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PH.D. THESIS

**MICRORNA PROFILATION FROM SERUM AND TOTAL AND
NEURONAL EXTRACELLULAR VESICLES IN PATIENTS
AFFECTED BY SCHIZOPHRENIA AND TREATMENT-RESISTANT
SCHIZOPHRENIA**

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Abstract

Background: Treatment-resistant schizophrenia (TRS), defined as the persistence of symptoms despite adequate antipsychotic treatment, remains frequently underrecognized, with clozapine, the gold standard, introduced only after an average delay of 4–9 years. In this study, we aimed to identify which Positive and Negative Syndrome Scale (PANSS) factors, executive function measures, and selected microRNAs (miRNAs) are most strongly associated with TRS, and to investigate the molecular underpinnings targeted by these miRNAs, thereby hypothesizing aberrant mechanisms contributing to the TRS condition.

Methods: We examined 60 patients with schizophrenia (25 treatment-responsive, 35 TRS) following a structured retrospective-prospective evaluation of antipsychotic response. Seventeen serum miRNAs were assessed. Principal Component Analysis (PCA) identified clinical variables and miRNAs with loading scores ≥ 0.4 , which were used to train three machine learning models. Random Forest (RF) provided the best balance of accuracy, sensitivity, specificity, and generalizability. Based on RF with nested cross-validation, selected miRNAs underwent Gene Ontology (GO) and KEGG enrichment analyses with Benjamini–Hochberg correction.

Results: PCA highlighted PANSS emotional (EMO), disorganization (DIS), and excitement (EXC) factors, processing speed, and miRNAs (miR-132-3p, miR-181-5p, miR-203a-3p, miR-199a-5p, miR-128-3p). RF classified TRS patients based on higher EMO, DIS, EXC, miR-132-3p, miR-181-5p, and miR-203a-3p, with 62.9% sensitivity, 60% specificity, and 0.71 AUC. GO analysis indicated that miR-132, miR-181b, and miR-203a regulate stress response, apoptosis, cell cycle, differentiation, and protein homeostasis, converging on synaptic signaling and neuroplasticity pathways (ErbB, glutamatergic, dopaminergic). Predicted targets included key neurotransmission genes (DRD1, HOMER1, MAPK1/3, GRIN2A/D), also modulated by antipsychotics.

Discussion: TRS is characterized by a combined clinical-molecular signature involving PANSS domains, and selected miRNAs converging on synaptic and neuroplasticity networks. Dopaminergic,

glutamatergic and ErbB pathways emerged as central hubs, suggesting that antipsychotic effects may be mediated, at least in part, through miRNA-driven mechanisms underlying TRS.

1. Introduction

Schizophrenia is conceptualized as a severe neurodevelopmental disorder affecting synaptic connectivity [1], resulting in a brain-wide derangement of neural networks [2-4]. Antipsychotics remain the cornerstone of pharmacological treatment in schizophrenia; however, up to 30% of patients exhibit an inadequate response, defining a subgroup known as treatment-resistant schizophrenia (TRS) [5-7]. Clozapine is currently the only medication specifically indicated for TRS [8]; yet up to 30% of TRS patients fail to respond even to clozapine, forming a further subgroup referred to as clozapine non-responders (CLZ-nR) [9]. TRS represents a major clinical challenge, particularly in addressing cognitive, social cognitive, and disorganization symptoms [10-15], which exert a profound impact on the long-term course and functional outcome of the disorder [16-18].

Given these challenges, there is a growing need to identify molecular markers capable of stratifying the patient population and guiding the exploration of specific pathophysiological pathways. Such biomarkers could shed new light on the etiopathogenesis of schizophrenia, particularly mechanisms involving dopaminergic and glutamatergic neurotransmission and their interplay at the level of the postsynaptic density (PSD). Despite the use of standardized diagnostic criteria such as the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), substantial disagreement among clinicians persists, and current diagnostic approaches remain limited by their reliance on clinical manifestations that typically emerge long after disease onset. This delay contributes to poor symptom control and limited therapeutic efficacy, especially for negative and cognitive symptoms.

In line with this objective, our work aimed to establish the foundation for investigating peripheral biomarkers that may nonetheless reflect central neurobiological processes. Specifically, we focused on the analysis of microRNAs, small non-coding RNAs implicated in aberrant neurodevelopmental and neurostructural processes, and on brain-derived extracellular vesicles (EVs), with the objective of obtaining a peripheral “snapshot” of the molecular events occurring within the brain.

Recent evidence summarized by Gangachannaiah et al. (2025) [19] reinforces the biological relevance of EVs in schizophrenia, identifying over one thousand differentially expressed molecules in EVs derived from patients. These molecular alterations converge on key pathways implicated in the disorder, including dopaminergic and glutamatergic signaling, mitochondrial homeostasis, immune regulation, and energy metabolism. Notably, specific EV-associated miRNAs (e.g., miR-206, miR-223, miR-137, and miR-675-3p) have been associated with synaptic plasticity, neuroinflammation, and treatment resistance, supporting their potential utility as diagnostic or prognostic biomarkers [20-22].

2. Aim of the study

The primary aim of this study was to identify potential peripheral biomarkers in patients with schizophrenia that may be associated with treatment-resistant schizophrenia (TRS). Furthermore, we sought to explore the possible contribution of these molecules to the etiopathogenesis of both schizophrenia and the TRS condition, focusing on circulating microRNAs and extracellular vesicles as key molecular mediators.

3. First experiment: Optimization of extracellular vesicles (EVs) isolation and following enrichment for neuronal vesicles (NEVs) protocol

3.1 Experimental design

Protocol optimization included testing different input plasma volumes, titrating antibody concentrations, and comparing two immunocapture strategies: (i) incubation of the antibody/magnetic bead complex with the sample (indirect method), and (ii) pre-incubation of the antibody with the sample followed by the addition of magnetic beads (direct method). Magnetic beads of both nanometer and micrometer scale were evaluated for their efficiency in vesicle capture. This study was carried out in collaboration with Professor Enza Torino's research group at the IIT Naples – University of Naples "Federico II", Psychiatry Unit, and the CNR-IEOS (Institute of Endocrinology and Experimental Oncology).

3.2 Materials and methods

3.2.1 Blood sample collection and plasma preparation

The whole blood samples (5 mL per participant) were obtained from an healthy controls in a fasting state (>12 hours without food consumption). After blood was allowed to clot by leaving it undisturbed at room temperature for 15–30 minutes, the clot was removed by centrifuging at 3000 rcf for 15 minutes in a refrigerated centrifuge for two time. Following centrifugation, the liquid component (plasma) was immediately filtered using a 0.22 μ m and transferred into a clean polypropylene RNase/DNase-free tube using a Pasteur pipette. Then, the plasma samples were apportioned into 2.0 ml aliquots and stored at -80°C until use.

3.2.2 EVs isolation protocol

In order to optimize the protocol, we tested various input volumes (500 μ l, 1 ml, and 3 ml) of plasma in different experimental paradigms to evaluate their impact on extracellular vesicle yield. Then, we isolated total extracellular vesicles using the Size Exclusion Chromatography (SEC) technique with IZON both two types of qEV columns (size=35 nm and size=70 nm) (Izon Science, New Zealand). Then, plasma was added on the top of the column. The EVs containing fractions (F2-F7, 700 μ l each) were collected by $1 \times$ PBS. The collected fractions were concentrated by ultrafiltration with 100 K Amicon Ultra-15 centrifugal filter units (EMD Millipore) and pooled in two different fractions' blocks: 2-5 fractions pool and 6-7 fractions pool.

3.2.3 Enrichment for neuronal vesicles (NEVs)

Through immunocapturing process, based on streptavidin–biotin interaction, employing a combination of multiple anti-L1CAM antibody concentrations (2.5, 3, 4, 5 ng) and 100 μ L of magnetic beads, we enriched for NEVs. These isolated NEVs underwent chemical and physical characterization using Nanoparticles Tracking Analysis (NTA). As part of the protocol optimization, we compared two experimental conditions: (i) incubation of the antibody/magnetic bead complex with the sample (indirect method), and (ii) pre-incubation of the antibody with the sample followed

by addition of magnetic beads (direct method). Magnetic beads of both nanometer (50 nm μ MACS Streptavidin MicroBeads) and micrometer (9.1 μ m Exo-Flow) scale were tested to evaluate their impact on yield and specificity.

3.2.4 Dynamic Light Scattering

After purification of both TEV and NEV, Dynamic Light Scattering (DLS) was used to determine the hydrodynamic diameter of particles and their concentrations for each SEC fraction. Each sample was diluted 1:5 with 1 mL of PBS in a polystyrene 12-mm square glass cuvette (square aperture for 90° sizing Malvern; # PCS1115) and measured in triplicate at 25°C using a Zetasizer Nano ZS (Model ZEN3600, Malvern Instruments Ltd. UK) equipped with a solid-state laser ($\lambda = 633$ nm) at a scattering angle of 173°.

3.4.5 RNA extraction and miRNA isolation

RNA was isolated using three different commercial kits: Qiagen Serum/Plasma Advanced Kit, miRNeasy Serum/Plasma Kit, and Zymo Quick-RNA Microprep Kit. Extractions were performed starting from 15 μ L of final volume of both NEVs and total extracellular vesicles following the manufacturers' instructions for each kit using optimized protocols designed to preserve the small RNA fraction. We transcribed 500 ng of RNA from NEVs and TEVs and amplified 20 ng of the resulting cDNA for Real-Time PCR analysis.

3.3 Results

3.3.1 Physicochemical characterization

Tables 1 and 2 summarize the results obtained by NTA across four independent experiments performed under different conditions.

Experiment	Protocol	Plasma Voume (ul)	TEVs concentration	Magnetic Beads Volume (ul)	Antibody volume (ng)	Experimental paradigm	NEEVs concentration
I	1	1000	2×10^{11}	80	2.5	(TEV + Ab) + Beads	1.6×10^{11}
	2	3000	6×10^{11}	150	5	(TEV + Ab) + Beads	6.8×10^{10}
II	1	500	3.5×10^{11}	100	2.5	(TEV + Ab) + Beads	2.9×10^{10}
						TEV + (Ab +Beads)	5.0×10^{10}
	2	1000	7×10^{11}	100	2.5	(TEV + Ab) + Beads	4.0×10^{10}
						TEV + (Ab +Beads)	1.1×10^{10}
	3	1000	7×10^{11}	100	5	(TEV + Ab) + Beads	6.4×10^{10}
						TEV + (Ab +Beads)	7.8×10^{10}

III	1 (Column size: 70 nm)	1000	3×10^{12}	100	4	(TEV + Ab) + Beads	4.1×10^{11}
						TEV + (Ab +Beads)	1.9×10^{11}
	2 (Column size: 35 nm)	1000	2.5×10^{12}	100	4	(TEV + Ab) + Beads	3.9×10^{11}
						TEV + (Ab +Beads)	1.1×10^{11}
IV	1 (Column size: μm)	1000	2.6×10^{12}	100	4	TEV + (Ab +Beads)	4.3×10^{11}
	2 (Column size: nm)	1000	2.6×10^{12}	100	3	TEV + (Ab +Beads)	4.2×10^{11}

Table 1. Summary of the results for SEC fractions 2–5 in terms of TEV and NEEV concentrations obtained by DLS under the different protocols tested. For each protocol, the plasma volume, the volume of magnetic beads, the amount of L1CAM-specific antibody, and the order of reagent addition used for NEEV enrichment are reported.

Esperimento	Protocollo	Volume di plasma (ul)	TEVs	Volume Magnetic Beads (ul)	Quantità di anticorpo (ng)	Ordine d'introduzione dei reagenti	NEEVs
I	1	1000	1.6×10^{11}	80	2.5	(TEV + Ab) + Beads	8.8×10^{10}
	2	3000	4.8×10^{11}	150	5	(TEV + Ab) + Beads	5.1×10^{10}
II	1	500	3.1×10^{11}	100	2.5	(TEV + Ab) + Beads	5.0×10^{10}
						TEV + (Ab +Beads)	5.7×10^{10}
	2	1000	6.2×10^{11}	100	2.5	(TEV + Ab) + Beads	1.1×10^{10}
						TEV + (Ab +Beads)	7.5×10^{10}
	3	1000	6.2×10^{11}	100	5	(TEV + Ab) + Beads	1.4×10^{11}
						TEV + (Ab +Beads)	4.1×10^{11}
III	1 (Column size: 70 nm)	1000	2.5×10^{12}	100	4	(TEV + Ab) + Beads	4.1×10^{11}
						TEV + (Ab +Beads)	1.9×10^{11}
	2 (Column size: 35 nm)	1000	1.2×10^{12}	100	4	(TEV + Ab) + Beads	3.5×10^{11}
						TEV + (Ab +Beads)	2.3×10^{11}
IV	1 (Column size: μm)	1000	2.6×10^{12}	100	4	TEV + (Ab +Beads)	2.1×10^{11}
	2 (Column size: nm)	1000	2.6×10^{12}	100	3	TEV + (Ab +Beads)	2.8×10^{11}

Table 2. Summary of the results for SEC fractions 6-7 in terms of TEV and NEEV concentrations obtained by DLS under the different protocols tested. For each protocol, the plasma volume, the volume of magnetic beads, the amount of L1CAM-specific antibody, and the order of reagent addition used for NEEV enrichment are reported.

Total extracellular vesicles (TEVs) were recovered in the range of 10^{11} – 10^{12} particles, of which approximately one-tenth consisted of neuron-enriched extracellular vesicles (NEEVs; 10^{10} – 10^{11} particles). The average vesicle size was around 100 nm, consistent with previously reported data [23]. Regarding the experimental conditions tested to isolate NEEVs as the final product, the following parameters were evaluated:

- the number of TEVs obtained from 0.5, 1.0, or 3.0 mL of starting plasma;
- the amount of antibody used (2.5–5 μg) and the volume of magnetic beads (80–150 μL), added to the sample in different sequences.

Specifically, two approaches were compared: (i) antibody conjugation to TEVs followed by binding of the complex to magnetic beads; (ii) antibody pre-conjugation to magnetic beads followed by binding to TEVs. While the optimal order of addition remains to be determined, subsequent experiments were standardized to 4 μg of antibody and 100 μL of magnetic beads.

Morphological analysis by TEM of the EV populations revealed greater dispersion when using 70 nm SEC columns, highlighting the presence of a more heterogeneous population, as shown in the images for both fraction groups (Figure 1).

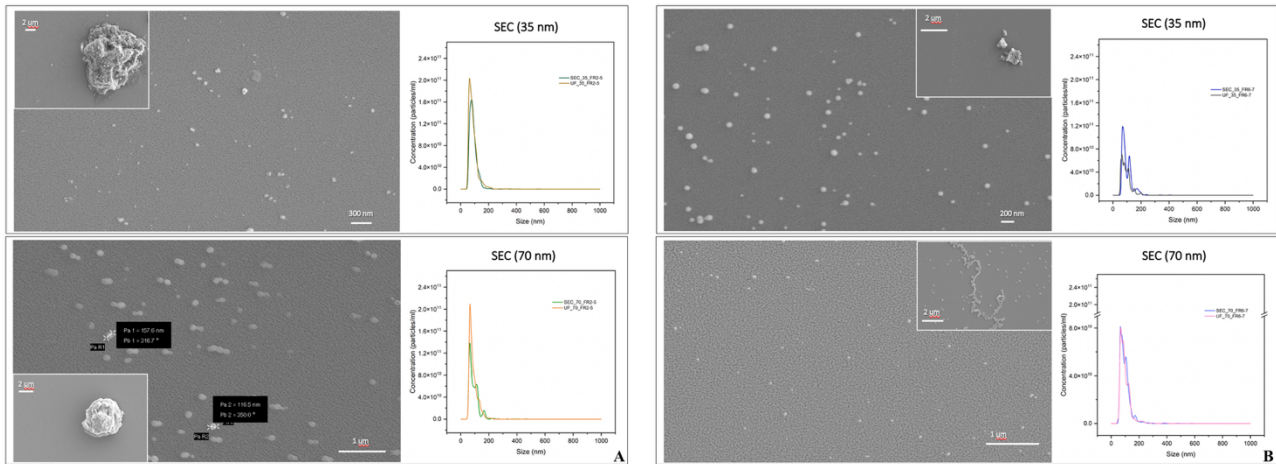


Figure 1. Morphological and physicochemical characterization of EV fractions. (A) TEM image of EVs and DLS size distribution profiles for fractions 2–5, comparing the two protocols using 35 nm and 70 nm SEC columns. (B) TEM image of EVs and DLS size distribution profiles for fractions 6–7 under the same experimental conditions. TEM images highlight vesicle morphology, while DLS graphs show particle size distribution and relative heterogeneity for each protocol.

3.3.2 Biological characterization

Table 3 summarizes the RNA values obtained using a NanoDrop spectrophotometer. For TEVs, total RNA concentrations ranged between 10–30 ng/μl, whereas NEEVs yielded approximately 100 ng/μl. These quantities appear inverted compared to the expected 10:1 ratio of TEV to NEEV vesicle numbers. RNA extraction was performed using silica membrane spin columns, optimized for small amounts of starting material, with elution in 15 μl. In the case of TEVs, we hypothesized that the reduced RNA yield might be due to column obstruction caused by excess input material. To test this, we employed alternative columns based on the same technology but with higher binding capacity. When RNA was eluted in 30 μl, the resulting concentration was only 3.9 ng/μl, thus ruling out this hypothesis. A more detailed qualitative and quantitative assessment of the RNA content in NEEVs is still required.

Esperimento	Protocollo	TEV	Concentrations (ng/ul)	260/280 (valore di riferimento 1.8-2)	260/230 (valore di riferimento >1)	NEEVs	Concentrations (ng/ul)	260/280 (valore di riferimento 1.8-2)	260/230 (valore di riferimento >1)
I	1	1.6×10^{11}	22.4	1.35	0.67	8.8×10^{10}	237.2	1.68	0.28
	2	4.8×10^{11}	-	-	-	5.1×10^{10}	247.6	1.70	0.30
II	1	3.1×10^{11}	-	-	-	5.0×10^{10}	105.5	1.58	0.26
						5.7×10^{10}	126.7	1.53	0.29
	2	6.2×10^{11}	3.9	1.58	0.03	1.1×10^{10}	103.5	1.58	0.27
						7.5×10^{10}	107.5	1.59	0.26
	3	6.2×10^{11}	-	-	-	1.4×10^{11}	99.6	1.49	0.27
						4.1×10^{11}	89.4	1.63	0.17
III	1 (Column size: 70 nm)	2.5×10^{12}	9.7	1.71	0.45	4.1×10^{11}	107.5	1.88	1.16
	2 (Column size: 35 nm)	1.2×10^{12}	9.3	1.48	0.48	1.9×10^{11}	121.9	1.86	1.85
						3.5×10^{11}	122.9	1.91	3.89
						2.3×10^{11}	122.1	1.89	1.33
IV	1 (Column size: um)	2.6×10^{12}	32.7 Q	1.48 Q	0.13 Q	2.1×10^{11}	83.4	1.9	0.23
	2 (Column size: nm)	2.6×10^{12}	6.8 Z	1.71 Z	0.01 Z	2.8×10^{11}	89.1	1.89	0.29

Table 3. Summary of the results for fractions 2–5 in terms of total RNA concentrations extracted from TEVs and NEEVs, as measured by NanoDrop under the different protocols tested. The 260/280 and 260/230 ratios for each total RNA sample are also reported.

4. Experiment #2

4.1 Experimental design

We carried out a cross-sectional study involving patients referred to the Outpatient Unit for Treatment-Resistant Psychosis, Section of Psychiatry, Department of Neuroscience, University of Naples “Federico II”. This unit functions as a tertiary care center, receiving referrals from community mental health services for specialized assessment of suspected treatment resistance. As such, the patients evaluated at our facility typically present with moderate to severe active symptoms. All consecutive patients who met the inclusion criteria were assessed, and a comprehensive battery of clinical, psychopathological, cognitive, and psychosocial measures was administered. Patient recruitment is still ongoing. All consecutive patients meeting eligibility criteria were screened and a large set of clinical, psychopathological, and cognitive variables was assessed.

This study aims to profile circulating microRNAs in serum samples from a population of patients diagnosed with schizophrenia, with the goal of stratifying individuals based on their response to standard antipsychotic treatments.

4.2 Materials and methods

4.2.1 Population

Patients were eligible for inclusion if they had a diagnosis of schizophrenia, were between 18 and 65 years of age, and exhibited stabilized symptoms—defined as no requirement for changes in antipsychotic medication or dosage in the past six months, no recent clinical deterioration, and no psychiatric hospitalization during the same period. The diagnosis of schizophrenia was confirmed by two experienced psychiatrists using the DSM-5 criteria and the Structured Clinical Interview for DSM Disorders (SCID). Definitions of treatment-resistant schizophrenia (TRS) and non-TRS were based on the American Psychiatric Association (APA) algorithm, further refined by the Treatment Response and Resistance in Psychosis (TRRIP) working group [6]. In accordance with these guidelines, patients were considered treatment-resistant if they had failed to respond to at least two antipsychotic drugs from different classes, administered at therapeutic doses for a minimum of six weeks. The severity of psychotic symptoms was assessed by Positive and Negative Syndrome Scale (PANSS) using the cut-off of 70. Above this score, patients were considered actively symptomatic at the time of the clinical assessment [24, 25].

None of the individuals meeting the eligibility criteria declined to participate. All research procedures were conducted in accordance with the ethical standards of the relevant national and institutional committees on human experimentation and with the principles outlined in the Declaration of Helsinki (1975), as revised in 2008. The study protocol was approved by the institutional review board, and all participants provided written informed consent prior to inclusion in the study.

This observational study included a total of 63 individuals diagnosed with schizophrenia, further classified as treatment-resistant ($n = 38$; 22 males, 16 females) or treatment-responsive ($n = 27$; 15 males, 12 females). All patients were receiving antipsychotic treatment at the time of the study. Exclusion criteria for patients included: (1) comorbidity with other major psychiatric disorders (e.g., bipolar disorder, major depressive disorder); (2) significant neurological conditions (e.g., brain tumors, stroke) or severe and unstable medical illnesses that could interfere with study procedures; (3) pregnancy or breastfeeding; (4) current substance abuse (including alcohol or illicit drugs); (5)

modified electroconvulsive therapy (ECT) within the previous three months; and (6) inability to complete study assessments or adhere to the protocol due to cognitive or other limitations.

4.2.2 Demographic and clinical variables

PANSS was administered by trained clinicians, and the 5-factor model for evaluating multidimensional psychopathology was applied [26]. This model includes the following factors: positive symptoms, negative symptoms, disorganization, excitement, and emotional distress. The following demographic clinical parameters were collected: age, sex, education years, age at onset of psychotic symptoms, illness duration, and current antipsychotic doses in chlorpromazine-equivalent milligrams (CPZ) [27]. The following tasks to assess cognitive performance

were included: the category instances task for verbal fluency; the list learning task for working memory; the token motor task for motor coordination; the symbol coding task for processing speed; and, finally, the Tower of London task for problem solving [28, 29].

4.2.3 Blood sample collection and serum preparation

The whole blood samples (5 mL *per* participant) were obtained from the 87 participants in a fasting state (>12 hours without food consumption). After blood was allowed to clot by leaving it undisturbed at room temperature for 15–30 minutes, the clot was removed by centrifuging at 1,000–2,000 x g for 10 minutes in a refrigerated centrifuge. Following centrifugation, the liquid component (serum) was immediately transferred into a clean polypropylene RNase/DNase-free tube using a Pasteur pipette and maintained at 2–8°C while handling. Then, the serum samples were apportioned into 0.5 ml aliquots and stored at –80 °C until use.

4.2.3.1 Detection of low level of hemolysis in serum samples

The release of miRNA content from red blood cells upon hemolysis dramatically alters the miRNA profile in blood-derived sources, such as serum, and creates confounding conditions in the search of

miRNAs as potential biomarkers, threatening the accuracy of serum-based tests. Excluding any samples with a pink discoloration at visual inspection because considered as a mark of severe hemolysis, a simple and cost-effective approach based on the use of a spectrophotometer and the measurement of oxy-hemoglobin absorbance at 414 nm was applied to determine the degree of hemolysis of all the 87 serum samples. $A_{414} \leq 0.2-0.25$ had previously been recommended as threshold for non-hemolyzed samples. Thus, quick absorbance measurements disqualified hemolyzed serum samples before time consuming and costly downstream sample processing took place. To identify putative hemolyzed samples, a further and subsequent approach based on the miRNA analysis in RNA samples was also applied. By RT-qPCR, the expression levels of miR-451a, known to be enriched in erythrocytes, were evaluated. As the levels of the miRNA are influenced by factors other than hemolysis, a simple threshold cannot be used as an indicator of hemolysis in this case. The level of the erythrocyte-specific miRNA must be related to a miRNA found to be un-affected by hemolysis and relatively stable in serum, such as miR-23a-3p. The relative expression of the erythrocyte-specific miR-451a and the stable miR-23a-3p, namely delta quantification cycle (ΔCq) (miR-23a-3p - miR-451a), is commonly used as an indicator of hemolysis in RNA samples: $\Delta Cq > 5$ indicates a possible hemolysis and $\Delta Cq > 7$ confers a high risk of hemolysis, affecting the data obtained. RNA samples with a value of $\Delta Cq > 7$ were excluded prior to further analysis in this study.

4.2.3.2 miRNA isolation from serum

For RNA isolation, a serum volume of 200 μ l was thawed on ice and mixed with 5 volumes of QIAzol Lysis Reagent from the miRNeasy Serum/Plasma Kit (Cat No: 217184, Qiagen), according to the instructions of the manufacturer. Finally, RNA was eluted in 15 μ L of RNase-free water by centrifugation through a RNeasy MinElute spin column, a silica-membrane column designed to retain short RNA species (defined as having fewer than 200 nucleotides) from small sample volumes.

It is a common practice to spike a synthetic miRNA into serum samples in order to monitor RNA recovery and reverse transcription efficiency. To avoid degradation by endogenous serum RNases,

the synthetic miRNA was added to the serum samples after the addition of denaturant (QIAzol Lysis Reagent), prior to chloroform addition and phase separation. Going through the entire RNA isolation process and ultimately measured by RT-qPCR, this synthetic miRNA was used as a qPCR-based method for quality control of RNA isolated from serum samples. It was also used as reference for normalization of differences in efficiency of RNA recovery between samples, since there is no endorsement of specific miRNAs or set of miRNAs as suitable endogenous controls in the case of circulating miRNAs. In RT-qPCR using the primer assay specific for the synthetic miRNA, the corresponding quantification cycle (C_q) values permitted normalization between samples. In this study, the synthetic Cel-miR39-3p (the miRNeasy Serum/Plasma Spike-In Control, Cat No: 219610, Qiagen) was added in 3.5 µl volume of 1.6 x 10⁸ copies/µl working solution.

4.2.4. miRNA quantitation

The concentration of extracted miRNA from serum samples was determined using the Qubit microRNA Assay Kit (Cat No: Q32880, Invitrogen) on the Qubit Fluorometer (Invitrogen), according to manufacturer's instructions. Indeed, the yield of RNA from a small volume of serum samples (200 µL) was below The Limit of Quantification (LOQ) to be quantitatively detected with a stated accuracy and precision by a UV-Vis Spectrophotometer. Specifically, 2 µL of previously extracted RNA were used for quantification. The resulting miRNA concentrations, expressed in ng/µL, were found to be comparable across samples (7.98 ± 2.17). Even if a fixed volume of eluted RNA samples was used as input for RT-qPCR rather than using a fixed mass of input RNA, the very similar miRNA concentration among the samples ensured uniformity and allowed for reliable downstream analyses.

4.2.4.1. miRNA cDNA synthesis

Reverse transcription of miRNA was performed in a single reaction step using the miRCURY LNA RT Kit (Cat No: 339340, Qiagen), according to the manufacturer's instructions. Given the comparable miRNA concentrations obtained, 10 µL of RNA samples (corresponding approximately to 80 ng of miRNA content) were used in a total of 20 µl reaction volume. The reaction was incubated

at 40–42 °C for 1 hour, followed by heat-inactivation for 5 min at 95°C and cooling to 4°C immediately after.

4.2.4.2. Real Time PCR (qRT-PCR)

Real-time quantitative PCR (qPCR) analyses were performed on a CFX96 thermocycler (Bio-Rad) using the miRCURY LNA SYBR Green PCR Kit (Cat. No: 339347, Qiagen) and miRCURY LNA miRNA SYBR PCR Assays (cat. no. 339306, Qiagen), LNA-enhanced primers specific for the selected miRNAs which are listed in Table 4.

Gene Globe ID	microRNA
YP02119317	hsa-miR-7-5p
YP00204714	hsa-miR30e-5p
YP00204486	hsa-miR34a-5p
YP00206026	hsa-mir124-3p
YP00204227	hsa-mir126-3p
YP00205995	hsa-mir128-3p
YP00206035	hsa-mir132-3p
YP00204530	hsa-mir181-5p
YP00205869	hsa-mir195-5p
YP00204494	hsa-mir199a-5p
YP00205914	hsa-mir203a-3p
YP00205986	hsa-mir223a-3p
YP00204222	hsa-mir590-5p
YP00205630	hsa-mir-1246
YP02100320	hsa-miR-3178
YP02112520	hsa-miR-5100
YP02110126	hsa-miR-7704

Table 4. LNA-enhanced primers and related Gene Globe ID

The reactions were performed in technical triplicate using 2 µL of the 5-fold diluted cDNA samples. The miRNAs that showed quantification cycle C_q values above 35 (detection threshold) were excluded.

The miRCURY LNA microRNA PCR system is characterized by higher sensitivity and specificity through the use of primers based on the Locked Nucleic Acids (LNA) technology. LNAs are a class of high-affinity nucleic acid analogs and their insertion into oligonucleotides increases the binding affinity to the complementary DNA or RNA sequence. In the case of the small miRNA sequence, LNA-based primers anneal directly to the miRNA sequence, thereby avoiding detrimental PCR-primer overlap with primer-dimer generation. In addition, LNA-modified oligonucleotides

considerably improve specificity, allowing single-nucleotide-mismatch discrimination that enables optimal differentiation between closely related members of the same miRNA family. Notably, the miRCURY LNA microRNA PCR system is especially well suited for the analysis of biofluid samples characterized by limited RNA content, such as serum. Indeed, in accordance with the manufacturing-based definition of quality, the miRNA assays are all validated to enable the detection of as few as 10 copies/ μL , which is essential for achieving accurate miRNA measurements without the potential biases which can be introduced by a pre-amplification reaction.

An absolute quantification is considered more suitable for the assessment of the small quantities of miRNAs in body fluids, such as serum. Since different laboratories customize the RT-qPCR experimental protocols differently, technical variations make it difficult to compare the results from different studies, leading to inconsistency or even contradiction among them. Thus, the concentrations of each analyzed miRNA in serum samples were determined by a standard calibration curve. Standard curves were generated by performing RT-qPCR of 10-fold serial dilutions (from 1×10^8 to 1×10^2 copy/ μL) of specific DNA amplicons made from the reverse transcription product of each miRNA to analyze and purified by the MinElute PCR Purification Kit (cat. no. 28004, Qiagen). The synthetic cel-miR-39-3p was used as an external standard for normalization and quality assessment. The calculation $\Delta C_q = C_q(\text{analyte}) - C_q(\text{standard})$ was applied to normalize C_q -values. Concentration of miRNAs was calculated using standard calibration curve (plotted logarithmic initial amount of dilution series of miRs against C_q -values).

4.2.5 Bioinformatic and statistical analysis

4.2.5.1 Descriptive analysis

Statistical analyses were performed using IBM SPSS Statistics 28.0.1 and RStudio (RStudio, 2020). Descriptive statistics were used to examine clinical and demographic variables, and the Shapiro Wilk test was conducted to assess the normality of continuous variable. To evaluate potential differences between diagnostic groups (i.e. TRS vs. SCZ), we performed either an independent-

sample two-tailed Student's t-test or, for non-normally distributed variables, a Mann-Whitney test. The Chi-square test was used for dichotomous variables. Statistical significance threshold was set at $p < 0.05$. A one-way ANOVA with Tukey's HSD post-hoc test was employed to assess differences among non-TRS and TRS subgroups (CLZ-R, and CLZ-nR), while a Kruskal-Wallis test with Dunn-Bonferroni post-hoc correction was applied for non-normally distributed variables. Analogously, analyses were performed to compare male and female participants within the same clinical group, using independent-sample two-tailed Student's t-tests for normally distributed variables or Mann-Whitney tests for non-normally distributed variables.

4.2.5.2 Principal Component Analysis

We applied Principal Component Analysis (PCA) to reduce the dimensionality of a complex dataset comprising clinical variables and circulating miRNA levels. This technique allows for the identification of the main directions of variance in the data, effectively addressing multicollinearity among variables and facilitating the visualization and interpretation of underlying latent structures. Moreover, the principal components derived from PCA serve as robust predictors in subsequent analyses, improving the efficiency and stability of predictive models related to pharmacological treatment response.

To identify the most influential variables contributing to the principal components derived from the dataset, we performed a PCA considering the first five principal components (PC1 to PC5) (Supplementary Table S3). Each component captures a distinct axis of variance within the multidimensional data. In particular, PC1 appears to represent a dimension contrasting severe clinical symptoms and cognitive/motor abilities. Specifically, it shows strong negative loadings on variables related to clinical symptom severity (e.g., total PANSS scores, positive and negative symptom scores), while cognitive and motor function variables (e.g., verbal memory, working memory, motor coordination) load positively. This suggests that PC1 separates subjects along a continuum from those

with more severe symptoms and poorer functioning to those with milder symptoms and better cognitive and motor performance.

PC2 seems to capture a different dimension, where certain molecular biomarkers (such as specific miRNAs) have positive loadings, whereas clinical symptoms and cognitive measures tend to have negative loadings. This indicates that PC2 may reflect a biological or molecular profile axis that is inversely related to clinical and cognitive features.

For each variable, we extracted the loadings (i.e., correlation coefficients) on all five PCs and calculated the combined contribution as the Euclidean norm (vector magnitude) of the loadings across these components. This combined loading score provides a summary measure of the overall importance of each variable in defining the multidimensional structure captured by the first five PCs. Variables were then ranked according to their combined loading scores in descending order and we selected the top-ranking variables as key contributors to the underlying data variance, thus serving as candidate features for subsequent predictive modeling and in-depth analysis. To identify variables that meaningfully contribute to the overall PCA structure, we computed a combined loading index across the first five principal components. Variables with a combined loading ≥ 0.4 were retained as relevant features, reflecting a stable and distributed contribution to the latent dimensionality of the dataset. This approach allowed us to focus on variables that collectively influence multiple principal components, enhancing interpretability and model efficiency.

4.2.5.3 Machine learning algorithms

We aimed to classify TRS patients using a set of top predictive variables selected based on their importance scores at PCA. The dataset included 60 subjects, labeled as TRS or non-TRS. Predictors, without causal link considering the cross-sectional nature of the study, comprised clinical scores and microRNA expression levels previously identified for their relevance.

Variables were selected based on mean decrease accuracy from Random Forest variable importance measures. The final set included clinical and molecular features hypothesized to best differentiate TRS status.

We conducted a comprehensive evaluation of three machine learning models, Random Forest, XGBoost, and Support Vector Machine (SVM), using nested cross-validation to rigorously assess their predictive performance and generalizability. The dataset was divided into outer folds ($k = 5$) for performance estimation and inner folds ($k = 5$) for hyperparameter tuning and model selection. To address class imbalance, we applied the Synthetic Minority Over-sampling Technique (SMOTE) exclusively on the training subsets within each outer fold. This approach prevents data leakage and ensures that the test data remain independent. For each outer fold, the training data underwent SMOTE balancing followed by hyperparameter optimization via grid search on the inner folds. Model performance metrics including accuracy, sensitivity, specificity, and area under the receiver operating characteristic curve (AUC) were computed on the held-out outer test sets. Predictions were binarized using a 0.5 probability threshold, and confusion matrices were used to derive sensitivity and specificity values. All analyses were performed using R, with packages including “caret” for cross-validation and model training, “smotefamily” for oversampling, “randomForest” for Random Forest implementation, “xgboost” for gradient boosting, and “e1071” for SVM. Statistical summaries of the performance metrics were reported as mean values with standard deviations across the outer folds.

4.2.5.4 Variable importance in random forest algorithm

The importance of variables in a Random Forest model is commonly assessed using the Mean Decrease Accuracy metric. This method measures how much the prediction accuracy decreases when the values of a particular variable are randomly permuted, breaking the association between that variable and the response. If permuting a variable’s values significantly reduces accuracy, it indicates that the variable is important for the model’s predictive performance. Conversely, if accuracy does not change or improves after permutation, the variable is considered less important or even

detrimental. This approach provides an intuitive way to rank predictors based on their contribution to the model's accuracy. To evaluate the impact of less important variables on model performance, we implemented a feature selection step excluding variables with negative importance scores, based on an initial Random Forest model.

4.2.5.5 Identification of validated miRNA targets with strong experimental support

To identify robustly validated targets of identified miRNAs (hsa-miR-132-3p, hsa-miR-181b-3p, hsa-miR-203a-3p), we utilized the Bioconductor package “multiMiR” within the R environment. Target data were retrieved using the `get_multimir()` function, specifying the validated interaction table for the miRNA of interest. The initial dataset was filtered to select targets with strong experimental support. Specifically, targets supported by experimental techniques such as Western blot, qRT-PCR, Functional MTI assays, Luciferase reporter assays, or CLIP-based methods were retained, using case-insensitive pattern matching on the `support_type` field. Interactions lacking PubMed identifiers were excluded to ensure traceability to primary literature. Targets were then grouped by gene symbol, summarizing the number of distinct supporting studies (`n_studies`), the experimental techniques reported (`experiments`), and the types of support evidence (`support_types`). Only targets supported by at least two independent studies ($n_studies \geq 2$) were considered strong candidates. To explore the overlap and uniqueness of predicted gene targets, we employed Venn diagram analysis as a visual and quantitative approach. This method was chosen to clearly depict shared and distinct target genes across the miRNAs, facilitating the identification of potentially common regulatory pathways or unique miRNA-specific effects. The filtered gene lists were then used to generate a three-set Venn diagram, using the “VennDiagram” package, which visually represents the intersections and exclusive elements among the datasets. This graphical representation aids in summarizing the data and guiding further functional enrichment analyses.

4.2.5.6 Gene Ontology Enrichment Analysis

Target genes for each microRNA (miR-132, miR-181b, and miR-203a) were extracted from the respective datasets and filtered to obtain unique gene symbols. Gene symbols were converted to Entrez Gene IDs using the `bitr` function from the `clusterProfiler` R package, with the `org.Hs.eg.db` annotation database for Homo sapiens. Genes lacking corresponding Entrez IDs were excluded from downstream analyses.

Gene Ontology (GO) enrichment analysis was performed separately for the three main GO categories: Biological Process (BP), Cellular Component (CC), and Molecular Function (MF). The `enrichGO` function of the `clusterProfiler` package was used for each category, applying the Benjamini-Hochberg procedure to control the false discovery rate. A significance threshold of adjusted p-value (q-value) < 0.05 was set to identify enriched GO terms.

4.2.5.7 miRNA Target Gene Analysis and Comparison with both Schizophrenia and TRS-Associated Genes

The gene lists from the three miRNA derived by GO analysis were then compared with schizophrenia-associated genes obtained from DisGeNET, filtered specifically for schizophrenia and TRS conditions using “`disgenet2r`”, “`dplyr`”, and “`tidy`” R packages. Only genes present in both the miRNA target lists and the filtered DisGeNET dataset were considered for subsequent analyses.

4.2.5.8 Kyoto Encyclopedia of Genes and Genomes pathway analysis

Pathway enrichment analysis was performed using the Kyoto Encyclopedia of Genes and Genomes (KEGG) database on predicted target genes of selected microRNAs (miR-132, miR-181b, and miR-203a). For each microRNA, the list of enriched pathways, including the associated gene sets, was extracted using “`clusterProfiler`”, “`org.Hs.eg.db`”, “`dplyr`” R packages. To investigate the potential relationship with schizophrenia, we compiled a reference dataset of pathways and genes previously annotated in KEGG as related to schizophrenia based on KEGG PATHWAY Database (<https://www.kegg.jp/kegg->

[bin/search?q=schizophrenia&display=disease&compound_thumbnail=&pathway_thumbnail=&dru](#)
[g_thumbnail=&from=disease&lang=&target=compound%2Bdrug%2Bdgroup%2Bdisease\)](#)

ID	geneID
Glutamatergic synapse	PLA2G4B/ADCY1/ADCY2/ADCY3/ADCY5/ADCY6/ADCY7/ADCY8/ADCY9/GNB5/GRIN3A/GRIN3B/PLA2G4E/GRK2/GRK3/DLG4/ADCY4/SHANK2/NCDN/PLCB1/SLC17A8/PLA2G4F/GLS2/GLS/GLUL/GNAI1/GNAI2/GNAI3/GNAO1/GNAQ/GNAS/GNB1/GNB2/GNB3/NG3/NG4/NG5/NG7/NG10/NG11/NGGT1/NGGT2/PLA2G4D/GRIA1/GRIA2/GRIA3/GRIA4/GRIK1/GRIK2/GRIK3/GRIK4/GRIK5/GRIN1/GRIN2A/GRIN2B/GRIN2C/GRIN2D/GRM1/GRM2/GRM3/GRM4/GRM5/GRM6/GRM7/GRM8/ITPR1/ITPR2/ITPR3/KCNJ3/SHANK1/NG13/PLA2G4A/PLCB2/PLCB3/PLCB4/PLD1/PLD2/NG2/SLC38A2/PPP3CA/PPP3CB/PPP3CC/PPP3R1/PPP3R2/PRKACA/PRKACB/PRKACG/MAPK1/MAPK3/NG12/SLC17A7/SLC17A6/GNB4/SLC1A1/SLC1A2/SLC1A3/SLC1A6/SLC1A7/TRPC1/CACNA1A/CACNA1C/CACNA1D/SLC38A1/SHANK3/PLA2G4C/JMJD7-PLA2G4B/DLGAP1/NG8/HOMER3/HOMER2/HOMER1/LZTS3 AKT3/CREB3/GNB5/ADCY5/COMT/CREB1/ATF2/ATF6B/MAPK14/CREB3L4/CALML6/DDC/DRD1/DRD2/DRD3/DRD4/DRD5/AKT1/AKT2/LRTOMT/PLCB1/FOS/GNAI1/GNAI2/GNAI3/GNAL/GNAO1/GNAQ/GNAS/GNB1/GNB2/GNB3/NG3/NG4/NG5/NG7/NG10/NG11/NGGT1/NGGT2/PPP2R3B/GRIA1/GRIA2/GRIA3/GRIA4/GRIN2A/GRIN2B/GSK3A/GSK3B/ITPR1/ITPR2/ITPR3/KCNJ3/KCNJ5/KCNJ6/KCNJ9/KIF5A/KIF5B/KIF5C/BMAL1/ARRB1/ARRB2/MAOA/MAOB/ATF4/CALY/NG13/CALML5/PLCB2/PLCB3/PLCB4/NG2/PPP1CA/PPP1CB/PPP1CC/PPP2R3C/PPP2CA/PPP2CB/PPP2R1A/PPP2R1B/PPP2R2A/PPP2R2B/PPP2R2C/PPP2R3A/PPP2R5A/PPP2R5B/PPP2R5C/PPP2R5D/PPP2R5E/PPP3CA/PPP3CB/PPP3CC/PRKACA/PRKACB/PRKACG/PRKCA/PRKCB/PRKCG/PPP2R2D/NG12/MAPK8/MAPK11/MAPK9/MAPK10/MAPK13/GNB4/MAPK12/SCN1A/CREB3D/SLC6A3/SLC18A1/SLC18A2/CACNA1A/CACNA1B/CACNA1C/CACNA1D/CALM1/CALM2/CALM3/CALML3/CAMK2A/CAMK2B/CAMK2D/CAMK2G/PPP1R1B/CREB3L3/CREB3L1/CALML4/NG8/CLOCK/CREB5
Dopaminergic synapse	PLA2G4B/RAPGEF3/GNB5/CYP2D6/ADCY5/TPH2/PLA2G4E/CYP2C9/CYP2C8/CYP2C18/CYP2D7/CYP2D6/CYP2J2/DDC/HTR3C/DUSP1/HTR3D/PLCB1/ALOX12/ALOX5/ALOX12B/ALOX15/ALOX15B/PLA2G4F/GABRB1/GABRB2/GABRB3/CYP4X1/GNAI1/GNAI2/GNAI3/GNAO1/GNAQ/GNAS/GNB1/GNB2/GNB3/NG3/NG4/NG5/NG7/NG10/NG11/NGGT1/NGGT2/PLA2G4D/HTR3E/HRAS/HTR1A/HTR1B/HTR1D/HTR1E/HTR1F/HTR2A/HTR2B/HTR2C/HTR3A/HTR4/HTR5A/HTR6/HTR7/APP/ARAF/ITPR1/ITPR2/ITPR3/KCND2/KCNJ3/KCNJ5/KCNJ6/KCNJ9/KCN22/KRAS/MAOA/MAOB/NRAS/NG13/PLA2G4A/PLCB2/PLCB3/PLCB4/NG2/PRKACA/PRKACB/PRKACG/PRKCA/PRKCB/PRKCG/MAPK1/MAPK3/NG12/MAP2K1/PTGS1/PTGS2/RAF1/GNB4/SLC6A4/SLC18A1/SLC18A2/BRAF/TPH1/TRPC1/CACNA1A/CACNA1B/CACNA1C/CACNA1D/CACNA1F/CACNA1S/CASP3/PLA2G4C/JMJD7-PLA2G4B/HTR3B/NG8
Serotoninerigic synapse	GNB5/ADCY1/ADCY2/ADCY3/CHAT/OGFR/ADCY5/ADCY6/HRH3/CHRM1/CHRM2/ADCY7/CHRM3/CHRM4/CHRM5/CHRNA3/CHRNA4/CHRNA7/ADCY8/CHRN2/CHRN4/ADCY9/GRIN3A/GRIN3B/ADORA1/ADORA2A/ADORA2B/ADORA3/SLC32A1/ADRA1D/ADRA1B/ADRA1A/ADRA2A/ADRA2B/ADRA2C/ADRB1/ADRB2/HTR3C/AGRP/DRD1/DRD2/DRD3/DRD4/DRD5/ADCY4/HTR3D/GABRR3/P2RX2/PLCB1/SLC17A8/GABBR1/TAC4/GABRA1/GABRA2/GABRA3/GABRA4/GABRA5/GABRA6/GABRB1/GABRB2/GABRB3/GABRD/GABRE/GABRG1/GABRG2/GABRG3/GABRP/GABRR1/GABRR2/GLRA1/GLRB/GNAI1/GNAI2/GNAI3/GNAL/GNAO1/GNAQ/GNAS/GNB1/GNB2/GNB3/NG3/NG4/NG5/NG7/NG10/NG11/NGGT1/NGGT2/HTR3E/GRIA1/GRIA2/GRIA3/GRIA4/GRIK1/GRIK2/GRIK3/GRIK4/GRIK5/GRIN1/GRIN2A/GRIN2B/GRIN2C/GRIN2D/GRM1/GRM2/GRM3/GRM4/GRM5/GRM6/GRM7/GRM8/HRH1/HRH2/HTR1A/HTR1B/HTR1D/HTR1E/HTR1F/HTR2A/HTR2B/HTR2C/HTR3A/HTR4/HTR5A/HTR6/HTR7/MC3R/MC4R/ACHE/OPRD1/OPRL1/OPRM1/OPRM2/P2RX1/P2RX3/P2RX4/P2RX5/P2RY1/P2RY2/P2RY4/P2RY6/P2RY11/PDYN/NG13/PENK/PLCB2/PLCB3/PLCB4/PNOC/P2RY13/NG2/POMC/PRKACA/PRKACB/PRKACG/PRKCA/PRKCB/PRKCG/GABRQ/NG12/SLC17A7/SLC17A6/GNB4/SLC5A7/SLC17A9/P2RY12/SLC1A1/SLC1A2/SLC1A3/SLC1A6/SLC1A7/SLC6A1/SLC6A2/SLC6A3/SLC6A4/SLC6A9/SLC6A11/SLC6A12/SLC6A13/SLC18A1/SLC18A2/SLC18A3/TAC1/TACR2/TAC3/TACR1/TACR3/OGFRL1/GLRA3/CHRNA6/CHRFAM7A/P2RX6/SLC6A5/HTR3B/NG8/GABBR2/P2RY14
Neuroactive ligand signaling	PATE3/INSL5/APELA/NPY4R2/LPAR6/CALCRL/NMUR1/PGRMC2/CYSLTR1/CGA/PGRMC1/NMU/NPFFR2/GPR83/UTS2/OGFR/HRH3/CHRM1/CHRM2/PTH2/CHRM3/CHRM4/CHRM5/CHRNA1/CHRNA2/CHRNA3/CHRNA4/CHRNA5/CHRNA7/CHRN1/CHRN2/UCN3/CHRN3/CHRN4/CHRN5/CHRN6/CHRN7/CHRN8/CHRN9/ADCYAP1/GRIN3A/GRIN3B/ADCYAP1/R1/RLN3/RXFP2/GPHB5/LTB4R/CNR1/CNR2/NMS/LYPD6/LYPD6B/CORT/ADM/ADORA1/TAAR9/TAAR1/ADORA2A/ADORA2B/CRH/CRHR1/CRHR2/ADORA3/CSH1/CSH2/CSHL1/ADRA1D/ADRA1B/ADRA1A/ADRA2A/ADRA2B/CTS/G/ADRA2C/ADRB1/ADRB2/ADRB3/PATE1/GPR156/GPHA2/DRD1/DRD2/DRD3/DRD4/DRD5/AGT/AGTR1/AGTR2/APLNR/S1PR1/LPAR1/S1PR3/EDN1/EDN2/EDN3/EDNRA/EDNRB/GABRR3/F2/F2R/F2RL1/F2RL2/P2RX2/LPAR3/FPR1/FPR2/FPR3/NTSR2/FSHB/FSHR/GABBR1/GABRA1/GABRA2/GABRA3/GABRA4/GABRA5/GABRA6/GABRB1/GABRB2/GABRB3/GABRD/GABRE/GABRG1/GABRG2/GABRG3/GABRP/GABRR1/NPB/GABRR2/UTS2B/GALR1/GCG/GCGR/GH1/GH2/GHR/GHRH/GHRHR/GHSR/GIP/GIPR/P2RY10/TMEM97/GLP1R/GLRA1/GLRA2/GLRB/GNRH1/GNRH2/GNRHR/NPBWR1/NPBWR2/PRLHR/UTS2R/NPW/LPAR4/MCHR1/GPR35/MLNR/P2RY8/GRIA1/GRIA2/GRIA3/GRIA4/GRI1/GRID2/GRIK1/GRIK2/GRIK3/GRIK4/GRIK5/GRIN1/GRIN2A/GRIN2B/GRIN2C/GRIN2D/NR3C1/GRM1/GRM2/GRM3/GRM4/GRM5/GRM6/GRM7/GRM8/GRP/GRPR/GZMA/HCTR1/HCTR2/TAAR6/HRH1/HRH2/HTR1A/HTR1B/HTR1D/HTR1E/HTR1F/HTR2A/HTR2B/HTR2C/HTR4/HTR5A/HTR6/HTR7/IAPP/RXFP4/PAQR9/QRFP/INSL3/KISS1/KNG1/NPSR1/LEP/LEPR/LHB/LHCGR/PATE2/PATE4/MAS1/MC1R/MC2R/MC3R/MC4R/MC5R/MLN/SLURP2/MTNR1A/MTNR1B/NMB/NMBR/NPY/NPY1R/NPY2R/NPY5R/NTS/NTSR1/OPRD1/OPRK1/OPRL1/OPRM1/OXT/OXTR/P2RX1/P2RX3/P2RX4/P2RX5/P2RX7/P2RY1/P2RY2/P2RY4/P2RY6/P2RY11/PRLH/GAL/RXFP3/PDYN/GHRL/PENK/PLG/S1PR5/P MCH/PNOC/P2RY13/POMC/AVP/AVPR1A/AVPR1B/PPY/AVPR2/NPY4R/CHRNA9/GABRQ/PRL/PRLR/LTB4R2/PRSS1/PRSS2/PRSS3/NMUR2/PYY/CHRNA10/CYSLTR2/SLURP1/PTAFR/PTGDR/PTGER1/PTGER2/PTGER3/PTGER4/PTGFR/PTGIR/PTH/PTH1R/PTH2R/HRH4/RXFP1/NPS/RLN1/RLN2/BDKRB1/BDKRB2/SCT/SCTR/NPFFR1/NPVF/LYNX1/SST1/SST2/SST3/SSTR4/SSTR5/BR3/TAC1/TACR2/TAC3/TACR1/TACR3/TBXA2R/TSPO/THRA/THRB/C3/C3AR1/TRH/TRHR/TSHB/TSHR/C5/C5AR1/UCN/VGF/VIP/VIPR1/VIPR2/TRPV1/CALCA/CALCB/CALCR/ADM2/PAQR6/GLRA3/TAAR8/QRFP/MCHR2/KISS1R/GALR3/GALP/NPFF/S1PR4/GALR2/CCK/CCKAR/APLN/CCKBR/CHRNA6/CHRFAM7A/F2RL3/UCN2/TAAR5/P2RX6/LPAR2/GPR50/TAAR2/S1PR2/GLP2R/GABBR2/P2RY14
Neuroactive ligand-receptor interaction	AKT3/CDKN1A/CDKN1B/PAK4/BUB1_PAK6/NG3/P3R3/URF_PIK3R3/CRK/CRKL/NG4/HBEGF/EGF/EGFR/EIF4E/BP1/ELK1/ERNB2/ERBB3/ERBB4/EREG/AKT1/AKT2/MTOR/ABL1/GAB1/SHC2/ABL2/GRB2/GSK3B/NGR1/HRAS/ARAF/JUN/AREG/KRAS/SHC4/MYC/NCK1/NRAS/PAK1/PAK2/PAK3/PIK3CA/PIK3CB/PIK3CD/PIK3R1/PIK3R2/PLCG1/S
ErbB signaling pathway	

HC3/PLCG2/PRKCA/PRKCB/PRKCG/MAPK1/MAPK3/MAPK8/MAPK9/MAPK10/MAP2K1/MAP2K2/MAP2K7/PAK6/PAK5/BAD/PTK2/RAF1/RPS6KB1/RPS6KB2/MAP2K4/SHC1/SOS1/SOS2/SRC/BRAF/STAT5A/STAT5B/BTC/TGFA/CAMK2A/CAMK2B/CAMK2D/CAMK2G/NCK2/PIK3R3/CBL/CBLB/NRG2

Table 5. Molecular pathway and related genes involved in schizophrenia pathophysiology.

We then performed a systematic comparison between the gene lists obtained from our microRNA-related enriched pathways and the reference schizophrenia-associated pathways by “tidyverse” R package. Gene identifiers were harmonized, and for each pathway we calculated the overlap between our input genes and the reference schizophrenia gene sets. The number of overlapping genes was recorded for each pathway–microRNA pair, and only those with a non-zero intersection were considered as putative links between the microRNA-regulated pathways and schizophrenia-related molecular mechanisms.

4.2.5.9 Construction and visualization of a gene–pathway network for schizophrenia-related miRNAs

To investigate the potential functional impact of miR-132, miR-181b, and miR-203a, we constructed a gene–pathway network linking their predicted target genes to significantly enriched KEGG pathways. Predicted targets were obtained from pathway enrichment analyses, and only genes overlapping with these pathways were included in the network.

Edges were defined as associations between pathways and their constituent genes, while nodes represented either genes or pathways. The dataset was processed in Rstudio using the “dplyr” and “tidyr” packages to separate multiple genes in each pathway into individual entries. The resulting edge list was used to generate an undirected network with the “igraph” package.

Network visualization was performed using ggraph with a Fruchterman–Reingold force-directed layout. This approach allowed identification of key network hubs corresponding to the glutamatergic synapse, dopaminergic synapse, and ErbB signaling pathway, highlighting potential mechanistic links between miRNA regulation and synaptic alterations implicated in schizophrenia.

4.2.5.10 Construction and visualization of a miRNA-Pathway-Drug network linking psychotropic compounds to schizophrenia

To better understand the potential mechanisms through which psychotropic compounds may modulate schizophrenia-related molecular pathways, we aimed to integrate information on miRNAs, their target pathways, and relevant drugs. This evaluation was particularly relevant given that our patients were under antipsychotic treatment, allowing us to contextualize the network in a clinically meaningful setting. The integrative network approach allows identification of convergence points where multiple miRNAs and compounds may act on shared signaling pathways, providing insights into the molecular interactions underlying drug effects and disease pathophysiology.

To investigate the relationship between psychotropic compounds and schizophrenia-related molecular pathways, we constructed an integrative miRNA–pathway–drug network. Candidate miRNAs (miR-132, miR-181b, and miR-203a) and their significantly enriched KEGG pathways were first identified through pathway enrichment analysis. We then compiled a comprehensive list of psychotropic compounds of interest, including both antipsychotic drugs and agents known to induce psychotomimetic effects (e.g., ketamine, phencyclidine, cocaine) based on KEGG pathways database. Drug–pathway associations were retrieved from KEGG and cross-referenced with our curated drug list. Only compounds with a direct match to KEGG drug entries linked to enriched pathways were retained. Nodes in the network were defined as miRNAs, pathways, or drugs, while edges represented validated or predicted associations between miRNAs and pathways, or KEGG-reported links between pathways and drugs. The network was implemented in Rstudio using the “igraph”, “ggraph”, and “tidyverse” packages. Graphs were generated in an undirected format, and node attributes were assigned by type (miRNA, pathway, drug). Network visualization was performed with a Fruchterman–Reingold force-directed layout. To enhance interpretability, we labeled the top 100 nodes ranked by degree centrality, highlighting the most connected elements in the network. Additionally, to assess the network specifically in the context of drugs actually administered to our patient cohort, we performed an analogous analysis filtering only the compounds

present in our sample. In this filtered network, the node ranking by degree centrality was omitted to focus on the direct relationships among miRNAs, pathways, and clinically relevant drugs.

4.3 Results

4.3.1 Descriptive analysis

We recruited 60 patients with schizophrenia, of whom 35 (58.3%) were classified as TRS and 25 (41.7%) as non-TRS (Table 6). The independent samples two-tailed Student's t-test and non-parametric Mann-Whitney test for normally and non-normally distributed variables, respectively, revealed significantly higher scores in PANSS subscale and factors - NEG TOT ($p=0.002$), GEN TOT($p=0.006$), PANSS tot ($p=0.001$), POS, NEG ($p=0.001$), EXC ($p=0.011$), EMO ($p=0.014$), PAUSS ($p=0.026$) and triglycerids levels ($p=0.004$) in TRS groups compared to SCZ. The only significances that survive the Bonferroni correction ($p < 0.0017$) are PANSS tot score and the PANSS POS factor.

Demographic and clinical variables	Mean±sd/Median±IQR		t_{gl}/Z	p-value	p-adj
	Schizophrenia patients (n = 25)	Treatment-Resistant Schizophrenia patients (n = 35)			
Age	47.00±23.00	39.00±23.00	-1.47	0.142	1.988
Sex (M%)	48.0%	54.3%	0.231 ₁	0.631	???
Age of onset	22.00±19.00	19.50±7.00	-1.28	0.202	2.828
Illness duration	20.58±12.83	19.66±11.06	0.30 ₅₇	0.384	11.14
CPZ equivalents	407.05±175.98	502.48±226.03	-1.58 ₄₇	0.060	1.74
PANSS Total score	75.21±14.19	90.61±20.18	-3.18 ₅₃	0.001	0.029
PANSS Positive score	15.00±8.00	20.50±7.00	-2.66	0.008	0.192
PANSS Negative score	18.63±4.69	22.84±5.69	-2.94 ₅₃	0.002	0.058
PANSS General score	40.38±7.78	48.87±10.05	-2.62 ₅₃	0.006	0.174
PANSS Disorganization factor	15.00±4.00	19.00±11.00	-2.80	0.005	0.07
PANSS Positive factor	16.21±4.03	21.87±7.19	-3.65 ₄₇	<0.001	<0.05
PANSS Negative factor	19.54±5.97	24.47±7.12	-2.71 ₅₂	0.005	0.145
PANSS Excitement factor	8.00±4.00	14.50±11.00	-2.78	0.005	0.07
PANSS Emotional factor	16.00±6.00	21.00±10.00	-3.02	0.003	0.042
PANSS PAUSS factor	23.00±7.00	26.00±7.00	-2.99	0.003	0.042
VM score	28.52±14.23	27.03±15.04	0.36 ₅₂	0.357	10.353
WM score	13.86±6.63	15.16±8.25	-0.62 ₅₂	0.268	7.772
CM score	37.50±22.33	33.87±17.76	0.66 ₅₂	0.255	7.395
VF score	31.89±15.22	32.42±17.20	-0.12 ₅₂	0.453	13.137
PS score	27.14±15.10	26.13±15.84	0.24 ₅₂	0.407	11.803
PSS score	14.00±13.50	12.50±12.00	-0.57	0.568	7.952
z score	±	±	-0.34	0.732	10.248
Fasting glucose (mg/dl)	81.96±18.37	82.81±13.68	-0.20 ₅₃	0.423	12.267
Total cholesterol (mg/dl)	166.17±48.45	178.71±28.36	-1.13 ₅₅	0.134	3.886
Triglycerides (mg/dl)	91.50±49.00	105.50±57.00	-2.71	0.007	0.098
LDL-cholesterol (mg/dl)	101.17±32.44	108.63±28.49	-0.88 ₄₉	0.193	5.597
HDL-cholesterol (mg/dl)	48.00±13.00	45.50±15.00	-1.50	0.134	1.876

Table 6. Demographic and clinical variables between treatment responsive and treatment-resistant schizophrenia

These sample sizes are consistent with the power analysis conducted prior to the study, which indicated that at least 25 patients per experimental group were necessary to achieve adequate statistical power. All participants were on antipsychotic treatment.

When we performed a one-way ANOVA with Tukey HSD post-hoc and non-parametric Kruskal-Wallis test with Dunn-Bonferroni post-hoc to investigate the differences between SCZ, CLZ-R, and CLZ-nR groups, for normally and non-normally distributed variables, respectively, we found lower CPZeq levels in SCZ group compare to CLZnR patients ($F_{2,56}=1.063$, $p=0.008$) and CLZR compared to CLZnR group ($F_{2,56}=1.063$, $p=0.013$). Regarding PANSS subscales and factor scores, significant differences were observed between patients with schizophrenia and those with treatment-resistant schizophrenia (TRS), further stratified by response to clozapine. Specifically, higher scores were found for the Negative Total (NEG TOT) scale, as well as for the GEN TOT, PANSS total score, POS, NEG, EXC, and EMO factors, as detailed in Table 7.

Demographic and clinical variables	Mean±sd/Median±IQR			F _{df} /H _{gl}	p-value	Post-hoc
	Schizophrenia patients (n = 25)	Treatment-Resistant Schizophrenia patients				
		CLZ-R (n = 23)	CLZ-nR (n = 12)			
Age	43.67±12.83	38.87±11.68	38.50±14.56	1.06 _{2,56}	0.352	-
Sex (M%)	48.0%	47.8%	66.7%	1.35 ₂	0.509	-
Age of onset	22.00±19.00	20.00±6.00	16.50±17.00	0.00 ₁	0.986	-
Illness duration	20.58±12.83	20.74±11.77	17.58±9.68	0.32 _{2,56}	0.725	-
CPZ equivalents	407.05±175.98	413.35±208.97	628.75±191.97	5.90 _{2,46}	0.005	CLZ-nR>CLZ-R>SCZ
PANSS Total score	75.21±14.19	90.55±21.56	90.78±17.53	4.95 _{2,52}	0.011	CLZ-nR>CLZ-R>SCZ
PANSS Positive score	15.00±8.00	21.50±9.00	23.00±6.00	0.02 ₁	0.879	-
PANSS Negative score	18.63±4.69	23.32±5.96	21.67±5.10	4.59 _{2,51}	0.015	CLZ-R>CLZ-nR>SCZ
PANSS General score	40.38±7.78	46.68±10.94	47.33±8.03	3.37 _{2,52}	0.042	CLZ-nR>CLZ-R>SCZ
PANSS Disorganization factor	15.00±4.00	14.50±6.00	31.00±13.00	9.24 ₁	0.002	CLZ-nR>SCZ>CLZ-R
PANSS Positive factor	16.21±4.03	20.90±7.31	24.11±6.80	6.92 _{2,51}	0.002	CLZ-nR>CLZ-R>SCZ
PANSS Negative factor	19.54±5.97	24.24±6.90	25.00±8.02	3.65 _{2,51}	0.033	CLZ-nR>CLZ-R>SCZ
PANSS Excitement factor	9.54±3.46	11.67±4.45	17.89±5.70	12.39 _{2,51}	<0.001	CLZ-nR>CLZ-R>SCZ
PANSS Emotional factor	16.42±3.01	19.48±4.92	25.33±7.19	12.13 _{2,51}	<0.001	CLZ-nR>CLZ-R>SCZ
PANSS PAUSS factor	23.00±7.00	26.00±7.00	27.50±11.00	0.74 ₁	0.388	-
VM score	28.52±14.23	26.77±14.82	27.67±16.49	0.08 _{2,51}	0.925	-
WM score	13.50±8.25	11.00±14.00	15.00±0.75	0.004 ₁	0.948	-
CM score	37.50±22.33	34.50±18.40	32.33±17.04	0.25 _{2,51}	0.776	-
VF score	31.89±15.22	31.04±17.23	35.78±17.65	0.27 _{2,51}	0.764	-
PS score	27.14±15.10	23.36±15.49	32.89±15.42	1.27 _{2,51}	0.291	-
PSS score	14.00±13.50	8.50±15.00	12.50±10.25	0.09 ₁	0.759	-
z score	20.50±37.48	22.00±45.50	-3.56±1.01	9.96 ₁	0.002	CLZ-R>SCZ>CLZ-nR
Fasting glucose (mg/dl)	81.96±18.37	80.14±11.48	88.40±16.71	0.95 _{2,52}	0.393	-
Total cholesterol (mg/dl)	166.17±48.45	173.76±29.13	189.10±24.86	1.26 _{2,49}	0.291	-
Triglycerides (mg/dl)	91.50±49.00	101.00±68.00	105.50±22.00	1.12 ₁	0.290	-
LDL-cholesterol (mg/dl)	101.17±32.44	100.53±27.35	122.40±26.11	2.11 _{2,48}	0.132	-
HDL-cholesterol (mg/dl)	54.67±18.19	45.94±7.45	47.60±8.66	0.56 ₁	0.456	-

Table 7. Demographic and clinical variables between treatment-responsive, clozapine-responsive and clozapine-resistant schizophrenia

When we investigated miRNAs levels, we found higher levels of hsa-mir-1246 in schizophrenia patients compared to TRS ones, but this differences was lost after Bonferroni correction (Table 8). No significantly differences were found among schizophrenia patients, clozapine responders and clozapine non responders (Table 9).

Gene Globe ID	microRNA	Mean±sd/Median±IQR		t_{gl}/Z	p-value	p-adj
		Schizophrenia patients (n = 23)	Treatment-Resistant Schizophrenia patients (n = 35)			
YP02119317	hsa-miR-7-5p	-2.503±0.19	-2.520±0.21	0.28 ₄₇	0.389	11.281
YP00204714	hsa-miR30e-5p	-0.285±0.16	0.262±0.16	-0.48 ₄₅	0.318	9.222
YP00204486	hsa-miR34a-5p	-2.442±0.25	-2.364±0.26	-1.13 ₅₅	0.131	3.799
YP00206026	hsa-mir124-3p	-3.088±0.29	-3.066±0.29	-0.28 ₅₆	0.392	11.368
YP00204227	hsa-mir126-3p	-2.924±0.76	-2.107±0.19	-1.14 ₄₁	0.132	3.828
YP00205995	hsa-mir128-3p	-3.186±0.22	-3.142±0.19	-0.81 ₅₆	0.212	6.148
YP00206035	hsa-mir132-3p	-2.957±0.19	-2.912±0.15	-0.84 ₅₆	0.201	5.829
YP00204530	hsa-mir181-5p	-3.534±0.21	-3.479±0.19	-1.08 ₅₆	0.142	4.118
YP00205869	hsa-mir195-5p	-3.327±0.17	-3.286±0.16	-0.90 ₅₆	0.186	5.394
YP00204494	hsa-mir199a-5p	-2.843±2.49	-3.686±2.53	-0.24	0.814	11.396
YP00205914	hsa-mir203a-3p	-3.657±0.29	-3.631±0.19	-0.27 ₂₃	0.397	11.513
YP00205986	hsa-mir223a-3p	-0.667±0.22	-0.626±0.20	-0.66 ₄₃	0.257	7.453
YP00204222	hsa-mir590-5p	-2.815±0.15	-2.778±0.15	-0.62 ₂₃	0.270	7.830
YP00205630	hsa-mir-1246	-2.140±0.14	-2.064±0.15	-1.94 ₅₆	0.029	0.841
YP02100320	hsa-miR-3178	-2.544±0.36	-2.572±0.27	-1.25	0.212	2.968
YP02112520	hsa-miR-5100	-2.188±0.30	-2.273±0.34	0.94 ₅₃	0.177	5.133
YP02110126	hsa-miR-7704	-2.943±0.34	-2.966±0.23	-1.01	0.313	4.382

Table 8. miRNA levels differences between treatment responsive and treatment-resistant schizophrenia

Gene Globe ID	microRNA	Mean±sd/Median±IQR			F _{df} /H _{gl}	p-value
		Schizophrenia patients (n = 26)	Treatment-Resistant Schizophrenia patients			
			CLZ-R (n = 23)	CLZ-nR (n = 12)		
YP02119317	hsa-miR-7-5p	-2.503±0.19	-2.529±0.23	-2.506±0.19	0.09 _{2,46}	0.918
YP00204714	hsa-miR30c-5p	-0.285±0.16	-0.271±0.16	-0.238±0.16	0.22 _{2,44}	0.803
YP00204486	hsa-miR34a-5p	-2.442±0.25	-2.366±0.25	-2.360±0.25	0.63 _{2,54}	0.535
YP00206026	hsa-mir124-3p	-3.088±0.29	-3.083±0.28	-3.036±0.33	0.14 _{2,55}	0.871
YP00204227	hsa-mir126-3p	-2.924±0.76	-2.104±0.22	-2.115±0.13	0.63 _{2,40}	0.538
YP00205995	hsa-mir128-3p	-3.186±0.22	-3.172±0.19	-3.085±0.19	1.05 _{2,55}	0.358
YP00206035	hsa-mir132-3p	-2.957±0.19	-2.940±0.15	-2.883±0.14	0.80 _{2,55}	0.454
YP00204530	hsa-mir181-5p	-3.534±0.21	-3.507±0.19	-3.424±0.19	1.27 _{2,55}	0.288
YP00205869	hsa-mir195-5p	-3.327±0.17	-3.283±0.18	-3.292±0.14	0.41 _{2,55}	0.666
YP00204494	hsa-mir199a-5p	-2.843±2.49	-4.760±2.56	-2.526±2.14	0.44 ₁	0.509
YP00205914	hsa-mir203a-3p	-3.657±0.29	-3.564±0.16	-3.720±0.21	0.79 _{2,22}	0.466
YP00205986	hsa-mir223a-3p	-0.667±0.22	-0.680±0.20	-0.531±0.16	1.76 _{2,42}	0.185
YP00204222	hsa-mir590-5p	-2.815±0.15	-2.836±0.17	-2.700±0.09	1.76 _{2,22}	0.195
YP00205630	hsa-mir-1246	-2.140±0.14	-2.052±0.15	-2.086±0.17	2.05 _{2,55}	0.138
YP02100320	hsa-miR-3178	-2.543±0.36	-2.468±0.29	-2.600±0.29	0.96 ₁	0.327
YP02112520	hsa-miR-5100	-2.188±0.30	-2.293±0.35	-2.235±0.31	0.56 _{2,52}	0.577
YP02110126	hsa-miR-7704	-2.943±0.34	-2.896±0.24	-2.986±0.26	0.70 ₁	0.404

Table 9. miRNA levels differences among treatment responsive, clozapine-responsive and clozapine-resistant schizophrenia.

4.3.2 Correlations between miRNA levels and clinical variables

We analyzed the correlations between circulating miRNA levels and clinical variables, identifying statistically significant associations that remained significant after false discovery rate (FDR correction). These results are presented in Figure 2 and detailed in Supplementary Table S1 and S2.

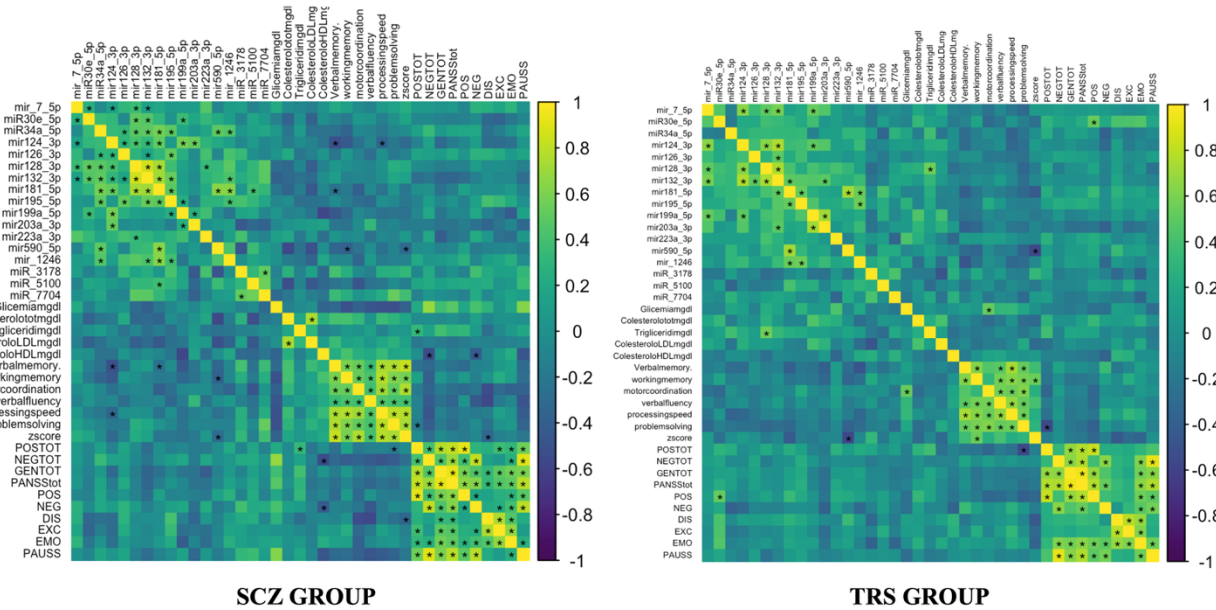


Figure 2. Correlation matrices between clinical variables and circulating miRNA levels in patients with schizophrenia (SCZ) and treatment-resistant schizophrenia (TRS). Direct and indirect correlations are represented by color intensity, with yellow color indicating higher correlation coefficients and blue lower correlation coefficients. Asterisks denoted statistically significant correlations.

We also compared the correlation matrices between groups, but no statistically significant differences were observed. The lack of significant group differences in the correlations between circulating miRNA levels and clinical measures suggests that the observed associations may reflect common underlying mechanisms, rather than being specific to treatment resistance or clinical subtypes. While no significant differences emerged from the comparison of correlation matrices, we observed more structured patterns in the SCZ group. Correlations among miRNAs may indicate co-expression or shared regulatory mechanisms, while associations among psychopathological scales suggest clinical coherence across symptom domains. Similar patterns were also present in the TRS group, though less pronounced, potentially reflecting greater heterogeneity or a weaker coupling between molecular and clinical dimensions.

4.3.3 Comparison of male and female miRNAs profiles across schizophrenia subtypes

4.3.3.1 Treatment Responsive Schizophrenia group

We found statistically significant differences in the levels of miR-30e-5p ($p = 0.049$), miR-124-3p ($p = 0.001$), miR-199a-5p ($p < 0.01$), miR-3178 ($p = 0.042$), miR-7704 ($p = 0.017$), glycemia ($p = 0.042$), verbal memory ($p = 0.028$), and working memory ($p = 0.016$). Specifically, all of the aforementioned miRNAs, except for miR-7704, were found to be more highly expressed in SCZ female compared to males of the same group. Only the differences in miR-124-3p and miR-199a-5p levels remained statistically significant after Bonferroni's adjustment ($p < 0.0016$) (Tables 10-11). No differences remained statistically significant for the non-parametric tests after Bonferroni correction.

Demographic and clinical variables	Mean±sd/Median±IQR		t_{gl}/Z	p-value	p-adj
	SCZ_M (n = 12)	SCZ_F (n = 13)			
Age	47.00±12.66	40.33±12.64	1.29 ₂₂	0.105	4.2
Age of onset	20.00±9.00	22.00±20.00	-0.06	0.054	0.162
Illness duration	23.42±13.25	17.75±12.30	1.09 ₂₂	0.145	5.8
CPZ equivalents	450.00±181.99	354.55±162.84	1.22 ₁₈	0.119	4.76
PANSS Total score	76.67±11.72	73.75±16.71	0.50 ₂₂	0.313	12.52
PANSS Positive score	15.00±6.00	17.50±8.00	-0.38	0.704	2.11
PANSS Negative score	19.83±3.69	17.42±5.40	1.28 ₂₂	0.107	4.28
PANSS General score	40.67±7.63	40.08±8.26	0.18 ₂₂	0.430	17.2
PANSS Disorganization factor	14.33±4.58	15.58±4.44	-0.68 ₂₂	0.252	10.08
PANSS Positive factor	15.75±4.00	16.67±4.19	-0.55 ₂₂	0.294	11.76
PANSS Negative factor	20.75±5.94	18.33±6.01	0.99 ₂₂	0.166	6.64
PANSS Excitement factor	9.33±3.96	9.75±3.05	-0.29 ₂₂	0.388	15.52
PANSS Emotional factor	15.67±3.23	17.17±2.69	-1.24 ₂₂	0.115	4.6
PANSS PAUSS factor	21.67±3.63	19.92±6.04	0.86 _{18,02}	0.200	8.0
VM score	22.64±13.51	33.92±13.14	-2.03 ₂₁	0.028	1.12
WM score	10.81±4.85	16.65±6.99	-2.30 ₂₁	0.016	0.64
CM score	36.82±24.94	38.12±20.76	-0.14 ₂₁	0.446	17.84
VF score	29.09±17.58	34.44±12.94	-0.84 ₂₁	0.206	8.24
PS score	21.91±14.27	31.94±14.77	-1.65 ₂₁	0.057	2.28
PSS score	10.55±7.58	15.32±4.98	-1.77 _{17,05}	0.047	1.88
z score	18.25±19.93	22.06±22.71	-0.42 ₂₀	0.340	13.6
Fasting glucose (mg/dl)	89.00±16.91	76.00±18.02	1.81 ₂₂	0.042	16.8
Total cholesterol (mg/dl)	162.73±59.96	169.08±44.30	-0.31 ₂₂	0.378	15.12
Triglycerides (mg/dl)	105.82±56.65	99.92±37.21	0.30 ₂₂	0.384	15.36
LDL-cholesterol (mg/dl)	90.18±38.36	110.46±24.22	-1.57 ₂₂	0.065	2.6
HDL-cholesterol (mg/dl)	42.00±10.00	52.50±26.00	-2.52	0.012	0.036

Table 10. Demographic and clinical variables differences based on sex: male schizophrenia patients compared to female schizophrenia patients.

Gene Globe ID	microRNA	Mean±sd/Median±IQR		t_{gl}/Z	p-value	p-adj
		SCZ_M (n = 12)	SCZ_F (n = 13)			
YP02119317	hsa-miR-7-5p	-2.39±0.20	-2.56±0.17	1.87 ₁₅	0.041	1.64

YP00204714	hsa-miR30e-5p	-0.22±0.15	-0.34±0.16	1.74 ₁₉	0.049	1.96
YP00204486	hsa-miR34a-5p	-2.40±0.24	-2.49±0.26	0.85 ₂₀	0.204	8.16
YP00206026	hsa-miR124-3p	-2.92±0.24	-3.27±0.22	3.69 ₂₁	0.001	0.04
YP00204227	hsa-miR126-3p	-2.38±1.04	-2.19±0.17	-0.54 ₁₈	0.297	11.88
YP00205995	hsa-miR128-3p	-3.16±0.23	-3.21±0.22	0.53 ₂₁	0.302	12.08
YP00206035	hsa-miR132-3p	-2.96±0.21	-2.95±0.19	-0.08 ₂₁	0.468	18.72
YP00204530	hsa-miR181-5p	-3.51±0.18	-3.57±0.25	0.62 ₂₁	0.270	10.8
YP00205869	hsa-miR195-5p	-3.31±0.15	-3.35±0.19	0.55 ₂₁	0.294	11.76
YP00204494	hsa-miR199a-5p	-2.44±0.28	-4.91±0.12	27.12 ₂₀	<0.001	<0.04
YP00205986	hsa-miR223a-3p	-0.61±0.22	-0.73±0.21	1.24 ₁₈	0.115	4.6
YP00205630	hsa-miR-1246	-2.14±0.09	-2.14±0.18	0.14 ₂₁	0.447	17.88
YP02100320	hsa-miR-3178	-2.72±0.25	-2.52±0.23	-1.83 ₁₈	0.042	1.68
YP02112520	hsa-miR-5100	-2.22±0.38	-2.15±0.18	-0.56 _{14,68}	0.294	11.76
YP02110126	hsa-miR-7704	-3.08±0.25	-2.82±0.29	-2.28 ₂₁	0.017	0.68

Table 11. miRNA levels differences based on sex: male schizophrenia patients compared to female schizophrenia patients.

4.3.3.2 Treatment Resistant Schizophrenia group

We found statistically significant differences in age, with higher values in female compared to male ($p = 0.021$), as well as increased levels in the same group for miR-7-5p ($p < 0.001$), miR-30e-5p ($p = 0.001$), miR-128-3p ($p = 0.002$), miR-132-3p ($p < 0.001$), miR-181-5p ($p = 0.004$), miR-195-5p ($p = 0.001$), miR-199a-5p ($p < 0.001$), and miR-1246 ($p = 0.014$), miR124-3p ($p=0.026$), and miR126-3p ($p=0.012$). After Bonferroni correction ($p < 0.016$), only the differences in miR-7-5p, miR-30e-5p, miR-132-3p, miR-195-5p, and miR-199a-5p remained statistically significant (Tables 12-13).

Demographic and clinical variables	Mean±sd/Median±IQR		t_{gl}/Z	p-value	p-adj
	TRS_M (n = 19)	TRS_F (n = 16)			
Age	34.84±10.35	43.38±13.60	-02.11 ₃₃	0.021	0.693
Age of onset	20.68±8.71	21.19±7.42	-0.18 ₃₃	0.428	14.12
Illness duration	17.53±9.99	22.19±12.03	-1.25 ₃₃	0.110	3.63
CPZ equivalents	525.00±302.50	350.00±431.50	-0.57	0.566	5.66
PANSS Total score	89.24±19.10	92.29±22.03	-0.41 ₂₉	0.341	11.253
PANSS Positive score	21.50±10.00	20.50±7.00	-0.28	0.781	7.81
PANSS Negative score	23.12±5.77	22.50±5.78	0.30 ₂₉	0.385	12.705
PANSS General score	45.41±10.02	48.64±10.17	-0.89 ₂₉	0.191	6.303
PANSS Disorganization factor	21.00±23.00	15.50±10.00	-1.25	0.211	2.11
PANSS Positive factor	22.44±7.09	21.21±7.53	0.46 ₂₈	0.325	10.725
PANSS Negative factor	25.19±8.31	23.64±5.65	0.59 ₂₈	0.281	9.273
PANSS Excitement factor	15.00±14.00	10.00±11.00	-0.50	0.616	6.16
PANSS Emotional factor	22.69±7.14	19.57±4.60	1.40 ₂₈	0.087	2.871
PANSS PAUSS factor	25.81±5.76	26.07±7.46	-0.11 ₂₈	0.458	15.114
VM score	22.82±13.93	32.14±15.25	-1.78 ₂₉	0.043	1.419
WM score	13.50±5.75	16.50±15.75	-1.25	0.210	2.10
CM score	35.77±21.12	31.57±12.99	0.65 ₂₉	0.261	8.613
VF score	32.06±18.80	32.86±15.72	-0.13 ₂₉	0.450	14.85
PS score	25.12±15.39	27.36±16.86	-0.39 ₂₉	0.351	11.583
PSS score	10.53±7.52	13.50±7.66	-1.09 ₂₉	0.143	4.719

z score	4.04±26.07	23.50±50.44	-2.14	0.032	0.32
Fasting glucose (mg/dl)	85.06±8.79	80.40±17.49	0.93 _{20,35}	0.182	6.006
Total cholesterol (mg/dl)	191.00±21.43	165.60±29.57	2.75 ₂₉	0.005	0.165
Triglycerides (mg/dl)	112.50±79.00	118.00±60	-0.53	0.593	5.93
LDL-cholesterol (mg/dl)	119.20±27.12	95.42±25.30	2.33 ₂₅	0.014	0.462
HDL-cholesterol (mg/dl)	47.47±8.93	45.46±6.40	0.67 ₂₆	0.253	8.349

Table 12. Demographic and clinical variables differences based on sex: male TRS patients compared to female TRS patients.

Gene Globe ID	microRNA	Mean±sd/Median±IQR		t _{gl} /Z	p-value	p-adj
		TRS_M (n = 19)	TRS_F (n = 16)			
YP02119317	hsa-miR-7-5p	-2.38±0.17	-2.66±0.16	4.84 ₃₀	<0.001	<0.033
YP00204714	hsa-miR30e-5p	-0.14±0.14	-0.34±0.12	3.71 ₂₄	0.001	0.033
YP00204486	hsa-miR34a-5p	-2.35±0.27	-2.38±0.25	0.25 ₃₃	0.401	13.233
YP00206026	hsa-miR124-3p	-2.97±0.25	-3.43±0.13	-3.28	0.001	0.01
YP00204227	hsa-miR126-3p	-2.00±0.17	-2.27±0.17	-3.14	0.002	0.02
YP00205995	hsa-miR128-3p	-3.06±0.18	-3.24±0.16	3.06 ₃₃	0.002	0.066
YP00206035	hsa-miR132-3p	-2.84±0.11	-3.01±0.12	4.40 ₃₃	<0.001	<0.033
YP00204530	hsa-miR181-5p	-3.40±0.14	-3.57±0.21	2.79 ₃₃	0.006	0.198
YP00205869	hsa-miR195-5p	-3.21±0.15	-3.37±0.14	3.28 ₃₃	0.001	0.033
YP00204494	hsa-miR199a-5p	-2.42±0.24	-4.88±0.09	37.11 _{17,35}	<0.001	<0.033
YP00205986	hsa-miR223a-3p	-0.53±0.33	-0.67±0.22	-1.31	0.189	1.89
YP00205630	hsa-miR-1246	-2.01±0.16	-2.12±0.12	2.29 ₃₃	0.014	0.462
YP02100320	hsa-miR-3178	-2.54±0.18	-2.46±0.30	-0.87 ₂₂	0.199	6.567
YP02112520	hsa-miR-5100	-2.24±0.34	-2.31±0.34	0.65 ₃₃	0.260	8.58
YP02110126	hsa-miR-7704	-2.89±0.24	-2.85±0.29	-0.42 ₃₃	0.337	11.121

Table 13. miRNA levels differences based on sex: male TRS patients compared to female TRS patients.

4.3.3.3 Clozapine responder Schizophrenia group

We found statistically significant differences in miR-7-5p ($p = 0.001$), miR-30e-5p ($p = 0.011$), miR-124-30 ($p = 0.039$), miR-126-3p ($p = 0.002$), miR-128-3p ($p = 0.030$), miR-132-3p ($p \leq 0.006$), miR-181-5p ($p = 0.049$), miR-195-5p ($p = 0.016$), miR-199a-5p ($p < 0.001$), and miR-1246 ($p = 0.046$) with higher levels in female compared to male. After Bonferroni correction ($p < 0.014$), only the differences in miR7-5p and miR199-5p remained statistically significant (Tables 14-15).

Demographic and clinical variables	Mean±sd/Median±IQR		t _{gl} /Z	p-value	p-adj
	CLZ-R_M (n = 11)	CLZ-R_F (n = 12)			
Age	43.00±13.00	42.50±28.00	-0.99	0.324	2.592
Age of onset	20.00±7.00	19.00±6.00	-0.80	0.422	3.376
Illness duration	19.91±10.13	21.50±13.50	-0.32 ₂₁	0.377	13.195
CPZ equivalents	402.09±205.17	434.00±234.02	-0.29 ₁₅	0.387	13.545
PANSS Total score	87.18±19.79	93.91±23.65	-0.72 ₂₀	0.239	8.365
PANSS Positive score	20.00±6.65	21.09±8.14	-0.34 ₂₀	0.367	12.845
PANSS Negative score	23.00±11.00	24.00±6.00	-0.60	0.551	4.408
PANSS General score	43.91±10.87	49.45±10.78	-1.20 ₂₀	0.122	4.27
PANSS Disorganization factor	17.00±13.00	14.50±4.00	-0.64	0.524	4.192
PANSS Positive factor	20.70±6.70	21.09±8.14	-0.12 ₁₉	0.453	15.855
PANSS Negative factor	24.10±8.13	24.36±5.97	-0.09 ₁₉	0.466	16.31
PANSS Excitement factor	11.90±5.38	11.45±3.78	0.22 ₁₉	0.414	14.49
PANSS Emotional factor	20.20±5.14	18.82±4.85	0.63 ₁₉	0.267	9.345
PANSS PAUSS factor	24.00±10.00	26.00±6.00	-0.14	0.888	7.104

VM score	21.73±13.11	31.82±15.27	-1.66 ₂₀	0.056	1.96
WM score	14.64±11.25	15.82±7.32	-0.29 ₂₉	0.387	13.545
CM score	36.18±23.96	32.82±11.44	0.42 _{14,33}	0.340	11.9
VF score	33.27±20.84	28.82±13.35	0.60 ₂₀	0.279	9.765
PS score	21.73±14.85	25.00±16.67	-0.49 ₂₀	0.316	11.06
PSS score	9.73±7.48	13.55±8.48	-1.12 ₂₀	0.138	4.83
z score	20.71±20.30	26.45±18.03	-0.67 ₁₈	0.256	8.96
Fasting glucose (mg/dl)	84.80±7.67	75.82±12.95	1.98 _{16,48}	0.033	1.155
Total cholesterol (mg/dl)	189.60±23.94	159.36±26.51	2.73 ₁₉	0.007	0.245
Triglycerides (mg/dl)	139.30±58.25	136.36±48.57	0.13 ₁₉	0.451	15.785
LDL-cholesterol (mg/dl)	110.56±29.32	89.25±21.27	1.70 ₁₅	0.055	1.925
HDL-cholesterol (mg/dl)	49.22±8.39	42.67±4.85	2.03 ₁₆	0.030	1.05

Table 14. Demographic and clinical variables differences based on sex: male CLZ_R patients copared to female CLZ_R patients.

Gene Globe ID	microRNA	Mean±sd/Median±IQR		t _{gl} /Z	p-value	p-adj
		CLZ-R_M (n = 11)	CLZ-R_F (n = 12)			
YP02119317	hsa-miR-7-5p	-2.35±0.17	-2.65±0.18	3.77 ₁₈	0.001	0.035
YP00204714	hsa-miR30e-5p	-0.17±0.15	-0.33±0.13	2.52 ₁₇	0.011	0.385
YP00204486	hsa-miR34a-5p	-2.35±0.24	-2.38±0.28	0.23 ₂₁	0.411	14.385
YP00206026	hsa-mir124-3p	-2.96±0.20	-3.39±0.13	-2.40	0.016	0.128
YP00204227	hsa-mir126-3p	-1.95±0.18	-2.24±0.15	3.51 ₁₃	0.002	0.07
YP00205995	hsa-mir128-3p	-3.09±0.18	-3.24±0.18	1.99 ₂₁	0.030	1.05
YP00206035	hsa-mir132-3p	-2.86±0.12	-3.01±0.14	2.78 ₂₁	0.006	0.21
YP00204530	hsa-mir181-5p	-3.44±0.14	-3.57±0.22	1.73 ₂₁	0.049	1.715
YP00205869	hsa-mir195-5p	-3.20±0.17	-3.36±0.16	2.30 ₂₁	0.016	0.56
YP00204494	hsa-mir199a-5p	-2.35±0.24	-4.88±0.08	29.19 _{8,16}	<0.001	<0.035
YP00205986	hsa-mir223a-3p	-0.63±0.21	-0.73±0.20	0.99 ₁₄	0.169	5.915
YP00205630	hsa-mir-1246	-2.00±0.16	-2.10±0.12	1.76 ₂₁	0.046	1.61
YP02100320	hsa-miR-3178	-2.50±0.33	-2.50±0.30	-0.21	0.834	6.672
YP02112520	hsa-miR-5100	-2.26±0.39	-2.32±0.33	0.42 ₂₁	0.341	11.935
YP02110126	hsa-miR-7704	-2.92±0.25	-2.90±0.22	-0.43	0.667	5.336

Table 13. miRNA levels differences based on sex: male CLZ_R patients copared to female CLZ_R patients.

4.3.3.4 Clozapine non responder Schizophrenia group

We found statistically significant differences in miR-7-5p (p =0.006), miR-30e-5p (p = 0.029), miR-124-30 (p=0.020), miR-126-3p (p = 0.030), miR-128-3p (p=0.031), miR-181-5p (p = 0.032), miR-195-5p (p = 0.008), and miR-199a-5p (p < 0.001) with higher levels in female compared to male. After Bonferroni adjustement (p < 0.016), only the differences in miR7-5p and miR199-5p remained statistically significant (Tables 16-17).

Demographic and clinical variables	Mean±sd/Median±IQR		t _{gl} /Z	p-value	p-adj
	CLZ-nR_M (n = 8)	CLZ-nR_F (n = 4)			
Age	32.50±10.09	50.50±15.89	-2.42 ₁₀	0.018	0.648
Age of onset	18.25±7.27	26.25±9.43	-1.64 ₁₀	0.066	2.376
Illness duration	14.25±9.41	24.25±6.95	-1.87 ₁₀	0.046	1.656
CPZ equivalents	591.50±203.73	703.25±164.86	-0.95 ₁₀	0.183	6.588
PANSS Total score	93.00±18.92	86.33±17.04	0.51 ₇	0.312	11.232
PANSS Positive score	20.33±4.59	21.33±6.11	-0.28 ₇	0.394	14.184
PANSS Negative score	18.00±5.43	21.00±???	-1.04	0.300	2.1

PANSS General score	48.17±8.42	45.67±8.62	0.42 ₇	0.345	12.42
PANSS Disorganization factor	27.00±8.56	22.67±2.52	0.83 ₇	0.216	7.776
PANSS Positive factor	25.33±7.39	21.67±6.03	0.74 ₇	0.241	8.676
PANSS Negative factor	27.00±9.06	21.00±4.00	1.07 ₇	0.161	5.796
PANSS Excitement factor	18.33±6.89	17.00±3.00	0.31 ₇	0.382	13.752
PANSS Emotional factor	26.83±8.52	22.33±2.31	0.87 ₇	0.206	7.416
PANSS PAUSS factor	26.00±6.99	21.67±3.22	0.99 ₇	0.176	6.336
VM score	30.00±5.32	43.00±3.67	-1.31	0.189	1.323
WM score	15.00±3.67	15.00±3.22	-1.13	0.258	1.806
CM score	35.00±16.67	27.00±20.07	0.64 ₇	0.272	9.792
VF score	29.83±15.90	47.67±17.21	-1.55 ₇	0.083	2.988
PS score	31.33±15.67	36.00±17.78	-0.41 ₇	0.349	12.564
PSS score	12.00±8.05	13.33±4.73	-0.26 ₇	0.401	14.436
z score	-3.62±2.82	12.38±23.51	-0.96 _{1.01}	0.256	9.216
Fasting glucose (mg/dl)	85.33±11.22	93.00±24.10	-0.60 _{3.88}	0.292	10.512
Total cholesterol (mg/dl)	193.33±18.33	182.75±34.70	0.64 ₈	0.271	9.756
Triglycerides (mg/dl)	142.17±61.00	103.25±19.36	1.46 _{6.38}	0.096	3.456
LDL-cholesterol (mg/dl)	132.17±18.66	107.75±31.43	1.56 ₈	0.079	2.844
HDL-cholesterol (mg/dl)	44.83±9.85	51.75±4.99	-1.28 ₈	0.118	4.248

Table 16. Demographic and clinical variables differences based on sex: male CLZ_nR patients copared to female CLZ_nR patients.

Gene Globe ID	microRNA	Mean±sd/Median±IQR		t _g /Z	p-value	p-adj
		CLZ-nR_M (n = 8)	CLZ-nR_F (n = 4)			
YP02119317	hsa-miR-7-5p	-2.42±0.17	-2.69±0.06	4.09 _{9.40}	0.001	0.036
YP00204714	hsa-miR30e-5p	-0.06±0.002	-0.30±0.003	-2.12	0.034	0.238
YP00204486	hsa-miR34a-5p	-2.27±0.04	-2.31±0.11	-0.17	0.865	6.055
YP00206026	hsa-miR124-3p	-2.90±0.32	-3.30±0.13	2.36 ₁₀	0.020	0.72
YP00204227	hsa-miR126-3p	-2.06±0.06	-2.21±0.13	2.32 ₆	0.030	1.08
YP00205995	hsa-miR128-3p	-3.01±0.18	-3.23±0.11	2.10 ₁₀	0.031	1.116
YP00206035	hsa-miR132-3p	-2.84±0.01	-3.01±0.12	-2.72	0.007	0.049
YP00204530	hsa-miR181-5p	-3.36±0.14	-3.56±0.21	2.07 ₁₀	0.032	1.152
YP00205869	hsa-miR195-5p	-3.23±0.12	-3.42±0.06	2.88 ₁₀	0.008	0.288
YP00204494	hsa-miR199a-5p	-2.50±0.24	-4.89±0.11	22.17 _{8.86}	<0.001	<0.036
YP00205986	hsa-miR223a-3p	-0.52±0.17	-0.56±0.16	0.33 ₇	0.377	13.572
YP00205630	hsa-miR-1246	-2.03±0.18	-2.19±0.10	1.69 ₁₀	0.062	2.232
YP02100320	hsa-miR-3178	-2.59±0.21	-2.55±0.25	-0.24 ₆	0.409	14.724
YP02112520	hsa-miR-5100	-2.21±0.29	-2.29±0.40	0.39 ₁₀	0.353	12.708
YP02110126	hsa-miR-7704	-2.42±0.22	-3.10±0.32	-0.17	0.865	6.055

Table 17. miRNA levels differences based on sex: male CLZ_nR patients copared to female CLZ_nR patients.

4.3.5 Principal Component Analysis

We performed a Principal Component Analysis (PCA) on the full dataset and retained the first five principal components (PCs) (Supplementary Table S3), which together captured the most relevant variance across variables with a cumulative variance = 55.1% and PC1 = 18.6%, PC2 = 14.3%, PC3 = 9.4%, PC4 = 6.8%, PC5 = 6.1% (Figure PCA_5D).

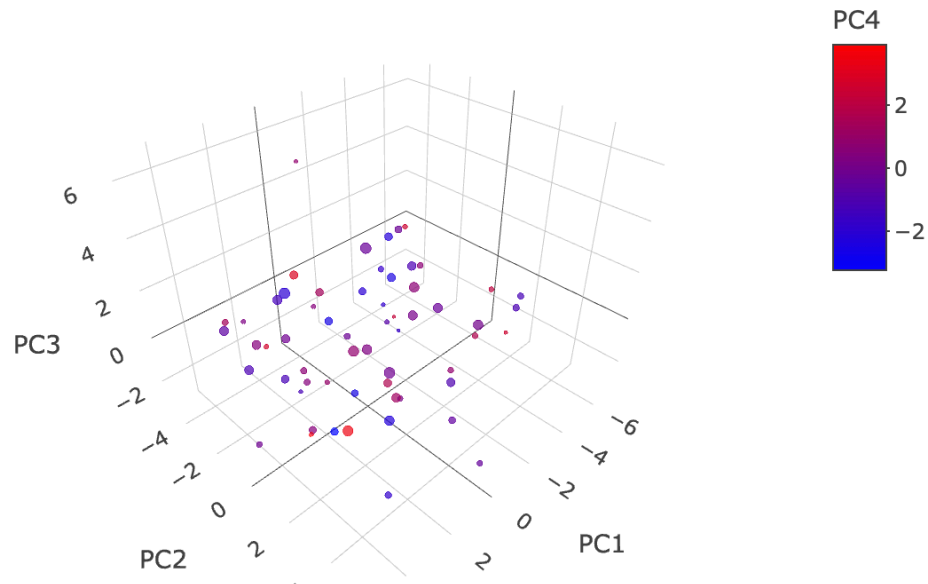


Figure 3. Principal component analysis (PCA) of circulating miRNA expression and clinical variables in patients. The plot displays the first five principal components, which together capture the largest proportion of variance in the dataset. Each point represents an individual subject, with grouping based on diagnostic category. The axes correspond to the respective principal components, illustrating how patients distribute across multivariate space according to shared molecular and clinical features.

In particular, PC1 appears to represent a dimension contrasting severe clinical symptoms and cognitive/motor abilities. Specifically, it shows strong negative loadings on variables related to clinical symptom severity (e.g., total PANSS scores, positive and negative symptom scores), while cognitive and motor function variables (e.g., verbal memory, working memory, motor coordination) load positively (Figure 4).

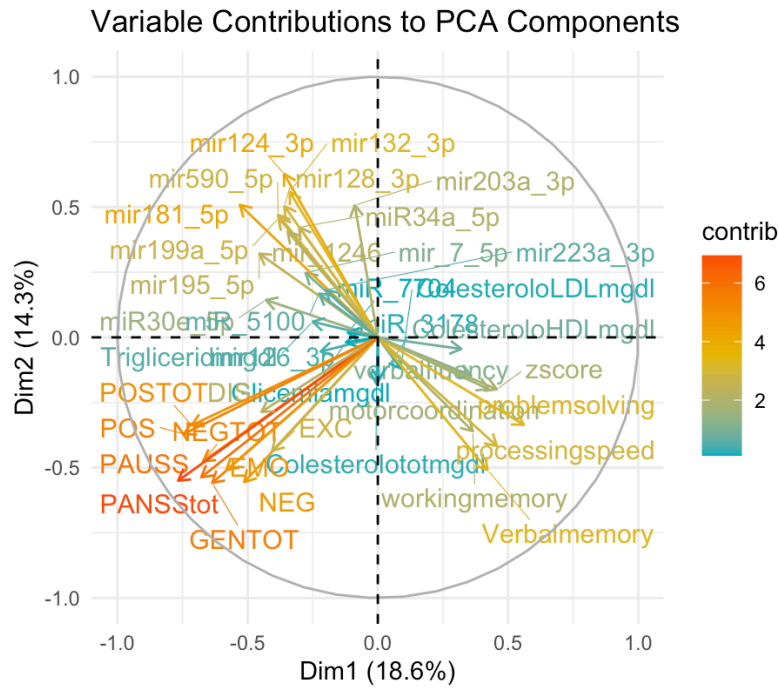


Figure 4. PCA loading plot for PC1 and PC2. The figure shows the correlation circle representing the contribution of individual variables to the first two principal components (PC1 and PC2). Each vector indicates the direction and strength of a variable's contribution, with length reflecting the magnitude of its influence and color denoting its relative weight in the component structure.

This suggests that PC1 separates subjects along a continuum from those with more severe symptoms and poorer functioning to those with milder symptoms and better cognitive and motor performance. PC2 seems to capture a different dimension, where certain molecular biomarkers (such as specific miRNAs) have positive loadings, whereas clinical symptoms and cognitive measures tend to have negative loadings. This indicates that PC2 may reflect a biological or molecular profile axis that is inversely related to clinical and cognitive features.

However, to identify the most influential features across the latent space, we computed a combined loading score for each variable, defined as the sum of the absolute loadings across the five retained PCs. Variables with a combined loading ≥ 0.4 were considered as contributing substantially to the overall principal component structure. Based on this criterion, the following variables were selected for further analysis: DIS (0.478), EXC (0.450), zscore (0.426), EMO (0.413), processing speed (0.412), mir199a_5p (0.410), mir128_3p (0.405), mir181_5p (0.403), mir203a_3p (0.400), and

mir132_3p (0.400). These variables demonstrated the highest multicomponent influence and were prioritized in downstream predictive modeling and interpretation.

4.3.6 Machine learning algorithm

We evaluated three machine learning algorithms represented by Random Forest, XGBoost, and SVM to predict the condition of TRS using selected clinical and molecular predictors.

Algorithm	Accuracy	Sensitivity	Specificity	AUC
Random Forest	0.633 $\pm$ 0.075	0.613 $\pm$ 0.172	0.693 $\pm$ 0.224	0.669 $\pm$ 0.102
XGBoost	0.567 $\pm$ 0.181	0.618 $\pm$ 0.251	0.537 $\pm$ 0.329	0.631 $\pm$ 0.122
SVM	0.583 $\pm$ 0.102	0.893 $\pm$ 0.147	0.190 $\pm$ 0.325	0.645 $\pm$ 0.139

Table 18. Performance metrics of three machine learning algorithms (Random Forest, XGBoost, and SVM) for the classification of patients with treatment-resistant schizophrenia (TRS) versus non-TRS. Accuracy, sensitivity, specificity, and area under the curve (AUC) are reported as mean $\pm$ standard deviation, estimated using nested cross-validation.

Results of the nested cross-validation revealed substantial differences in the performance of the models evaluated on the dataset balanced using SMOTE. The Nested Cross-Validation results indicate a moderate overall classification performance of the Random Forest model. The mean accuracy across the outer folds was 0.633 ($\pm$ 0.075), reflecting a reasonable level of correct classifications. Sensitivity and specificity values were 0.613 ($\pm$ 0.172) and 0.693 ($\pm$ 0.224), respectively, suggesting the model has a slightly better ability to correctly identify negative cases compared to positive cases, although with notable variability across folds. The mean AUC of 0.669 ($\pm$ 0.102) further supports the model's moderate discriminatory power. These results demonstrate acceptable but improvable predictive capability and highlight some inconsistency likely due to sample size or data heterogeneity. In contrast, the XGBoost model exhibited generally poorer performance compared to Random Forest, with a mean accuracy of 0.567 $\pm$ 0.181 and an AUC of 0.631 $\pm$ 0.122. The higher standard deviations, particularly for sensitivity (0.251) and specificity (0.329), indicate greater variability in performance across folds, potentially reflecting reduced robustness of this model for the current dataset.

The Support Vector Machine (SVM) approach presented a more nuanced pattern. It achieved a high mean sensitivity of 0.893 $\pm$ 0.147, highlighting a strong capacity to identify true positive cases. However, this came at the expense of specificity, which was markedly lower 0.190 $\pm$ 0.325, indicating

poor ability to correctly classify negative cases and a high false positive rate. The overall accuracy was 0.583 ± 0.102 and the AUC reached 0.645 ± 0.139 , both lower than those of Random Forest, but potentially acceptable depending on the clinical or practical context, particularly where sensitivity is prioritized.

Overall, these findings suggest that, for this dataset, the Random Forest model balanced with SMOTE provides the most reliable trade-off between accuracy, sensitivity, and specificity, along with good generalizability. While XGBoost remains a powerful algorithm, it appeared less stable in this setting. SVM, despite its high sensitivity, showed limited overall discriminatory ability.

Considering the best algorithm, Random Forest model, the most relevant variables contributing to the classification performance were found to be DIS, EMO, EXC, miR132-3p, miR181-5p, and miR203-3p (Fig. 5).

The prominence of DIS, EMO, and EXC highlights the significant role of clinical and behavioral features in distinguishing between groups. Notably, the involvement of specific microRNAs such as miR132-3p, miR181-5p, and miR203-3p suggests a potential molecular underpinning related to the biological mechanisms associated with the condition under study. These findings emphasize the importance of integrating both phenotypic and molecular markers for improved predictive modeling and provide insights into possible pathways for further investigation.

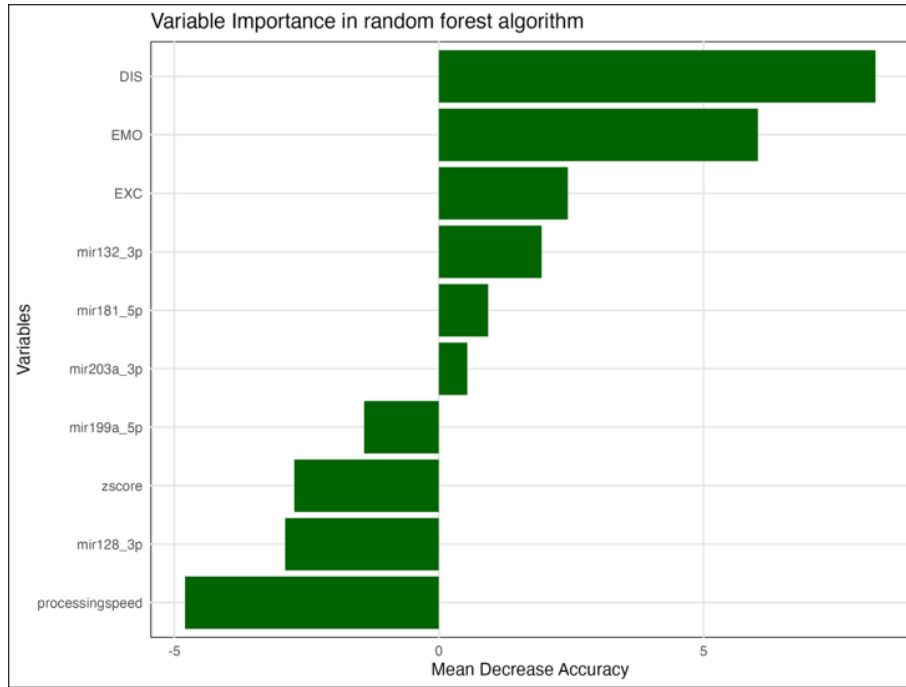


Figure 5. Variable importance plot from the Random Forest model for the classification of treatment-resistant schizophrenia (TRS) versus non-TRS. Importance values are expressed as Mean Decrease Accuracy, indicating the reduction in model performance when each variable is permuted. Higher values reflect stronger contributions of the corresponding variable to the predictive performance of the model.

Given that variables with negative Mean Decrease Accuracy can potentially introduce noise or reduce model interpretability, we decided to rerun the model excluding these less informative features. Specifically, we retained only the variables with positive importance values: the Disorganization factor, Emotional factor, Excitement factor, miR-132-3p, miR-181-5p, and miR-203a-3p. This refined model showed a mixed pattern of performance changes: the mean outer AUC improved to approximately 0.714, indicating enhanced overall discrimination ability. Sensitivity increased slightly to 0.629, while specificity decreased to 0.600, suggesting a trade-off between better detection of positive cases and a higher rate of false positives. The Mean Decrease Accuracy values for these selected variables (EMO = 5.88, DIS = 4.65, mir132_3p = 3.21, EXC = 2.34, mir181_5p = 1.31, mir203a_3p = 0.79) confirm their relative importance in the classification task (Figure 6).

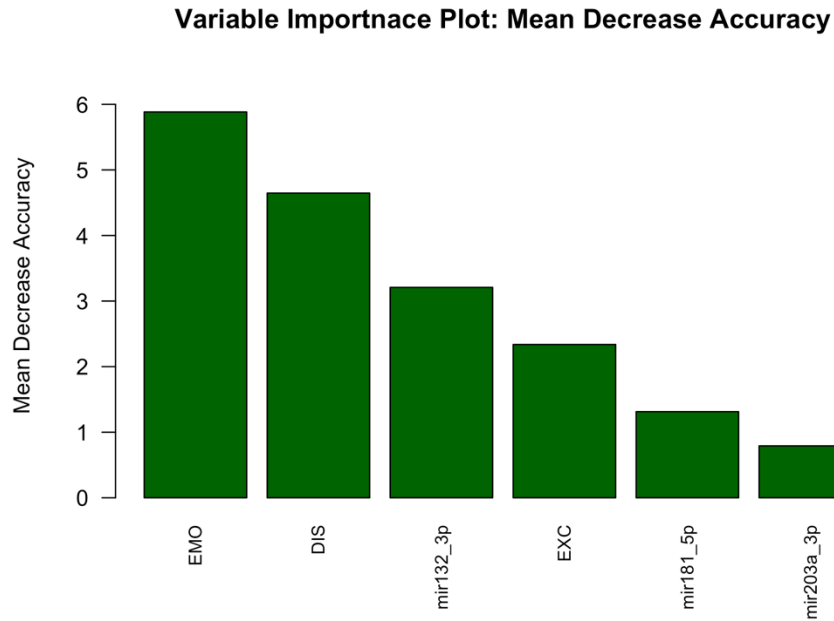


Figure 6. Variable importance plot from the Random Forest model including only predictors that contributed to the classification of treatment-resistant schizophrenia (TRS) versus non-TRS. Importance values are expressed as Mean Decrease Accuracy, with higher values indicating stronger contributions to model performance.

4.3.7 Characterization of validated target genes for key miRNAs

Starting from the miRNAs identified as significant by the machine learning algorithm, we investigated the validated filtered gene targets associated with each miRNA (Table 19).

miR-132	miR-181	miR-203a
VMP1	CBX4	BIRC5
HS3ST3B1	ETS1	BMI1
ARHGAP32	HSPA1B	DUSP5
CDKN1A	TIMP3	ATM
ELOC	ZNF667	BCL2L2
FOXO1	ZNF669	COX20
FXR1	ZNF83	SNAI2
HBEGF	ATM	TP63
PSMA2	BCL2	ABL1
TJAP1	FKBP14	ANKRD13B
AMD1	GIGYF1	ARID3B
CRK	NPM3	FBXL5
DAZAP2	TMCC1	MXRA7
EML4	UNC5B	NARS1
FZD6	ZFAND6	PI4K2B
KPNA1	ZNF487	RAN
MUC13	ZNF791	SOCS3
NUP50	ADCY9	SRC

OCN	AP5M1	CDK6
PLAGL2	C2orf69	CIAO1
POLR1F	CAPRIN2	CPEB4
RAB5B	CCNK	DHX33
SIRT1	CHD9	DLX5
SLC38A2	CYLD	DNAAF2
SPRED1	DDX3X	DNAJB6
TLN2	E2F1	DYNLT1
TRUB1	ELK4	EN2
UBXN2A	EPS8	ENAH
	FKBP1C	GABRB1
	FOXL1	GLRX2
	GATA6	GPR156
	GRK2	GXYLT1
	HK2	HNRNPDL
	HMGA2	LASP1
	HSP90B1	LCOR
	IRAK1BP1	LIFR
	KIF2C	LOH12CR2

	LBR	MAFK
	LCLAT1	MTPN
	NR6A1	NR2F2
	NSD2	NUFIP2
	PHC3	PARD6B
	PTEN	PIK3CA
	RASSF1	PLD2
	RNF187	PRNP
	RNF6	PSAT1
	RPL13A	RUNX2
	SCD	SERTAD3
	SEPTIN2	SNX4

	ZBTB4	SOD2
	ZFP69B	STMP1
	ZNF440	TCF4
	ZNF556	TMEM97
	ZNF844	TRMT5
		TSC22D2
		TSR1
		UBXN2A
		VGLL4
		ZBED3
		ZNF200
		ZNF367

Table 19. Target genes of miR-132, miR-181b, and miR-203a. Only genes meeting the filtering criteria defined in the Methods section were included. Each column lists the target genes associated with the corresponding miRNA.

The filtered gene targets were visualized using a Venn diagram (Figure 7) to assess overlaps among the three miRNAs.

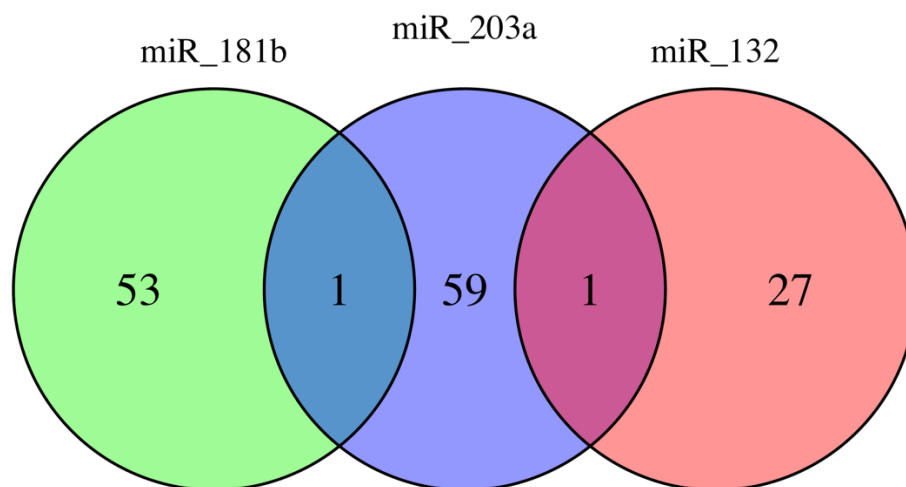


Figure 7. Venn diagram showing the overlap of target genes regulated by miR-132, miR-181b, and miR-203a. The diagram highlights genes uniquely regulated by each miRNA as well as those shared between two or all three miRNAs, illustrating potential convergent regulatory pathways.

The comparative analysis revealed the following: no gene targets were common between miR-132 and miR-181b; ii) one gene target, UBXN2A, was shared between miR-132 and miR-203a; iii) one gene target, ATM, was shared between miR-181b and miR-203a; iv) no gene targets were common

to all three miRNAs. These results suggest limited overlap in the experimentally validated target genes among the three miRNAs, highlighting potentially distinct regulatory roles.

4.3.8 Functional enrichment analysis across miR-132, miR-181b, and miR-203a targets

GO enrichment analysis was performed for miR-132, miR-181b, and miR-203a to explore the BP, CC, and MF associated with their predicted target genes (Table 20).

miR-132 Biological Process								
ID	Description	GeneRatio	BgRatio	pvalue	p.adjust	qvalue	geneID	Count
GO:0009267	cellular response to starvation	4/28	179/18870	0.000134	0.03849	0.028178	CDKN1A/FOXO1/SIRT1/SLC38A2	4
GO:0030330	DNA damage response, signal transduction by p53 class mediator	3/28	73/18870	0.00017	0.03849	0.028178	CDKN1A/SIRT1/SPRED1	3
GO:0060148	positive regulation of post-transcriptional gene silencing	2/28	15/18870	0.00022	0.03849	0.028178	FXR1/TRUB1	2
GO:0071732	cellular response to nitric oxide	2/28	15/18870	0.00022	0.03849	0.028178	FOXO1/CRK	2
GO:1900370	positive regulation of post-transcriptional gene silencing by RNA	2/28	15/18870	0.00022	0.03849	0.028178	FXR1/TRUB1	2
GO:2000637	positive regulation of miRNA-mediated gene silencing	2/28	15/18870	0.00022	0.03849	0.028178	FXR1/TRUB1	2
GO:1902170	cellular response to reactive nitrogen species	2/28	17/18870	0.000285	0.03849	0.028178	FOXO1/CRK	2
GO:0042594	response to starvation	4/28	218/18870	0.000285	0.03849	0.028178	CDKN1A/FOXO1/SIRT1/SLC38A2	4
GO:0042060	wound healing	5/28	423/18870	0.000355	0.03849	0.028178	CDKN1A/HBEGF/CRK/FZD6/OCN	5
GO:0055093	response to hyperoxia	2/28	20/18870	0.000397	0.03849	0.028178	CDKN1A/FOXO1	2
GO:0071731	response to nitric oxide	2/28	20/18870	0.000397	0.03849	0.028178	FOXO1/CRK	2
GO:0045722	positive regulation of gluconeogenesis	2/28	21/18870	0.000438	0.03849	0.028178	FOXO1/SIRT1	2
GO:1990830	cellular response to leukemia inhibitory factor	3/28	104/18870	0.000482	0.03849	0.028178	POLR1F/SIRT1/UBXN2A	3
GO:0031669	cellular response to nutrient levels	4/28	251/18870	0.000487	0.03849	0.028178	CDKN1A/FOXO1/SIRT1/SLC38A2	4
GO:1990823	response to leukemia inhibitory factor	3/28	106/18870	0.00051	0.03849	0.028178	POLR1F/SIRT1/UBXN2A	3
GO:0036296	response to increased oxygen levels	2/28	27/18870	0.000728	0.048366	0.035409	CDKN1A/FOXO1	2
GO:0031668	cellular response to extracellular stimulus	4/28	281/18870	0.000744	0.048366	0.035409	CDKN1A/FOXO1/SIRT1/SLC38A2	4
GO:0060964	regulation of miRNA-mediated gene silencing	2/28	28/18870	0.000784	0.048366	0.035409	FXR1/TRUB1	2
GO:1900368	regulation of post-transcriptional gene silencing by regulatory ncRNA	2/28	29/18870	0.000841	0.048366	0.035409	FXR1/TRUB1	2
GO:0060147	regulation of post-transcriptional gene silencing	2/28	30/18870	0.0009	0.048366	0.035409	FXR1/TRUB1	2
GO:0060966	regulation of gene silencing by regulatory ncRNA	2/28	31/18870	0.000961	0.048366	0.035409	FXR1/TRUB1	2
GO:0061041	regulation of wound healing	3/28	133/18870	0.000986	0.048366	0.035409	HBEGF/CRK/OCN	3
GO:0001933	negative regulation of protein phosphorylation	4/28	304/18870	0.000997	0.048366	0.035409	CDKN1A/OCN/SIRT1/SPRED1	4
GO:0046685	response to arsenic-containing substance	2/28	32/18870	0.001025	0.048366	0.035409	CDKN1A/SLC38A2	2
miR-132 Cellular Component								
GO:0016327	apicolateral plasma membrane	2/28	22/19886	0.000434	0.046872	0.037461	FZD6/OCN	2
miR-132 Molecular Function								
GO:0031625	ubiquitin protein ligase binding	5/27	308/18496	7.41E-05	0.007317	0.004859	CDKN1A/FOXO1/CRK/DAZAP2/FZD6	5
GO:0044389	ubiquitin-like protein ligase binding	5/27	327/18496	9.82E-05	0.007317	0.004859	CDKN1A/FOXO1/CRK/DAZAP2/FZD6	5
GO:0019887	protein kinase regulator activity	4/27	226/18496	0.000305	0.015171	0.010075	CDKN1A/HBEGF/DAZAP2/SPRED1	4
GO:0019207	kinase regulator activity	4/27	256/18496	0.00049	0.018238	0.012112	CDKN1A/HBEGF/DAZAP2/SPRED1	4
GO:0030295	protein kinase activator activity	3/27	124/18496	0.000765	0.022791	0.015135	CDKN1A/HBEGF/DAZAP2	3
GO:0019209	kinase activator activity	3/27	133/18496	0.000937	0.02327	0.015453	CDKN1A/HBEGF/DAZAP2	3
GO:0030291	protein serine/threonine kinase inhibitor activity	2/27	37/18496	0.001324	0.028189	0.01872	CDKN1A/SPRED1	2
miR-181b Biological Process								
GO:2001236	regulation of extrinsic apoptotic signaling pathway	7/53	158/18870	2.82E-07	0.000445	0.000373	HSPA1B/TIMP3/BCL2/UNC5B/CYLD/DDX3X/PTEN	7
GO:0097191	extrinsic apoptotic signaling pathway	7/53	229/18870	3.39E-06	0.002676	0.002244	HSPA1B/TIMP3/BCL2/UNC5B/CYLD/DDX3X/PTEN	7
GO:0019079	viral genome replication	5/53	131/18870	3.28E-05	0.017258	0.014471	BCL2/CCNK/DDX3X/GRK2/HMGA2	5
GO:0045926	negative regulation of growth	6/53	247/18870	6.49E-05	0.025347	0.021253	HSPA1B/BCL2/CAPRIN2/DDX3X/PTEN/RNF6	6
GO:0008625	extrinsic apoptotic signaling pathway via death domain receptors	4/53	86/18870	9.93E-05	0.025347	0.021253	TIMP3/BCL2/DDX3X/PTEN	4
GO:2001233	regulation of apoptotic signaling pathway	7/53	398/18870	0.000118	0.025347	0.021253	HSPA1B/TIMP3/BCL2/UNC5B/CYLD/DDX3X/PTEN	7
GO:1901099	negative regulation of signal transduction in absence of ligand	3/53	35/18870	0.000128	0.025347	0.021253	HSPA1B/BCL2/UNC5B	3
GO:2001240	negative regulation of extrinsic apoptotic signaling pathway in absence of ligand	3/53	35/18870	0.000128	0.025347	0.021253	HSPA1B/BCL2/UNC5B	3
GO:2000045	regulation of G1/S transition of mitotic cell cycle	5/53	183/18870	0.00016	0.026652	0.022347	ATM/BCL2/DDX3X/E2F1/PTEN	5
GO:2001237	negative regulation of extrinsic apoptotic signaling pathway	4/53	99/18870	0.000171	0.026652	0.022347	HSPA1B/BCL2/UNC5B/DDX3X	4
GO:0030308	negative regulation of cell growth	5/53	189/18870	0.000186	0.026652	0.022347	HSPA1B/BCL2/CAPRIN2/DDX3X/RNF6	5
GO:0019058	viral life cycle	6/53	321/18870	0.000271	0.033364	0.027975	HSPA1B/BCL2/CCNK/DDX3X/GRK2/HMGA2	6
GO:2001239	regulation of extrinsic apoptotic signaling pathway in absence of ligand	3/53	46/18870	0.000292	0.033364	0.027975	HSPA1B/BCL2/UNC5B	3
GO:1902806	regulation of cell cycle G1/S phase transition	5/53	209/18870	0.000296	0.033364	0.027975	ATM/BCL2/DDX3X/E2F1/PTEN	5
GO:1902041	regulation of extrinsic apoptotic signaling pathway via death domain receptors	3/53	50/18870	0.000374	0.039296	0.03295	TIMP3/DDX3X/PTEN	3
GO:2001238	positive regulation of extrinsic apoptotic signaling pathway	3/53	53/18870	0.000444	0.043771	0.036702	TIMP3/CYLD/PTEN	3
miR-181b Molecular Function								
GO:0001227	DNA-binding transcription repressor activity, RNA polymerase II-specific	6/52	326/18496	0.000295	0.030679	0.023293	ZNF669/ZNF487/ZBTB4/ZFP69B/ZNF440/ZNF556	6

GO:0001217	DNA-binding transcription repressor activity	6/52	334/18496	0.000335	0.030679	0.023293	ZNF669/ZNF487/ZBTB4/ZFP69B/ZNF440/ZNF556	6
miR-203a Biological Process								
GO:0008630	intrinsic apoptotic signaling pathway in response to DNA damage	6/58	102/18870	6.93E-07	0.001318	0.000975	ATM/BCL2L2/SNAI2/TP63/ABL1/SOD2	6
GO:0051402	neuron apoptotic process	8/58	278/18870	2.03E-06	0.001933	0.001429	ATM/TP63/ABL1/CPEB4/EN2/PIK3CA/PRNP/SOD2	8
GO:0043523	regulation of neuron apoptotic process	7/58	232/18870	6.84E-06	0.004339	0.003208	ATM/ABL1/CPEB4/EN2/PIK3CA/PRNP/SOD2	7
GO:2000811	negative regulation of anoikis	3/58	18/18870	2.18E-05	0.010348	0.007651	SNAI2/SRC/PIK3CA	3
GO:0046854	phosphatidylinositol phosphate biosynthetic process	4/58	66/18870	5.02E-05	0.0144	0.010647	ATM/PI4K2B/SOCS3/PIK3CA	4
GO:0097193	intrinsic apoptotic signaling pathway	7/58	319/18870	5.3E-05	0.0144	0.010647	ATM/BCL2L2/SNAI2/TP63/ABL1/SRC/SOD2	7
GO:2000209	regulation of anoikis	3/58	24/18870	5.33E-05	0.0144	0.010647	SNAI2/SRC/PIK3CA	3
GO:0002433	immune response-regulating cell surface receptor signaling pathway involved in phagocytosis	3/58	26/18870	6.81E-05	0.0144	0.010647	ABL1/SRC/PLD2	3
GO:0038096	Fc-gamma receptor signaling pathway involved in phagocytosis	3/58	26/18870	6.81E-05	0.0144	0.010647	ABL1/SRC/PLD2	3
GO:0034614	cellular response to reactive oxygen species	5/58	154/18870	0.00011	0.020862	0.015425	ATM/ABL1/SRC/GLRX2/SOD2	5
GO:0002431	Fc receptor mediated stimulatory signaling pathway	3/58	32/18870	0.000128	0.02194	0.016222	ABL1/SRC/PLD2	3
GO:0038094	Fc-gamma receptor signaling pathway	3/58	33/18870	0.000141	0.02194	0.016222	ABL1/SRC/PLD2	3
GO:0043276	anoikis	3/58	34/18870	0.000154	0.02194	0.016222	SNAI2/SRC/PIK3CA	3
GO:0048145	regulation of fibroblast proliferation	4/58	89/18870	0.000161	0.02194	0.016222	BMI1/ABL1/CDK6/SOD2	4
GO:0042542	response to hydrogen peroxide	4/58	101/18870	0.000263	0.032245	0.023842	ABL1/SRC/GLRX2/SOD2	4
GO:0061138	morphogenesis of a branching epithelium	5/58	187/18870	0.000271	0.032245	0.023842	SNAI2/TP63/ABL1/SOCS3/SRC	5
GO:0048144	fibroblast proliferation	4/58	107/18870	0.000328	0.034475	0.02549	BMI1/ABL1/CDK6/SOD2	4
GO:0090398	cellular senescence	4/58	110/18870	0.000364	0.034475	0.02549	ATM/TP63/ABL1/CDK6	4
GO:0001763	morphogenesis of a branching structure	5/58	203/18870	0.000396	0.034475	0.02549	SNAI2/TP63/ABL1/SOCS3/SRC	5
GO:0048732	gland development	7/58	443/18870	0.000401	0.034475	0.02549	ATM/SNAI2/TP63/ABL1/SRC/PIK3CA/SOD2	7
GO:0000302	response to reactive oxygen species	5/58	205/18870	0.000414	0.034475	0.02549	ATM/ABL1/SRC/GLRX2/SOD2	5
GO:0062197	cellular response to chemical stress	6/58	317/18870	0.000416	0.034475	0.02549	ATM/ABL1/SRC/GLRX2/PIK3CA/SOD2	6
GO:2001243	negative regulation of intrinsic apoptotic signaling pathway	4/58	114/18870	0.000417	0.034475	0.02549	BCL2L2/SNAI2/SRC/SOD2	4
GO:0048568	embryonic organ development	7/58	453/18870	0.000458	0.035141	0.025983	BMI1/SOCS3/DLX5/DNAJB6/EN2/NR2F2/RUNX2	7
GO:0046474	glycerophospholipid biosynthetic process	5/58	210/18870	0.000462	0.035141	0.025983	ATM/PI4K2B/SOCS3/PIK3CA/PLD2	5
GO:0046660	female sex differentiation	4/58	120/18870	0.000506	0.036862	0.027255	ATM/TP63/SRC/NR2F2	4
GO:0002065	columnar/cuboidal epithelial cell differentiation	4/58	123/18870	0.000556	0.036862	0.027255	TP63/ABL1/SRC/CDK6	4
GO:0048146	positive regulation of fibroblast proliferation	3/58	53/18870	0.000579	0.036862	0.027255	BMI1/ABL1/CDK6	3
GO:0030111	regulation of Wnt signaling pathway	6/58	338/18870	0.000584	0.036862	0.027255	SNAI2/ABL1/SRC/DLX5/VGLL4/ZBED3	6
GO:0002757	immune response-activating signaling pathway	7/58	473/18870	0.000593	0.036862	0.027255	ABL1/SRC/DHX33/PIK3CA/PLD2/PRNP/STMP1	7
GO:0002327	immature B cell differentiation	2/58	12/18870	0.000601	0.036862	0.027255	ATM/ABL1	2
GO:0050673	epithelial cell proliferation	7/58	480/18870	0.000646	0.03744	0.027682	BCL2L2/SNAI2/TP63/CDK6/DLX5/NR2F2/RUNX2	7
GO:0038093	Fc receptor signaling pathway	3/58	56/18870	0.00068	0.03744	0.027682	ABL1/SRC/PLD2	3
GO:0043525	positive regulation of neuron apoptotic process	3/58	56/18870	0.00068	0.03744	0.027682	ATM/ABL1/PRNP	3
GO:0006661	phosphatidylinositol biosynthetic process	4/58	131/18870	0.000704	0.03744	0.027682	ATM/PI4K2B/SOCS3/PIK3CA	4
GO:1900272	negative regulation of long-term synaptic potentiation	2/58	13/18870	0.000709	0.03744	0.027682	ABL1/PRNP	2
GO:0030522	intracellular receptor signaling pathway	6/58	353/18870	0.000733	0.037664	0.027848	SNAI2/TP63/SRC/DHX33/NR2F2/STMP1	6
GO:0002764	immune response-regulating signaling pathway	7/58	500/18870	0.000822	0.04024	0.029753	ABL1/SRC/DHX33/PIK3CA/PLD2/PRNP/STMP1	7
GO:0035791	platelet-derived growth factor receptor-beta signaling pathway	2/58	14/18870	0.000825	0.04024	0.029753	ABL1/SRC	2
GO:0010639	negative regulation of organelle organization	6/58	363/18870	0.000847	0.040284	0.029785	BIRC5/ATM/BCL2L2/SRC/MTPN/PIK3CA	6
GO:2001234	negative regulation of apoptotic signaling pathway	5/58	243/18870	0.000893	0.041434	0.030636	BMI1/BCL2L2/SNAI2/SRC/SOD2	5
GO:0048863	stem cell differentiation	5/58	246/18870	0.000944	0.042499	0.031423	SNAI2/TP63/ABL1/CDK6/RUNX2	5
GO:0033002	muscle cell proliferation	5/58	247/18870	0.000961	0.042499	0.031423	ABL1/SRC/PIK3CA/SOD2/VGLL4	5
GO:0045017	glycerolipid biosynthetic process	5/58	250/18870	0.001014	0.043832	0.032409	ATM/PI4K2B/SOCS3/PIK3CA/PLD2	5
GO:0030177	positive regulation of Wnt signaling pathway	4/58	146/18870	0.001055	0.043882	0.032446	ABL1/SRC/DLX5/ZBED3	4
GO:1900034	regulation of cellular response to heat	2/58	16/18870	0.001084	0.043882	0.032446	ATM/DNAJB6	2
GO:0008654	phospholipid biosynthetic process	5/58	254/18870	0.001088	0.043882	0.032446	ATM/PI4K2B/SOCS3/PIK3CA/PLD2	5
GO:0034599	cellular response to oxidative stress	5/58	255/18870	0.001107	0.043882	0.032446	ATM/ABL1/SRC/GLRX2/SOD2	5
GO:0001649	osteoblast differentiation	5/58	257/18870	0.001147	0.044362	0.032801	SNAI2/TP63/CDK6/DLX5/RUNX2	5
GO:0045667	regulation of osteoblast differentiation	4/58	150/18870	0.001166	0.044362	0.032801	SNAI2/TP63/CDK6/RUNX2	4
GO:1901522	positive regulation of transcription from RNA polymerase II promoter involved in cellular response to chemical stimulus	2/58	17/18870	0.001226	0.044838	0.033153	DLX5/RUNX2	2
GO:1902036	regulation of hematopoietic stem cell differentiation	2/58	17/18870	0.001226	0.044838	0.033153	ABL1/CDK6	2
GO:0046488	phosphatidylinositol metabolic process	4/58	155/18870	0.001316	0.047239	0.034928	ATM/PI4K2B/SOCS3/PIK3CA	4
GO:2001233	regulation of apoptotic signaling pathway	6/58	398/18870	0.00136	0.047908	0.035423	BMI1/BCL2L2/SNAI2/TP63/SRC/SOD2	6
GO:0006979	response to oxidative stress	6/58	400/18870	0.001395	0.048255	0.035679	ATM/ABL1/SRC/GLRX2/PRNP/SOD2	6
GO:0051881	regulation of mitochondrial membrane potential	3/58	73/18870	0.001471	0.049973	0.036949	ABL1/SRC/SOD2	3
GO:0030900	forebrain development	6/58	407/18870	0.001524	0.04998	0.036955	NARS1/RAN/SRC/CDK6/DLX5/NR2F2	6
GO:0050678	regulation of epithelial cell proliferation	6/58	407/18870	0.001524	0.04998	0.036955	SNAI2/TP63/CDK6/DLX5/NR2F2/RUNX2	6
miR-203 Biological Process								
GO:0052742	phosphatidylinositol kinase activity	3/58	26/18496	7.23E-05	0.018504	0.015902	ATM/PI4K2B/PIK3CA	3
GO:0001727	lipid kinase activity	3/58	41/18496	0.000287	0.036516	0.031381	ATM/PI4K2B/PIK3CA	3
GO:0016303	1-phosphatidylinositol-3-kinase activity	2/58	10/18496	0.000428	0.036516	0.031381	ATM/PIK3CA	2

Table 20. GO enrichment analysis of predicted target genes for miR-132, miR-181b, and miR-203a. The table lists significantly enriched biological processes, molecular functions, and cellular components, along with their associated genes and adjusted p-values. P-values were corrected for multiple comparisons using the Benjamini–Hochberg (BH) method

Following Benjamini-Hochberg correction, several BP, MF, and CC showed significant enrichment, highlighting pathways potentially regulated by these miRNAs as reported also in the Venn diagram

(Figure 7). While some GO terms were commonly enriched across all three miRNAs, suggesting coordinated roles in key cellular processes, others were unique to individual miRNAs, indicating specific regulatory functions. This integrative analysis provides a comprehensive overview of the functional landscape associated with these miRNAs and offers insights into their potential contributions to cellular and molecular regulation (Figure 8).

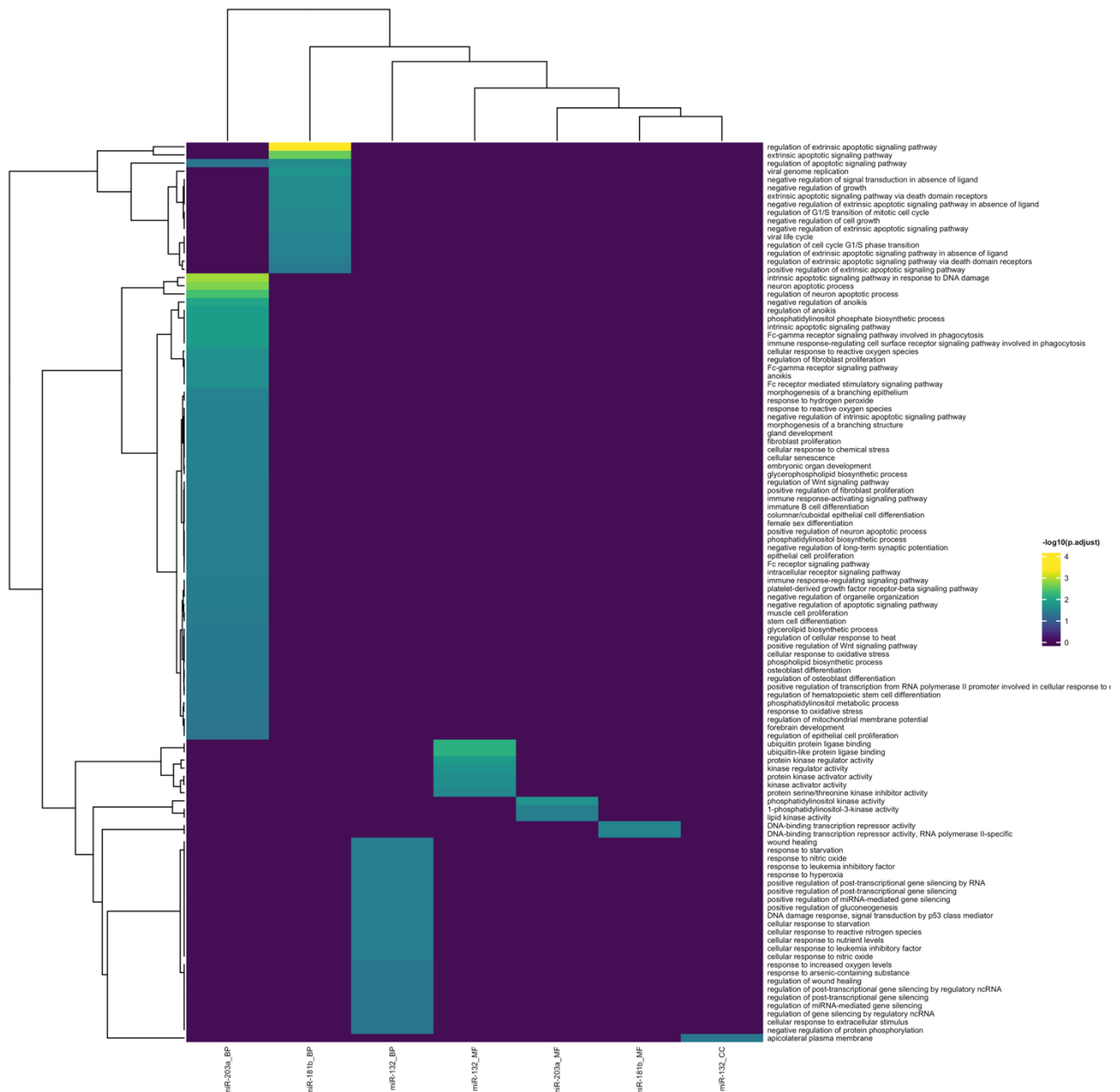


Figure 8. Category-gene heatmap showing Gene Ontology (GO) enrichment for miR-132, miR-181b, and miR-203a. Each row represents a GO term, and each column corresponds to a miRNA. Colors indicate the level of enrichment expressed as $-\log_{10}(\text{adjusted p-value})$, with lighter colors representing stronger enrichment. Dendrograms on the rows and columns depict hierarchical clustering of GO terms and miRNAs, highlighting functional relationships and similarities in enrichment patterns across the three miRNAs.

4.3.8.1 Gene ontology enrichment of miR-132 target genes

Analysis of miR-132 target genes revealed significant enrichment in biological processes related to cellular stress responses, nutrient sensing, and DNA damage signaling. At the cellular component level, these targets are primarily localized to the apicolateral plasma membrane, suggesting involvement in membrane-associated signaling pathways. Functionally, the genes show strong associations with ubiquitin protein ligase binding and kinase regulatory activities, indicating potential roles in post-translational modifications and the modulation of protein signaling networks. Together, these results highlight miR-132 as a regulator of stress response and protein homeostasis pathways.

4.3.8.2 Gene Ontology enrichment of miR-181b target genes

GO enrichment analysis of miR-181b target genes revealed significant associations primarily within BP and molecular functions MF. In the BP category, targets were strongly enriched in apoptotic signaling pathways, particularly the extrinsic apoptotic signaling pathway and its regulation, as well as negative regulation of cell growth and G1/S cell cycle transition. Viral-related processes, including viral genome replication and viral life cycle, were also significantly enriched. In the MF category, target genes were predominantly involved in DNA-binding transcription repressor activity, specifically RNA polymerase II-specific repression. No significant enrichment was observed in the CC category. Overall, these results suggest that miR-181b may regulate genes involved in apoptosis, cell growth control, cell cycle progression, and transcriptional repression.

4.3.8.3 Gene ontology enrichment of miR-203a target genes

GO BP enrichment analysis of miR-203a target genes revealed a prominent involvement in apoptotic processes and the regulation of cell survival. Significantly enriched terms included intrinsic apoptotic signaling in response to DNA damage, neuronal apoptosis, and regulation of anoikis, suggesting a potential role of miR-203a in modulating cell death and neuronal resilience. Additional enriched processes encompassed responses to oxidative and chemical stress, fibroblast proliferation,

and cellular differentiation, including neuronal and epithelial lineages. Pathways related to intracellular signal regulation, such as Fc receptor and Wnt signaling, as well as embryonic development and organogenesis, were also highlighted. Overall, these findings indicate that miR-203a may play a multifaceted role in regulating key processes of cell survival, differentiation, and tissue development.

4.3.9 miRNA target gene analysis and comparison with both schizophrenia and TRS-associated genes

Comparison with schizophrenia-associated genes obtained from DisGeNET, filtered for schizophrenia and TRS, for which NOTCH4 was the only gene retrieved, revealed that a subset of miRNA target genes overlapped with known schizophrenia-related genes (Table 21).

miRNA	Gene	GO_types
miR-181b	ATM	BP
miR-203a	ATM	BP, MF
miR-181b	BCL2	BP
miR-203a	EN2	BP
miR-181b	HSPA1B	BP
miR-203a	PI4K2B	BP, MF
miR-203a	PIK3CA	BP, MF
miR-181b	PTEN	BP
miR-132	SIRT1	BP
miR-132	SLC38A2	BP
miR-203a	SOD2	BP

Table 21. Overlapping genes between miRNA targets and schizophrenia/TRS-associated genes. The table lists genes identified as targets of miR-132, miR-181b, and miR-203a that are also associated with schizophrenia or TRS according to DisGeNET. The corresponding miRNA regulating each gene is indicated, along with the Gene Ontology (GO) categories in which each gene is enriched. BP, Biological Process; CC, Cellular Component; MF, Molecular Function; ATM, Ataxia Telangiectasia Mutated; BCL2, B-cell lymphoma 2; EN2, Engrailed Homeobox 2; HSPA1B, Heat Shock Protein Family A (Hsp70) Member 1B; PI4K2B, Phosphatidylinositol 4-Kinase Type 2 Beta; PIK3CA, Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha; PTEN, Phosphatase and Tensin Homolog; SIRT1, Sirtuin 1; SLC38A2, Solute Carrier Family 38 Member 2; SOD2, Superoxide Dismutase 2.

4.3.10 KEGG analysis

KEGG pathway enrichment analysis identified multiple signaling pathways associated with the predicted target genes of miR-132, miR-181b, and miR-203a (Figure 9).

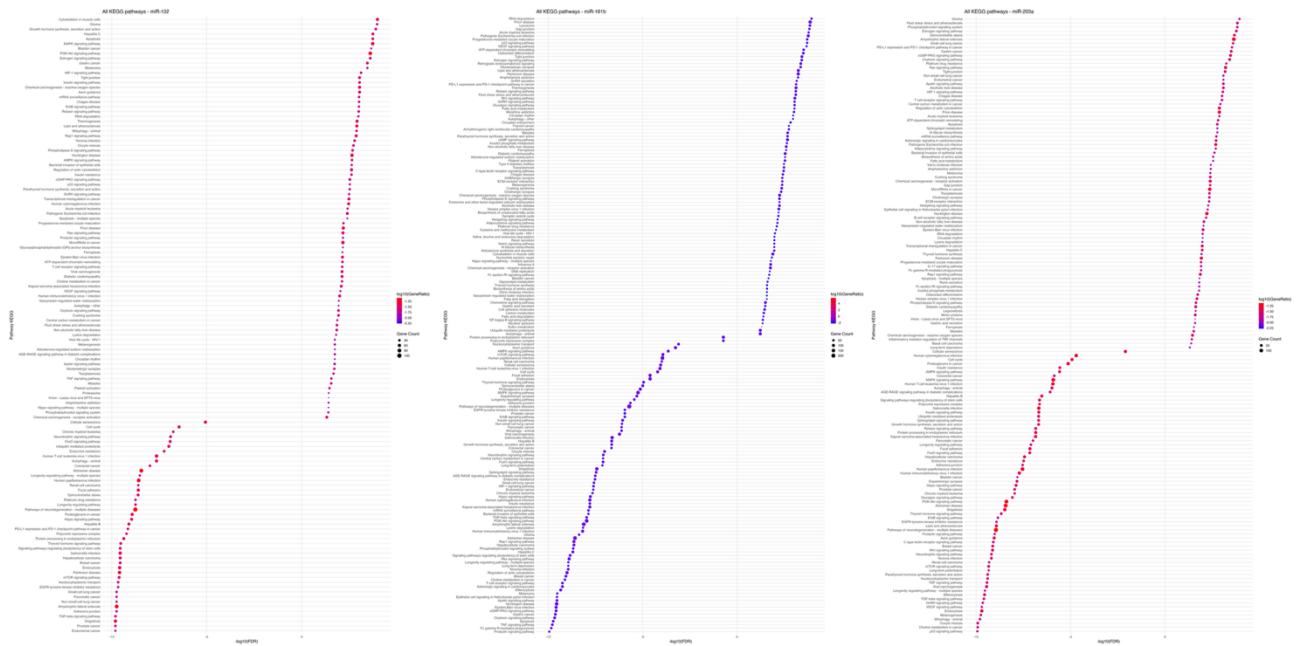


Figure 9. KEGG pathway enrichment analysis for miR-132, miR-181b, and miR-203a. Each panel shows the enriched pathways for the corresponding miRNA, highlighting biological processes and signaling pathways potentially regulated by their target genes. Pathway significance is indicated by adjusted p-values or enrichment scores (as defined in the Methods section).

To evaluate their potential relevance to schizophrenia, we compared the enriched pathways for each microRNA with reference pathways annotated in KEGG as schizophrenia-related (Table 22 – for a comprehensive overview please see supplementary Tables S4-S5-S6).

miRNA	Pathway	n_miRNA_genes	n_sch_genes	n_overlap	Overlap_genes	pval	fdr	bonf
miR-132	ErbB signaling pathway	28	86	28	CDKN1A;EGFR;RAF1;CRK;HBEGF;GSK3B;MAPK1;PIK3R3;KRAS;PIK3R1;AKT2;HRAS;AKT3;ABL2;CAMK2D;EREG;GRB2;PAK2;PIK3CA;PIK3CB;MAPK3;MAPK8;MAP2K4;SOS2;STAT5B;SHC3;CBL;SOS1	$< 1e^{-10}$	$< 1e^{-10}$	$< 1e^{-10}$
	Glutamatergic synapse	30	112	29	GNB1;MAPK1;PLA2G4C;SLC38A2;GRIA2;ADCY6;GNAI2;PPP3CA;ADCY3;ADCY7;ADCY9;GLS;GLUL;GNAS;GNB3;GRIN2D;PLD1;PPP3R1;MAPK3;SLC1A3;TRPC1;HOMER1;NCDN;SLC38A1;CACNA1A;DLGAP1;PPP3CB;ADCY5;LZTS3	$< 1e^{-10}$	$< 1e^{-10}$	$< 1e^{-10}$
miR-181b	Dopaminergic synapse	81	131	81	GRIA2;CREB1;FOS;ARRB2;PPP2R5E;CLOCK;MAPK14;GNAI3;MAPK9;AKT2;PPP2R2A;GNAI2;AKT1;PPP3CA;AKT3;ARRB1;ATF4;CACNA1B;CALM1;CALM2;CALM3;CAMK2G;COMT;ATF2;ATF6B;DRD1;GNAI1;GNAQ;GNB1;GNB2;GRIA1;GRIN2A;GSK3B;ITPR1;ITPR2;KCNJ9;KIF5A;KIF5B;KIF5C;MAOA;PPP1CA;PPP1CB;PPP1CC;PPP2CB;PPP2R1A;PPP2R1B;PPP2R2C;PPP2R3A;PPP2R5A;PPP2R5C;PRKACA;PRKACB;PRKCA;PRKCB;MAPK8;CREB3;PPP2R3C;PPP2R2D;GNB4;GNG7;CACNA1A;CACNA1D;GRIA3;MAOB;PPP2R2B;GNAL;PPP3CB;SCN1A;ADCY5;PPP3CC;ITPR3;KCNJ3;PPP2CA;MAPK10;MAPK13;PPP2R5D;PLCB1;GNAO1;CREB3L1;GRIN2B;CACNA1C	$< 1e^{-35}$	$< 1e^{-35}$	$< 1e^{-35}$
	ErbB signaling pathway	57	86	56	MAP2K1;MTOR;ERBB2;ERBB3;KRAS;NRAS;PTK2;CDKN1A;CDKN1B;MYC;EGFR;ARAF;PIK3R1;PAK1;GAB1;MAPK9;CRKL;ABL1;RAF1;AKT2;ERBB4;AKT1;AKT3;ABL2;CAMK2G;CRK;EREG;GRB2;GSK3B;PAK2;PIK3CA;PIK3CB;PLCG1;PLCG2;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;RPS6KB1;MAP2K4;SOS2;STAT5B;NCK2;PAK4;SHC3;PIK3R3;NRG2;NCK1;MAPK10;BAD;BRAF;SOS1;MAP2K7;CBLB;PAK5	$< 1e^{-35}$	$< 1e^{-35}$	$< 1e^{-35}$

miR-202a	Dopaminergic synapse	53	131	53	CLOCK;MAPK9;CREB1;AKT2;FOS;GNAS;GSK3B;KIF5B;PPP1CB;PRKACB;PRKCA;MAPK8;MAPK14;GNAI3;PPP2R2A;AKT1;PPP3CA;AKT3;MAPK11;ATF4;CALM1;CALM2;CAMK2G;COMT;ATF2;GNAI1;GNAQ;GNB1;GNG5;ITPR1;ITPR2;KIF5C;MAOA;PPP1CC;PPP2CB;PPP2R1A;PPP2R3A;PPP2R5A;PPP2R5C;PPP2R3B;GNB4;CREB3L2;PPP2R2B;PPP3CB;PPP3CC;GNG11;ARRB2;PLCB1;GNG12;GSK3A;CREB3L1;CREB3L4;GRIN2B	$< 1e^{-19}$	$< 1e^{-19}$	$< 1e^{-19}$
	ErbB signaling pathway	37	86	37	ABL1;JUN;MAPK9;AKT2;SHC1;GSK3B;PIK3CA;PRKCA;MAPK8;SRC;ERBB2;KRAS;NRAS;CDKN1A;PIK3R1;PAK1;MAP2K1;ERBB4;HRAS;AKT1;AKT3;CAMK2G;CRK;HBEGF;EIF4EBP1;ELK1;EREG;MTOR;PAK2;PLCG2;RPS6KB1;MAP2K4;SOS2;TGFA;CBL;SOS1;SHC2	$< 1e^{-21}$	$< 1e^{-21}$	$< 1e^{-21}$

Table 22. KEGG pathway enrichment of selected miRNA target genes associated with schizophrenia. The table lists pathways significantly enriched for selected miRNA targets that overlap with schizophrenia-related genes. Columns report the total number of miRNA target genes (n_miRNA_genes), total number of schizophrenia-related genes (n_scz_genes), number of overlapping genes (n_overlap), the names of overlapping genes (Overlap_genes), and statistical significance values (p-value, FDR, and Bonferroni correction). Only pathways relevant to schizophrenia are shown.

Enrichment analysis revealed a highly significant convergence of these miRNAs on key schizophrenia-related pathways. Specifically, miR-132 displayed strong enrichment in the ErbB signaling pathway (hsa04012; $FDR = 3.5 \times 10^{-16}$) and glutamatergic synapse (hsa04724; $FDR = 1.2 \times 10^{-11}$), with consistent overlap across genes involved in synaptic plasticity and intracellular signaling (e.g., HOMER, GRIA1/2, MAPK1, MAPK3, AKT2, PI3K family members). Similarly, miR-181b showed robust enrichment in multiple pathways, including dopaminergic synapse (hsa04728; $FDR = 3.1 \times 10^{-34}$) and ErbB signaling (hsa04012; $FDR = 3.1 \times 10^{-34}$), regulating a wide set of genes implicated in neurotransmission and neurodevelopment (e.g., AKT1/2/3, GSK3B, GRIN2A/B, CREB1). miR-202a also exhibited significant enrichment in both dopaminergic synapse (hsa04728; $FDR = 2.3 \times 10^{-20}$) and ErbB signaling (hsa04012; $FDR = 8.6 \times 10^{-22}$) with consistent overlap across genes such as MAPK, AKT, COMT.

Consistent with previous reports showing increased expression of these miRNAs in schizophrenia patients, our findings suggest that their upregulation may exert a convergent effect on synaptic signaling cascades and neuroplasticity-related pathways. Since increased miRNA levels are expected to enhance gene silencing, it can be hypothesized that this mechanism leads to reduced downstream protein expression, ultimately contributing to the dysfunction of critical genes involved in neurotransmission and synaptic plasticity in schizophrenia.

4.3.11 Convergent Targeting by miR-132, miR-181b, and miR-203a across dopaminergic, glutamatergic, and ErbB pathways

To further explore the biological relevance of the identified miRNAs, we constructed a gene–pathway network linking the predicted target genes of miR-132, miR-181b, and miR-203a to the most significantly enriched pathways (Figure 10).

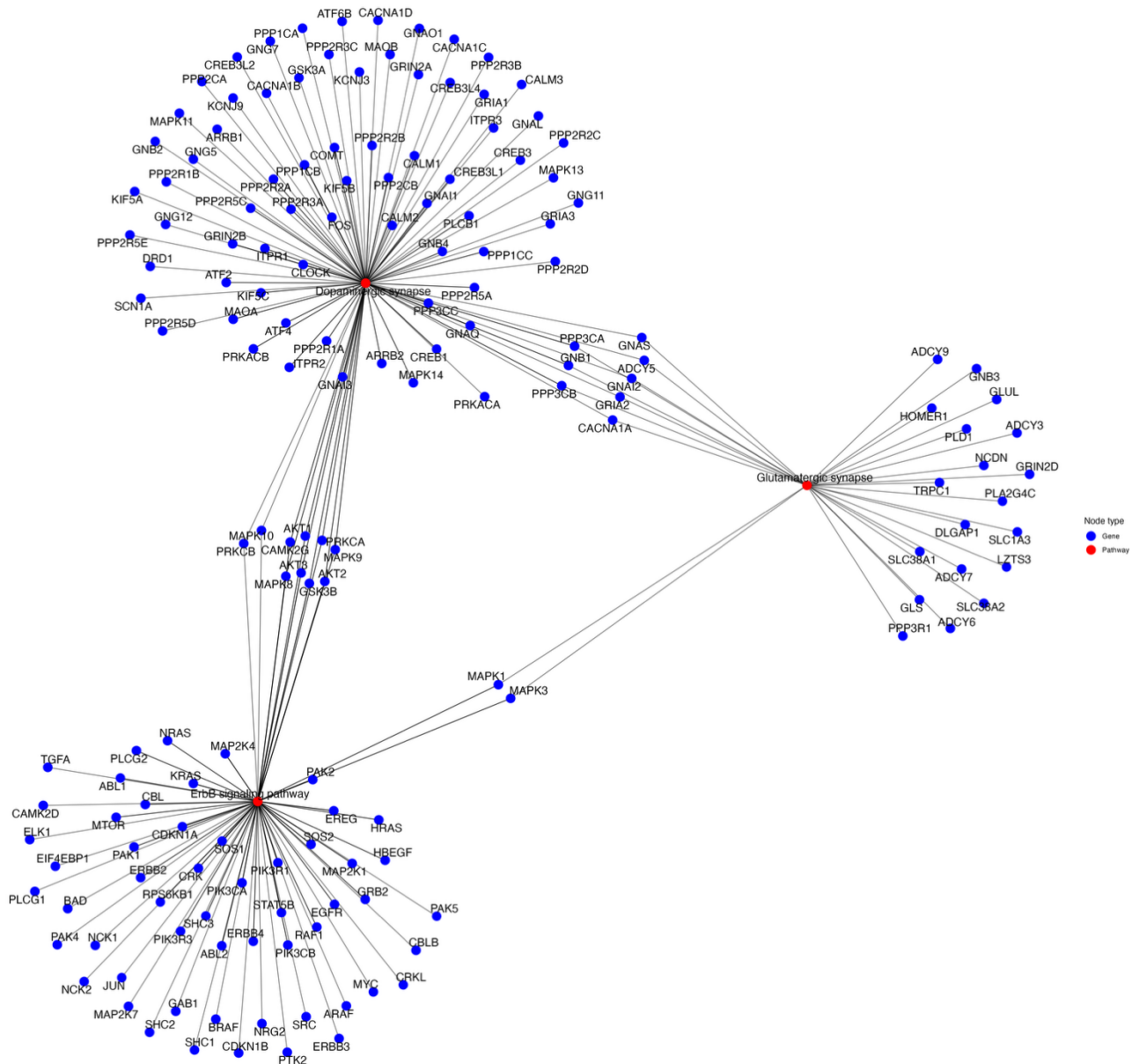


Figure 10. Gene–pathway network linking the predicted target genes of miR-132, miR-181b, and miR-203a to the most significantly enriched pathways associated with schizophrenia. Nodes represent either miRNA target genes or enriched pathways, and edges indicate gene participation in specific pathways. This network highlights the potential regulatory roles of the three miRNAs in schizophrenia-related biological processes.

The network revealed three major hubs corresponding to the glutamatergic synapse, dopaminergic synapse, and ErbB signaling pathway, all of which are critically implicated in schizophrenia pathophysiology.

Within this network, the dopaminergic synapse node was highly connected, encompassing numerous genes involved in neurotransmitter signaling and intracellular cascades (DRD1, AKT1/2/3, GSK3B, CREB1). The glutamatergic synapse node displayed selective associations with genes regulating excitatory transmission and synaptic plasticity (HOMER1, GRIN2A/D, SLC1A3), while the ErbB signaling pathway was enriched for genes mediating neurodevelopmental and intracellular signaling processes (ERBB4, MAPK1/3, PI3K family members).

Altogether, this network representation highlights a convergent effect of the three miRNAs on interconnected signaling pathways that regulate neurotransmission and neuroplasticity, suggesting a potential mechanistic link between their dysregulation and the synaptic alterations observed in schizophrenia.

4.3.12 miRNA-pathway-psychotropic compounds integration

To explore the interactions between schizophrenia-related miRNAs, molecular pathways, and psychotropic compounds, we constructed an integrative miRNA-pathway-drug network. The full network, including both antipsychotic drugs and psychotomimetic agents, is shown in Figure 11. Nodes were classified as miRNAs, pathways, or drugs, and edges represented validated or predicted associations. Visualization of the network revealed several highly connected elements, with the top nodes ranked by degree centrality corresponding to key miR-181b and schizophrenia-related pathways related to our miRNAs targets. These hubs represent potential convergence points where multiple miRNAs and drugs interact, highlighting pathways that may be particularly sensitive to pharmacological modulation.

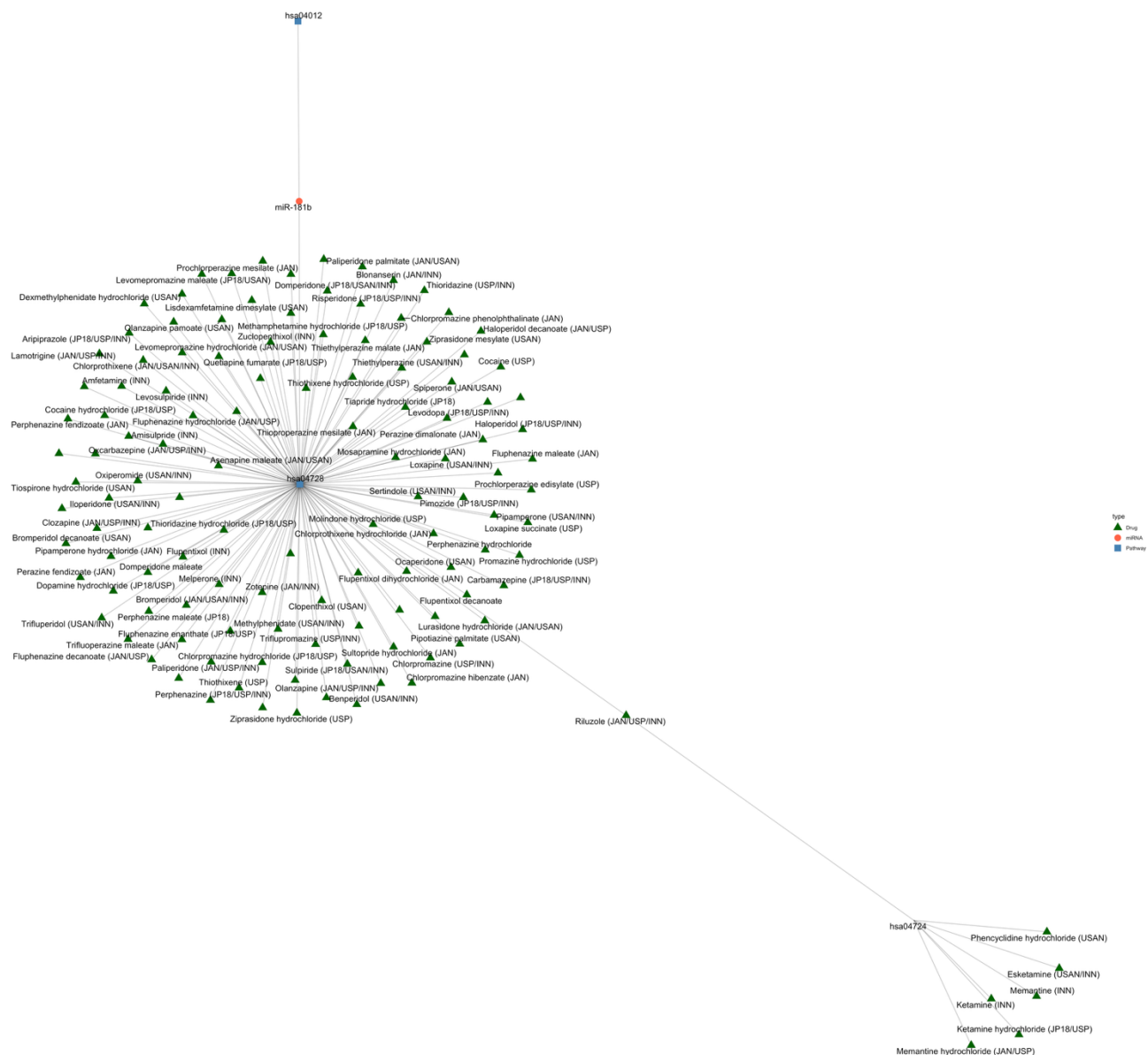


Figure 11. Integrative miRNA-pathway-drug network for schizophrenia-related miRNAs. The network links miR-132, miR-181b, and miR-203a with enriched molecular pathways and psychotropic compounds, including antipsychotics and psychotomimetic agents. Nodes represent miRNAs, pathways, or drugs, while edges indicate validated associations. Highly connected nodes, ranked by degree centrality, correspond to key miR-181b targets and schizophrenia-related pathways, highlighting potential convergence points for pharmacological modulation.

To contextualize the network with our patient cohort, we performed an analogous analysis filtering only the drugs actually administered to the patients. The filtered network is shown in Figure 12. While overall connectivity was reduced compared to the full network, the main pathway-miRNA relationships were preserved, emphasizing clinically relevant interactions. Notably, the dopaminergic synapse and Erb signaling pathway remained prominent hubs, suggesting that antipsychotic treatment may specifically modulate these pathways via miRNA-mediated mechanisms.

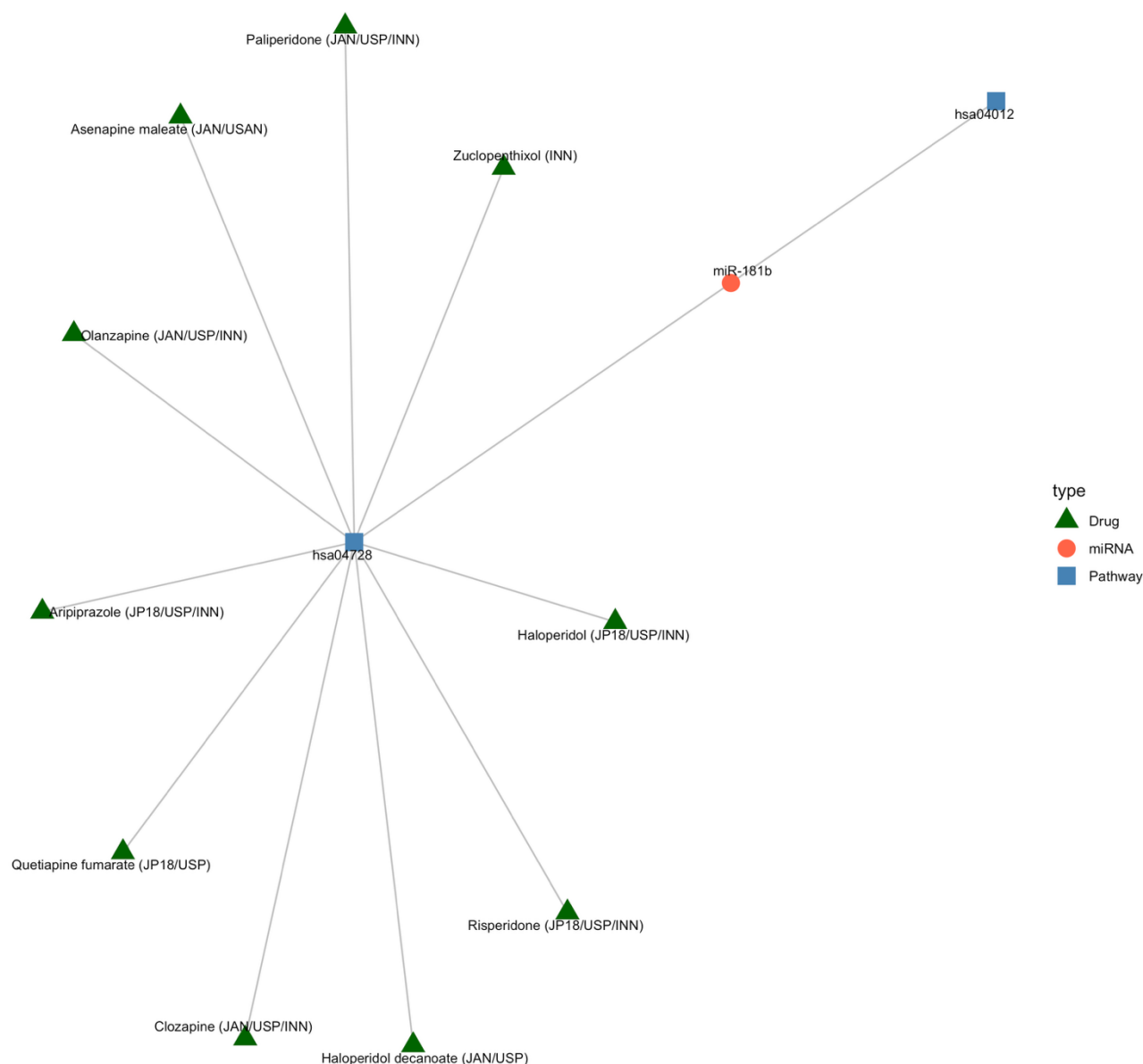


Figure 12. Integrative miRNA–pathway–drug network for schizophrenia-related miRNAs. The network links miR-132, miR-181b, and miR-203a with enriched molecular pathways and psychotropic compounds observed in the study population. Nodes represent miRNAs, pathways, or drugs, and edges indicate validated associations. Highly connected nodes, ranked by degree centrality, correspond to key miR-181b targets and schizophrenia-related pathways, highlighting potential points where multiple miRNAs and clinically relevant drugs converge.

5. Discussion

The present study aimed to investigate peripheral biomarkers, specifically circulating microRNAs and extracellular vesicles, in patients with schizophrenia and TRS. Our findings provide insight into the molecular alterations that may underlie the heterogeneity of the disorder and its variable response to pharmacological treatment. By focusing on molecules accessible in peripheral blood, we sought to

bridge the gap between clinically observable symptoms and central neurobiological processes, highlighting pathways that could contribute to synaptic dysfunction, aberrant neurotransmission, and treatment resistance. The results are discussed in the context of current knowledge on dopaminergic and glutamatergic signaling, synaptic plasticity, and the role of EVs as carriers of disease-relevant molecular information, offering potential avenues for patient stratification and targeted interventions. No statistically significant differences in miRNA levels were observed in our sample after Bonferroni correction. However, patients with TRS exhibited more severe symptomatology and greater cognitive impairment, consistent with previous literature [10, 30, 31]. Regarding the correlations between miRNA levels and schizophrenia psychopathological domains, we identified statistically significant associations between multiple miRNAs and clinical symptoms. These findings likely reflect shared expression patterns or common molecular mechanisms underlying the miRNAs, as well as clinical coherence across the measured symptom domains.

Although descriptive analyses did not reveal statistically significant differences, the machine learning approach was able to differentiate the TRS condition with acceptable accuracy based on the EMO, DIS, and EXC PANSS factors - as reported in our previous study, [31] - and the miRNAs miR-132_3p, miR-181b_5p, and miR203a_3p. A targeted analysis was conducted to investigate the association of these miRNAs with schizophrenia, but only one gene, *UBXN2A*, emerged as a validated target of both miR-181b_5p and miR-203a_3p in the context of schizophrenia. *UBXN2A* functions to repress the ubiquitination and subsequent endoplasmic reticulum-associated degradation of the $\alpha 3$ subunit of nicotinic acetylcholine receptors (*CHRNA3*) in cortical neurons. By promoting the translocation of *CHRNA3* to the plasma membrane, *UBXN2A* enhances acetylcholine-gated ion-channel activation at the membrane, thereby impacting acetylcholine neurotransmission, a pathway known to be disrupted in schizophrenia [32, 33].

When analyzing the pathways targeted by the miRNAs identified through the machine learning approach, we found that miR-132 was enriched in pathway related to glutamatergic neurotransmission, particularly involving genes such as *Homer1* and *GRIA1/2*. These genes have been

implicated in the pathophysiology of schizophrenia and TRS in both human and animal studies, due to their critical role in synaptic plasticity at glutamatergic PSD and in mediating responses to antipsychotic treatment [34-38]. In contrast, miR-181b was primarily enrichment in dopaminergic pathway, regulating a broad set of genes, including AKT1/2/3 and GRIN2A/B, which are involved in neurotransmission and neurodevelopmental processes. This aligns with evidence linking N-methyl-d-aspartate receptor (NMDAR) hypofunction to cognitive deficits and hypofrontality in schizophrenia [39-43]. Finally, miR202a showed strong enrichment in genes regulating COMT, which is closely related to dopaminergic signaling and has been primarily associated with TRS [44-46].

Another crucial findings in our work, is related to the effects of antipsychotics on investigated pathways and miRNAs and we demonstrated that psychotropic drugs in general, and specifically antipsychotics administered to our patients, are obviously, able to modulate dopaminergic and Erb signaling particularly via miR181b confirming literature data [47-49].

In summary, our study provides novel insights into the molecular underpinnings of schizophrenia and TRS through the analysis of peripheral biomarkers, including circulating microRNAs and extracellular vesicles. While traditional statistical analyses did not reveal significant differences in miRNA levels between groups, machine learning approaches successfully differentiated TRS patients based on clinical dimensions and specific miRNAs, highlighting the potential of integrative computational methods in identifying clinically relevant molecular signatures. These findings underscore the relevance of peripheral biomarkers as potential tools for patient stratification, the identification of treatment-resistant profiles, and the elucidation of molecular mechanisms underlying symptom heterogeneity.

Overall, this study lays the groundwork for future investigations aimed at integrating peripheral molecular signatures with clinical phenotypes, paving the way for more personalized and targeted therapeutic strategies in schizophrenia and TRS.

6. Limitations

This study has several limitations that should be acknowledged. The cross-sectional design precludes definitive predictions, and the classification model requires testing in independent cohorts for external validation. Moreover, the sample size is relatively small; however, we used the RF approach with nested-cross validation to minimize optimism and overfitting. A possible selection bias cannot be excluded at this stage, as patients were recruited from a specialized center for TRS. Importantly, these findings should be considered preliminary, and ongoing analyses aim to extend the evaluation to include healthy control groups. Despite these limitations, the present study represents a first attempt to specifically investigate the potential role of miRNAs in predicting TRS diagnosis.

7. Conclusions

In conclusion, this preliminary study highlights the potential of circulating miRNAs and possibly extracellular vesicles as peripheral biomarkers in schizophrenia and TRS. Although limited by sample size and study design, our findings suggest that specific miRNA signatures may reflect key molecular pathways involved in treatment resistance, particularly within the dopaminergic and glutamatergic systems. Machine learning approaches have proven valuable in identifying clinically relevant patterns that traditional analyses were unable to detect. Further studies including healthy controls and larger cohorts are needed to validate these findings and refine their translational potential. Ultimately, this work contributes to the development of biomarker-based tools for patient stratification and personalized treatment strategies in schizophrenia.

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9. Supplementary Tables

SCZ correlations				
Var1	Var2	Correlation	p_value	p_fdr
GENTOT	PANSSStot	0.952838	1E-31	7.45E-29
NEGTOT	PAUSS	0.934229	1.2E-27	4.44E-25
POS	POSTOT	0.866629	3.68E-19	9.08E-17
mir128_3p	mir132_3p	0.799683	1.83E-14	3.39E-12
PANSSStot	POSTOT	0.794365	3.61E-14	5.21E-12
DIS	EXC	0.79312	4.22E-14	5.21E-12
PANSSStot	PAUSS	0.785324	1.1E-13	1.16E-11
NEGTOT	PANSSStot	0.768656	7.46E-13	6.91E-11
processingspeed	Verbalmemory	0.748072	6.46E-12	5.32E-10
GENTOT	POSTOT	0.744328	9.35E-12	6.93E-10
PANSSStot	POS	0.727395	4.63E-11	3.12E-09
NEG	NEGTOT	0.706867	2.76E-10	1.7E-08
mir181_5p	mir590_5p	0.699249	5.15E-10	2.94E-08
EMO	EXC	0.685265	1.54E-09	8.17E-08
processingspeed	workingmemory	0.675278	3.26E-09	1.61E-07
problemsolving	processingspeed	0.667218	5.83E-09	2.7E-07
GENTOT	POS	0.655343	1.33E-08	5.81E-07
GENTOT	PAUSS	0.652914	1.57E-08	6.47E-07
NEG	PAUSS	0.646439	2.42E-08	9.43E-07
EMO	PANSSStot	0.63248	5.93E-08	2.2E-06
DIS	EMO	0.630807	6.58E-08	2.32E-06
motorcoordination	processingspeed	0.627411	8.12E-08	2.73E-06
GENTOT	NEGTOT	0.620152	1.26E-07	4.06E-06
Verbalmemory.	workingmemory	0.610452	2.23E-07	6.9E-06
EMO	GENTOT	0.605722	2.93E-07	8.69E-06
processingspeed	verbalfluency	0.604724	3.1E-07	8.84E-06
problemsolving	workingmemory	0.600162	4.01E-07	1.1E-05
motorcoordination	problemsolving	0.59957	4.15E-07	1.1E-05
mir132_3p	mir181_5p	0.597699	4.6E-07	1.14E-05
problemsolving	Verbalmemory.	0.598223	4.47E-07	1.14E-05
NEG	PANSSStot	0.582718	1.04E-06	2.47E-05
mir124_3p	mir132_3p	0.57772	1.34E-06	3.11E-05
mir_1246	mir181_5p	0.576387	1.44E-06	3.23E-05
mir128_3p	mir181_5p	0.572357	1.77E-06	3.86E-05
Verbalmemory.	zscore	0.56773	2.24E-06	4.74E-05
EMO	NEGTOT	0.561101	3.11E-06	6.4E-05
mir124_3p	mir128_3p	0.557172	3.77E-06	7.55E-05
ColesteroloLDLmgdl	Colesterolototmgdl	0.556027	3.98E-06	7.77E-05
mir124_3p	mir199a_5p	0.548729	5.64E-06	0.000105
workingmemory	zscore	0.548609	5.67E-06	0.000105
mir199a_5p	mir203a_3p	0.535643	1.03E-05	0.000187

EMO	POS	0.521078	1.97E-05	0.000347
PAUSS	POS	0.516362	2.41E-05	0.000415
mir181_5p	mir195_5p	0.513532	2.72E-05	0.000457
EMO	PAUSS	0.512863	2.79E-05	0.00046
motorcoordination	verbalfluency	0.512136	2.88E-05	0.000464
verbalfluency	workingmemory	0.504428	3.97E-05	0.0006
problemsolving	verbalfluency	0.504515	3.95E-05	0.0006
PAUSS	POSTOT	0.505137	3.85E-05	0.0006
motorcoordination	Verbalmemory.	0.502909	4.22E-05	0.000625
mir132_3p	mir195_5p	0.502334	4.32E-05	0.000628
GENTOT	NEG	0.498912	4.96E-05	0.000707
mir_1246	mir195_5p	0.490469	6.94E-05	0.000971
EMO	NEG	0.485767	8.34E-05	0.001144
problemsolving	zscore	0.481647	9.77E-05	0.001317
motorcoordination	zscore	0.479554	0.000106	0.0014
processingspeed	zscore	0.475352	0.000124	0.001612
miR_3178	miR_7704	0.469934	0.000152	0.001938
mir124_3p	mir203a_3p	0.468582	0.000159	0.002002
mir_7_5p	mir124_3p	0.467129	0.000168	0.002076
mir128_3p	miR34a_5p	0.462806	0.000197	0.00235
mir126_3p	mir195_5p	0.462847	0.000196	0.00235
mir181_5p	miR34a_5p	0.455109	0.000259	0.003043
ColesteroloHDLmgdl	NEG	-0.45016	0.000308	0.003562
EXC	GENTOT	0.444371	0.000375	0.004278
mir128_3p	miR30e_5p	0.442825	0.000396	0.004441
EXC	PANSStot	0.439729	0.000439	0.004856
verbalfluency	zscore	0.436043	0.000497	0.005412
verbalfluency	Verbalmemory.	0.435238	0.00051	0.005478
mir124_3p	mir181_5p	0.434311	0.000526	0.005489
mir590_5p	zscore	-0.43472	0.000519	0.005489
motorcoordination	workingmemory	0.431945	0.000569	0.005851
NEGTOT	POS	0.427731	0.000652	0.006621
mir195_5p	miR34a_5p	0.423653	0.000744	0.007447
mir_7_5p	mir128_3p	0.420813	0.000814	0.008043
DIS	PANSStot	0.41344	0.001026	0.010001
mir132_3p	miR34a_5p	0.412454	0.001058	0.010177
mir132_3p	miR30e_5p	0.411318	0.001095	0.010405
POSTOT	Trigliceridimgdl	0.410518	0.001123	0.010529
POSTOT	problemsolving	-0.40837	0.001199	0.011103
NEGTOT	POSTOT	0.403806	0.001377	0.012594
DIS	GENTOT	0.401893	0.001458	0.013175
mir_1246	miR34a_5p	0.401284	0.001485	0.013255
miR_5100	mir181_5p	0.397774	0.001648	0.014536
mir199a_5p	miR30e_5p	0.393701	0.001857	0.01619
miR34a_5p	mir590_5p	0.387391	0.002228	0.019201
mir124_3p	Verbalmemory.	-0.38475	0.002403	0.020463

mir126_3p	mir132_3p	0.383409	0.002496	0.021014
mir195_5p	mir199a_5p	0.374364	0.003211	0.026734
mir_7_5p	miR30e_5p	0.371721	0.003452	0.027639
mir124_3p	mir126_3p	0.371924	0.003433	0.027639
mir_1246	mir132_3p	0.371541	0.003469	0.027639
EXC	POSTOT	0.371885	0.003436	0.027639
mir128_3p	mir223a_3p	0.370338	0.003584	0.028254
EMO	POSTOT	0.367871	0.003831	0.029884
mir_7_5p	mir132_3p	0.366605	0.003964	0.030597
mir126_3p	miR34a_5p	0.361811	0.004504	0.034404
DIS	zscore	-0.35841	0.004925	0.03724
EXC	NEG	0.355093	0.005369	0.040185
ColesteroloHDLmgdl	NEGTOT	-0.35349	0.005595	0.041459
mir124_3p	processingspeed	-0.3516	0.005873	0.04309
mir181_5p	Verbalmemory.	-0.347	0.006603	0.0475
mir590_5p	workingmemory	-0.34734	0.006547	0.0475
NEG	POS	0.346118	0.006751	0.048098

Supplementary tables S1. Significant correlation coefficients between clinical variables and circulating miRNA levels in patients with schizophrenia (SCZ). This table displays only the statistically significant correlations (e.g., $p < 0.05$ or adjusted p-values per FDR), highlighting associations between clinical measures (e.g., PANSS subscales, cognitive indices) and circulating miRNA expression levels. Positive and negative correlations are indicated by the sign of the coefficient; magnitude reflects the strength of the relationship.

Var1	Var2	Correlation	p_value	p_fdr
GENTOT	PANSStot	0.948018	5.64E-18	4.18E-15
NEGTOT	PAUSS	0.929649	7.24E-16	2.68E-13
POS	POSTOT	0.829133	7.61E-10	1.88E-07
DIS	EXC	0.784265	2.49E-08	4.61E-06
PANSStot	POSTOT	0.767696	7.38E-08	1.09E-05
PANSStot	POS	0.763768	9.43E-08	1.16E-05
NEGTOT	PANSStot	0.75674	1.44E-07	1.34E-05
PANSStot	PAUSS	0.758248	1.32E-07	1.34E-05
processingspeed	Verbalmemory.	0.735039	4.95E-07	4.07E-05
mir124_3p	mir132_3p	0.754902	8.58E-07	6.23E-05
mir181_5p	mir590_5p	0.72314	9.25E-07	6.23E-05
mir128_3p	mir132_3p	0.746499	1.09E-06	6.72E-05
mir199a_5p	mir203a_3p	0.714787	1.41E-06	8.03E-05
DIS	EMO	0.684824	5.69E-06	0.000301
GENTOT	POSTOT	0.67791	7.67E-06	0.000379
GENTOT	POS	0.673501	9.25E-06	0.000428
processingspeed	verbalfluency	0.67153	1E-05	0.000438
GENTOT	NEGTOT	0.65111	2.28E-05	0.000938
mir_7_5p	mir124_3p	0.646634	2.71E-05	0.001056
NEG	NEGTOT	0.640894	3.36E-05	0.001185
EMO	PANSStot	0.641074	3.34E-05	0.001185
GENTOT	PAUSS	0.638362	3.69E-05	0.001243
processingspeed	workingmemory	0.634166	4.3E-05	0.001387
mir124_3p	mir128_3p	0.634454	6.25E-05	0.001852

Verbalmemory.	workingmemory	0.62412	6.16E-05	0.001852
motorcoordination	problemsolving	0.620934	6.89E-05	0.001964
EMO	EXC	0.618994	7.37E-05	0.002023
EMO	NEGTOT	0.614869	8.49E-05	0.002247
mir_7_5p	mir132_3p	0.584577	0.000226	0.005591
problemsolving	workingmemory	0.585284	0.000221	0.005591
motorcoordination	verbalfluency	0.578656	0.000271	0.006482
verbalfluency	workingmemory	0.576496	0.000289	0.006498
EMO	GENTOT	0.577106	0.000284	0.006498
NEG	PAUSS	0.57003	0.000351	0.007641
mir590_5p	zscore	-0.56785	0.000374	0.007913
problemsolving	processingspeed	0.559321	0.000478	0.009707
POSTOT	problemsolving	-0.55881	0.000485	0.009707
mir128_3p	Trigliceridimgdl	0.557432	0.000504	0.009826
EMO	PAUSS	0.553917	0.000556	0.010567
EMO	POS	0.551511	0.000595	0.011016
motorcoordination	processingspeed	0.549512	0.000628	0.011357
workingmemory	zscore	0.54726	0.000668	0.011793
mir_1246	mir195_5p	0.553221	0.000693	0.011936
mir_1246	mir181_5p	0.539496	0.000984	0.016576
problemsolving	Verbalmemory.	0.527493	0.001129	0.018112
Glicemiamgdl	motorcoordination	0.526815	0.001149	0.018112
problemsolving	verbalfluency	0.528266	0.001107	0.018112
NEG	PANSSStot	0.525635	0.001184	0.018279
miR30e_5p	POS	0.521786	0.001306	0.019747
mir_7_5p	mir199a_5p	0.520384	0.001353	0.020048
mir181_5p	mir195_5p	0.521849	0.001516	0.022023
mir126_3p	mir132_3p	0.505854	0.001935	0.027568
mir_7_5p	mir128_3p	0.504027	0.002021	0.02826
mir124_3p	mir199a_5p	0.496533	0.002414	0.033124
mir132_3p	mir181_5p	0.495518	0.002777	0.036752
PAUSS	POS	0.491123	0.002737	0.036752
mir132_3p	mir203a_3p	0.488058	0.002937	0.038175
EMO	NEG	0.485959	0.00308	0.039353
verbalfluency	Verbalmemory.	0.481776	0.003385	0.042514

Supplementary tables S2. Significant correlation coefficients between clinical variables and circulating miRNA levels in patients with Treatment-Resistant Schizophrenia (TRS). This table displays only the statistically significant correlations (e.g., $p < 0.05$ or adjusted p-values per FDR), highlighting associations between clinical measures (e.g., PANSS subscales, cognitive indices) and circulating miRNA expression levels. Positive and negative correlations are indicated by the sign of the coefficient; magnitude reflects the strength of the relationship.

PC1	PC2	PC3	PC4	PC5
-3.3810346	3.70927791	1.43649828	-1.0813584	0.98448512
2.82513024	1.28606873	0.57488538	1.00084371	-0.2838847
-0.3153997	0.45899721	2.88452735	-1.7189969	0.6145548
1.58520956	3.22705897	0.36560412	0.20064847	-0.4778827
-3.7254339	3.60923353	1.68425519	-1.2653559	0.83565438

-0.5960965	1.63128068	1.50195038	0.04295265	-2.1931069
3.32427725	-1.0864808	0.89449938	2.69074284	0.32929308
-1.9126312	-0.5395682	-0.4633739	2.27725058	-0.0072556
0.24547593	4.21704569	-0.8124318	-0.5238659	1.02879565
1.67930146	0.77719832	-2.7828719	3.42580269	2.72778258
3.28899308	0.88717872	0.62236018	0.53390957	-0.8328718
2.09583511	-0.9425041	3.14535332	2.98676149	-1.6680369
0.5347248	-0.3684085	0.1246087	-0.1917016	0.76713588
2.63737973	-3.5642031	-2.1066254	-1.0889358	-2.1038826
4.06067429	-2.120484	1.71249495	1.4122411	0.81093587
3.95669857	0.71361914	1.06864819	-1.2081718	-1.4606337
2.08882191	1.70936768	-0.0915683	-2.4907514	-0.9738794
-0.6436975	0.94038931	0.45360414	-1.68467	0.00079097
2.90692019	4.02614251	-2.2702391	-1.8709431	-0.9149065
1.89535068	0.3014019	-3.0170614	-3.2287489	1.28058165
4.89853879	0.26834823	-1.3809111	-0.1365136	0.69238044
0.39896698	-4.549113	-0.566067	-1.3302063	2.20815326
1.27405542	-1.4366025	6.55351809	0.85736655	0.06322447
2.67110909	0.0921882	-2.5180561	0.54671366	-1.2863882
-0.2982452	0.56981086	1.53043645	-1.8424467	-0.0785063
-4.5175545	-4.850488	-0.542926	-0.3180674	-3.0666145
-4.805856	1.1595537	-1.5030545	-0.0119489	-2.4817676
-0.8880736	-0.9480364	-1.6595549	0.36595752	-2.4339922
-4.6856386	-2.151235	-1.3125315	0.64434597	-2.4631317
0.06332921	1.53251464	-1.7898054	1.36121889	-1.9075958
-2.0554582	4.30634833	1.47594579	2.57810256	-0.05459
-1.4439667	2.70425345	-1.2890138	-0.9328013	1.79933722
-1.7763462	2.39952999	-1.1351402	0.93101865	0.61420986
3.16675053	-1.9347331	0.37024107	0.48808982	-2.0386928
2.09174851	-1.2041246	-1.9836092	-1.2539202	0.10008309
-0.3443066	-2.8631294	0.26869757	1.41893796	1.37728174
-0.8363396	-1.0444474	0.98414133	-2.0287859	-1.2238939
0.75852305	1.90136382	-2.1392828	-2.2488263	-2.4129085
-2.7380972	0.84986864	0.25412928	-0.2646559	-2.3218939
-0.5800155	0.46263338	-2.2290965	1.69730441	-1.5426774
-0.9498977	0.07737001	0.16978793	-0.7962333	0.27258264
2.64597032	-0.0458809	-2.8629045	3.93025577	0.20071184

-4.7366308	-2.7441838	1.28951027	2.57130454	-0.35142
0.4063588	5.54883912	-1.6119442	-0.3888569	0.60064072
-4.712647	1.69320731	0.4985568	2.17375256	0.42900729
-0.7721204	1.74609029	3.42058141	0.73802999	0.67136518
-1.305613	-2.2021862	-2.7406295	0.88771616	2.73912688
-3.1880207	2.26869021	-0.4748781	1.7385673	0.65162955
1.29174251	-2.9566418	-1.0405616	-0.089071	1.70154305
-0.6476207	0.48617884	-1.7521243	-0.0940476	3.04271994
-6.9452533	-4.4337048	-2.4002908	-1.0610693	1.89430144
3.59735727	-3.1569806	0.51380909	-0.6400957	2.14491384
2.55543153	-0.2536407	-0.098368	0.76007714	0.8596707
-0.7914401	-3.0009699	-1.3955558	-2.4966024	1.46916312
-1.7355554	-0.6337542	3.0237281	-2.1632442	1.44311533
-3.8339108	-2.228344	1.76183721	-0.2221064	1.15890159
-0.1024765	1.14969681	2.99971751	-2.3784615	1.66663526
1.53792144	-0.8039966	1.69391767	0.56584427	0.20773179
3.73921445	-1.5549205	1.87542728	0.23549285	0.20164467
1.04356692	-3.0919841	0.81720534	-2.0097892	-3.0096716

Supplementary Table S3. Principal component analysis (PCA) scores for the first five principal components. The table reports the individual subject loadings across the first five principal components (PC1–PC5), which together capture the major sources of variance in the dataset. These values represent the position of each subject in the multivariate space defined by the PCA.

hsa-miR-132						
Subcategory	ID	Description	GeneRatio	p.adjust	Count	GeneSymbol
Cell growth and death	hsa04218	Cellular senescence	62/1557	1,17E+05	62	RB1;CDKN1A;CCNA2;SMAD2;CCNB1;GSK3B;STAG1;SMC1A;E2F3;CDK6;TK;E2F5;CDC25A;TGFB2;CDC25B;AURKB;YWHAZ;E2F2;PRKDC;ATM;RAD21;ATR;BUB1B;CDKN2C;CHEK1;CREBBP;E2F4;EP300;HDAC1;HDAC2;SMAD4;MCM3;MCM6;MDM2;ORC5;PPP2CB;PPP2R5A;SKP2;WEE1;YWHAG;YWHAH;SMC3;BUB3;TRIP13;ESPL1;STAG2;YWHAQ;PDS5B;ANAPC7;CCNB2;MAD2L1BP;PPP2CA;PPP2R5E;SKP1;TFDP1;ZBTB17;PTTG1;WAPL;CDC14C
Cell growth and death	hsa04110	Cell cycle	59/1557	2,84E+06	59	CCNB1;MAPK1;SMC1A;FBXW11;ADCY6;YWHAZ;PPP3CA;ADCY3;ADCY7;ADCY9;CALM1;CAMK2D;IGF1R;PGR;PPP1CB;PPP1CC;PPP2CB;PPP2R5A;PPP3R1;MAPK3;RPS6KA3;AURKA;YWHAG;YWHAH;SMC3;ESPL1;SLK;YWHAQ;CPEB3;ANAPC7;CPEB4;CPEB2;CCNB2;PPP3CB;ADCY5;PPP2CA;PPP2R5E;SKP1;PTTG1
Cancer: specific types	hsa05220	Chronic myeloid leukemia	36/1557	5,74E+06	36	THBS1;CDKN1A;CCNB1;PTEN;BCL2;CDK6;APAF1;CCNG1;IGFBP3;BAX;BCL2L1;ATM;BBC3;CHEK1;MDM2;MDM4;SERPINE1;SLAH1;RRM2B;ZMAT3;SESN2;SESN3;CCNB2;PIDD1
Signal transduction	hsa04068	FoxO signaling pathway	51/1557	8,41E+06	51	CASP7;RAF1;MAPK1;PIK3R3;BCL2;TUBA1A;KRAS;LMNB1;APAF1;IKBKB;PIK3R1;BCL2L1;BAX;AKT2;FOS;HRAS;AKT3;BCL2L1;ATM;BBC3;ACTG1;XIAP;BIRC5;CAPN2;CHUK;LMNA;NFKBIA;PIK3CA;PIK3CB;MAPK3;MAPK8;SPTAN1;TUBA1B;DIABLO;LMNB2;DAB2IP;CTSO;CTSB;MAP3K5;PIDD1;DAXX;MCL1
Folding, sorting and degradation	hsa04120	Ubiquitin mediated proteolysis	53/1557	9,89E+06	53	CASP7;BCL2;APAF1;BCL2L1;BAX;BCL2L1;BBC3;XIAP;BIRC5;NGFR;MAPK8;DIABLO;BIRC6
Drug resistance: antineoplastic	hsa01522	Endocrine resistance	41/1557	1,74E+07	41	ACSL4;VDAC2;ACSL1;ACSL3;SLC11A2;PCBP1;SAT1;TFRC;SLC39A14;MAP1LC3B;CP;CYBB;VDAC3;GCLM;SAT2
Transport and catabolism	hsa04140	Autophagy - animal	58/1557	4,37E+07	58	RB1;CDKN1A;SIRT1;RAF1;FOXO1;CCNA2;SMAD2;CCNB1;NBN;MAPK1;VDAC2;PIK3R3;PTEN;FBXW11;E2F3;CDK6;KRAS;E2F5;HIPK3;CDC25A;TGFB2;IGFBP3;PIK3R1;AKT2;HRAS;PPP3CA;E2F2;AKT3;ATM;ZFP36L1;CALM1;CAPN2;CHEK1;E2F4;MDM2;SERPINE1;PIK3CA;PIK3CB;PPP1CB;PPP1CC;PPP3R1;MAPK3;MAP2K3;RAD1;RAD9A;TSC1;MAPKAPK2;RRAS2;HIPK2;TRP

						M7;SLC25A31;LIN54;HIPK1;CCNB2;RBBP4;VDAC3;PPP3CB;SLC25A4;SLC25A5;VDAC1;HUS1;CXCL8
Infectious disease: viral	hsa05166	Human T-cell leukemia virus 1 infection	71/1557	4,37E+07	71	EGFR;RAF1;CRK;FGF2;MAPK1;PIP5K1A;ACTR2;NCKAP1;FGF22;PIK3R3;KRAS;CFL2;IQGAP1;PIK3R1;RHOA;AKT2;ITGB4;HRAS;RDX;AKT3;ACTG1;ACTN4;DIAPH1;LPAR1;FN1;ITGAV;ITGB1;ITGB8;MYLK;PPP1R12A;PAK2;PFN2;PIK3CA;PIK3CB;PIP4K2A;PPP1CB;PPP1CC;MAPK3;PXN;SOS2;VCL;WASF1;ARPC3;RRAS2;ARHGEF12;SSH1;ENAH;ARPC5L;SSH2;PIKFYVE;DOCK1;WASL;SOS1;MYH10;DIAPH2;CYFIP1;CYRIB;CYR1A
Nervous system	hsa04722	Neurotrophin signaling pathway	45/1557	8,05E+06	45	THBS1;EGFR;RAF1;CRK;GSK3B;MAPK1;PIP5K1A;TLN2;PIK3R3;PTEN;LAMC2;BCL2;VEGFA;COL1A1;COL1A2;TLN1;PIK3R1;RHOA;AKT2;ITGB4;HRAS;AKT3;ACTG1;ACTN4;XIAP;ARHGAP5;CAPN2;COL6A2;CTNNA1;DIAPH1;EMP1;FLNA;FLNB;FLT1;FN1;GRB2;RAPGEF1;IGF1R;ITGAV;ITGB1;ITGB8;LAMB1;MYLK;PPP1R12A;PAK2;PIK3CA;PIK3CB;PPP1CB;PPP1CC;MAPK3;MAPK8;PXN;RAP1A;SOS2;VCL;ZFYX;SHC3;COL6A6;LAMA1;DOCK1;TNR;SOS1;LAMB2
Cancer: specific types	hsa05210	Colorectal cancer	36/1557	9,79E+07	36	EGFR;MAPK1;CTNND1;IQGAP1;RHOA;CDH1;NLK;ACTG1;ACTN4;CREBBP;CSNK2A2;CTNNA1;CTNNA1;EP300;IGF1R;INSR;LMO7;SMAD4;MAPK3;PTPRJ;RAP1A;VCL;WASF1;HEG1;SMURF2;SSX2IP;CTNNA2;SMURF1;WASL;AFDN;NECTIN2;NECTIN3;ARHGAP29
Aging	hsa04213	Longevity regulating pathway - multiple species	28/1557	3,34E+08	28	CFTR;ACTR2;TJAP1;OCLN;NF2;TUBA1A;EPB41L4B;RHOA;PPP2R2A;RDX;ACTG1;ACTN4;CLDN4;DLG2;HSPA4;ITGB1;LLGL2;MAP3K1;NEDD4;PPP2CB;PRKAA1;PRKAB2;MAPK8;RAP1A;STK11;YBX3;ARHGEF2;MAGI1;RAPGEF2;ARPC3;TUBA1B;NEDD4L;ARHGAP17;PPP2R2D;CGN;RAP2C;ARPC5L;CRB3;PRKAG2;PPP2CA;MAP3K5;MYH10;SCRIB;AMOTL1;AFDN;PATJ;PALM1
Infectious disease: viral	hsa05165	Human papillomavirus infection	92/1557	3,83E+08	92	RAF1;WNT3A;SMAD2;FGF2;GSK3B;LIFR;MAPK1;FZD6;PIK3R3;KRAS;SMA5D5;BMPR2;PCGF5;ID3;ID1;PIK3R1;LIF;BMI1;AKT2;JAK1;HRAS;AKT3;WNT10B;ACVR1;ACVR2A;ACVR2B;ZFHX3;CTNNA1;DUSP9;DVL3;GRB2;IGF1R;IL6ST;INHBB;SMAD4;PAX6;PIK3CA;PIK3CB;MAPK3;SKIL;TCF3;FZD5;FZD3;KAT6A;FZD1;SMARCA1
Cancer: specific types	hsa05211	Renal cell carcinoma	30/1557	4,02E+08	30	RPTOR;PPP2CB;ULK2;GABARAPL2;ATG4B;ATG2B;ATG3;ATG9A;ATG4A;WIPI2;ATG13;PPP2CA
Cellular community - eukaryotes	hsa04510	Focal adhesion	63/1557	4,02E+08	63	RAB5B;USP8;KRAS;SP1;MITF;HIF1A;HRAS;BCL2L1;CSNK2A2;OPA1;MAPK8;RAB5C;SLAH1;TFE3;UBB;UBC;VCP;MFN2;HUWE1;PHB2;GABARAPL2;RRAS2;BCL2L13;SMURF2;TBC1D15;ATG9A;MAP1LC3B;SMURF1;ARIH1;MUL1;MFN1;TOMM70
Neurodegenerative disease	hsa05017	Spinocerebellar ataxia	49/1557	4,11E+08	49	RAF1;VMP1;MAPK1;YKT6;PIK3R3;PTEN;BCL2;KRAS;IRS1;PIK3R1;TRAF6;HIF1A;RPTOR;AKT2;DDIT4;HRAS;AKT3;BCL2L1;TP53INP2;IGF1R;LAMP2;PIK3CA;PIK3CB;PPP2CB;PRKAA1;MAPK3;MAPK8;RAB1A;STK11;TSC1;UBB;UBC;UVRAG;MTMR4;ULK2;RB1CC1;GABARAPL2;RRAS2;ATG4B;SH3GLB1;ZFYVE1;ATG2B;BIRC6;ATG3;VPS3A;ATG9A;MAP1LC3B;ATG4A;EIF2AK4;WIPI2;ATG13;TANK;CTSB;PPP2CA;STX17;WDR45B;EPG5;RUBCN
Drug resistance: antineoplastic	hsa01524	Platinum drug resistance	31/1557	5,60E+08	31	EGFR;LDLR;SMAD2;ARF6;HSPA1B;RAB5B;PIP5K1A;ACTR2;USP8;RAB11FIP2;ARF3;VPS26A;RHOA;TRAF6;TSG101;AP2M1;HRAS;AP2B1;CAPZA1;CAPZB;CLTC;IGF1R;KIF5B;KIF5C;MDM2;NEDD4;PLD1;RAB5C;TFRC;GBF1;ASAP2;RABEP1;CYTH3;VPS4B;ZFYVE16;ARPC3;RNF41;ARHGEF1;EHD1;EPN2;NEDD4L;SNX12;EHD4;SH3GLB1;CHMP3;MAPK8;RAB1A;STK11;VPS37B;ARPC5L;VPS25;ARFGAP2;ARAP2;CHMP4B;VPS37A;GRK4;DNM1;MVH12B;ARF1;SH3KBP1;AGAP3;EPS15;SMURF1;AMPH;WASL;CBL;HSPA8;VPS29;RAB11FIP4;WIPF2;WASHC5
Aging	hsa04211	Longevity regulating pathway	35/1557	5,60E+08	35	BDNF;EGFR;IRAK1;RAF1;RASA1;STMN1;MAP3K3;CRK;FGF2;HSPA1B;MAPK1;PLA2G4C;FGF22;IRAK4;KRAS;VEGFA;IKBKB;EFNA3;TGFB2;STK4;TRAF6;AKT2;CDC25B;FOS;HRAS;PPP3CA;NLK;AKT3;CACNB4;CHUK;ATF2;DUSP6;DUSP9;EFNA1;EREG;FLNA;FLT1;GRB2;IGF1R;INSR;MAPT;MEF2C;MAP3K1;MAP3K4;MAP3K9;MYD88;NF1;NGFR;PAK2;PPP3R1;MAPK3;MAPK8;MAP2K3;PTPRR;RAP1A;RPS6KA3;MAP2K4;SOS2;STK3;TEK;RPS6KA5;MAPKAPK2;RAPGEF2;MAP3K2;RRAS2;TAOK1;DUSP16;CACNA1A;MAPK8IP3;PPP3CB;MAP4K4;SOS1;MAP3K5;HSPA8;TAOK3;MAP3K20;DAXX
Neurodegenerative disease	hsa05022	Pathways of neurodegeneration - multiple diseases	122/1557	5,75E+08	122	CDKN1A;EGFR;RAF1;CRK;HBEGF;GSK3B;MAPK1;PIK3R3;KRAS;PIK3R1;AKT2;HRAS;AKT3;ABL2;CAMK2D;EREG;GRB2;PAK2;PIK3CA;PIK3CB;MAPK3;MAPK8;MAP2K4;SOS2;STAT5B;SHC3;CBL;SOS1
Cancer: overview	hsa05205	Proteoglycans in cancer	62/1557	8,43E+08	62	BDNF;EGFR;RAF1;RASA1;ARF6;FGF2;GNB1;MAPK1;RAB5B;PLA2G4C;FGF22;PIK3R3;KRAS;VEGFA;IKBKB;EFNA3;STK4;PIK3R1;RHOA;AKT2;HRAS;AKT3;BCL2L1;ABL2;CALM1;CHUK;EFNA1;FLT1;GNB3;GRB2;IGF1R;INSR;NF1;NGFR;PAK2;PIK3CA;PIK3CB;PLD1;MAPK3;MAPK8;PTPN11;RAB5C;RAP1A;REL;SOS2;TEK;SHOC2;BRAP;RRAS2;SHC3;RALGAPB;RALGAP2;RASAL1;SOS1;SYNGAP1;KSR2;AFDN
Signal transduction	hsa04390	Hippo signaling pathway	51/1557	9,03E+08	51	THBS1;EGFR;RAF1;CRK;FGF2;MAPK1;FGF22;TLN2;PIK3R3;KRAS;VEGFA;EFNA3;ADCY6;TLN1;CTNND1;ID1;PIK3R1;RHOA;PRKD2;AKT2;CDH1;GNAI2;HRAS;AKT3;ACTG1;ADCY3;ADCY7;ADCY9;CALM1;CTNNA1;LPAR1;EFNA1;FLT1;GNAS;RAPGEF1;IGF1R;INSR;ITGB1;NGFR;PFN2;PIK3CA;PIK3CB;MAPK3;MAP2K3;RAP1A;TEK;MAGI1;RAPGEF2;DOCK4;ENAH;SIPA1L2;MAGI3;CNR1;ADCY5;AFDN

Infectious disease: viral	hsa05161	Hepatitis B	52/1557	1,25E+09	52	RAF1;MEF2A;MAPK1;VDAC2;IRS1;ADCY6;RHOA;AKT2;ATP2B1;GNAI2;MEF2D;PPP3CA;AKT3;ATP1A2;ADCY3;ADCY7;ADCY9;ATP1A3;ATP2A2;ATP2B4;CALM1;ATF2;INSR;KCNMA1;MEF2C;MYLK;PPP1R12A;PDE3A;PPP1CB;PPP1CC;PPP3R1;MAPK3;RGS2;CREB3;SLC25A31;ADRA1B;ATP2B3;VDAC3;PPP3CB;ATP1B4;SLC25A4;SLC25A5;ADCY5;VDAC1
Cancer: overview	hsa05235	PD-L1 expression and PD-1 checkpoint pathway in cancer	34/1557	1,42E+09	34	CDKN1A;EGFR;MAPK1;PIK3R3;SLC2A1;ELOC;BCL2;VEGFA;IL6R;PIK3R1;HIF1A;AKT2;AKT3;ARNT;CAMK2D;CREBBP;EP300;FLT1;IFNGR2;IGF1R;INSR;SERPINE1;PDHA1;PFKFB3;PIK3CA;PIK3CB;MAPK3;RPS6;TEK;TFRC;EGLN1;ENO1;CYBB;PFKL
Chromosome	hsa03083	Polycomb repressive complex	32/1557	1,67E+09	32	CDKN1A;EGFR;SIRT1;RAF1;FOXO1;CCNB1;MAPK1;PIK3R3;PTEN;KRAS;SGK3;IRS1;IKBKB;TGFB2;STK4;PIK3R1;BCL2L11;AKT2;HRAS;NLK;AKT3;ATM;CHUK;CREBBP;EP300;FOXG1;GRB2;PRMT1;IGF1R;INSR;SMAD4;MDM2;PIK3CA;PIK3CB;PRKAA1;PRKAB2;MAPK3;MAPK8;SKP2;SOS2;STK11;USP7;HOMER1;PLK4;PLK2;GABARAPL2;CCNB2;PRKAG2;SOS1;SOD2;C8orf44-SGK3
Folding, sorting and degradation	hsa04141	Protein processing in endoplasmic reticulum	53/1557	2,33E+09	53	IMPA1;PIP5K1A;PIK3R3;PTEN;PIK3R1;CALM1;PIK3CA;PIK3CB;PI4KB;PIP4K2A;MTMR4;DGKI;PI4K2B;PLCD3;DGKH;MTM1;PIKFYVE;SYNJ2;ITPKB;PI4KA;DGKE;MTMR1;PIK3C2G;PPP5K2;PIP4P1
Neurodegenerative disease	hsa05010	Alzheimer disease	100/1557	2,77E+08	100	EGFR;RAF1;ARF6;MAPK1;PIP5K1A;PLA2G4C;PIK3R3;KRAS;ADCY6;PIK3R1;RHOA;AKT2;HRAS;AKT3;ADCY3;ADCY7;ADCY9;LPAR1;GNAS;GRB2;INSR;PIK3CA;PIK3CB;PLD1;MAPK3;PTPN11;SOS2;TSC1;DGKI;CYTH3;RRAS2;SHC3;AGPAT3;AGPAT4;DGKH;DNM1;ARF1;ADCY5;DGKE;SOS1;CXCL8
Endocrine system	hsa04919	Thyroid hormone signaling pathway	41/1557	3,39E+09	41	RAF1;WNT3A;GSK3B;MAPK1;FZD6;PIK3R3;PTEN;KRAS;IRS1;IKBKB;PIK3R1;RHOA;RPTOR;AKT2;DDIT4;HRAS;AKT3;WNT10B;ATP6V1A;ATP6V1E1;CHUK;DVL3;GRB2;GRB10;IGF1R;INSR;LRP6;LRP5;PIK3CA;PIK3CB;PRKAA1;MAPK3;RPS6;RPS6KA3;SKP2;SOS2;STK11;TSC1;FZD5;FZD3;SLC7A5;FZD1;ATP6V1G1;ULK2;PRR5L;SESN2;FNIP1;SOS1;SLC38A9
Cancer: specific types	hsa05224	Breast cancer	47/1557	3,61E+09	47	BDNF;THBS1;CDKN1A;EGFR;RAF1;FGF2;GNB1;GSK3B;MAPK1;FGF22;PIK3R3;PTEN;LAMC2;BCL2;CDK6;KRAS;VEGFA;IL6R;SGK3;IRS1;COL1A1;COL1A2;IKBKB;EFNA3;HSP90B1;PIK3R1;BCL2L11;MYB;BRCA1;RPTOR;AKT2;ITGB4;PPP2R2A;JAK1;YWHAZ;DDIT4;HRAS;AKT3;BCL2L1;CHUK;COL6A2;ATF2;LPAR1;EFNA1;EREG;FLT1;FN1;GNB3;GRB2;HSP90AA1;IGF1R;INSR;ITGAV;ITGB1;ITGB8;LAMB1;MDM2;NGFR;PIK3CA;PIK3CB;PPP2CB;PPP2R5A;PRKAA1;MAPK3;RPS6;SOS2;STK11;TEK;TSC1;YWHAG;YWHAH;MAGI1;CREB3;YWHAG;CDC37;PHLPP2;PKN3;PPP2R2D;COL6A6;LAMA1;GHR;PPP2CA;TNR;SOS1;PPP2R5E;CRTC2;LAMB2;MCL1;C8orf44-SGK3
Infectious disease: bacterial	hsa05132	Salmonella infection	70/1557	3,61E+09	70	SIRT1;FOXO1;CCNA2;CFTR;PIK3R3;IRS1;PIK3R1;RPTOR;AKT2;PPP2R2A;PPARG;AKT3;ELAVL1;EEF2;IGF1R;INSR;PFKFB3;PIK3CA;PIK3CB;PPP2CB;PPP2R5A;PRKAA1;PRKAB2;SREBF1;STK11;TSC1;CREB3;RAB14;PPP2R2D;ADIPOR2;PRKAG2;PPP2CA;PPP2R5E;CRTC2;PFKL
Cancer: specific types	hsa05225	Hepatocellular carcinoma	52/1557	3,61E+09	52	THBS1;SMAD2;MAPK1;GDF5;E2F5;SMAD5;BMPR2;SP1;FBN1;TGFB2;ID3;ID1;RHOA;ACVR1;ACVR2A;ACVR2B;CREBBP;E2F4;EP300;HDAC1;HDAC2;INHBB;SMAD4;PPP2CB;MAPK3;SKIL;TFRC;ZFYVE16;LEMD3;SMURF2;RGM;NBL1;NCOR1;SMURF1;PPP2CA;SKP1;TFDP1
Cellular community - eukaryotes	hsa04550	Signaling pathways regulating pluripotency of stem cells	46/1557	3,61E+09	46	RAF1;PTGS2;MAPK1;PLA2G4C;PIK3R3;KRAS;VEGFA;PIK3R1;AKT2;HRAS;PPP3CA;AKT3;PIK3CA;PIK3CB;PPP3R1;MAPK3;PXN;MAPKAPK2;PPP3CB
Transport and catabolism	hsa04144	Endocytosis	70/1557	3,84E+09	70	RAF1;SMAD2;GNB1;MEF2A;MAPK1;KRAS;ADCY6;NOTCH3;AKT2;CDH1;JAG1;GNAI2;HRAS;MEF2D;AKT3;ADCY3;ADCY7;ADCY9;CALM1;GNB3;SMAD4;MEF2C;MYLK;SERPINE1;PRKAA1;PRKAB2;MAPK3;RPS6;RYSR3;RRAS2;MAP1LC3B;PRKAG2;ADCY5;APLN;CCN2
Neurodegenerative disease	hsa05012	Parkinson disease	74/1557	3,91E+09	74	WNT3A;SMAD2;GSK3B;GDF5;FZD6;FBXW11;NF2;LATS2;BMPR2;TGFB2;ID1;PPP2R2A;YAP1;CDH1;YWHAB;BBC3;WNT10B;ACTG1;AFP;BIRC5;CTNNA1;CTNNA1;DLG2;DVL3;GLI2;LLGL2;SMAD4;SERPINE1;PPP1CB;PPP1CC;PPP2CB;STK3;YWHAG;YWHAH;FZD5;FZD3;FZD1;LIMD1;LATS1;DLG5;YWHAG;WWTR1;PPP2R2D;SAV1;FRMD6;CTNNA2;PPP2CA;SCRIB;PATJ;CCN2;PALS1
Signal transduction	hsa04150	mTOR signaling pathway	49/1557	4,07E+09	49	FAT4;NF2;LATS2;YAP1;STK3;LIMD1;LATS1;WWTR1;SAV1;FRMD6
Drug resistance: antineoplastic	hsa01521	EGFR tyrosine kinase inhibitor resistance	30/1557	4,62E+09	30	CASP7;PTGS2;MMP9;MAPK1;PIK3R3;IKBKB;PIK3R1;LIF;AKT2;JAG1;FOS;AKT3;XIAP;CHUK;ATF2;MMP14;NFKBIA;PIK3CA;PIK3CB;MAPK3;MAPK8;MAP2K3;CXCL5;MAP2K4;TRAF3;RPS6KA5;CREB3;DAB2IP;DNM1L;MAP3K5
Translation	hsa03013	Nucleocytoplasmic transport	37/1557	4,62E+09	37	ARID2;ACTR8;ACTG1;CHD3;BPTF;HDAC1;HDAC2;RBBP7;SMARCA4;SMARCB1;SMARCC2;SMARCD1;SMARCD2;SS18;ARID1A;TRRAP;MORF4L2;BAZ2B;RSF1;CHAC1;GATAD2A;INO80D;ACTR5;EPC1;RBBP4;NFRKB;KAT5;SRCAP;BAZ2A;INO80;ING3;C17orf49

Cancer: specific types	hsa05223	Non-small cell lung cancer	28/1557	5,55E+09	28	PCGF5;ASXL2;BMI1;AURKB;CREBBP;EP300;HDAC1;HDAC2;FOXK2;RBBP7;RNF2;UBE2D1;UBE2D3;USP7;DCAF7;MTF2;MGA;RYBP;CBX6;SFMBT1;BCOR;BCORL1;PHC3;LCOR;FOXK1;RBBP4;FBRSL1;HCFC1;SKP1;TFDP1;ASXL1;OGT
Cancer: specific types	hsa05212	Pancreatic cancer	29/1557	5,55E+09	29	HSPD1;CNOT6;BTG2;DDX6;HSPA9;CNOT4;PABPC4;C1D;TOB2;XRN2;CNOT10;PABPC1;CNOT7;EDC3;DCP2;DHX36;PATL1;PAN3;ENO1;NUDT16;CNOT2;CNOT1;PABPC3;PFKL;CNOT9;TENT4B
Neurodegenerative disease	hsa05014	Amyotrophic lateral sclerosis	94/1557	5,55E+09	94	PSMA2;PSMD12;PSMB5;PSMC4;PSMD1;PSMD11;PSME3;PSME4;PSMA5;PSMA1;PSMB2;PSMD3;PSMC5;SEMI
Cellular community - eukaryotes	hsa04520	Adherens junction	33/1557	5,55E+09	33	UBE2W;ELOC;FBXW11;UBE2I;TRAF6;BRCA1;FBXW7;XIAP;DDB1;MDM2;MAP3K1;TRIM37;NEDD4;SIAH1;SKP2;UBB;UBC;UBE2B;UBE2D1;UBE2D3;UBE2E1;UBE2G1;UBE2L3;UBE2N;CUL4B;CUL4A;HERC3;PIAS2;TRIP12;UBE3C;KEAP1;UBA2;HUWE1;STUB1;UBE4B;NEDD4L;UBR5;ANAPC7;UBE2R2;UBA6;BIRC6;SMURF2;UBE2Z;UBE2J2;UBE2F;SMURF1;UBA1;UBE2A;HERC1;CBL;SKP1;PPIL2;UBE2E2
Cancer: specific types	hsa05222	Small cell lung cancer	33/1557	5,55E+09	33	HSPA1B;SSR3;SEC61A1;UBXN2A;BCL2;HSP90B1;BAX;XBP1;CAPN2;PDIA3;HSPA5;HSP90AA1;NFE2L2;MAPK8;RPN1;RPN2;SEC62;UBE2D1;UBE2D3;UBE2G1;VCP;SEC24C;STUB1;UBE4B;DNAJA2;SEC24B;SEC23A;HYOU1;SEC24A;HSPH1;MAN1A2;SEC31A;TRAM1;UBQLN2;UBQLN1;DNAJC10;DERL1;EDEM3;MAGT1;UBE2J2;TXNDC5;PLAA;SAR1B;BAG1;MAP3K5;HSPA8;SKP1;UBXN4;OSTC;BCAP31;STT3B;MARCF6;EDEM2
Signal transduction	hsa04350	TGF-beta signaling pathway	37/1557	6,40E+09	37	MDFIC;MAP1B;TSG101;CCNT2;CREBBP;EP300;FURIN;SMARCB1;SUPT4H1;XPO1;VPS4B;NUP153;CPSF6;TNPO3;AFF4;NELFCD;CHMP4B;APOBEC3C;RANBP2
Cancer: specific types	hsa05215	Prostate cancer	36/1557	6,44E+09	36	KPNA1;NUP50;PNN;UBE2I;TNPO1;KPNA5;NUP98;TPR;XPO1;DDX39B;NUP214;RAE1;NUP155;NUP153;IPO8;IPO7;XPO7;CASC3;XPO7;TNPO3;KPNA6;AHCTF1;UPF2;IPO11;TMEM33;NDC1;NUP107;SEN2;XPO4;KPNB1;IPO5;NUP88;RANBP2;NUP205;NUP188;NUP58;POM121C
Infectious disease: bacterial	hsa05131	Shigellosis	69/1557	6,44E+09	69	CSTF3;CSTF2T;PNN;PPP2R2A;CSTF2;FUS;GSPT1;PPP1CB;PPP1CC;PPP2CB;PPP2R5A;DDX39B;PABPC4;SMG7;PAPOLA;CLP1;CPSF6;CASC3;SMG1;SMG6;TARDBP;UPF2;PABPC1;CPSF3;WDR33;PPP2R2D;PAPOLG;MSI2;PPP2CA;ETFI;PPP2R5E;PABPC3
Cancer: specific types	hsa05213	Endometrial cancer	24/1557	6,44E+09	24	CDKN1A;MMP9;FOXO1;CCNA2;POLK;TAF15;SP1;HMGA2;MITF;WT1;IGFBP3;BMI1;BAX;PPARG;BMP2K;PLAU;BCL2L1;ATM;CCNT2;CDKN2C;DUSP6;ETV1;FLT1;FUS;FUT8;HDAC1;HDAC2;HOXA9;IGF1R;JUP;MDM2;MEF2C;KMT2A;NGFR;PBX3;RARA;REL;SS18;TCF3;TFE3;PER2;EWSR1;AFF1;NCOR1;TSPAN7;DOT1L;ZBTB17;CXCL8;NSD2;H3-5;H3C13
NA	hsa04820	Cytoskeleton in muscle cells	64/1557	0.0001	64	RB1;CDKN1A;CCNA2;MAPK1;PIK3R3;HDAC3;GTF2H1;CDK6;KRAS;PIK3R1;RHOA;BAX;JAK1;YWHAZ;HRAS;ACTN4;C3;CHEK1;ATF2;CREBBP;DDB1;DDX3X;EP300;GRB2;GTF2A1;HDAC1;HDAC2;IL6ST;MDM2;NFKBIA;PIK3CA;PIK3CB;PKM;MAPK3;PXN;REL;SKP2;STAT5B;TRAF3;YWHAG;YWHAH;USP7;ATP6V0D1;MAPKAPK2;CREB3;YWHQA;UBR4;VDAC3;SCRIB;H2BC18
Cancer: specific types	hsa05214	Glioma	28/1557	0.0001	28	THBS1;CDKN1A;EGFR;RAF1;WNT3A;MMP9;SMAD2;HBEGF;FGF2;MAPK1;FZD6;PIK3R3;KRAS;SDC4;PDCD4;VEGFA;COL1A1;COL1A2;TGFB2;IQGAP1;PIK3R1;RHOA;HIF1A;AKT2;HRAS;PLAU;RDX;AKT3;ANK2;WNT10B;ACTG1;CAMK2D;CD63;CTNNB1;FLNA;FN1;GRB2;IGF1R;ITGAV;ITGB1;MDM2;PPP1R12A;PIK3CA;PIK3CB;PPP1CB;PPP1CC;MAPK3;PTPN11;PXN;RPS6;SOS2;FZD5;FZD3;FZD1;FRS2;RRAS2;ARHGEF12;DROSHA;ANK3;SDC2;CBL;SOS1
Endocrine system	hsa04935	Growth hormone synthesis, secretion and action	39/1557	0.0001	39	THBS1;ZEB2;CDKN1A;SOX4;EGFR;SIRT1;RAF1;PTGS2;WNT3A;STMN1;MMP9;CRK;MAPK1;PIK3R3;PTEN;BCL2;E2F3;CDK6;KRAS;PDCD4;VEGFA;SLC7A1;BMP2;CDC25A;IRS1;DNMT3A;IKBKB;HMGA2;EFNA3;CCNG1;TGFB2;KIF23;UBE2I;PIK3R1;NOTCH3;NOTCH2;RHOA;BCL2L1;DICER1;BCL2L2;BRCA1;VIM;BMI1;RPTOR;CDC25B;DDIT4;DNMT1;HRAS;E2F2;PLAU;STI4;RDX;FOXP1;ATM;CREBBP;EFNA1;EP300;GLS;GRB2;HDAC1;HDAC2;MDM2;MDM4;PIK3CA;PIK3CB;MAPK3;SOS2;FZD3;RPS6KA5;TNR;SOS1;MARKS;MCL1
Infectious disease: viral	hsa05160	Hepatitis C	47/1557	0.0001	47	RB1;EGFR;RAF1;FGF2;KPNA1;MAPK1;FGF22;PIK3R3;BCL2;KRAS;VEGFA;CDC25A;ADCY6;HSP90B1;PIK3R1;NOTCH2;AKT2;JAG1;FOS;GNAI2;HRAS;AKT3;ADCY3;ADCY7;ADCY9;XIAP;BIRC5;ARNT;CHRNA7;ATF2;GNAS;GRB2;HSP90AA1;KPNA5;MGST3;PGR;PIK3CA;PIK3CB;MAPK3;RPS6KA3;SOS2;STAT5B;CREB3;KPNA6;CACNA1A;ADCY5;KPNB1;SOS1
Cell growth and death	hsa04210	Apoptosis	42/1557	0.0001	42	EGFR;RAF1;CYP2E1;MAPK1;VDAC2;PIK3R3;COX8C;NDUFB10;PTEN;KRAS;VEGFA;IKBKB;PIK3R1;PRKD2;HIF1A;AKT2;FOS;HRAS;AKT3;ABL2;ARNT;CHUK;GRB2;MGST3;NDUFA9;NFE2L2;NFKBIA;PIK3CA;PIK3CB;PLD1;MAPK3;MAPK8;PTPN11;PTPRJ;SDHC;MAP2K4;SOS2;UQCRC2;KEAP1;UQCRCQ;SLC25A31;NDUFA13;VDAC3;SLC25A4;SLC25A5;UQCRCU;UQCRC1;VDAC1;SDHA;SOS1;MAP3K5;UQCRCF1;NDUFV1;ATP5F1A;ATP5MC2;ATP5PF;ATP5F1B;ATP5F1D;SOD2
Signal transduction	hsa04010	MAPK signaling pathway	77/1557	0.0001	77	EGFR;RAF1;MAPK1;PIK3R3;SLC2A1;PTEN;KRAS;PIK3R1;HIF1A;AKT2;HRAS;AKT3;GLS;IDH1;PDHA1;PIK3CA;PIK3CB;PKM;MAPK3;SLC7A5;PFKL

Cancer: specific types	hsa05219	Bladder cancer	18/1557	0.0002	18	EGFR;RAF1;MAPK1;PI3K1A;PLA2G4C;PIK3R3;KRAS;SP1;PIK3R1;HIF1A;AKT2;FOS;HRAS;AKT3;GRB2;PIK3CA;PIK3CB;PLD1;MAPK3;MAPK8;SOS2;TSC1;WASF1;DGKI;DGKH;DGKE;SOS1;LYPLA1
Endocrine system	hsa04915	Estrogen signaling pathway	42/1557	0.0002	42	EML4;EGFR;RAF1;MAP3K3;ALK;MAPK1;PIK3R3;PTEN;KRAS;IKBKB;PIK3R1;TRAF6;HIF1A;AKT2;JAK1;FOS;HRAS;PPP3CA;AKT3;CHUK;CSNK2A2;IFNGR2;MYD88;NFKBIA;PIK3CA;PIK3CB;PPP3R1;MAPK3;MAP2K3;PTPN11;BATF;TICAM1;CD3G;PPP3CB
Signal transduction	hsa04151	PI3K-Akt signaling pathway	89/1557	0.0002	89	CDKN1A;EGFR;RAF1;SMAD2;GSK3B;MAPK1;POLK;PIK3R3;BCL2;KRAS;TGFB2;MSH2;PIK3R1;RHOA;BCL2L1;BAX;AKT2;FOS;HRAS;AKT3;BBC3;BIRC5;CTNNB1;DCC;EREG;GRB2;MSH6;SMAD4;MSH3;PIK3CA;PIK3CB;MAPK3;MAPK8;SOS2;APPL1;SOS1
Cancer: specific types	hsa05226	Gastric cancer	44/1557	0.0003	44	CDKN1A;RAF1;CRK;MAPK1;PIK3R3;SLC2A1;ELOC;KRAS;VEGFA;TGFB2;PIK3R1;HIF1A;AKT2;HRAS;AKT3;ARNT;CREBBP;EP300;GRB2;RAPGEF1;PAK2;PIK3CA;PIK3CB;MAPK3;PTPN11;RAP1A;SOS2;TFE3;EGLN1;SOS1
Cancer: specific types	hsa05218	Melanoma	26/1557	0.0003	26	RB1;CDKN1A;EGFR;RAF1;SMAD2;MAPK1;POLK;PIK3R3;E2F3;CDK6;KRAS;VEGFA;IKBKB;TGFB2;PIK3R1;BAX;AKT2;JAK1;E2F2;AKT3;BCL2L1;CHUK;SMAD4;PIK3CA;PIK3CB;PLD1;MAPK3;MAPK8;RAD51
Signal transduction	hsa04066	HIF-1 signaling pathway	34/1557	0.0007	34	CDKN1A;EGFR;RAF1;GSK3B;MAPK1;POLK;PIK3R3;PTEN;KRAS;PIK3R1;BAX;AKT2;CDH1;HRAS;AKT3;CTNNA1;CTNNB1;GRB2;PIK3CA;PIK3CB;MAPK3;SOS2;CTNNA2;SOS1
Development and regeneration	hsa04360	Axon guidance	50/1557	0.0008	50	RB1;CDKN1A;EGFR;RAF1;MAPK1;POLK;PIK3R3;PTEN;E2F3;CDK6;KRAS;PIK3R1;BAX;AKT2;HRAS;E2F2;AKT3;CALM1;CAMK2D;GRB2;IGF1R;MDM2;PIK3CA;PIK3CB;MAPK3;SOS2;SHC3;SOS1
Cellular community - eukaryotes	hsa04530	Tight junction	47/1557	0.0008	47	RB1;CDKN1A;EGFR;RAF1;MMP9;FOXO1;GSK3B;MAPK1;PIK3R3;PTEN;BCL2;E2F3;KRAS;IKBKB;HSP90B1;PIK3R1;AKT2;HRAS;E2F2;PLAU;AKT3;CHUK;CREBBP;CTNNB1;EP300;GRB2;HSP90AA1;IGF1R;MDM2;NFKBIA;PIK3CA;PIK3CB;MAPK3;SOS2;CREB3;SOS1
Endocrine system	hsa04910	Insulin signaling pathway	40/1557	0.0008	40	RB1;CDKN1A;EGFR;RAF1;FGF2;MAPK1;FGF22;POLK;PIK3R3;PTEN;E2F3;CDK6;KRAS;MITF;PIK3R1;BAX;AKT2;CDH1;HRAS;E2F2;AKT3;IGF1R;MDM2;PIK3CA;PIK3CB;MAPK3
Cancer: overview	hsa05208	Chemical carcinogenesis - reactive oxygen species	59/1557	0.0008	59	THBS1;RB1;CDKN1A;EGFR;RAF1;MMP9;HBEGF;MAPK1;E2F3;KRAS;VEGFA;CDH1;HRAS;E2F2;MDM2;MAPK3;RPS6KA5;CXCL8
Translation	hsa03015	mRNA surveillance pathway	32/1557	0.0009	32	RB1;CDKN1A;RAF1;CRK;MAPK1;POLK;PIK3R3;E2F3;CDK6;KRAS;IKBKB;TGFB2;PIK3R1;BAX;AKT2;HRAS;E2F2;AKT3;BCL2L1;CHUK;CTBP1;GRB2;HDAC1;HDAC2;SMAD4;MDM2;NFKBIA;PIK3CA;PIK3CB;MAPK3;PTPN11;SOS2;STAT5B;SHC3;CBL;SOS1
Infectious disease: parasitic	hsa05142	Chagas disease	32/1557	0.0009	32	RAF1;CCNA2;MAPK1;PIK3R3;KRAS;IKBKB;PIK3R1;AKT2;HRAS;AKT3;CHUK;DUSP6;GRB2;JUP;PIK3CA;PIK3CB;MAPK3;RARA;SOS2;STAT5B;PER2;SOS1
Signal transduction	hsa04012	ErbB signaling pathway	28/1557	0.0009	28	RB1;CDKN1A;PTGS2;POLK;PIK3R3;PTEN;LAMC2;BCL2;E2F3;CDK6;APAF1;IKBKB;PIK3R1;TRAF6;BAX;AKT2;E2F2;AKT3;BCL2L1;XIAP;CHUK;FN1;ITGAV;ITGB1;LAMB1;NFKBIA;PIK3CA;PIK3CB;SKP2;TRAF3;LAMA1;ZBTB17;LAMB2
Endocrine system	hsa04926	Relaxin signaling pathway	38/1557	0.001	38	RB1;EML4;CDKN1A;EGFR;RAF1;ALK;MAPK1;POLK;PIK3R3;E2F3;CDK6;KRAS;STK4;PIK3R1;BAX;AKT2;HRAS;E2F2;AKT3;GRB2;KIF5B;KIF5C;PIK3CA;PIK3CB;MAPK3;SOS2;STAT5B;SOS1
Folding, sorting and degradation	hsa03018	RNA degradation	26/1557	0.001	26	RB1;CDKN1A;EGFR;RAF1;WNT3A;FGF2;GSK3B;MAPK1;FZD6;FGF22;POLK;PIK3R3;PTEN;NCOA3;E2F3;CDK6;KRAS;SP1;PIK3R1;NOTCH3;NOTCH2;BRCA1;BAX;AKT2;JAG1;FOS;HRAS;E2F2;AKT3;WNT10B;CSNK1A1;CTNNB1;DVL3;GRB2;IGF1R;LRP6;LRP5;SMAD4;MGST3;NFE2L2;PIK3CA;PIK3CB;MAPK3;SMARCA4;SMARCB1;SMARCC2;SMARCD1;SMARCD2;SOS2;FZD5;FZD3;ARID1A;FZD1;KEAP1;SHC3;SOS1
Environmental adaptation	hsa04714	Thermogenesis	60/1557	0.001	60	RB1;CDKN1A;EGFR;RAF1;WNT3A;SMAD2;GSK3B;MAPK1;FZD6;POLK;ARID2;PIK3R3;PTEN;E2F3;CDK6;KRAS;TGFB2;PIK3R1;BAX;AKT2;HRAS;E2F2;AKT3;BCL2L1;WNT10B;ACTG1;CSNK1A1;CTNNB1;DVL3;GRB2;IGF1R;LRP6;LRP5;SMAD4;MGST3;NFE2L2;PIK3CA;PIK3CB;MAPK3;SMARCA4;SMARCB1;SMARCC2;SMARCD1;SMARCD2;SOS2;FZD5;FZD3;ARID1A;FZD1;KEAP1;SHC3;SOS1
Cardiovascular disease	hsa05417	Lipid and atherosclerosis	56/1557	0.001	56	RB1;CDKN1A;EGFR;RAF1;WNT3A;SMAD2;FGF2;GSK3B;MAPK1;FZD6;FGF22;POLK;PIK3R3;BCL2;E2F3;KRAS;TGFB2;PIK3R1;BAX;AKT2;CDH1;HRAS;E2F2;AKT3;WNT10B;CSNK1A1;CTNNA1;CTNNB1;DVL3;GRB2;JUP;LRP6;LRP5;SMAD4;PIK3CA;PIK3CB;MAPK3;SOS2;FZD5;FZD3;FZD1;SHC3;CTNNA2;SOS1
Transport and catabolism	hsa04137	Mitophagy - animal	32/1557	0.001	32	MMP9;SMAD2;GSK3B;VDAC2;PIK3R3;SLC2A1;COX8C;NDUFB10;PTEN;SP1;IRS1;COL1A1;COL1A2;TGFB2;PIK3R1;AKT2;AKT3;ATP2A2;CAMK2D;CPRT2;INSR;NDUFA9;PDHA1;PIK3CA;PIK3CB;PPP1CB;PPP1CC;MAPK8;SDHC;UQCRC2;TBC1D4;UQCRCQ;SLC25A31;NDUFA13;CYBB;VDAC3;SLC25A4;SLC25A5;UQCRCB;UQCRC1;VDAC1;SDHA;UQCRCF1;NDUFV1;PTPA;ATP5F1A;ATP5MC2;ATP5PF;ATP5F1B;ATP5F1D
Signal transduction	hsa04015	Rap1 signaling pathway	55/1557	0.001	55	CASP7;IRAK1;MMP9;LDLR;GSK3B;HSPA1B;MAPK1;IRAK4;PIK3R3;BCL2;HSPD1;KRAS;APAF1;IKBKB;HSP90B1;PIK3R1;RHOA;TRAF6;BAX;AKT2;FOS;PPARG;HRAS;PPP3CA;XBP1;AKT3;BCL2L1;CALM1;CAMK2D;CHUK;HSPA4;HSPA5;HSP90AA1;MYD88;NFE2L2;NFKBIA;OLR1;PIK3CA;PIK3CB;PPP3

						R1;MAPK3;MAPK8;MAP2K3;RAP1A;MAP2K4;TRAF3;VLDLR;TICAM1;CYBB;PPP3CB;TANK;MAP3K5;HSPA8;LY96;CXCL8;SOD2
Infectious disease: bacterial	hsa05135	Yersinia infection	39/1557	0.001	39	MMP9;MEF2A;PIK3R3;BCL2;SDC4;VEGFA;BMP2;IKBKB;HSP90B1;PIK3R1;RHOA;AKT2;FOS;AKT3;ACTG1;ACVR1;ACVR2A;ACVR2B;CALM1;CHUK;CTNNB1;HSP90AA1;ITGAV;MEF2C;MGST3;NFE2L2;PIK3CA;PIK3CB;PRKAA1;MAPK8;MAP2K4;ARHGEF2;KEAP1;TXN2;SDC2;MAP3K5
Cell growth and death	hsa04114	Oocyte meiosis	39/1557	0.001	39	EGFR;RAF1;FGF2;GSK3B;MAPK1;PIK3R3;PTEN;BCL2;KRAS;AXL;VEGFA;IL6R;PIK3R1;BCL2L11;BAX;AKT2;JAK1;HRAS;AKT3;BCL2L1;GRB2;IGF1R;NF1;PIK3CA;PIK3CB;MAPK3;RPS6;SOS2;SHC3;SOS1
Signal transduction	hsa04072	Phospholipase D signaling pathway	41/1557	0.002	41	RB1;CDKN1A;EGFR;RAF1;MMP9;HBEGF;MAPK1;PIK3R3;BCL2;NCOA3;E2F3;KRAS;SP1;ADCY6;PIK3R1;NOTCH3;NOTCH2;BAX;AKT2;JAG1;FOS;HRAS;E2F2;AKT3;ADCY3;ADCY7;ADCY9;CDKN2C;GNAS;GRB2;IGF1R;MDM2;PIK3CA;PIK3CB;MAPK3;MAPK8;SOS2;SHC3;NCOR1;ADCY5;SOS1
Neurodegenerative disease	hsa05016	Huntington disease	74/1557	0.002	74	CDKN1A;MAPK1;PIK3R3;BCL2;APAF1;MSH2;PIK3R1;BRCA1;BAX;AKT2;AKT3;BCL2L1;ATM;BBC3;XIAP;BIRC5;ATP7A;SLC31A1;MSH6;MDM2;MGST3;MSH3;PIK3CA;PIK3CB;MAPK3;REV3L;TOP2A;TOP2B;ERCC1;MAP3K5;POLH
Signal transduction	hsa04152	AMPK signaling pathway	35/1557	0.002	35	FOXO1;GSK3B;PIK3R3;SLC2A1;PTEN;IRS1;IKBKB;PIK3R1;AKT2;AKT3;INSR;NFKBIA;PIK3CA;PIK3CB;PPP1CB;PPP1CC;PPP1R3C;PRKAA1;PRKAB2;MAPK8;PTPN11;PYGB;RPS6KA3;SREBF1;TBC1D4;CREB3;MLXIP;PRKAG2;OGT;CRTC2;PTPA;OGA
Infectious disease: bacterial	hsa05100	Bacterial invasion of epithelial cells	25/1557	0.002	25	CASP7;CYP2E1;GSK3B;PIK3R3;COX8C;NDUFB10;IL6R;IRS1;IKBKB;PIK3R1;BCL2L11;BAX;AKT2;FOS;PPARG;XBP1;AKT3;INSR;NDUFA9;PIK3CA;PIK3CB;PRKAA1;PRKAB2;MAPK8;SDHC;SREBF1;UQCRC2;MLXIP;UQCRCQ;ADIPOR2;NDUFA13;PRKAG2;UQCRCB;UQCRC1;SDHA;MAP3K5;UQCRCF1;NDUFV1;CXCL8
Cell motility	hsa04810	Regulation of actin cytoskeleton	58/1557	0.002	58	FOXO1;SMAD2;MAPK1;PIK3R3;BCL2;KRAS;VEGFA;COL1A1;COL1A2;TGFB2;PIK3R1;BAX;AKT2;HRAS;AKT3;DIAPH1;FN1;SMAD4;SERPINE1;PIK3CA;PIK3CB;MAPK3;MAPK8;STAT5B;PLCD3;CYBB;CXCL8
Endocrine and metabolic disease	hsa04931	Insulin resistance	32/1557	0.002	32	RB1;CDKN1A;EGFR;WNT3A;LDLR;GSK3B;MAPK1;FZD6;USP8;E2F3;CDK6;SP1;ADCY6;GNAI2;E2F2;WNT10B;ADCY3;ADCY7;ADCY9;ARNT;CAMK2D;SCARB1;CDKN2C;ATF2;CTNNB1;DVL3;GNAS;KMT2A;MAPK3;RAP1A;RBBP5;FZD5;FZD3;KMT2D;FZD1;ASH2L;CREB3;ARMC5;ADCY5
Signal transduction	hsa04022	cGMP-PKG signaling pathway	44/1557	0.002	44	CRK;ACTR2;PIK3R3;PIK3R1;RHOA;CDH1;ACTG1;CLTC;CTNNA1;CTNNB1;FN1;ITGB1;PIK3CA;PIK3CB;PXN;VCL;WASF1;ARPC3;SHC3;ARPC5L;DNM1;CTNNA2;DOCK1;WASL;CBL
Cell growth and death	hsa04115	p53 signaling pathway	24/1557	0.002	24	CASP7;IRAK1;ARF6;MAPK1;ACTR2;NCKAP1;IRAK4;OCN;TUBA1A;IKBKB;RHOA;TRAF6;BAX;FOS;ACTG1;CHUK;CLDN4;LPAR1;ITGB1;MYD88;MYO1D;MYO1E;MYO5A;MYO6;NFKBIA;PAK2;MAPK3;MAPK8;PTPN11;RAB1A;TMBIM6;WASF1;ARHGEF2;CYTH3;SEC24C;ARPC3;TUBA1B;SEC24B;SEC24A;TMED10;ARHGEF12;ARPC5L;TUBB;ARF1;FCGR2A;WASL;MYH10;WIPF2;RPS3;CXCL8;CYFIP1
Endocrine system	hsa04928	Parathyroid hormone synthesis, secretion and action	33/1557	0.002	33	EGFR;FOXO1;ARF6;GSK3B;MAPK1;ACTR2;TLN2;PIK3R3;FBXW11;BCL2;IKBKB;TLN1;PIK3R1;RHOA;TRAF6;RPTOR;BAX;AKT2;AKT3;BCL2L1;ATM;ACTG1;ACTN4;C3;CAPN2;CHUK;DIAPH1;ITGB1;MDM2;MYD88;NFKBIA;PFN2;PIK3CA;PIK3CB;MAPK3;MAPK8;PXN;UBB;UBE2D1;UBE2D3;UBE2N;UBE2V1;UBE2V2;VCL;RIPK2;WASF1;ARHGEF2;RPS6KA5;CYTH3;ARPC3;FBNP1;MAP1LC3B;ARPC5L;TIFA;PLCD3;ARF1;FBNP1L;WIP2;DOCK1;VDAC1;WASL;SKP1;SHARPIN;CXCL8;SEPTIN7;H3-5;H3C13
Endocrine system	hsa04912	GnRH signaling pathway	28/1557	0.003	28	CASP7;IRAK1;RAF1;ANXA2;ARF6;KPN1A;MAPK1;RAB5B;ACTR2;EXOC5;NCKAP1;IRAK4;BCL2;TUBA1A;IKBKB;HSP90B1;RHOA;TRAF6;BAX;AKT2;FOS;HRAS;AKT3;ACTG1;CHUK;CTNNB1;DYNC1H1;DYNC1L1;DYNC1L2;FNLNA;HSP90AA1;KIF5B;KIF5C;KLC1;M6PR;MYD88;MYO6;NFKBIA;PFN2;PIK3CA;PIK3CB;MAPK3;MAPK8;MAP2K3;RAB5C;MAP2K4;RIPK2;CYTH3;ARPC3;TUBA1B;DCTN6;PLEKHM2;TXN2;VPS33A;AHNAK;DYNC2H1;ARPC5L;TUBB;ARF1;DCTN1;WASL;PIK3C2G;DCTN2;DYNLT1;SKP1;RPS3;LY96;DYNLL2;CXCL8;CYFIP1
Cancer: overview	hsa05202	Transcriptional misregulation in cancer	51/1557	0.003	51	IRAK1;ARF6;CRK;GSK3B;MAPK1;PIP5K1A;ACTR2;IRAK4;PIK3R3;IKBKB;PIK3R1;RHOA;TRAF6;AKT2;FOS;AKT3;ACTG1;CHUK;FN1;ITGB1;MYD88;NFKBIA;PIK3CA;PIK3CB;MAPK3;MAPK8;MAP2K3;PXN;RPS6KA3;MAP2K4;ARPC3;ARHGEF12;ARPC5L;TICAM1;FCGR2A;DOCK1;WASL;WIPF2;CXCL8
Infectious disease: viral	hsa05163	Human cytomegalovirus infection	56/1557	0.003	56	IRAK1;SMAD2;MAPK1;IRAK4;PIK3R3;IKBKB;TGFB2;PIK3R1;TRAF6;AKT2;PPP2R2A;FOS;GNAI2;AKT3;C3;CHUK;GNAS;IFNGR2;MYD88;NFKBIA;SERPINE1;PIK3CA;PIK3CB;PPP2CB;MAPK3;MAPK8;MAP2K4;PPP2R2D;TICAM1;CD3G;PPP2CA;CXCL8
Cancer: specific types	hsa05221	Acute myeloid leukemia	22/1557	0.003	22	IRAK1;LDLR;HSPA1B;MAPK1;IRAK4;LAMC2;BCL2;IKBKB;TGFB2;TRAF6;AKT2;JAK1;GNAI2;AKT3;BCL2L1;XIAP;CHUK;IFNGR2;ITGB1;LAMB1;MYD88;NFKBIA;MAPK3;MAPK8;MAP2K3;LAMA1;HSPA8;LY96;LAMB2
Infectious disease: bacterial	hsa05130	Pathogenic Escherichia coli infection	51/1557	0.003	51	RB1;CDKN1A;EGFR;RAF1;LDLR;GSK3B;OAS2;MAPK1;PIK3R3;OCN;E2F3;CDK6;KRAS;APAF1;IKBKB;PIK3R1;TRAF6;BAX;AKT2;PPP2R2A;JAK1;YWHAZ;HRAS;E2F2;AKT3;SCARB1;CHUK;CLDN4;CTNNB1;GRB2;NFKBIA;PIK3CA;PIK3CB;PPP2CB;MAPK3;SOS2;TRAF3;YWHAG;YWHAH;PSME3;YWHAQ;PPP2R2D;TICAM1;EIF2AK4;PPP2CA;SOS1;OAS3

Cell growth and death	hsa04215	Apoptosis - multiple species	13/1557	0.003	13	RB1;CDKN1A;IRAK1;RAF1;MMP9;CCNA2;MAPK1;IRAK4;PIK3R3;BCL2;E2F3;KRAS;APAF1;IKBKB;TGFB2;PIK3R1;TRAF6;BAX;AKT2;JAK1;FOS;YWHAZ;HRAS;E2F2;AKT3;BIRC5;CHUK;ATF2;CREBBP;DDI1;DDX3X;EP300;GRB2;SMAD4;MAP3K1;MYD88;NFKBIA;PIK3CA;PIK3CB;MAPK3;MAPK8;MAP2K3;MAP2K4;SOS2;STAT5B;TRAF3;CREB3;YWHAQ;TICAM1;VDAC3;SOS1;CXCL8
Endocrine system	hsa04914	Progesterone-mediated oocyte maturation	31/1557	0.006	31	IRAK1;GSK3B;HSPA1B;OAS2;IRAK4;PIK3R3;RACK1;BCL2;CDK6;ADAR;APAF1;IKBKB;PIK3R1;TRAF6;BAX;AKT2;JAK1;FOS;AKT3;BCL2L1;BBC3;CHUK;CSNK2A2;MYD88;NFKBIA;PIK3CA;PIK3CB;MAPK8;STAT5B;TRAF3;CD3G;EIF2AK4;OAS3;HSPA8
Neurodegenerative disease	hsa05020	Prion disease	65/1557	0.006	65	RB1;CDKN1A;EGFR;RAF1;PTGS2;CRK;GNB1;GSK3B;MAPK1;PIK3R3;E2F3;CDK6;KRAS;VEGFA;IL6R;SP1;IKBKB;ADCY6;PIK3R1;RHOA;BAX;AKT2;JAK1;GNAI2;HRAS;PPP3CA;E2F2;AKT3;ADCY3;ADCY7;ADCY9;CALM1;CHUK;ATF2;CTNNB1;GNAS;GNB3;GRB2;PDIA3;ITGAV;MDM2;NFKBIA;PIK3CA;PIK3CB;PPP3R1;MAPK3;PXN;SOS2;TSC1;CREB3;AKAP13;ARHGFE12;PPP3CB;ADCY5;SOS1;CXCL8
Signal transduction	hsa04014	Ras signaling pathway	57/1557	0.006	57	THBS1;RB1;ATP6V0E1;CDKN1A;EGFR;RAF1;PTGS2;WNT3A;FOXO1;CCNA2;GSK3B;LFNG;MAPK1;FZD6;PIK3R3;PTEN;LAMC2;CDK6;KRAS;VEGFA;COL1A1;COL1A2;IKBKB;PIK3R1;NOTCH3;NOTCH2;BAX;AKT2;ITGB4;PPP2R2A;JAG1;JAK1;HRAS;AKT3;ATM;WNT10B;ATP6V1A;ATP6V1E1;CHUK;COL6A2;CREBBP;CSNK1A1;CTNNB1;DLG2;DVL3;EP300;FNI1;GNAS;GRB2;HDAC1;HDAC2;ITGAV;ITGB1;ITGB8;LAMB1;LLGL2;MDM2;PIK3CA;PIK3CB;PKM;PPP2CB;PPP2R5A;MAPK3;PXN;SOS2;TRAF3;TSC1;FZD5;FZD3;FZD1;ATP6V0D1;MAGI1;ATP6V1G1;MAML1;CREB3;UBR4;PPP2R2D;CRB3;COL6A6;TICAM1;LAMA1;HES4;NFX1;PPP2CA;TNF;SOS1;PPP2R5E;SCRIB;BCAP31;LAMB2;PATJ;PALS1
Endocrine system	hsa04917	Prolactin signaling pathway	22/1557	0.006	22	RB1;CDKN1A;CCNA2;SMAD2;MAP3K3;MAPK1;VDAC2;TLN2;CRTCI;PIK3R3;SLC2A1;PTEN;E2F3;KRAS;IKBKB;ADCY6;TGFB2;TLN1;PIK3R1;BAX;AKT2;JAK1;FOS;HRAS;PPP3CA;E2F2;AKT3;BCL2L1;ATM;ADCY3;ADCY7;ADCY9;XIAP;BUB1B;CDKN2C;CHEK1;CHUK;ATF2;CREBBP;EP300;SMAD4;MAP3K1;NFKBIA;PIK3CA;PIK3CB;PPP3R1;MAPK3;MAPK8;MAP2K4;STAT5B;TCF3;XPO1;TRRAP;NRP1;BUB3;ESPL1;CREB3;ANAPC7;CRTC3;SLC25A31;CCNB2;CD3G;VDAC3;PPP3CB;SLC25A4;SLC25A5;ADCY5;KAT5;VDAC1;CRTC2;PTTG1
Cancer: overview	hsa05206	MicroRNAs in cancer	73/1557	0.006	73	RB1;CDKN1A;RAF1;PTGS2;FGF2;GNB1;GSK3B;MAPK1;PIK3R3;E2F3;CDK6;KRAS;VEGFA;IKBKB;PIK3R1;HIF1A;BAX;AKT2;JAK1;FOS;HRAS;PPP3CA;E2F2;AKT3;C3;CALM1;CHUK;CREBBP;CTNNB1;EP300;GNB3;IL6ST;NFKBIA;PIK3CA;PIK3CB;PPP3R1;MAPK3;MAPK8;MAP2K4;TRAF3;UBB;UBC;MAPKAPK2;ATG3;MAP1LC3B;TICAM1;PPP3CB;CXCL8
Glycan biosynthesis and metabolism	hsa00563	Glycosylphosphatidylinositol (GPI)-anchor biosynthesis	12/1557	0.006	12	RB1;CDKN1A;IRAK1;CCNA2;CR2;OAS2;PSMD12;IRAK4;POLK;PIK3R3;BCL2;E2F3;CDK6;APAF1;IKBKB;PIK3R1;TRAF6;BCL2L1;VIM;BAX;AKT2;JAK1;E2F2;AKT3;CHUK;PDIA3;HDAC1;HDAC2;MDM2;MYD88;NEDD4;NFKBIA;PIK3CA;PIK3CB;MAPK8;MAP2K3;PSMC4;PSMD1;PSMD11;MAP2K4;SKP2;TRAF3;USP7;NCOR2;SAP30L;CD3G;PSMD3;OAS3;PSMC5;SEM1
Infectious disease: viral	hsa05169	Epstein-Barr virus infection	50/1557	0.007	50	IRAK1;RAF1;CCNB1;CRK;GNB1;MAPK1;IRAK4;PIK3R3;ELOC;FBXW11;BCL2;KRAS;CFL2;IKBKB;PIK3R1;TRAF6;BAX;AKT2;FOS;GNAI2;HRAS;PPP3CA;AKT3;BCL2L1;ATM;APIG1;CALM1;CHEK1;CHUK;DDI1;GNB3;PDIA3;MYD88;NFKBIA;PAK2;PIK3CA;PIK3CB;PPP3R1;MAPK3;MAPK8;MAP2K3;PXN;WEE1;CUL4B;CUL4A;APOBEC3C;CCNB2;CD3G;PPP3CB;SKP1;DCAF1
Chromosome	hsa03082	ATP-dependent chromatin remodeling	32/1557	0.007	32	CASP7;RAF1;PTGS2;WNT3A;GSK3B;MAPK1;PSMA2;PSMD12;VDAC2;FZD6;RTN4;PIK3R3;COX8C;NDUFB10;TUBA1A;KRAS;BACE1;APAF1;IRS1;IKBKB;PIK3R1;APP;AKT2;HRAS;PPP3CA;XBP1;AKT3;WNT10B;ATP2A2;CALM1;CAPN2;CHRNA7;CHUK;CSNK1A1;CSNK2A2;CTNNB1;DVL3;GRIN2D;INSR;KIF5B;KIF5C;KLC1;LRP6;LRP5;MAPT;NDUFA9;SLC11A2;PIK3CA;PIK3CB;PPP3R1;MAPK3;MAPK8;PSMB5;PSMC4;PSMD1;PSMD11;RYR3;SDHC;UQCRC2;FZD5;FZD3;FZD1;CDK5R1;ULK2;RB1CC1;RTN3;TUBA1B;SLC39A14;UQCRCQ;SLC39A1;ATG2B;SLC39A9;SLC25A31;TUBB;NDUFA13;CYBB;WIP1;VDAC3;PPP3CB;ATG13;SLC25A4;SLC25A5;PSMA5;UQCRCB;PSMA1;PSMB2;PSMD3;UQCRC1;VDAC1;SDHA;MAP3K5;UQCRCF1;NDUFB1;PSMC5;SEM1;ATP5F1A;ATP5MC2;ATP5PF;ATP5F1B;ATP5F1D
Cell growth and death	hsa04216	Ferroptosis	15/1557	0.007	15	PSMA2;PSMD12;VDAC2;COX8C;NDUFB10;TUBA1A;APAF1;BAX;GNAI2;XBP1;BCL2L1;CALM1;CAMK2D;GNAS;GPR37;HSPA5;KIF5B;KIF5C;KLC1;MAPT;NDUFA9;NFE2L2;SLC11A2;MAPK8;PSMB5;PSMC4;PSMD1;PSMD11;RYR3;SDHC;UBB;UBC;UBE2G1;UBE2L3;UQCRC2;KEAP1;MFN2;TRAP1;TUBA1B;SLC39A14;TXN2;UQCRCQ;SLC39A1;SLC39A9;SLC25A31;UBE2J2;TUBB;NDUFA13;VDAC3;SLC25A4;SLC25A5;ADCY5;PSMA5;UQCRCB;PSMA1;PSMB2;PSMD3;UBA1;UQCRC1;VDAC1;SDHA;MAP3K5;UQCRCF1;MFN1;NDUFB1;PSMC5;SEM1;ATP5F1A;ATP5MC2;ATP5PF;SEPTIN5;DAXX;ATP5F1B;ATP5F1D
Immune system	hsa04660	T cell receptor signaling pathway	33/1557	0.007	33	PSMA2;PSMD12;NUP50;COX8C;NDUFB10;BCL2;TUBA1A;GRIA2;APAF1;MAP3K3;BAX;PPP3CA;XBP1;ANXA11;BCL2L1;ACTG1;ANXA7;FUS;GRIN2D;HNRNPA2B1;HSPA5;KIF5B;KIF5C;KLC1;NDUFA9;NUP98;PFN2;PPP3R1;MAP2K3;PSMB5;PSMC4;PSMD1;PSMD11;RAB1A;SDHC;TPR;UQCRC2;VCP;NUP14;RAE1;NUP155;ULK2;RB1CC1;FIG4;NUP153;TUBA1B;DCTN6;ATXN2L;SETX;TARDBP;UQCRCQ;UBQLN2;UBQLN1;ATG2B;NDC1;NUP107;DERL1;SPG11;MAP1LC3B;TUBB;HNRNPA3;NDUFA13;WIP1;DCTN1;PPP3CB;ATG13;TANK;PSMA5;UQCRCB;NUP88;PSMA1;PSMB2;PSMD3;UQCRC1;VDAC1;SDH

						A;MAP3K5;UQCRFS1;RANBP2;DCTN2;NUP205;NUP188;CHCHD10;NDUFV1;PSMC5;NUP58;POM121C;SEM1;ATP5F1A;ATP5MC2;ATP5PF;DAXX;ATP5F1B;ATP5F1D
Cancer: overview	hsa05231	Choline metabolism in cancer	28/1557	0.007	28	BDNF;PSMA2;PSMD12;VDAC2;COX8C;NDUFB10;TUBA1A;GRIA2;APAF1;SP1;RCOR1;BAX;PPARG;AP2M1;BBC3;AP2B1;CLTC;CREBBP;EP300;HTT;HDAC1;HDAC2;KIF5B;KIF5C;KLC1;NDUFA9;POLR2A;MAPK8;PSMB5;PSMC4;PSMD1;PSMD11;SDHC;SLC1A3;STX1A;TAF4;UQCRC2;ULK2;RB1CC1;TUBA1B;CREB3;DCTN6;UQCRCQ;ATG2B;SLC25A31;TUBB;NDUFA13;WIPI2;DCTN1;VDAC3;ATG13;SLC25A4;SLC25A5;PSMA5;UQCRB;HIP1;PSMA1;PSMB2;PSMD3;UQCRC1;VDAC1;SDHA;MAP3K5;UQCRFS1;DCTN2;NDUFV1;PSMC5;SEM1;ATP5F1A;ATP5MC2;ATP5PF;ATP5F1B;ATP5F1D;SOD2
Cancer: overview	hsa05203	Viral carcinogenesis	50/1557	0.007	50	PSMA2;PSMD12;VDAC2;PIK3R3;GRIA2;SP1;PIK3R1;ATXN1;AKT2;XBP1;AKT3;ATP2A2;GRIN2D;NFYA;OPA1;PIK3CA;PIK3CB;MAPK8;PSMB5;PSMC4;PSMD1;PSMD11;RORA;VLDLR;PUM1;ULK2;RB1CC1;NOP56;ATXN2L;PUM2;ATG2B;SLC25A31;CACNA1A;WIPI2;VDAC3;ATXN1L;ATG13;SLC25A4;SLC25A5;PSMA5;KAT5;PSMA1;PSMB2;PSMD3;VDAC1;MAP3K5;DAB1;PSMC5;SEM1
Cardiovascular disease	hsa05415	Diabetic cardiomyopathy	50/1557	0.007	50	GSK3B;HSPA1B;MAPK1;PSMA2;PSMD12;VDAC2;PIK3R3;COX8C;NDUFB10;TUBA1A;APAF1;PIK3R1;BAX;PPP3CA;ATF2;CSNK2A2;GRIN2D;HSPA5;KIF5B;KIF5C;KLC1;NCAM2;NDUFA9;PIK3CA;PIK3CB;PPP3R1;MAPK3;MAPK8;PSMB5;PSMC4;PSMD1;PSMD11;RYP3;SDHC;UQCRC2;TUBA1B;CREB3;STIP1;UQCRCQ;SLC25A31;TUBB;NDUFA13;CYBB;VDAC3;PPP3CB;SLC25A4;SLC25A5;PSMA5;UQCRB;PSMA1;PSMB2;PSMD3;UQCRC1;VDAC1;SDHA;UQCRFS1;HSPA8;NDUFV1;PSMC5;SEM1;ATP5F1A;ATP5MC2;ATP5PF;ATP5F1B;ATP5F1D
Infectious disease: viral	hsa05167	Kaposi sarcoma-associated herpesvirus infection	48/1557	0.008	48	BDNF;CASP7;RAF1;PTGS2;WNT3A;GSK3B;MAPK1;PSMA2;PSMD12;VDAC2;FZD6;COX8C;NDUFB10;BCL2;TUBA1A;KRAS;GRIA2;APAF1;ATXN1;APP;BAX;HRAS;PPP3CA;XBP1;BCL2L1;WNT10B;ATP2A2;CALM1;CAMK2D;CAPN2;CHRNA7;CSNK1A1;CSNK2A2;CTNNB1;DVL3;FUS;GPR37;GRIN2D;HTT;HSPA5;KIF5B;KIF5C;KLC1;LRP6;LRP5;MAPT;NDUFA9;PPP3R1;MAPK3;MAPK8;MAP2K3;PSMB5;PSMC4;PSMD1;PSMD11;RAB1A;RYP3;SDHC;STX1A;UBB;UBC;UBE2G1;UBE2L3;UQCRC2;VCP;FZD5;FZD3;FZD1;CDK5R1;ULK2;RB1CC1;FIG4;MFN2;TRAP1;TUBA1B;DCTN6;ATXN2L;TARDBP;UQCRCQ;ZFYVE1;ATG2B;DERL1;SPG11;MAP1LC3B;SLC25A31;UBE2J2;TUBB;NDUFA13;CYBB;WIPI2;DCTN1;VDAC3;ATXN1L;PPP3CB;ATG13;SLC25A4;SLC25A5;TANK;PSMA5;UQCRB;HIP1;PSMA1;PSMB2;PSMD3;UBA1;UQCRC1;VDAC1;SDHA;MAP3K5;UQCRFS1;DCTN2;MFN1;NDUFV1;PSMC5;SEM1;ATP5F1A;ATP5MC2;ATP5PF;SEPTIN5;DAXX;ATP5F1B;ATP5F1D
Signal transduction	hsa04370	VEGF signaling pathway	19/1557	0.009	19	SIRT1;GRIA2;FOS;PPP3CA;CALM1;CAMK2D;ATF2;GNAS;GRIN2D;HDAC1;HDAC2;PPP1CB;PPP1CC;PPP3R1;STX1A;CREB3;FOSB;PPP3CB;ADCY5
Infectious disease: viral	hsa05170	Human immunodeficiency virus 1 infection	51/1557	0.01	51	PLOD3;ALDH9A1;KMT2A;PLOD1;KMT2D;SETD1B;ASH1L;KMT2E;KMT2C;CAMKMT;SETDB2;SUV39H2;DLST;SETD2;SETD1A;DHTKD1;NSD1;DOT1L;NSD2
Excretory system	hsa04962	Vasopressin-regulated water reabsorption	15/1557	0.01	15	PIGB;PIGX;PIGM;PIGS;PIGU;PIGO;PIGV;DPM2;PIGK;PIGY;PIGW;PGAP4
Transport and catabolism	hsa04136	Autophagy - other	12/1557	0.01	12	DAG1;LAMP2;PCDH9;TFRC;NRP2;PCDH11X;MYH10
Endocrine system	hsa04921	Oxytocin signaling pathway	39/1557	0.01	39	THBS1;PDLIM7;TLN2;FBN3;SYNE3;SDC4;LMNB1;COL1A1;COL1A2;FBN1;TLN1;VIM;ITGB4;ATP1A2;ANK2;ACTG1;ATP1A3;CAPZA1;CAPZB;COL5A2;COL6A2;DAG1;DIAPH1;DSC2;DSP;EMD;FHL1;FHL2;FN1;ITGAV;ITGB1;ITGB8;JUP;LMNA;MYBPC1;MYH2;PLEC;SGCB;SNTB2;SPTAN1;SPTBN1;TPM2;VCL;ZYX;DAAM1;SYNE2;SUN1;TMEM43;LMNB2;FMNL2;MAP6A6;LAMA1;ENO1;DTNA;ATP1B4;ANK3;NEB;CSR2P2;DES;SDC2;TTN;MYH10;DIAPH2;MYH13
Endocrine and metabolic disease	hsa04934	Cushing syndrome	39/1557	0.01	39	SIRT1;FOXO1;PIK3R3;KRAS;IRS1;ADCY6;PIK3R1;RPTOR;BAX;AKT2;PPARG;HRAS;AKT3;ADCY3;ADCY7;ADCY9;ATF2;IGF1R;INSR;PIK3CA;PIK3CB;PRKAA1;PRKAB2;STK11;TSC1;RB1CC1;CREB3;APPL1;ADIPOR2;SESN2;SESN3;PRKAG2;ATG13;ADCY5;SOD2
Cancer: overview	hsa05230	Central carbon metabolism in cancer	21/1557	0.01	21	SIRT1;FOXO1;HSPA1B;PIK3R3;KRAS;IRS1;ADCY6;PIK3R1;RPTOR;AKT2;HRAS;AKT3;ADCY3;ADCY7;ADCY9;HDAC1;HDAC2;FOXO2;IGF1R;INSR;PIK3CA;PIK3CB;PRKAA1;PRKAB2;PRKAG2;ADCY5;HSPA8;SOD2
Cardiovascular disease	hsa05418	Fluid shear stress and atherosclerosis	36/1557	0.01	36	RAF1;RASA1;EPHA4;GSK3B;MAPK1;PIK3R3;KRAS;BMPR2;CFL2;EFNA3;PIK3R1;RHOA;GNAI2;HRAS;PPP3CA;CAMK2D;DCC;DPYSL2;EFNA1;EFNB2;EPHB4;ITGB1;ABLIM1;PAK2;PIK3CA;PIK3CB;PLXNA1;PPP3R1;MAPK3;PTPN11;ROBO2;TRPC1;FZD3;NRP1;PLXNC1;ARHGEF12;PLXNB2;SSH1;ENAH;SRGAP1;SSH2;PLXNA4;UNC5D;SEMA5B;SRGAP3;PPP3CB;SEMA6D;SEMA4G;EPHA3;TRPC5
Endocrine and metabolic disease	hsa04932	Non-alcoholic fatty liver disease	39/1557	0.01	39	RAF1;FOXO1;CRK;GSK3B;MAPK1;PIK3R3;KRAS;IRS1;IKBKB;PIK3R1;RPTOR;AKT2;HRAS;AKT3;CALM1;GRB2;RAPGEF1;INSR;PIK3CA;PIK3CB;PPP1CB;PPP1CC;PPP1R3C;PRKAA1;PRKAB2;PRKAR1A;MAPK3;MAPK6;PYGB;

						RPS6;SOS2;SREBF1;TSC1;SOCS2;TRIP10;SHC3;PRKAG2;PRKAR1B;CBL;SO S1
Amino acid metabolism	hsa00310	Lysine degradation	19/1557	0.01	19	EGFR;RAF1;MAP3K3;HBEGF;MAPK1;PLA2G4C;KRAS;ADCY6;HRAS;ADCY3;ADCY7;ADCY9;CALM1;CAMK2D;GNAS;GRB2;MAP3K1;MAP3K4;MMP14;PLD1;MAPK3;MAPK8;MAP2K3;MAP2K4;SOS2;MAP3K2;ADCY5;SOS1
Excretory system	hsa04960	Aldosterone-regulated sodium reabsorption	13/1557	0.01	13	RAF1;CCNA2;CCNB1;MAPK1;PIK3R3;KRAS;CDC25A;ADCY6;PIK3R1;AKT2;CDC25B;GNAI2;AKT3;ADCY3;ADCY7;ADCY9;HSP90AA1;IGF1R;PGR;PIK3CA;PIK3CB;MAPK3;MAPK8;RPS6KA3;AURKA;CPEB3;ANAPC7;CPEB4;CPEB2;CCNB2;ADCY5
Information processing in viruses	hsa03250	Viral life cycle - HIV-1	19/1557	0.01	19	EGFR;RAF1;MMP9;HBEGF;HSPA1B;KCNJ9;MAPK1;PIK3R3;BCL2;NCOA3;KRAS;NCOA2;SP1;ADCY6;HSP90B1;PIK3R1;AKT2;FOS;GNAI2;HRAS;AKT3;ADCY3;ADCY7;ADCY9;CALM1;ATF2;GABBR1;GNAS;GRB2;HSP90AA1;PGR;PIK3CA;PIK3CB;MAPK3;RARA;SOS2;GREB1;CREB3;SHC3;ADCY5;SOS1;HSPA8
Endocrine system	hsa04916	Melanogenesis	27/1557	0.01	27	RAF1;WNT3A;GSK3B;MAPK1;FZD6;KRAS;ADCY6;MITF;GNAI2;HRAS;WNT10B;ADCY3;ADCY7;ADCY9;CALM1;CAMK2D;CREBBP;CTNNB1;DVL3;EP300;GNAS;MAPK3;FZD5;FZD3;FZD1;CREB3;ADCY5
Endocrine and metabolic disease	hsa04933	AGE-RAGE signaling pathway in diabetic complications	27/1557	0.01	27	RAF1;GSK3B;MAPK1;PIK3R3;KRAS;PIK3R1;AKT2;FOS;HRAS;AKT3;GRB2;PIK3CA;PIK3CB;MAPK3;MAPK8;SOS2;STAT5B;SOCS2;SOCS6;SHC3;SOS1;SOCS7
Environmental adaptation	hsa04710	Circadian rhythm	12/1557	0.01	12	RAF1;FOXO1;GSK3B;MAPK1;PIK3R3;HDAC3;SLC2A1;NCOA3;KRAS;NCOA2;PIK3R1;NOTCH3;NOTCH2;HIF1A;AKT2;HRAS;AKT3;ATP1A2;ACTG1;ATP1A3;ATP2A2;CREBBP;CTNNB1;EP300;HDAC1;HDAC2;ITGAV;MDM2;PIK3CA;PIK3CB;MAPK3;MED24;TBC1D4;MED13;MED13L;PLCD3;ATP1B4;NCOR1;MED14;MED12;PFKL
Signal transduction	hsa04371	Apelin signaling pathway	35/1557	0.01	35	CDKN1A;EGFR;RAF1;PTGS2;KCNJ9;MAPK1;PLA2G4C;KCNJ2;KRAS;ADCY6;RHOA;FOS;GNAI2;HRAS;PPP3CA;ACTG1;ADCY3;ADCY7;ADCY9;CACNB4;CALM1;CAMK2D;EEF2;GNAS;MEF2C;MYLK;PPP1R12A;PPP1CB;PPP1CC;PPP3R1;PRKAA1;PRKAB2;MAPK3;RGS2;RYP3;PRKAG2;PPP3CB;ADCY5;TRPM2
Nervous system	hsa04724	Glutamatergic synapse	30/1557	0.01	30	EGFR;RAF1;MMP9;MMP13;SMAD2;GNB1;MAPK1;PIK3R3;KRAS;VEGFA;COL1A1;COL1A2;ADCY6;PIK3R1;AKT2;FOS;GNAI2;HRAS;AKT3;ADCY3;ADCY7;ADCY9;ATF2;GNAS;GNB3;GRB2;NFKBIA;PIK3CA;PIK3CB;MAPK3;MAPK8;MAP2K4;SOS2;CREB3;SHC3;RXFP1;ADCY5;SOS1
Infectious disease: parasitic	hsa05145	Toxoplasmosis	29/1557	0.02	29	CDKN1A;EGFR;RAF1;MMP13;HBEGF;GATA3;MEF2A;MAPK1;BCL2;SP1;ADCY6;RHOA;FOS;GNAI2;MEF2D;WNK1;ADCY3;ADCY7;ADCY9;ATF2;GNAS;LRP6;LRP5;MEF2C;MMP14;PLD1;MAPK3;OXSR1;CREB3;AKAP13;ADCY5;WNK2;STK39
Signal transduction	hsa04668	TNF signaling pathway	30/1557	0.02	30	RAF1;CRK;GSK3B;MAPK1;PIK3R3;KRAS;IRS1;ADCY6;IGFBP3;PIK3R1;AKT2;FOS;GNAI2;HRAS;AKT3;ADCY3;ADCY7;ADCY9;ATF2;CREBBP;EP300;GNAS;GRB2;MAP3K1;PIK3CA;PIK3CB;MAPK3;MAPK8;MAP2K3;MAP2K4;SOS2;STAT5B;SOCS2;CREB3;SHC3;GHR;SSTR2;ADCY5;SOS1
Infectious disease: viral	hsa05162	Measles	34/1557	0.02	34	NR1D2;FBXW11;CRY2;NPAS2;PRKAA1;PRKAB2;RORA;RORB;PER3;PER2;PRKAG2;SKP1
Immune system	hsa04611	Platelet activation	31/1557	0.03	31	ACSL4;COX8C;NDUFB10;KRAS;ADCY6;RPTOR;PPARG;HRAS;ACTG1;ADCY3;ADCY7;ADCY9;COX10;CPT2;ATF2;ACSL1;ACSL3;GNAS;GRB2;NDUFA9;PRKAA1;PRKAB2;MAP2K3;RPS6;RPS6KA3;SDHC;SMARCA4;SMARCB1;SMARCC2;SMARCD1;SMARCD2;SOS2;TSC1;UQCRC2;ARID1A;CREB3;FRS2;KDM1A;UQCRCQ;KDM3B;NDUFA13;SLC25A20;COX19;PRKAG2;CNR1;ADCY5;UQCRB;UQCRC1;SDHA;SOS1;MAP3K5;UQCRCF1;ZNF516;NDUFB1;NDUFA8;ATP5F1A;ATP5MC2;ATP5PF;ATP5F1B;ATP5F1D
Folding, sorting and degradation	hsa03050	Proteasome	14/1557	0.03	14	MAPK1;PIK3R3;KRAS;IRS1;PIK3R1;ATP1A2;ATP1A3;INSR;PIK3CA;PIK3CB;MAPK3;NEDD4L;ATP1B4
NA	hsa03273	Virion - Lassa virus and SFTS virus	7/1557	0.03	7	RAB5B;ADCY6;ADCY3;ADCY9;DYNC1H1;DYNC1H1;DYNC1L1;GNAS;RAB5C;CREB3;DCTN6;DYNC2H1;DCTN1;DCTN2;DYNLL2
Substance dependence	hsa05031	Amphetamine addiction	19/1557	0.03	19	MAPK1;PLA2G4C;TLN2;PIK3R3;COL1A1;COL1A2;ADCY6;TLN1;PIK3R1;RHOA;AKT2;GNAI2;AKT3;ACTG1;ADCY3;ADCY7;ADCY9;GNAS;ITGB1;MYLK;PPP1R12A;PIK3CA;PIK3CB;PPP1CB;PPP1CC;MAPK3;RAP1A;ARHGEF12;FCGR2A;ADCY5;FERMT3
Signal transduction	hsa04392	Hippo signaling pathway - multiple species	10/1557	0.03	10	RAF1;GSK3B;MAPK1;PIK3R3;KRAS;IKBKB;PIK3R1;RHOA;AKT2;PPP2R2A;FOS;HRAS;PPP3CA;AKT3;CHUK;GRB2;NFKBIA;PAK2;PIK3CA;PIK3CB;PPP2CB;PPP2R5A;PPP3R1;MAPK3;MAPK8;PTPN11;SOS2;PPP2R2D;CD3G;PPP3CB;PPP2CA;SOS1;PPP2R5E
Signal transduction	hsa04070	Phosphatidylinositol signaling system	25/1557	0.03	25	BDNF;IRAK1;RAF1;MAP3K3;CRK;GSK3B;MAPK1;IRAK4;PIK3R3;BCL2;KRAS;IRS1;IKBKB;PIK3R1;RHOA;TRAF6;BAX;AKT2;HRAS;AKT3;CALM1;CAMK2D;GRB2;RAPGEF1;MAP3K1;NFKBIA;NGFR;PIK3CA;PIK3CB;MAPK3;MAPK8;PTPN11;RAP1A;RPS6KA3;SOS2;RIPK2;RPS6KA5;MAPKAPK2;FRS2;PRDM4;SHC3;KIDINS220;SH2B1;SOS1;MAP3K5
Cancer: overview	hsa05207	Chemical carcinogenesis	48/1557	0.04	48	GNB1;MAPK1;PLA2G4C;SLC38A2;GRIA2;ADCY6;GNAI2;PPP3CA;ADCY3;ADCY7;ADCY9;GLS;GLUL;GNAS;GNB3;GRIN2D;PLD1;PPP3R1;MAPK3;SL

		is - receptor activation				C1A3;TRPC1;HOMER1;NCDN;SLC38A1;CACNA1A;DLGAP1;PPP3CB;ADCY5;SHANK2;LZTS3
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Supplementary Table S4. KEGG pathway enrichment of miR-132 target genes associated with schizophrenia. The table lists pathways significantly enriched for miR-132 targets that overlap with schizophrenia-related genes. Columns report the total number of miRNA target genes (n_miRNA_genes), total number of schizophrenia-related genes (n_scz_genes), number of overlapping genes (n_overlap), the names of overlapping genes (Overlap_genes), and statistical significance values (p-value, FDR, and Bonferroni correction). Only pathways relevant to schizophrenia are shown.

hsa-miR-181b-3p						
Subcategory	ID	Description	GeneRatio	p.adjust	Count	GeneSymbol
Transport and catabolism	hsa04140	Autophagy - animal	114/3285	5,81E-02	97	E2F1;ATM;EP300;STAG1;PPP2R5E;SMC1A;E2F3;CDK6;RB1;E2F5;CCND1;CDKN1A;CDKN1B;MYC;TGFB2;CCNE1;RBL1;ABL1;CDC25B;YWHAZ;CCNA2;SMAD2;PDS5A;CDK2;PRKDC;RAD21;ATR;BUB1;BUB1B;CCNB1;CDK1;CDC6;CDC20;CD C27;CREBBP;GADD45A;SFN;GSK3B;HDAC1;MAD2L1;SMAD3;SMAD4;MCM2;M CM3;MCM4;MCM6;MDM2;ORC5;PPP2CB;PPP2R1A;PPP2R1B;PPP2R5A;PPP2R5C; SKP2;TFDP2;WEE1;YWHAE;YWHAG;YWHAH;CDC7;CUL1;CDC14A;CDC23;SMC 3;CCNE2;BUB3;TRIP13;ESPL1;NDC80;STAG2;DBF4;YWHAQ;PDS5B;ORC6;NIPBL ;ANAPC13;ANAPC15;FBXO5;ANAPC7;ANAPC16;ESCO2;CCNB2;CDC16;ATR;PPP 2CA;YWHAB;PPP2R5D;SKP1;TFDP1;RBX1;MAU2;MTBP;ZBTB17;PTTG1;SGO1;W APL;KNL1
Folding, sorting and degradation	hsa04120	Ubiquitin mediated proteolysis	100/3285	5,81E-02	81	MAP2K1;ADCY9;IGF1R;RPS6KA3;CPEB4;PPP2R5E;MAPK14;SMC1A;FBXW11;AD CY6;CCNE1;YWHAZ;BTRC;PPP3CA;CDK2;ADCY3;AR;BUB1;CALM1;CALM2;CA LM3;CAMK2G;CCNB1;CDK1;CDC20;CDC27;ITPR1;ITPR2;MAD2L1;PGR;PPP1CA; PPP1CB;PPP1CC;PPP2CB;PPP2R1A;PPP2R1B;PPP2R5A;PPP2R5C;PPP3R1;PRKACA ;PRKACB;MAPK1;MAPK3;AURKA;YWHAE;YWHAG;YWHAH;CUL1;CDC23;SMC 3;CCNE2;ESPL1;SLK;YWHAQ;CPEB3;ANAPC13;ANAPC15;FBXO5;RPS6KA6;AN APC7;ANAPC16;CPEB2;CCNB2;IGF1;RPS6KA1;FBXO43;CDC16;PPP3CB;ADCY5;P PP3CC;ITPR3;PPP2CA;MAPK13;YWHAB;PPP2R5D;SKP1;RBX1;ADCY1;PTTG1;RE C8;SGO1
Chromosome	hsa03083	Polycomb repressive complex	65/3285	5,21E+00	43	BCL2;CCNG1;ATM;PMAIP1;PTEN;CDK6;THBS1;CCND1;CDKN1A;SESN1;APAF1; CASP3;CCNE1;CDK2;CCNB1;CDK1;DDB2;GADD45A;SFN;MDM2;MDM4;SERPIN E1;RRM2;SIAH1;PPM1D;TNFRSF10B;TNFRSF10A;CCNE2;E124;ZNF385A;RRM2B; STEAP3;ZMAT3;SESN2;SESN3;CCNB2;IGF1;TSC2;RCHY1;GORAB;ATR;GTSE1;A DGRB1
Folding, sorting and degradation	hsa04141	Protein processing in endoplasmic reticulum	111/3285	5,21E+00	72	BCL2;MCL1;BCL2L11;MAP2K1;FOS;ATM;XIAP;PMAIP1;TUBA1A;KRAS;NRAS;L MNB1;APAF1;BAK1;IKBKB;RELA;CASP7;CASP6;PIK3R1;CASP3;MAPK9;RAF1;A KT2;CTSC;NFKB1;AKT1;AKT3;ACTB;PARP1;PARP4;BIRC2;BIRC5;ATF4;CAPN2;C HUK;CTSD;CTSH;CTSL;GADD45A;EIF2S1;ITPR1;ITPR2;PDPK1;PIK3CA;PIK3CB; MAPK1;MAPK3;MAPK8;PTPN13;SPTAN1;CTSF;TNFRSF10B;TNFRSF10A;AIFM1; EIF2AK3;TUBA1B;TUBA8;PARP2;TNFRSF1A;PIK3R3;CTSS;CTSO;ERN1;ITPR3;M APK10;RIPK1;HRK;BAD;MAP3K5;CASP2;DAXX;P3R3URF-PIK3R3
Translation	hsa03013	Nucleocytop lasmic transport	75/3285	1,25E+03	25	TFRC;SLC7A11;ACSL1;ACSL3;ACSL4;FTL;GPX4;PCBP1;SLC3A2;TF;ATG7;ACSL6 ;SLC39A14;ACSL5;STEAP3;MAP1LC3B;MAP1LC3A;CP;CYBB;PCBP2;VDAC3;GC LM;ATG5;SLC40A1;NCOA4
Development and regeneration	hsa04360	Axon guidance	112/3285	1,82E+03	97	E2F1;ZFP36L2;SIRT1;ETS1;MAP2K1;ATM;ZFP36L1;MTOR;IL1A;PTEN;MAPK14;F BXW11;E2F3;CDK6;KRAS;NRAS;TGFB2;RB1;E2F5;CCND1;CDKN1A;HIPK3;MY C;TGFB2;RELA;PIK3R1;CCNE1;RBL1;RAF1;AKT2;FOXO3;CCNA2;TGFB1;NFKB 1;AKT1;SMAD2;BTRC;PPP3CA;CDK2;AKT3;SLC25A6;CALM1;CALM2;CALM3;C APN2;CCNB1;CDK1;GADD45A;FOXO1;HLA-A;ITPR1;ITPR2;SMAD3;MDM2;NFATC2;NFATC3;SERPINE1;PIK3CA;PIK3CB;PPP1 CA;PPP1CB;PPP1CC;PPP3R1;MAPK1;MAPK3;MAP2K6;RHEB;TSC1;SQSTM1;CCN E2;MAPKAPK2;HIPK2;TRPM7;LIN54;HIPK1;CCNB2;TSC2;CACNA1D;MRAS;PIK3 R3;RBBP4;VDAC3;PPP3CB;SLC25A4;SLC25A5;ATR;PPP3CC;HLA-C;ITPR3;MAPK13;VDAC1;HUS1;HLA-B;HLA-E;RAD50;MRE11;P3R3URF-PIK3R3
Signal transduction	hsa04152	AMPK signaling pathway	81/3285	4,39E+03	115	MAP2K1;FGFR1;ARHGAP35;KRAS;NRAS;ARPC1B;PTK2;CFL2;EGFR;ARAF;GSN; IQGAP1;PIK3R1;CDC42;PAK1;CRKL;RAF1;APC;ITGB3;AKT2;ITGB4;ROCK2;AKT 1;RDX;AKT3;ACTB;ACTN4;ACTN1;C5;CRK;DIAPH1;LPAR1;FGF7;FGF9;FG F10;FGFR2;FN1;ITGA6;ITGA3;ITGA4;ITGA9;ITGAV;ITGB1;ITGB2;ITGB5;I TGB8;LIMK1;PAK2;PAK3;PDGFA;PDGFRA;PIK3CA;PIK3CB;PIP4K2A;PPP1CA;PP P1CB;PPP1CC;MAPK1;MAPK3;PXN;RAC1;ROCK1;SLC9A1;SOS2;TIAM1;ARHGEF 7;WASF1;ARPC5;ARPC3;ACTR3;ACTR2;ABI2;WASF2;PAK4;GNA13;NCKAP1;ITG A11;ARHGEF12;GIT1;ARHGEF4;SSH1;PPP1R12C;ENAH;PDGFC;PIP4K2C;DIAPH3 ;ARPC5L;SSH2;SPATA13;MYLK4;CYFIP2;ACTR3B;MRAS;PIK3R3;ITGAL;ITGA7;P PP1R12B;BCAR1;PIKFYVE;ARPC1A;DOCK1;F2R;WASL;BRAF;SOS1;MYH10;IQG AP2;DIAPH2;PIP4K2B;PAK5;CYRIB;CYRIA;P3R3URF-PIK3R3
Signal transduction	hsa04150	mTOR signaling pathway	98/3285	8,42E+03	117	BCL2;MAP2K1;XIAP;IGF1R;RAP1B;SPP1;ARHGAP35;PTEN;LAMC2;ERBB2;THBS 1;LAMC1;PTK2;CCND1;VEGFA;COL4A1;COL1A2;EGFR;CAV1;TLN1;PIK3R1;CDC 42;PAK1;MAPK9;CRKL;RAF1;MET;ITGB3;AKT2;ITGB4;ROCK2;AKT1;RELN;AKT 3;ACTB;ACTN4;ACTN1;BIRC2;ARHGAP5;CAPN2;COL4A5;COL6A1;CRK;CTNNB 1;DIAPH1;EMP1;FLNA;FLNB;FLT1;FN1;GRB2;GSK3B;TNC;ILK;ITGA6;ITGA2;ITG A3;ITGA4;ITGA9;ITGAV;ITGB1;ITGB5;ITGB8;LAMA3;LAMA5;LAMB1;PAK2;PAK 3;PDGFA;PDGFRA;PDPK1;PIK3CA;PIK3CB;PPP1CA;PPP1CB;PPP1CC;PRKCA;PRK CB;MAPK1;MAPK3;MAPK8;PXN;RAC1;RAP1A;ROCK1;SOS2;VEGFC;ZYX;PAK4;I TGA11;PARVB;SHC3;PPP1R12C;PARVA;PDGFC;TLN2;IGF1;TNXB;LAMA2;VWF;H

						GF;MYLK4;PIK3R3;ITGA7;PPP1R12B;BCAR1;DOCK1;COL4A6;MAPK10;TNR;BA D;BRAF;COL6A3;SOS1;LAMB2;PAK5;P3R3URF-PIK3R3
Infectious disease: viral	hsa05165	Human papillomavir us infection	177/3285	8,95E+03	60	NLK;FGFR1;EP300;IGF1R;RAP1B;PDCD10;SSX2IP;ERBB2;TGFB2;TJP1;EGFR;SN A12;CTNND1;IQGAP1;CDC42;MET;CDH1;ROCK2;TGFB2;ACTB;ACTN4;ACTN1; CREBBP;CSNK2A1;CSNK2A2;CTNNA1;CTNNB1;INSR;LMO7;SMAD3;SMAD4;M APK1;MAPK3;PTPRB;PTPRF;PTPRJ;PTPRM;RAC1;RAP1A;ROCK1;MAP3K7;WASF 1;WASF2;WASF3;LEF1;HEG1;SMURF2;KRIT1;SORBS1;CTNNA3;TCF7L2;PARD3;C SNK2B;WASL;FARP2;FER;AFDN;NECTIN2;NECTIN3;NECTIN4
Cancer: specific types	hsa05211	Renal cell carcinoma	53/3285	9,64E+03	83	PALS1;ERBB2;TUBA1A;EPB41L4B;ARPC1B;CCND1;TJP1;F11R;CDC42;MAPK9;PR KCE;PPP2R2A;ROCK2;RDX;ACTB;ACTN4;ACTN1;CLDN7;DLG1;DLG2;CTTN;HS PA4;ITGB1;LLGL2;MAP3K1;NEDD4;PPP2CB;PPP2R1A;PPP2R1B;PPP2R2C;PRKAA 1;PRKAA2;PRKAB1;PRKAB2;PRKACA;PRKACB;PRKCI;MAPK8;RAC1;RAP1A;R OCK1;TIAM1;SYMPK;YBX3;MPDZ;CLDN12;CLDN1;MAGI1;RAPGEF2;ARPC5;AR PC3;ACTR3;ACTR2;TUBA1B;BVES;NEDD4L;RAPGEF6;RAB8B;TUBA8;ARHGAP1 7;PPP2R2D;RAP2C;ARPC5L;CGNL1;OCLN;CACNA1D;ACTR3B;PRKAG2;WHAM M;PPP2R2B;PARD3;ARPC1A;JAM3;PPP2CA;MAPK10;MAP3K5;MYH10;SCRIB;MY L6;AMOTL1;MAP2K7;AFDN;PATJ
Cell growth and death	hsa04218	Cellular senescence	97/3285	1,11E+04	51	MAP2K1;ADCY9;TUBB;TUBB2A;GJA1;TUBA1A;KRAS;NRAS;TJP1;ADCY6;EGFR ;GNAI3;RAF1;GNAI2;ADCY3;CDK1;CSNK1D;DRD1;LPAR1;GNAI1;GNAQ;GRB2; GRM1;GRM5;GUCY1A2;ITPR1;ITPR2;PDGFA;PDGFRA;PRKACA;PRKACB;PRKC A;PRKCB;MAPK1;MAPK3;MAP2K5;SOS2;TUBA1B;TUBB4B;MAP3K2;TUBA8;PD GFC;HTR2A;PRKG1;ADCY5;ITPR3;SOS1;PLCB1;ADCY1;GUCY1A1;GUCY1B1
Infectious disease: viral	hsa05166	Human T- cell leukemia virus 1 infection	128/3285	1,21E+04	78	BMPR2;MAP2K1;FGFR1;ZFHX3;ID4;IGF1R;SMAD1;MAPK14;HOXA1;KRAS;NRA S;SMAD5;MYC;ACVR1B;DVL2;PCGF5;JARID2;PIK3R1;RAF1;LIF;BMI1;REST;MEI S1;APC;AKT2;JAK1;AKT1;SMAD2;BMPR1B;JAK2;AKT3;WNT10B;STAT3;ACVR1; ACVR2A;ACVR2B;BMPR1A;CTNNB1;DVL3;FGF2;FGFR2;GRB2;GSK3B;IL6ST;IN HBB;LIFR;SMAD3;SMAD4;OTX1;PIK3CA;PIK3CB;MAPK1;MAPK3;SKIL;TBX3;W NT2;WNT9A;FZD5;FZD3;KAT6A;FZD4;FZD6;FZD8;PCGF3;RIF1;SMARCAD1;PCG F6;ACVR1C;IGF1;PIK3R3;SETDB1;COMMD3- BMI1;MAPK13;WNT2B;DVL1;HOXD1;PCGF2;P3R3URF-PIK3R3
Cell growth and death	hsa04110	Cell cycle	97/3285	1,61E+04	21	MTOR;ATG2B;RPTOR;PIK3C3;PPP2CB;BECN1;ATG12;ULK2;ATG7;GABARAPL2; ATG4B;PIK3R4;ATG3;ATG9A;ATG4A;ATG4C;ATG13;MLST8;PPP2CA;ATG5;ATG4D
Cellular community - eukaryotes	hsa04510	Focal adhesion	117/3285	4,06E+04	67	E2F1;UBB;ULK1;HUWE1;MTX3;KRAS;NRAS;SP1;MITF;RELA;RHOT1;MAPK9;HI F1A;FOXO3;TBK1;ATF4;BNIP3;CSNK2A1;CSNK2A2;EIF2S1;MAPK8;RAB5A;RAB 5C;SIAH1;UBC;VCP;TFEB;BECN1;SQSTM1;TAX1BP1;EIF2AK3;TOMM20;MFN2;U SP15;CALCOCO2;CITED2;PHB2;GABARAPL2;RABGEF1;SMURF2;TBC1D15;ATG 9A;MAP1LC3B;MAP1LC3A;UBA52;MRAS;USP8;RPS27A;AMFR;CSNK2B;MAPK1 0;RAB7A;ARIH1;NBR1;MTX2;MON1B;SAMM50;FIS1;AMBRA1;MUL1;TOMM40L; PINK1;USP30;MFN1;FUNDC1;TOMM70;MARCF5
Transport and catabolism	hsa04144	Endocytosis	139/3285	4,06E+04	114	BCL2;HMGB1;MAP2K1;DDIT4;MTOR;IGF1R;UBB;ULK1;ATG2B;PRKCD;WDFY3; PTEN;SMCR8;KRAS;NRAS;IRS1;IRS2;PIK3R1;TRAF6;MAPK9;HIF1A;RAF1;RPTO R;AKT2;TBK1;AKT1;AKT3;TP53INP2;VMP1;BNIP3;CTSD;CTSL;DAPK1;EIF2S1;IT PR1;LAMP2;PDPK1;PIK3C3;PIK3CA;PIK3CB;PPP2CB;PRKAA1;PRKAA2;PRKACA ;PRKACB;MAPK1;MAPK3;MAPK8;RAB1A;RHEB;RPS6KB1;MAP3K7;TSC1;UBC; UVRAG;STX7;VAMP8;BECN1;SQSTM1;TAX1BP1;MTMR3;MTMR4;ATG12;EIF2A K3;ULK2;RB1CC1;CALCOCO2;RRAGB;ATG7;RRAGA;GABARAPL2;ATG4B;GOR ASP2;PIK3R4;SH3GLB1;BIRC6;VPS18;RRAGC;MTMR14;ATG3;VPS33A;ATG9A;M AP1LC3B;MAP1LC3A;ATG4A;C9orf72;ATG4C;TSC2;EIF2AK4;SUPT20H;UBA52;M RAS;PIK3R3;RPS27A;ATG13;MLST8;ERN1;PPP2CA;MAPK10;BAD;RAB7A;ATG5; NBR1;PLEKHM1;AMBRA1;STX17;WDR41;WDR45B;EPG5;DEPTOR;RAB33B;ATG 4D;RUBCN;P3R3URF-PIK3R3
Endocrine system	hsa04919	Thyroid hormone signaling pathway	78/3285	8,93E+04	69	AP3M2;GNS;SORT1;LAPTM4B;NCOA7;MEAK7;CD164;SLC17A5;IGF2R;CTSC;EN TPD4;ACP2;AP1G1;AGA;ARSB;ASAH1;ATP6V0A1;ATP6AP1;SCARB2;CD63;AP1S 1;TPP1;CLTA;CLTB;CLTC;CTSD;CTSH;CTSL;DMXL1;GLB1;GUSB;IDS;LAMP2;LIP A;MANBA;NAGA;NPC1;CTSA;PPT1;LGMN;PSAP;AP3B1;CTSE;AP3D1;ATP6V0D1; PPT2;GGA2;DMXL2;WDR7;AP4E1;ABCB9;AP3M1;GNPTAB;FUCA1;NAGLU;GGA 1;ATP6V0C;CTSS;CTSO;DNASE2;ABCA2;NPC2;PLA2G15;ATP6V0A2;FUCA2;HGS NAT;MFSD8;AP1G2;AP4B1
Cancer: overview	hsa05205	Proteoglycan s in cancer	116/3285	1,34E+05	139	TSG101;LDLR;ARF6;HSPA1B;IGF1R;TFRC;CHMP2B;EPS15;ARRB2;GRK2;WASHC 5;TGFB2;ARF4;RAB11FIP2;ARF3;ARPC1B;VPS37C;EGFR;CAV1;DNM2;VPS26A; PDCD6IP;CDC42;TRAF6;IGF2R;ITCH;HGS;AP2M1;TGFB1;SMAD2;AP2A1;AP2B1 ;BIN1;ARRB1;CAPZA1;AP2S1;CLTA;CLTB;CLTC;FGFR2;HLA- A;HSPA1L;KIF5A;KIF5B;KIF5C;SMAD3;MDM2;NEDD4;PDGFRA;PLD1;PRKCI;RA B5A;RAB5C;SH3GL2;SNX2;STAM;EEA1;SNX4;SNX3;GBF1;ASAP2;RABEP1;ZFYV E16;GIT2;DNAJC6;ARPC5;ARPC3;ACTR3;ACTR2;STAM2;ARFGEF1;RAB10;EHD1; EPN2;NEDD4L;DNM3;SNX5;GIT1;EHD3;ASAP1;VPS36;SH3GLB1;CHMP3;RUFY2; VPS35;RAB22A;SMURF2;CHMP6;VPS37B;ARPC5L;VPS25;ARFGAP2;CHMP7;ARA P2;AGAP1;VPS37A;GRK4;ARF1;SH3KBP1;ACTR3B;RUFY1;AGAP3;SMAP1;IQSEC 2;AGAP2;SPG21;USP8;IQSEC1;ARFGAP3;RAB35;PARD3;ARPC1A;HLA- C;WASL;RAB11B;RAB4A;RAB7A;ZFYVE9;GRK5;HLA-B;HLA- E;ARFGEF2;HSPA8;WWP1;SNF8;ACAP2;PSD3;VPS28;VTA1;CHMP1B;EPS15L1;AR AP3;PSD2;VPS26B;WIPF2;CBLB;GRK3;WASHC3;SPART
Signal transduction	hsa04010	MAPK signaling pathway	158/3285	1,78E+05	82	SIRT1;CREB1;MAP2K1;ADAM17;DUSP5;TMEM30A;MAPK14;SLC16A1;THBS1;A XL;PTK2;MERTK;DNMT3A;ADAM9;CASP7;CASP3;HIF1A;CRKL;PTGS2;ITGB3;A BCA1;PPARG;CEBPB;JAK2;ADAM10;ARNT;ATP2A2;CALR;CAMK2G;CD47;CPT1 A;CRK;ITGAV;ITGB5;LIPA;LRP1;NFATC2;NFATC3;ODC1;MAPK1;MAPK3;PROS1; RAB5A;RAB5C;RAC1;SGK1;MAPKAPK2;TGFBRAPI;ATP8A1;ATP11B;VPS8;PANX

						1;RAB14;ATP8A2;VPS18;ANO3;VPS33A;XKR4;SIRPA;ANO6;ATP11C;PECAM1;ALOX5;PTGER4;PLA2G6;ELMO1;CPT1C;BCAR1;PPARD;DOCK1;DUSP4;S1PR1;MAPK13;ATP2A1;RAB7A;TYRO3;SLC2A1;PLA2G15;P2RY12;MEGF10;ANO4;ADGRB1
Nervous system	hsa04728	Dopaminergic synapse	82/3285	2,05E+05	158	NLK;MAP2K1;FOS;FGFR1;MAP3K3;DUSP5;HSPA1B;IGF1R;IL1A;MAP3K10;RAP1B;RPS6KA3;ELK4;ARRB2;CSF1;MAPK14;KIT;ERBB2;ERBB3;KRAS;NRAS;TGFB2;VEGFA;MYC;IKBKB;MAP3K8;EGFR;TGFB2;ARAF;RELA;STK4;CDC42;IRAK1;TRAF6;CASP3;PAK1;MAPK9;CRKL;RAF1;MET;RASA1;AKT2;CDC25B;ERBB4;TGFBR1;NFKB1;AKT1;PPP3CA;AKT3;EFNA5;ARRB1;ATF4;CACNA1B;CACNA2D1;CACNB2;CACNB4;CHUK;ATF2;CRK;GADD45A;DUSP3;DUSP6;EFNA1;EPHA2;EREG;FGF2;FGF7;FGF9;FGF10;FGFR2;FLNA;FLT1;MKNK2;GRB2;HSPA1L;IL1B;IL1R1;INSR;MAPT;MEF2C;MAP3K1;MAP3K4;MAP3K9;MYD88;NF1;NFATC3;NTRK2;PAK2;PDGFA;PDGFRA;PLA2G4A;PPM1A;PPP3R1;PPP5C;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;MAP2K5;MAP2K6;PTPRR;RAC1;RAP1A;RASA2;RELB;RET;MAP2K4;SOS2;SRF;STK3;MAP3K7;VEGFC;MAPKAPK3;MAP4K3;LAMTOR3;RPS6KA4;MAPKAPK2;RAPGEF2;MAP3K2;RPS6KA6;IRAK4;PDGFC;TAOK1;CACNG8;CACNA2D4;IGF1;CACNA1A;HGF;CACNA1D;KITLG;KITLG;CACNA2D2;RPS6KA1;TNFRSF1A;MRAS;MECOM;PPP3CB;MAP4K4;PPP3CC;DUSP4;MAPK10;MAPK13;MAPKAPK5;BRAF;SOS1;MAP3K5;HSPA8;RASGRF2;MAPK8IP2;CACNA2D3;MAP2K7;HSPB1;MAP3K21;DAXX;CACNA1C
Aging	hsa04211	Longevity regulating pathway	61/3285	2,80E+05	58	MAP2K1;MTOR;ERBB2;ERBB3;KRAS;NRAS;PTK2;CDKN1A;CDKN1B;MYC;EGFR;ARAF;PIK3R1;PAK1;GAB1;MAPK9;CRKL;ABL1;RAF1;AKT2;ERBB4;AKT1;AKT3;ABL2;CAMK2G;CRK;EREG;GRB2;GSK3B;PAK2;PAK3;PIK3CA;PIK3CB;PLCG1;PLCG2;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;RPS6KB1;MAP2K4;SOS2;STAT5B;NCK2;PAK4;SHC3;PIK3R3;NRG2;NCK1;MAPK10;BAD;BRAF;SOS1;MAP2K7;CBLB;PAK5;P3R3URF-PIK3R3
Neurodegenerative disease	hsa05022	Pathways of neurodegeneration - multiple diseases	233/3285	5,17E+05	118	ETS1;MAP2K1;FGFR1;ARF6;IGF1R;RAP1B;SHOC2;RASSF1;CSF1;KIT;KRAS;NRAS;VEGFA;IKBKB;EGFR;RELA;STK4;PIK3R1;CDC42;PAK1;GAB1;MAPK9;ABL1;RAF1;MET;RASA1;AKT2;TBK1;NFKB1;AKT1;AKT3;EFNA5;ABL2;CALM1;CALM2;CALM3;CHUK;EFNA1;EPHA2;ETS2;FGF2;FGF7;FGF9;FGF10;FGFR2;FLT1;GNB1;GNB2;GRB2;GRIN2A;INSR;NF1;NTRK2;PAK2;PAK3;PDGFA;PDGFRA;PIK3CA;PIK3CB;PLA2G4A;PLCG1;PLCG2;PLD1;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;RGL2;RAB5A;RAB5C;RAC1;RALA;RAP1A;RASA2;REL;SOS2;TIAM1;VEGFC;BRAP;RASAL2;GAB2;PAK4;PLCE1;SHC3;EXOC2;PDGFC;RALGAPB;RALGAP2;GNB4;GNG7;IGF1;HGF;KITLG;PLA2G6;MRAS;PIK3R3;RASAL1;MAPK10;BAD;SOS1;SYNGAP1;RALBP1;RASGRF2;GRIN1;RAPGEF5;KSR1;RALGAP1;RGL1;PLA2G12A;KSR2;GRIN2B;AFDN;PAK5;PLAAT3;P3R3URF-PIK3R3
Drug resistance: antineoplastic	hsa01521	EGFR tyrosine kinase inhibitor resistance	55/3285	8,87E+05	108	MAP2K1;FGFR1;ADCY9;IGF1R;RAP1B;SIPA1L1;CSF1;MAPK14;KIT;THBS1;KRAS;NRAS;VEGFA;ADCY6;EGFR;TLN1;GNAI3;CTNND1;PIK3R1;CDC42;PRKD2;CRKL;RAF1;MET;ITGB3;AKT2;ADORA2B;CDH1;GNAI2;AKT1;AKT3;EFNA5;ACTB;ADCY3;CALM1;CALM2;CALM3;CRK;CTNND1;LPA1;EFNA1;EPHA2;FGF2;FGF7;FGF9;FGF10;FGFR2;FLT1;GNAI1;GNAQ;GRIN2A;INSR;ITGB1;ITGB2;PDGFA;PDGFRA;PIK3CA;PIK3CB;PLCG1;PRKCA;PRKCB;PRKCI;MAPK1;MAPK3;MAP2K6;RAC1;RALA;RAP1A;RAP1GAP;TIAM1;VEGFC;MAGI1;RAPGEF2;DOCK4;RAPGEF4;PRKD3;PLCE1;RAPGEF6;ENAH;PDGFC;SIPA1L2;TLN2;IGF1;HGF;KITLG;KRIT1;MRAS;PIK3R3;ITGAL;MAGI3;CNR1;BCAR1;PAR3;ADCY5;F2R;MAPK13;BRAF;GRIN1;RAPGEF5;MAGI2;FARP2;PLCB1;GNAO1;ADCY1;ARAP3;GRIN2B;AFDN;P3R3URF-PIK3R3
Cancer: specific types	hsa05215	Prostate cancer	68/3285	8,90E+05	85	CREB1;ATP2B1;MAP2K1;ADCY9;IRS1;ADCY6;IRS2;GNAI3;RAF1;PRKCE;AKT2;ROCK2;GNAI2;AKT1;MEF2D;PPP3CA;AKT3;ATP1A2;ADCY3;SLC25A6;ATF4;ATP1A1;ATP1B1;ATP1B2;ATP2A2;ATP2B4;CALM1;CALM2;CALM3;ATF2;ATF6B;GNAI1;GNAQ;GUCY1A2;INSR;ITPR1;ITPR2;KCNMA1;MEF2A;MEF2C;NFATC2;NFATC3;PDE2A;PDE3A;PDE3B;PPP1CA;PPP1CB;PPP1CC;PPP3R1;MAPK1;MAPK3;RGS2;ROCK1;SRF;PDE5A;CREB3;GNAI3;EDNRB;ADRA1B;CACNA1D;OPRD1;ATP2B2;ATP2B3;MYLK4;PRKG1;SLC8A1;VDAC3;PPP3CB;ATP1B4;SLC25A4;SLC25A5;ADCY5;PPP3CC;ITPR3;VDAC1;ATP2A1;BAD;PLCB1;ADCY1;CREB3L1;PIK3R6;GTF2I;GUCY1A1;GUCY1B1;CACNA1C
Signal transduction	hsa04012	ErbB signaling pathway	58/3285	8,91E+05	102	GRIA2;CREB1;ATP2B1;MAP2K1;FOS;ADCY9;EP300;RAP1B;PPARA;ADCY6;HCN2;GNAI3;RELA;PIK3R1;PAK1;MAPK9;RAF1;AKT2;ROCK2;GNAI2;NFKB1;AKT1;AKT3;ATP1A2;ADCY3;ATP1A1;ATP1B1;ATP1B2;ATP2A2;ATP2B4;CALM1;CALM2;CALM3;CAMK4;CAMK2G;CREBBP;DRD1;GABBR1;GNAI1;GRIA1;GRIN2A;KCNK2;PDE3A;PDE3B;PDE4D;PIK3CA;PIK3CB;PLD1;PPP1CA;PPP1CB;PPP1CC;PRKACA;PRKACB;MAPK1;MAPK3;MAPK8;RAC1;RAP1A;ROCK1;ROR2;SLC9A1;TIAM1;V1P;GABBR2;ABCC4;CREB3;RAPGEF4;BVES;PLCE1;GLI3;PTCH1;CACNA1D;GRIA3;GRIA4;HTR1F;ATP2B2;ATP2B3;SSTR1;SSTR2;ADCYAP1;ACOX3;PIK3R3;ADCYAP1R1;ATP1B4;ADCY5;F2R;GLP1R;MAPK10;ATP2A1;BAD;BRAF;GRIN1;ADCY1;HHIP;ARAP3;CREB3L1;LIPE;GRIN2B;AFDN;PDE10A;CACNA1C;P3R3URF-PIK3R3
Neurodegenerative disease	hsa05017	Spinocerebellar ataxia	86/3285	9,90E+04	47	BCL2;VCAM1;ATM;XIAP;CYLD;TNFSF11;CARD10;IKBKB;RELA;UBE2I;IRAK1;TRAF6;PTGS2;ICAM1;NFKB1;PLAU;PARP1;BIRC2;CHUK;CSNK2A1;CSNK2A2;GADD45A;CXCL1;CXCL2;CXCL3;IL1B;IL1R1;LTBR;MYD88;PLCG1;PLCG2;PRKCB;RELB;MAP3K7;TNFAIP3;TRAF3;MALT1;ERCC1;IRAK4;TAB3;LYN;TRAF5;TNFRSF1A;CSNK2B;RIPK1;PIAS4;RIGI
Endocrine system	hsa04910	Insulin signaling pathway	83/3285	1,16E+06	66	BCL2;MAP2K1;EP300;MTOR;HK2;IFNGR1;IGF1R;TFRC;EIF4E2;ERBB2;CDKN1A;VEGFA;ALDOA;CDKN1B;IL6R;EGFR;RELA;PIK3R1;HIF1A;AKT2;NFKB1;AKT1;VHL;AKT3;STAT3;ARNT;CAMK2G;CREBBP;EIF4E;EPAS1;FLT1;GAPDH;MKNK2;HK1;INSR;LDHA;LDHB;LTBR;SERPINE1;PFKFB3;PFKP;PIK3CA;PIK3CB;PLCG1;PLCG2;PRKCA;PRKCB;MAPK1;MAPK3;RPS6KB1;TF;TIMP1;CUL2;EGLN1;ENO1;EN

						O2;IGF1;PFKM;CYBB;PIK3R3;SLC2A1;RBX1;EGLN2;PFKL;ELOC;P3R3URF-PIK3R3
Cancer: specific types	hsa05223	Non-small cell lung cancer	51/3285	1,26E+06	78	NLK;SIRT1;BCL2L11;MAP2K1;ATM;CAT;EP300;IGF1R;PTEN;MAPK14;BCL6;KRAS;NRAS;TGFB2;CCND1;CDKN1A;CDKN1B;IRS1;IKBKB;IRS2;EGFR;TGFB2;ARAF;STK4;PIK3R1;MAPK9;RAF1;AKT2;FOXO3;TGFB1;AKT1;CDK2;AKT3;STAT3;BINP3;CCNB1;CHUK;CREBBP;GADD45A;FOXG1;GRB2;GRM1;PRMT1;INSR;SMAD3;SMAD4;MDM2;PDPK1;PIK3CA;PIK3CB;PRKAA1;PRKAA2;PRKAB1;PRKAB2;MAPK1;MAPK3;MAPK8;SGK1;SKP2;SOS2;USP7;ATG12;HOMER1;PLK2;GABARAPL2;CCNB2;IGF1;PRKAG2;PIK3R3;AGAP2;FBXO32;S1PR1;MAPK10;MAPK13;BRAF;SOS1;SOD2;P3R3URF-PIK3R3
Cancer: specific types	hsa05212	Pancreatic cancer	53/3285	1,32E+06	55	PTEN;INPP5F;MTMR6;PIK3R1;CALM1;CALM2;CALM3;CDS1;IMPA1;INPP5B;ITPR1;ITPR2;PIK3C2A;PIK3C2B;PIK3C3;PIK3CA;PIK3CB;PI4KB;PIP4K2A;PLCG1;PLCG2;PRKCA;PRKCB;CDS2;SYNJ1;MTMR3;MTMR4;DGKI;CDIPT;SACM1L;PLCE1;PI4K2A;MTMR14;IPPK;PIP4K2C;DGKH;IPMK;OCRL;IP6K1;DGKG;INPP4B;PIK3R3;INPP4A;ITPK1;PIKFYVE;ITPR3;DGKE;MTMR1;DGKB;MTMR7;PLCB1;PIIP5K2;PIP4K2B;BPNT2;P3R3URF-PIK3R3
Transport and catabolism	hsa04137	Mitophagy - animal	67/3285	1,32E+06	72	BCL2;MAP2K1;SPTLC3;PPP2R5E;PTEN;MAPK14;KRAS;NRAS;GNAI3;RELA;SGPL1;PIK3R1;MAPK9;RAF1;PRKCE;AKT2;PPP2R2A;ROCK2;GNAI2;NFKB1;AKT1;AKT3;ASA1;CTSD;GNAI1;GNAQ;ABCC1;PDPK1;PIK3CA;PIK3CB;PLD1;PPP2CB;PPP2R1A;PPP2R1B;PPP2R2C;PPP2R3A;PPP2R5A;PPP2R5C;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;RAC1;ROCK1;NSMAF;DEGS1;GAB2;SPTLC1;GNAI3;S1PR5;PPP2R3C;PPP2R2D;SGPP1;SGMS2;SPTSSA;SGMS1;OPRD1;TNFRSF1A;PIK3R3;PPP2R2B;S1PR1;PPP2CA;MAPK10;MAPK13;S1PR2;SPTLC2;MAP3K5;PPP2R5D;PLCB1;DEGS2;P3R3URF-PIK3R3
Cancer: overview	hsa05203	Viral carcinogenes is	113/3285	1,70E+06	69	MAP2K1;ADCY9;ARF6;MTOR;PLPP3;KIT;KRAS;NRAS;ADCY6;EGFR;DNM2;PIK3R1;GAB1;RAF1;AKT2;AKT1;AKT3;ADCY3;AGT;LPAR1;PTK2B;GRB2;GRM1;GRM5;INSR;PDGFA;PDGFRA;PIK3CA;PIK3CB;PLA2G4A;PLCG1;PLCG2;PLD1;PRKCA;MAPK1;MAPK3;RALA;RHEB;SOS2;TSC1;DGKI;GAB2;AGPAT1;GNAI3;RAPGEF4;DNM3;SHC3;AGPAT5;PDGFC;AGPAT3;AGPAT4;DGKH;TSC2;AVPR1A;KITLG;ARF1;DGKG;MRAS;PIK3R3;ADCY5;F2R;DGKE;DGKB;SOS1;PLCB1;ADCY1;PIK3R6;PLPP1;P3R3URF-PIK3R3
Infectious disease: bacterial	hsa05132	Salmonella infection	132/3285	4,20E+06	98	MAP2K1;DDIT4;MTOR;IGF1R;RPS6KA3;ULK1;EIF4E2;TBC1D7;PTEN;KRAS;NRAS;IRS1;IKBKB;DVL2;PIK3R1;RAF1;RPTOR;AKT2;ATP6V1B2;AKT1;AKT3;WNT10B;ATP6V1A;ATP6V1C1;ATP6V1E1;CHUK;DVL3;EIF4E;GRB2;GRB10;GSK3B;INSR;LRP6;PDPK1;PIK3CA;PIK3CB;PRKAA1;PRKAA2;PRKCA;PRKCB;MAPK1;MAPK3;RHEB;RPS6KB1;CLIP1;SGK1;SKP2;SLC3A2;SOS2;TSC1;WNT2;WNT9A;FZD5;FZD3;SLC7A5;FZD4;FZD6;FZD8;LAMTOR3;ATP6V1G1;TTI1;DEPDC5;ULK2;RRAGB;RRAGA;RPS6KA6;CAB39;MIOS;RRAGC;MAPKAP1;WDR59;SEH1L;SESN2;FNIP1;F1LCN;RICTOR;LAMTOR4;IGF1;TSC2;STRADA;RPS6KA1;NPRL3;TNFRSF1A;PIK3R3;MLST8;WNT2B;BRAAF;DVL1;SOS1;ATP6V1D;FNIP2;DEPTOR;SLC38A9;RNF152;PRR5;CASTOR1;CASTOR2;P3R3URF-PIK3R3
Infectious disease: viral	hsa05161	Hepatitis B	93/3285	4,42E+06	173	TCL1A;BCL2;MCL1;HSP90B1;BCL2L11;CREB1;MAP2K1;DDIT4;FGFR1;MTOR;IGF1R;SPP1;EIF4E2;PPP2R5E;PTEN;CSF1;LAMC2;KIT;ERBB2;ERBB3;CDK6;THBS1;KRAS;NRAS;LAMC1;PTK2;CCND1;CDKN1A;VEGFA;GYS1;CDKN1B;IL6R;IRS1;MYC;COL4A1;COL1A2;IKBKB;EGFR;RELA;PIK3R1;CCNE1;MYB;BRCA1;RAF1;MET;ITGB3;RPTOR;AKT2;ITGB4;PPP2R2A;FOXO3;JAK1;YWHAZ;ERBB4;NFKB1;AKT1;RELN;JAK2;CDK2;AKT3;OSMR;EFNA5;ATF4;CHUK;COL4A5;COL6A1;ATF2;ATF6B;LPAR1;EFNA1;EPHA2;EIF4E;EREG;FGF2;FGF7;FGF9;FGF10;FGFR2;FLT1;F1N1;GNB1;GNB2;GRB2;GSK3B;HSP90AA1;HSP90AB1;TNC;IFNAR1;IFNAR2;INSR;ITGA6;ITGA2;ITGA3;ITGA4;ITGA9;ITGAV;ITGB1;ITGB5;ITGB8;LAMA3;LAMA5;LAMB1;MDM2;NTRK2;PDGFA;PDGFRA;PDPK1;PIK3CA;PIK3CB;PPP2CB;PPP2R1A;PPP2R1B;PPP2R2C;PPP2R3A;PPP2R5A;PPP2R5C;PRKAA1;PRKAA2;PRKCA;PKN2;MAPK1;MAPK3;PRLR;RAC1;RET;RHEB;RPS6KB1;SGK1;SOS2;TSC1;VEGFC;YWHAZ;YWHAG;YWHAH;CCNE2;MAGI1;CREB3;YWHAQ;ITGA11;PHLPP2;PHLPP1;PPP2R3C;PPP2R2D;PDGFC;GNB4;GNG7;IGF1;TNXB;GHR;LAMA2;TSC2;VWF;HGF;KITLG;PIK3R3;PPP2R2B;ITGA7;MLST8;COL4A6;F2R;PPP2CA;TNR;YWHAB;BAD;COL6A3;SOS1;PPP2R5D;MAGI2;CREB3L1;CRTC2;LAMB2;PIK3R6;P3R3URF-PIK3R3
Endocrine system	hsa04935	Growth hormone synthesis, secretion and action	74/3285	4,42E+06	81	SIRT1;CREB1;MTOR;IGF1R;SCD;ULK1;PPP2R5E;CCND1;GYS1;IRS1;IRS2;PIK3R1;RPTOR;AKT2;PPP2R2A;FOXO3;PPARG;CCNA2;AKT1;AKT3;ELAVL1;ACACB;CPT1A;EEF2;HMGCR;HNF4A;INSR;LEPR;PDPK1;PFKFB2;PFKFB3;PFKFB4;PFKP;PIK3CA;PIK3CB;PPP2CB;PPP2R1A;PPP2R1B;PPP2R2C;PPP2R3A;PPP2R5A;PPP2R5C;PRKAA1;PRKAA2;PRKAB1;PRKAB2;RAB2A;RHEB;RPS6KB1;SREBF1;MAP3K7;TSC1;CREB3;RAB10;TBC1D1;EEF2K;RAB14;CAB39;PPP2R3C;PPP2R2D;ADIPOR2;SCD5;IGF1;PFKM;TSC2;STRADA;PRKAG2;PIK3R3;PPP2R2B;CPT1C;PPP2CA;FASN;RAB11B;PPP2R5D;ADIPOR1;CREB3L1;CRTC2;LIPE;PFKL;ACACA;P3R3URF-PIK3R3
Cellular community - eukaryotes	hsa04520	Adherens junction	60/3285	4,48E+05	83	NLK;SIRT1;CSNK1A1;EP300;TBL1XR1;CCDC88C;FBXW11;CCND1;MYC;DVL2;MAPK9;APC;ROCK2;CTNNB1P1;BTRC;PPP3CA;WNT10B;CAMK2G;CREBBP;CSNK2A1;CSNK2A2;CTNNB1;DVL3;GSK3B;PRICKLE3;LRP6;SMAD3;SMAD4;MCC;NFATC2;NFATC3;ROR1;PPP3R1;PRKACA;PRKACB;PRKCA;PRKCB;MAPK8;PSEN1;RAC1;SIAH1;MAP3K7;TBL1X;TLE3;TLE4;WNT2;WNT9A;FZD5;FZD3;FZD4;FZD6;FZD8;CUL1;RUVBL1;WIF1;DAAM1;DAAM2;LEF1;RNF43;CHD8;SENP2;VANGL1;ZNRNF3;PRICKLE1;PRICKLE2;RSPO2;CACYPB;PPP3CB;TCF7L2;PPARD;PPP3CC;CSNK2B;CTNND2;MAPK10;WNT2B;DVL1;FOSL1;SKP1;RBX1;PLCB1;CXXC4;TBL1Y;CCAR2

Cancer: specific types	hsa05210	Colorectal cancer	57/3285	4,53E+06	32	ADAM17;EP300;KAT2B;NOTCH1;DVL2;NOTCH3;NOTCH2;ATXN1;ITCH;JAG1;NUMBL;CREBBP;DVL3;KAT2A;HDAC1;RBPJ;PSEN1;TLE3;TLE4;NCOR2;SPEN;HEY1;HEY2;MAML2;DTX3L;NRARP;ATXN1L;DVL1;CIR1;MAML3;DLL4;DTX3
Cell growth and death	hsa04114	Oocyte meiosis	81/3285	1,06E+07	30	BCL2;CSNK1A1;ARRB2;GRK2;FBXW11;CCND1;BTRC;ARRB1;CSNK1D;CSNK1G2;CSNK1G3;GAS1;GSK3B;PRKACA;PRKACB;CUL3;CUL1;CDON;CSNK1G1;SMURF2;BOC;SPOPL;GLI3;PTCH1;SPOP;EVC2;LRP2;HHIP;EFCAB7;GRK3
Nervous system	hsa04722	Neurotrophin signaling pathway	72/3285	1,23E+07	65	BMPT2;EP300;ID4;TFRC;SMAD1;THBS1;TGFB2;E2F5;SMAD5;SP1;MYC;ACVR1B;FBN1;TGFB2;RBL1;TGFB1;SMAD2;BMP1B;ACVR1;ACVR2A;ACVR2B;BMP6;BMP1A;CREBBP;LRRC32;HDAC1;INHBB;LTBP1;SMAD3;SMAD4;SMAD7;NEO1;PPP2CB;PPP2R1A;PPP2R1B;MAPK1;MAPK3;ROCK1;RPS6KB1;SKI;SKIL;TF;TGIF1;CUL1;ZFYVE16;LEMD3;SIN3A;GREM1;RGMA;TGIF2;SMURF2;THSD4;ACVR1C;RGM;HFE;NCOR1;DCN;PPP2CA;ZFYVE9;FST;SKP1;TFDP1;RBX1;HAMP;BMP5
Signal transduction	hsa04068	FoxO signaling pathway	78/3285	1,27E+07	36	MAP2K1;MAPK14;KRAS;NRAS;PTK2;VEGFA;PIK3R1;CDC42;RAF1;PTGS2;AKT2;AKT1;PPP3CA;AKT3;NFATC2;PIK3CA;PIK3CB;PLA2G4A;PLCG1;PLCG2;PPP3R1;PRKCA;PRKCB;MAPK1;MAPK3;PXN;RAC1;MAPKAPK3;MAPKAPK2;PIK3R3;PPP3CB;PPP3CC;MAPK13;BAD;HSPB1;P3R3URF-PIK3R3
Nervous system	hsa04720	Long-term potentiation	46/3285	1,39E+07	74	MAP2K1;ADCY9;MTOR;SPP1;TFAM;KRAS;NRAS;CCND1;ADCY6;GNAI3;NOTCH3;RAF1;HDAC4;PRKCE;AKT2;CDH1;JAG1;GNAI2;TGFB1;AKT1;MEF2D;SMAD2;AKT3;ADCY3;CALM1;CALM2;CALM3;CAMK4;EGR1;GNAI1;GNAQ;GNB1;GNB2;ITPR1;ITPR2;SMAD3;SMAD4;MEF2A;MEF2C;NRF1;SERPINE1;PDE3B;PIK3C3;PRKAA1;PRKAA2;PRKAB1;PRKAB2;PRKACA;PRKACB;MAPK1;MAPK3;RPS6KB1;RYYR2;RYYR3;SLC9A1;BECN1;GNAI3;PIK3R4;GNB4;MAP1LC3B;MAP1LC3A;GNG7;MYLK4;PRKAG2;MRAS;SLC8A1;ADCY5;ITPR3;APLN;PLCB1;ADCY1;LIPE;PIK3R6;CCN2
Infectious disease: bacterial	hsa05131	Shigellosis	130/3285	2,71E+07	87	LATS2;BMP2;RASSF1;PALS1;SMAD1;FBXW11;TGFB2;CCND1;MYC;TGFB2;SNAIL2;TEAD1;DVL2;TP53BP2;APC;PPP2R2A;YAP1;CDH1;YWHAZ;TGFB1;SMAD2;BTRC;BMP1B;WNT10B;ACTB;AFP;BIRC2;BIRC5;BMP6;BMP1A;CSNK1D;CTNNA1;CTNNB1;DLG1;DLG2;DVL3;GSK3B;ITGB2;LLGL2;SMAD3;SMAD4;SMAD7;SERPINE1;PPP1CA;PPP1CB;PPP1CC;PPP2CB;PPP2R1A;PPP2R1B;PPP2R2C;PRKCI;STK3;TEAD4;WNT2;WNT9A;YWHAE;YWHAG;YWHAH;FZD5;FZD3;FZD4;FZD6;FZD8;LATS1;DLG5;YWHAQ;WWC1;CRB1;WWTR1;LEF1;MOB1A;PPP2R2D;SAV1;AJUBA;FRMD6;PPP2R2B;CTNNA3;TCF7L2;PARD3;PPP2CA;YWHAB;WNT2B;DVL1;SCRIB;BMP5;PATJ;CCN2
Signal transduction	hsa04071	Sphingolipid signaling pathway	72/3285	2,93E+07	17	LATS2;RASSF1;TEAD1;PAK1;YAP1;STK3;TEAD4;LATS1;RASSF2;WWC1;WWTR1;MOB1A;SAV1;FAT4;AJUBA;FRMD6;DCHS1
Endocrine and metabolic disease	hsa04933	AGE-RAGE signaling pathway in diabetic complications	62/3285	3,31E+07	64	VCAM1;CREB1;MAP2K1;FOS;ADAM17;XIAP;CYLD;CSF1;MAPK14;IKKBK;MAP3K8;SOCS3;RELA;CASP7;PIK3R1;CASP3;MAPK9;ITCH;PTGS2;LIF;AKT2;JAG1;CEBPB;ICAM1;NFKB1;AKT1;AKT3;BIRC2;ATF4;CHUK;ATF2;ATF6B;CXCL1;CXCL2;CXCL3;IL1B;PIK3CA;PIK3CB;MAPK1;MAPK3;MAPK8;MAP2K6;CXCL5;MAP2K4;MAP3K7;TNFAIP3;TRAF3;VEGFC;RPS6KA4;BAG4;CREB3;TAB3;CXCL10;TRAF5;TNFRSF1A;PIK3R3;MAPK10;MAPK13;RIPK1;DNM1L;MAP3K5;CREB3L1;MAP2K7;P3R3URF-PIK3R3
Drug resistance: antineoplastic	hsa01522	Endocrine resistance	61/3285	3,40E+07	45	SPP1;LAMC2;THBS1;LAMC1;SDC4;CD44;COL4A1;COL1A2;ITGB3;ITGB4;RELN;CD47;COL4A5;COL6A1;DAG1;FN1;HSPG2;TNC;ITGA6;ITGA2;ITGA3;ITGA4;ITGA9;ITGAV;ITGB1;ITGB5;ITGB8;LAMA3;LAMA5;LAMB1;SV2B;ITGA11;MEPE;FRAS1;NPNT;AGRN;TNXB;LAMA2;VWF;ITGA7;COL4A6;TNR;COL6A3;SV2A;LAMB2
Cancer: specific types	hsa05222	Small cell lung cancer	58/3285	3,84E+07	69	VCAM1;SLITRK1;SDC4;F11R;CDH1;ICAM1;PTPRD;CD276;NCAM1;LRRC4;ALCAM;CDH3;CDH4;CLDN7;GLG1;HLA-A;HLA-DRB5;ITGA6;ITGA4;ITGA9;ITGAV;ITGB1;ITGB2;ITGB8;L1CAM;NCAM2;NEO1;PTPRF;PTPRM;PVR;CNTNAP1;CLDN12;CLDN1;NRXN3;SDC3;NLGN4Y;NTNG1;CNTNAP2;NLGN3;ESAM;SLITRK4;OCLN;PECAM1;CD4;NFASC;NRCAM;LRRC4B;ITGAL;VCAN;CADM3;NRXN1;SLITRK2;JAM3;CNTN1;HLA-C;PTPRC;SDC2;HLA-B;HLA-E;SLITRK3;NLGN1;NRXN2;SLITRK5;NLGN2;LRRC4C;SLITRK6;NEGR1;NECTIN2;NECTIN3
Signal transduction	hsa04066	HIF-1 signaling pathway	66/3285	4,06E+07	61	BPTF;TRRAP;RSF1;PBRM1;INO80B;BAZ2A;INO80D;BAZ1A;ACTB;CHD3;CHD4;HDAC1;RBBP7;SMARCA2;SMARCA4;SMARCB1;SMARCC1;SMARCC2;SMARCD1;YY1;DPF3;ARID1A;RUVBL1;MBD2;BAZ1B;MTA2;MORF4L2;ZNHIT1;BRD8;MORF4L1;BRD7;BAZ2B;GATAD2A;PHF10;DMAP1;GATAD2B;EP400;MEAF6;ACTR5;EPC1;PHF6;ARID2;RBBP4;NFRKB;UCHL5;KAT5;SMARCA5;YEATS4;SRCAP;EPC2;ARID1B;INO80;MTA3;CECR2;SS18L1;YY2;RUVBL2;MACROH2A1;H2AZ2;BICRA;H2AJ
Cancer: specific types	hsa05213	Endometrial cancer	41/3285	4,19E+07	65	CBX7;EP300;RNF2;CBX4;EED;PHC3;E2F6;PHF19;PHC2;PCGF5;ASXL2;JARID2;EZH2;BMI1;BAP1;CREBBP;EZH1;HDAC1;FOXK2;RBBP7;SCML1;UBE2D1;UBE2D3;YY1;USP7;YAF2;DCAF7;PCGF3;SCML2;CBX3;MTF2;KDM2A;MGA;RYBP;CBX6;SUZ12;AUTS2;SFBMT1;BCOR;TEX10;MBD5;ASXL3;PCGF6;LCOR;KDM2B;CBX2;USP45;MBD6;AEBP2;FOXK1;USP16;RBBP4;FBRSL1;COMMD3-BMI1;CSNK2B;PHF1;HCFC1;SKP1;TFDP1;ASXL1;CBX8;L3MBTL2;OGT;YY2;PCGF2
Cancer: specific types	hsa05220	Chronic myeloid leukemia	50/3285	4,62E+07	45	CNOT9;TENT4B;HSPD1;CNOT6;BTG3;BTG2;DDX6;HSPA9;CNOT4;PARN;PFKP;PABPC4;CNOT8;TOB1;TOB2;DIS3;EDC4;PABPC1;LSM3;CNOT7;XRN1;EDC3;PNPT1;DIS3L;DCP2;PATL1;PAN3;ENO1;ENO2;PFKM;PABPC4B;PAN2;LSM5;CNOT2;DCPS;EXOSC7;CNOT1;ZCCHC7;EXOSC6;CNOT6L;PFKL;DCP1A;TENT4A;MTREX;SKI C8

Signal transduction	hsa04390	Hippo signaling pathway	87/3285	5,93E+07	100	XIAP;UBB;CUL5;HUWE1;FBXW11;SOCS3;UBE2I;CDC34;TRAF6;UBE2Q1;BRCA1;ITCH;BTRC;VHL;FBXW7;RHOB;BIRC2;CDC20;CDC27;DDB1;DDB2;UBE2K;MDM2;MAP3K1;TRIM37;NEDD4;SIAH1;SKP2;UBC;UBE2B;UBE2D1;UBE2D3;UBE2E1;UBE2G1;UBE2H;UBE2L3;UBE2N;UBE3A;CUL4B;CUL4A;CUL3;CUL2;CUL1;PIAS1;CDC23;HERC3;HERC2;UBE2M;TRIP12;UBE4A;RNF7;UBE3C;KEAP1;CUL7;UBA2;UBE4B;TRIM32;NEDD4L;ANAPC13;ANAPC15;HERC4;UBE2S;UBR5;ANAPC7;UBE2J1;UBE2R2;DET1;UBA6;UBE2W;BIRC6;UBE2O;SMURF2;UBE2Z;UBE3B;UBE2Q2;ANAPC16;RCHY1;UBA52;CDC16;FANCL;RPS27A;UBE2QL1;SAE1;RHOB;UBA1;UBE2A;UBE2G2;HERC1;UBE2L6;PIAS3;SKP1;WWP1;WWP2;RBX1;PPL1;PIAS4;UBE2E2;CBLB;NHLRC1;ELOC
Infectious disease: viral	hsa05163	Human cytomegalovirus infection	117/3285	6,39E+07	111	BCL2;DNAJB11;HSP90B1;HSPA1B;LMAN1;SEC24C;PDIA6;MAN1A2;GANAB;BAK1;DNAJC1;HERPUD1;MAPK9;DAD1;SEC24D;ATF4;CALR;CAPN2;ATF6B;EIF2S1;PDIA3;DNAJA1;HSPA1L;HSPA5;HSP90AA1;HSP90AB1;DNAJB1;STT3A;MAPK8;DNAJC3;RAD23B;RPN1;RPN2;SEL1L;SSR3;SEC62;UBE2D1;UBE2D3;UBE2G1;VCP;WFS1;MOGS;CUL1;EIF2AK3;BAG2;EDEM1;UBE4B;DNAJA2;SEC24B;SEC23B;SEC23A;HYOU1;SEC24A;HSPH1;CKAP4;SEC63;HSPA4L;SEC31A;ATF6;TRAM1;SEC61A1;UBQLN2;UBQLN1;UBE2J1;DNAJC10;DNAJB12;YOD1;NPLOC4;UGGT2;NSFL1C;SAR1A;UGGT1;UBQLN4;MAN1C1;DERL1;EDEM3;DNAJC5;MAGT1;RNF5;TXNDC5;PRKCSH;OS9;CANX;PLAA;SAR1B;ERLEC1;ATXN3;AMFR;NGLY1;UBXN6;ERN1;MAPK10;UBE2G2;MBTPS1;MAP3K5;HSPA8;SKP1;RBX1;SEC31B;MBTPS2;DERL2;OSTC;MAP2K7;SIL1;PPP1R15A;KRTCAP2;ERO1A;SELENOS;ERO1B;UFD1;MARCHF6
Endocrine and metabolic disease	hsa04931	Insulin resistance	65/3285	6,40E+07	33	TSG101;EP300;RAN;KAT2B;AFF4;PDCD6IP;HGS;BICD1;CCNT1;CCNT2;CREBBP;KAT2A;MAP1A;MAP1B;MLLT3;MX2;FURIN;SMARCB1;SUPT5H;XPO1;NUP153;CPSF6;ELL2;BICD2;TNPO3;SAMHD1;NELFD;CHMP6;CD4;PIN1;RANBP2;NELFB;MAP1S
Infectious disease: viral	hsa05167	Kaposi sarcoma-associated herpesvirus infection	104/3285	6,42E+07	20	FEN1;MCM2;MCM3;MCM4;MCM6;POLA1;POLD2;POLE;RFC2;RFC3;RFC5;RPA2;RPA3;POLE4;RNASEH1;RNASEH2B;RFC1;RPA1;SSBP1;RNASEH2A
Translation	hsa03015	mRNA surveillance pathway	62/3285	7,51E+07	32	POLR2K;GTF2H1;DDB1;DDB2;ERCC5;GTF2H3;MNAT1;POLD2;POLE;POLR2B;POLR2C;POLR2D;POLR2E;POLR2H;RAD23B;RFC2;RFC3;RFC5;RPA2;RPA3;XPC;CUL4B;CUL4A;POLE4;UVSSA;ERCC1;POLR2M;RFC1;RPA1;CETN2;RBX1;BIVM-ERCC5
Infectious disease: bacterial	hsa05100	Bacterial invasion of epithelial cells	50/3285	7,57E+07	75	TNPO1;XPO6;KPNA1;KPNA2;KPNA4;RAN;NDC1;KPNB1;IPO5;THOC3;POM121;PNN;UBE2I;RBM8A;GLE1;KPNA3;KPNA5;NCBP1;NUP98;RANGAP1;TPR;XPO1;DDX39B;NUP214;NUP155;EIF4A3;NUP153;IPO8;IPO7;NUP50;XPO7;CASC3;NCBP2;ACIN1;XPO7;NUP210;NUP160;TNPO3;KPNA6;AHCTF1;UPF2;NXT1;TNPO2;NMD3;IPO11;NUP54;TMEM33;IPO9;NUP107;THOC2;XPO5;SEN2;XPO4;THOC6;THOC7;SEH1L;SUMO1;SUMO2;SNUPN;NXF1;NUP88;THOC1;SAP18;RANBP2;RNPS1;IPO13;NUP205;NUP188;MAGOHB;NUP133;RANBP17;UPF3A;NUP37;NUP58;POM121C
Signal transduction	hsa04151	PI3K-Akt signaling pathway	173/3285	9,43E+07	62	FUS;RNMT;PPP2R5E;WDR82;PNN;RBM8A;PPP2R2A;SMG5;CSTF2;GLE1;GSTP1;NCBP1;PPP1CA;PPP1CB;PPP1CC;PPP2CB;PPP2R1A;PPP2R1B;PPP2R2C;PPP2R3A;PPP2R5A;PPP2R5C;DDX39B;SYMPK;PABPC4;EIF4A3;SMG7;HBS1L;PAPOLA;NUDT21;CPSF6;CASC3;NCBP2;ACIN1;SMG1;SMG6;TARDBP;UPF2;PABPC1;NXT1;CPSF1;CPSF3;PELO;PPP2R3C;WDR33;PPP2R2D;PAPOLG;FIP1L1;MSI2;NXF1;PABPC4L;PPP2R2B;MSI1;PPP2CA;RNGTT;ETF1;SAP18;PPP2R5D;RNPS1;PCF11;MAGOHB;UPF3A
Signal transduction	hsa04350	TGF-beta signaling pathway	65/3285	9,43E+07	113	CREB1;DDX3X;EP300;PMAIP1;KAT2B;H4C15;CDK6;KRAS;NRAS;RB1;CCND1;CDKN1A;CDKN1B;BAK1;GSN;RELA;GTF2H1;PIK3R1;CDC42;CASP3;CCNE1;RBL1;HDAC4;HNRNPK;JAK1;YWHAZ;CCNA2;NFKB1;CDK2;STAT3;ACTN4;ACTN1;ATF4;C3;CDK1;CDC20;CHD4;ATF2;CREBBP;ATF6B;DDB1;DLG1;EGR3;KAT2A;GRB2;GTF2A1;GTF2E1;GTF2H3;HDAC1;HLA-A;RBPJL;IL6ST;LTBR;MDM2;PIK3CA;PIK3CB;PKM;PRKACA;PRKACB;MAPK1;MAPK3;PXN;RAC1;RAS2;REL;SKP2;SP100;SRF;STAT5B;TRAF3;UBE3A;YWHAE;YWHAG;YWHAB;USP7;DNAJA3;ATP6V0D1;CCNE2;MAPKAPK2;TBPL1;IRF9;CREB3;YWHAG;UBR4;SND1;MRPS18B;VAC14;LYN;TRAF5;PIK3R3;VDAC3;HDAC11;HDAC9;GTF2E2;HLA-C;YWHAB;HDAC3;BAD;HLA-B;HLA-E;SCRIB;CREB3L1;H4C8;H4C3;H4C11;H4C16;H4C14;H4C5;H4C2;P3R3URF-PIK3R3;H4C12;H4C13;H4C6
Neurodegenerative disease	hsa05014	Amyotrophic lateral sclerosis	176/3285	1,34E+08	116	ESR1;TIMP3;PDCD4;MAP2K1;FGFR1;MTOR;IGF1R;MAPK14;ERBB2;ERBB3;THBS1;KRAS;NRAS;DDX5;SDC4;PTK2;CCND1;CDKN1A;VEGFA;CD44;MYC;COL1A2;EGFR;TGFB2;CAV1;ARAF;IQGAP1;PIK3R1;CDC42;CASP3;PAK1;HIF1A;RAF1;MET;ITGB3;AKT2;ROCK2;ERBB4;AKT1;SMAD2;PLAU;RDX;AKT3;ANK2;WNT10B;STAT3;ACTB;CAMK2G;CD63;CTNBNB1;CTSL;CTTN;FGF2;FLNA;FN1;GPC3;GRB2;HSPG2;ITGA2;ITGAV;ITGB1;ITGB5;ITPR1;ITPR2;MDM2;PDPK1;PIK3CA;PIK3CB;PLAUR;PLCG1;PLCG2;PPP1CA;PPP1CB;PPP1CC;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;PXN;RAC1;ROCK1;RPS6KB1;SLC9A1;SOS2;TIAM1;WNT2;WNT9A;FZD5;FZD3;FZD4;FZD6;FZD8;FRS2;ARHGAP12;DROSHA;PLCE1;PPP1R12C;IGF1;PTCH1;HGF;MRAS;PIK3R3;ANK3;PPP1R12B;DCN;ITPR3;LUM;MAPK13;SDC2;WNT2B;BRAF;SOS1;P3R3URF-PIK3R3
Amino acid metabolism	hsa00310	Lysine degradation	42/3285	1,45E+08	93	ESR1;BCL2;E2F1;HSP90B1;CREB1;MAP2K1;FOS;ADCY9;XIAP;MTOR;KPNA1;KPNA2;KPNA4;RPS6KA3;TNFSF11;KPNB1;ARRB2;BCL6;KRAS;NRAS;RB1;CCND1;PARA;VEGFA;MYC;ADCY6;EGFR;GNAI3;RELA;PIK3R1;NOTCH2;RAF1;AKT2;JAG1;GNAI2;NFKB1;AKT1;JAK2;AKT3;STAT3;ADCY3;BIRC5;AR;ARNT;ARRB1;ATF4;CACNA1B;CDC6;ATF2;ATF6B;FGF2;FGF7;FGF9;FGF10;GNAI1;GRB2;GSTM3;HS

						P90AA1;HSP90AB1;KPNA3;KPNA5;MGST3;PGR;PIK3CA;PIK3CB;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;RPS6KB1;SOS2;STAT5B;CREB3;KPNA6;RPS6KA6;CHRFAM7A;CACNA1A;CACNA1D;CHRNA2;RPS6KA1;PIK3R3;ADCY5;BAD;SOS1;PTGES3;DLL4;ADCY1;CREB3L1;PAQR7;CACNA1C;P3R3URF-PIK3R3
Infectious disease: viral	hsa05170	Human immunodeficiency virus 1 infection	110/3285	1,54E+08	100	MAP2K1;FOS;CAT;PRKCD;PTEN;MAPK14;KRAS;NRAS;PTK2;VEGFA;IKBKB;EGFR;ARAF;RELA;PIK3R1;PRKD2;MAPK9;HIF1A;ABL1;RAF1;MET;AKT2;FOXO3;NFKB1;AKT1;AKT3;ABL2;SLC25A6;ARNT;CHUK;COX7B;COX8A;SLC26A2;GRB2;GSTM3;MGST3;NDUFA4;NDUFA9;NDUFB1;NDUFB5;NDUFS4;PDPK1;PIK3CA;PIK3CB;PLD1;MAPK1;MAPK3;MAPK8;PTPRJ;RAC1;MAP2K4;SOD1;SOS2;UQCRC2;KEAP1;AKR1A1;PRKD3;NOX4;HGF;NQO1;SLC26A6;UQCRH;PIK3R3;VDAC3;SLC25A4;SLC25A5;NDUFA2;UQCRB;NDUFS1;NDUFC2;CBR1;COX7C;NDUFA6;MAPK10;MAPK13;UQCRC1;VDAC1;COX5A;BAD;BRAF;NDUFA10;NDUFA7;NDUFAB1;SOS1;MAP3K5;NDUFA12;MAP2K7;NDUFV1;NDUFV2;COX6A1;ATP5F1A;ATP5MC2;ATP5MC3;ATP5F1B;ATP5PB;ATP5F1E;ATP5PO;ATP5PD;SOD2;P3R3URF-PIK3R3
Cancer: specific types	hsa05214	Glioma	48/3285	2,36E+08	44	MAP2K1;FGFR1;MTOR;HK2;PTEN;G6PD;KIT;ERBB2;KRAS;NRAS;MYC;NTRK3;EGFR;PIK3R1;HIF1A;RAF1;MET;AKT2;AKT1;AKT3;FGFR2;GLS;HK1;IDH1;LDHA;LDHB;PDGFRA;PFKP;PIK3CA;PIK3CB;PKM;MAPK1;MAPK3;RET;SLC1A5;SLC7A5;PFKM;PIK3R3;SIRT6;PGAM1;SLC2A1;PFKL;TIGAR;P3R3URF-PIK3R3
Neurodegenerative disease	hsa05010	Alzheimer disease	182/3285	3,91E+08	57	MAP2K1;FOS;MTOR;PLPP3;KRAS;NRAS;SLC44A1;SP1;EGFR;SLC22A5;PIK3R1;MAPK9;HIF1A;RAF1;AKT2;AKT1;AKT3;GRB2;PDGFA;PDGFRA;PDPK1;PIK3CA;PIK3CB;PLA2G4A;PLCG1;PLD1;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;RAC1;RHEB;RPS6KB1;SOS2;TSC1;WASF1;DGKI;WASF2;WASF3;PDGFC;CHPT1;SLC44A2;DGKH;SLC44A5;TSC2;DGKG;PIK3R3;CHKA;MAPK10;DGKE;DGKB;SOS1;LYPLA1;GPCPD1;PLPP1;P3R3URF-PIK3R3
Cancer: specific types	hsa05225	Hepatocellular carcinoma	90/3285	4,42E+08	48	MAP2K1;FOS;MAP3K3;MTOR;IFNGR1;PTEN;MAPK14;KRAS;NRAS;EML4;IKBKB;EGFR;RELA;PIK3R1;TRAF6;HIF1A;RAF1;AKT2;JAK1;NFKB1;AKT1;PPP3CA;JAK2;STAT1;AKT3;STAT3;ALK;CHUK;CSNK2A1;CSNK2A2;MYD88;NFATC2;NFATC3;PIK3CA;PIK3CB;PLCG1;PPP3R1;MAPK1;MAPK3;MAP2K6;RPS6KB1;CD4;PIK3R3;PPP3CB;PPP3CC;CSNK2B;MAPK13;P3R3URF-PIK3R3
Signal transduction	hsa04015	Rap1 signaling pathway	108/3285	4,42E+08	57	BCL2;BCL2L1;MAP2K1;FOS;MTOR;PMAIP1;KRAS;NRAS;TGFB2;CCND1;CDKN1A;BAK1;MYC;EGFR;TGFB2;ARAF;MSH2;PIK3R1;CASP3;MAPK9;RAF1;APC;AKT2;TGFB1;AKT1;SMAD2;AKT3;BIRC5;CTNNB1;DCC;DDB2;GADD45A;EREG;GRB2;GSK3B;MSH6;SMAD3;SMAD4;PIK3CA;PIK3CB;MAPK1;MAPK3;MAPK8;RAC1;RALA;RPS6KB1;SOS2;APPL1;LEF1;POLK;PIK3R3;TCF7L2;MAPK10;BAD;BRAF;SOS1;P3R3URF-PIK3R3
Infectious disease: viral	hsa05160	Hepatitis C	85/3285	5,06E+08	53	ETS1;MAP2K1;EP300;RAP1B;KRAS;NRAS;CDKN1A;VEGFA;TGFB2;ARAF;PIK3R1;CDC42;PAK1;GAB1;HIF1A;CRKL;RAF1;MET;AKT2;AKT1;VHL;AKT3;ARNT;CRBBP;CRK;EPAS1;GRB2;PAK2;PAK3;PIK3CA;PIK3CB;MAPK1;MAPK3;RAC1;RAP1A;SOS2;CUL2;ARNT2;PAK4;EGLN1;FLCN;FH;HGF;PIK3R3;BAD;BRAF;SOS1;SLC2A1;RBX1;EGLN2;PAK5;ELOC;P3R3URF-PIK3R3
Cellular community - eukaryotes	hsa04550	Signaling pathways regulating pluripotency of stem cells	78/3285	7,02E+08	53	E2F1;MAP2K1;MTOR;ERBB2;E2F3;CDK6;KRAS;TGFB2;RB1;CCND1;CDKN1A;VEGFA;BAK1;IKBKB;EGFR;TGFB2;ARAF;RELA;PIK3R1;CDC42;MAPK9;BRCA2;RAF1;AKT2;JAK1;TGFB1;NFKB1;AKT1;SMAD2;STAT1;AKT3;STAT3;CHUK;DDB2;GADD45A;SMAD3;SMAD4;PIK3CA;PIK3CB;PLD1;MAPK1;MAPK3;MAPK8;RAC1;RALA;RPS6KB1;POLK;PIK3R3;MAPK10;BAD;BRAF;RALBP1;P3R3URF-PIK3R3
Signal transduction	hsa04014	Ras signaling pathway	118/3285	7,97E+08	41	MAP2K1;PTEN;ERBB2;KRAS;NRAS;CCND1;CDKN1A;BAK1;MYC;EGFR;ARAF;PIK3R1;RAF1;APC;AKT2;CDH1;FOXO3;AKT1;AKT3;CTNNA1;CTNNB1;DDB2;GADD45A;GRB2;GSK3B;ILK;PDPK1;PIK3CA;PIK3CB;MAPK1;MAPK3;SOS2;LEF1;POLK;PIK3R3;CTNNA3;TCF7L2;BAD;BRAF;SOS1;P3R3URF-PIK3R3
Aging	hsa04213	Longevity regulating pathway - multiple species	40/3285	8,80E+08	48	E2F1;MAP2K1;MTOR;IGF1R;PTEN;E2F3;CDK6;KRAS;NRAS;RB1;CCND1;CDKN1A;BAK1;EGFR;ARAF;PIK3R1;RAF1;AKT2;AKT1;AKT3;CALM1;CALM2;CALM3;CAMK4;CAMK2G;DDB2;GADD45A;GRB2;MDM2;PDGFA;PDGFRA;PIK3CA;PIK3CB;PLCG1;PLCG2;PRKCA;PRKCB;MAPK1;MAPK3;SOS2;POLK;SHC3;IGF1;PIK3R3;BRAF;SOS1;CAMK1D;P3R3URF-PIK3R3
Nervous system	hsa04730	Long-term depression	39/3285	8,84E+08	68	BCL2;E2F1;HSP90B1;CREB1;MAP2K1;FGFR1;EP300;MTOR;IGF1R;PTEN;ERBB2;E2F3;KRAS;NRAS;RB1;CCND1;CDKN1A;CDKN1B;IKBKB;EGFR;ARAF;RELA;PIK3R1;CCNE1;RAF1;AKT2;NFKB1;AKT1;PLAU;CDK2;AKT3;AR;ATF4;CHUK;CREBBP;CTNNB1;ERG;FGFR2;GRB2;GRM1;GRM5;GSK3B;GSTP1;HSP90AA1;HSP90AB1;MDM2;NFKB1;PDGFA;PDGFRA;PDPK1;PIK3CA;PIK3CB;MAPK1;MAPK3;SOS2;CCNE2;CREB3;LEF1;PDGFC;IGF1;PIK3R3;TCF7L2;SLC46A1;BAD;BRAF;SOS1;CREB3L1;P3R3URF-PIK3R3
Infectious disease: bacterial	hsa05135	Yersinia infection	75/3285	8,89E+08	23	MAP2K1;KRAS;NRAS;CCND1;CDKN1A;BAK1;MYC;CDH1;PPARG;CTNNB1;DDB2;GADD45A;MAPK1;MAPK3;RET;TPR;CCDC6;LEF1;POLK;TCF7L2;PAX8;BRAF;NCOA4
Cell motility	hsa04810	Regulation of actin cytoskeleton	115/3285	1,03E+09	44	E2F1;MAP2K1;FGFR1;IGF1R;PTEN;E2F3;CDK6;KRAS;NRAS;RB1;CCND1;CDKN1A;BAK1;MITF;EGFR;ARAF;PIK3R1;RAF1;MET;AKT2;CDH1;AKT1;AKT3;DDB2;GADD45A;FGF2;FGF7;FGF9;FGF10;MDM2;PDGFA;PDGFRA;PIK3CA;PIK3CB;MAPK1;MAPK3;POLK;PDGFC;IGF1;HGF;PIK3R3;BAD;BRAF;P3R3URF-PIK3R3
Cancer: specific types	hsa05224	Breast cancer	79/3285	1,18E+09	22	E2F1;MAP2K1;RASSF1;ERBB2;E2F3;THBS1;KRAS;NRAS;RB1;CCND1;CDKN1A;VEGFA;MYC;EGFR;ARAF;RAF1;CDH1;DAPK1;MDM2;MAPK1;MAPK3;BRAF
Cancer: overview	hsa05230	Central carbon metabolism in cancer	44/3285	1,26E+07	50	E2F1;MAP2K1;E2F3;CDK6;KRAS;NRAS;TGFB2;RB1;CCND1;CDKN1A;CDKN1B;BAK1;MYC;IKBKB;TGFB2;ARAF;RELA;PIK3R1;CRKL;ABL1;RAF1;AKT2;TGFB1;NFKB1;AKT1;AKT3;CHUK;CRK;DDB2;GADD45A;GRB2;HDAC1;SMAD3;SMAD4;MDM2;PIK3CA;PIK3CB;MAPK1;MAPK3;SOS2;STAT5B;GAB2;POLK;SHC3;MECOM;PIK3R3;BAD;BRAF;SOS1;P3R3URF-PIK3R3

Cancer: overview	hsa05231	Choline metabolism in cancer	57/3285	1,33E+09	40	MAP2K1;MTOR;PER2;KIT;KRAS;NRAS;CCND1;MYC;IKBKB;ARAF;RELA;PIK3R1;RAF1;RUNX1T1;AKT2;CCNA2;NFKB1;AKT1;AKT3;STAT3;CHUK;DUSP6;GRB2;JUP;PIK3CA;PIK3CB;MAPK1;MAPK3;RPS6KB1;SOS2;STAT5B;LEF1;ZBTB16;PIK3R3;TCF7L2;PPARD;BAD;BRAF;SOS1;P3R3URF-PIK3R3
Immune system	hsa04660	T cell receptor signaling pathway	67/3285	1,80E+09	58	BCL2;E2F1;XIAP;PTEN;LAMC2;E2F3;CDK6;RB1;LAMC1;PTK2;CCND1;CDKN1A;CDKN1B;APAF1;BAK1;MYC;COL4A1;IKBKB;RELA;PIK3R1;TRAF6;CASP3;CCNE1;PTGS2;AKT2;NFKB1;AKT1;CDK2;AKT3;BIRC2;CHUK;COL4A5;DDB2;GADD45A;FN1;ITGA6;ITGA2;ITGA3;ITGAV;ITGB1;LAMA3;LAMA5;LAMB1;PIK3CA;PIK3CB;SKP2;TRAF3;CCNE2;POLK;LAMA2;TRAF5;PIK3R3;FHIT;CKS1B;COL4A6;ZBTB17;LAMB2;P3R3URF-PIK3R3
Circulatory system	hsa04261	Adrenergic signaling in cardiomyocytes	81/3285	1,80E+09	51	E2F1;MAP2K1;RASSF1;ERBB2;E2F3;CDK6;KRAS;NRAS;RB1;EML4;CCND1;CDKN1A;BAK1;EGFR;ARAF;STK4;PIK3R1;RAF1;MET;AKT2;FOXO3;AKT1;AKT3;STAT3;ALK;DDB2;GADD45A;GRB2;KIF5A;KIF5B;KIF5C;PDPK1;PIK3CA;PIK3CB;PLCG1;PLCG2;PRKCA;PRKCB;MAPK1;MAPK3;RET;SOS2;STAT5B;POLK;HGF;PIK3R3;FHIT;BAD;BRAF;SOS1;P3R3URF-PIK3R3
Transport and catabolism	hsa04148	Efferocytosis	82/3285	2,22E+09	79	ESR1;NCOA3;E2F1;MAP2K1;FOS;FGFR1;CSNK1A1;MTOR;IGF1R;TNFSF11;PTEN;NOTCH1;KIT;ERBB2;E2F3;CDK6;KRAS;NRAS;RB1;CCND1;CDKN1A;SP1;BAK1;MYC;EGFR;DVL2;ARAF;PIK3R1;NOTCH3;NOTCH2;BRCA2;BRCA1;RAF1;APC;AKT2;JAG1;AKT1;AKT3;WNT10B;CTNNB1;DDB2;GADD45A;DVL3;FGF2;FGF7;FGF9;FGF10;GRB2;GSK3B;LRP6;PGR;PIK3CA;PIK3CB;MAPK1;MAPK3;RPS6KB1;SOS2;WNT2;WNT9A;FZD5;FZD3;FZD4;FZD6;FZD8;HEY1;HEY2;LEF1;POLK;SHC3;IGF1;PIK3R3;TCF7L2;NCOA1;WNT2B;BRAF;DVL1;SOS1;DLL4;P3R3URF-PIK3R3
Cancer: specific types	hsa05218	Melanoma	44/3285	3,37E+09	90	E2F1;MAP2K1;CSNK1A1;MTOR;IGF1R;PBRM1;PTEN;E2F3;CDK6;KRAS;NRAS;TGFB2;RB1;CCND1;CDKN1A;BAK1;MYC;EGFR;TGFB2;DVL2;ARAF;PIK3R1;GAB1;GAB1;ABC1;ABC1;RAF1;MET;APC;AKT2;TGFB1;AKT1;SMAD2;AKT3;CTNNB1;DDB2;GADD45A;DVL3;GRB2;GSK3B;GSTM3;GSTP1;LRP6;SMAD3;SMAD4;MGST3;PIK3CA;PIK3CB;PLCG1;PLCG2;PRKCA;PRKCB;MAPK1;MAPK3;RPS6KB1;SMARCA2;SMARCA4;SMARCB1;SMARCC1;SMARCC2;SMARCD1;SOS2;TXNRD1;WNT2;WNT9A;FZD5;FZD3;DPF3;ARID1A;FZD4;FZD6;FZD8;KEAP1;BRD7;LEF1;POLK;SHC3;PHF10;ARID2;HGF;NQO1;PIK3R3;TCF7L2;TXNRD3;WNT2B;BAD;BRAF;DVL1;SOS1;ARID1B;P3R3URF-PIK3R3
Infectious disease: bacterial	hsa05120	Epithelial cell signaling in Helicobacter pylori infection	43/3285	3,51E+09	78	CDX2;BCL2;E2F1;MAP2K1;CSNK1A1;MTOR;ERBB2;E2F3;KRAS;NRAS;TGFB2;RB1;CCND1;CDKN1A;CDKN1B;BAK1;MYC;EGFR;TGFB2;DVL2;ARAF;PIK3R1;CNE1;GAB1;ABC1;ABC1;RAF1;MET;APC;AKT2;CDH1;TGFB1;AKT1;SMAD2;CDK2;AKT3;WNT10B;CTNNA1;CTNNB1;DDB2;GADD45A;DVL3;FGF2;FGF7;FGF9;FGF10;FGFR2;GRB2;GSK3B;JUP;LRP6;SMAD3;SMAD4;PIK3CA;PIK3CB;MAPK1;MAPK3;RPS6KB1;SOS2;WNT2;WNT9A;FZD5;FZD3;FZD4;FZD6;FZD8;CCNE2;LEF1;POLK;SHC3;HGF;PIK3R3;CTNNA3;TCF7L2;WNT2B;BRAF;DVL1;SOS1;P3R3URF-PIK3R3
Signal transduction	hsa04371	Apelin signaling pathway	74/3285	3,51E+09	45	GJA1;ITGB3;ITGB4;ACTB;ACTN2;ATP2A2;CACNA2D1;CACNB2;CACNB4;CTNNA1;CTNNB1;DAG1;DSC2;DSG2;DSP;ITGA6;ITGA2;ITGA3;ITGA4;ITGA9;ITGAV;ITGB1;ITGB5;ITGB8;JUP;PKP2;RYR2;SGCB;SNTB2;ITGA11;LEF1;CACNG8;CACNA2D4;LAMA2;CACNA1D;CACNA2D2;SLC8A1;CTNNA3;DTNA;ITGA7;TCF7L2;DES;ATP2A1;CACNA2D3;CACNA1C
Neurodegenerative disease	hsa05016	Huntington disease	145/3285	3,64E+09	93	MTOR;PDK3;PRKCD;PTEN;G6PD;MAPK14;TGFB2;PPARA;GYS1;SP1;IRS1;COL3A1;COL1A2;TGFB2;RELA;PIK3R1;MAPK9;AKT2;TGFB1;NFKB1;AKT1;SMAD2;AKT3;PARP1;AGT;SLC25A6;ATP2A2;CAMK2G;COX7B;COX8A;CPT2;CTSD;GAPDH;GFP1;GSK3B;GSR;INSR;SMAD3;NDUFA4;NDUFA9;NDUFB1;NDUFB5;NDUFS4;PDK4;PIK3CA;PIK3CB;PPP1CA;PPP1CB;PPP1CC;PRKCA;PRKCB;MAPK8;RAC1;RYR2;UQCRC2;TBC1D4;CYBB;UQCRC1;PIK3R3;VDAC3;SLC25A4;SLC25A5;NDUFA2;PDK2;UQCRCB;NDUFS1;NDUFC2;COX7C;NDUFA6;MAPK13;UQCRC1;VDAC1;COX5A;ATP2A1;NDUFA10;NDUFA7;NDUFAB1;SLC2A1;PLCB1;NDUFA12;NDUFV1;NDUFV2;COX6A1;ATP5F1A;ATP5MC2;ATP5MC3;ATP5F1B;ATP5PB;ATP5F1E;ATP5PO;ATP5PD;P3R3URF-PIK3R3
Signal transduction	hsa04022	cGMP-PKG signaling pathway	85/3285	3,88E+09	101	BCL2;VCAM1;HSP90B1;FOS;LDLR;HSPA1B;RAP1B;MAPK14;HSPD1;KRAS;NRAS;PTK2;APAF1;IKBKB;RELA;CASP7;CASP6;PIK3R1;CDC42;IRAK1;TRAF6;CASP3;MAPK9;ABCA1;AKT2;ROCK2;PPARG;TBK1;ICAM1;NFKB1;AKT1;PPP3CA;JAK2;AKT3;STAT3;ATF4;CALM1;CALM2;CALM3;CAMK2G;CHUK;CYP2C8;EIF2S1;CXCL1;CXCL2;CXCL3;GSK3B;HSPA1L;HSPA2;HSPA4;HSPA5;HSP90AA1;HSP90AB1;IL1B;ITPR1;MYD88;NFATC2;NFATC3;PDPK1;PIK3CA;PIK3CB;PLCG1;POU2F1;POU2F2;PPP3R1;PRKCA;MAPK1;MAPK3;MAPK8;MAP2K6;RAC1;RAP1A;MAP2K4;MAP3K7;TRAF3;VLDLR;TNFRSF10B;TNFRSF10A;EIF2AK3;ATF6;IRAK4;LYN;ABC G1;APOB;CYBB;TNFRSF1A;PIK3R3;PPP3CB;PPP3CC;ERN1;MAPK10;MAPK13;BAD;MAP3K5;HSPA8;PLCB1;MAP2K7;APOA1;ERO1A;SOD2;P3R3URF-PIK3R3
Infectious disease: viral	hsa05169	Epstein-Barr virus infection	101/3285	3,88E+09	70	BCL2;VCAM1;BMPR2;HSP90B1;FOS;IL1A;MAPK14;SDC4;PTK2;VEGFA;IKBKB;CAV1;RELA;PIK3R1;MAPK9;ASS1;ITGB3;AKT2;ICAM1;NFKB1;AKT1;BMPR1B;AKT3;ACTB;ACVR1;ACVR2A;ACVR2B;BMPR1A;CALM1;CALM2;CALM3;CHUK;CTNNB1;CTSL;GSTM3;GSTP1;HSP90AA1;HSP90AB1;IL1B;IL1R1;ITGAV;MEF2A;MEF2C;MGST3;PDGFA;PIK3CA;PIK3CB;PRKAA1;PRKAA2;MAP2K5;MAP2K6;RAC1;MAP2K4;MAP3K7;SQSTM1;KEAP1;PECAM1;NQO1;SUMO1;SUMO2;TNFRSF1A;PIK3R3;MAPK10;MAPK13;SDC2;MAP3K5;PIAS4;MAP2K7;P3R3URF-PIK3R3
Cancer: specific types	hsa05226	Gastric cancer	78/3285	4,24E+09	55	BCL2;BCL2L1;MAP2K1;MTOR;IGF1R;EIF4E2;PTEN;ERBB2;ERBB3;KRAS;NRAS;AXL;VEGFA;IL6R;EGFR;ARAF;PIK3R1;GAB1;RAF1;MET;AKT2;FOXO3;JAK1;AKT1;JAK2;AKT3;STAT3;EIF4E;FGF2;FGFR2;GRB2;GSK3B;NF1;PDGFA;PDGFRA;PIK3CA;PIK3CB;PLCG1;PLCG2;PRKCA;PRKCB;MAPK1;MAPK3;RPS6KB1;SOS2;SHC3;PDGFC;IGF1;HGF;PIK3R3;NRG2;BAD;BRAF;SOS1;P3R3URF-PIK3R3

Endocrine system	hsa04921	Oxytocin signaling pathway	80/3285	4,66E+09	61	ESR1;BCL2;NCOA3;E2F1;MAP2K1;FOS;ADCY9;MTOR;IGF1R;CARM1;NOTCH1;MAPK14;ERBB2;E2F3;KRAS;NRAS;RB1;PTK2;CCND1;CDKN1A;CDKN1B;SP1;ADCY6;EGFR;ARAF;PIK3R1;NOTCH3;NOTCH2;MAPK9;RAF1;AKT2;JAG1;MED1;AKT1;AKT3;ADCY3;GRB2;MDM2;PIK3CA;PIK3CB;PRKACA;PRKACB;MAPK1;MAPK3;MAPK8;RPS6KB1;SOS2;SHC3;IGF1;PIK3R3;NCOR1;ADCY5;MAPK10;MAPK13;BAD;BRAF;SOS1;DLL4;ADCY1;GPER1;P3R3URF-PIK3R3
Signal transduction	hsa04070	Phosphatidylinositol signaling system	55/3285	4,85E+08	38	BCL2;ATM;XIAP;PMAIP1;ERBB2;CDKN1A;APAF1;BAK1;MSH2;PIK3R1;CASP3;BRCA1;AKT2;AKT1;AKT3;BIRC2;BIRC5;ATP7A;SLC31A1;GSTM3;GSTP1;MSH6;MDM2;MGST3;PDPK1;PIK3CA;PIK3CB;MAPK1;MAPK3;REV3L;TOP2A;TOP2B;ABCC2;ERCC1;PIK3R3;BAD;MAP3K5;P3R3URF-PIK3R3
Cell growth and death	hsa04210	Apoptosis	72/3285	5,52E+09	27	MTOR;HK2;PRKCD;IRS1;IKKBK;SOS3;IRS2;PIK3R1;MAPK9;PRKCE;CACNA1B;HK1;INSR;PIK3CA;PIK3CB;PKM;MAPK1;MAPK3;MAPK8;SOS4;CACNA1A;CACNA1D;CACNA1E;PIK3R3;MAPK10;CACNA1C;P3R3URF-PIK3R3
Signal transduction	hsa04668	TNF signaling pathway	64/3285	6,22E+09	65	CREB1;MTOR;RPS6KA3;PRKCD;PTEN;PPARA;GYS1;IRS1;IKKBK;SOS3;IRS2;RELA;PIK3R1;MAPK9;PRKCE;AKT2;NFKB1;AKT1;AKT3;STAT3;ACACB;AGT;CPT1A;GFP1;GSK3B;INSR;PDPK1;PIK3CA;PIK3CB;PPP1CA;PPP1CB;PPP1CC;PPP1R3C;PPP1R3D;PRKAA1;PRKAA2;PRKAB1;PRKAB2;PRKCB;MAPK8;PTPRF;PYGB;PYGL;RPS6KB1;SREBF1;TBC1D4;CREB3;MLXIP;RPS6KA6;PPP1R3B;SLC27A1;RPS6KA1;PRKAG2;TNFRSF1A;PIK3R3;PPARGC1B;MAPK10;SLC2A1;MLXIPL;CREB3L1;OGT;CRTC2;PPP1R3E;OGA;P3R3URF-PIK3R3
Immune system	hsa04666	Fc gamma R-mediated phagocytosis	55/3285	7,00E+09	74	BCL2L11;FOS;IL1A;MAPK14;PPARA;IL6R;IRS1;IKKBK;SOS3;IRS2;RELA;CASP7;PIK3R1;CDC42;CASP3;MAPK9;ITCH;AKT2;PPARG;NFKB1;AKT1;AKT3;ATF4;COX7B;COX8A;EIF2S1;GSK3B;IL1B;INSR;LEPR;NDUFA4;NDUFA9;NDUFB1;NDUFB5;NDUFS4;PIK3CA;PIK3CB;PRKAA1;PRKAA2;PRKAB1;PRKAB2;MAPK8;RAC1;SREBF1;UQCRC2;EIF2AK3;MLXIP;ADIPOR2;PRKAG2;TNFRSF1A;UQCRRH;PIK3R3;NDUFA2;UQCRB;NDUFS1;NDUFC2;ERN1;COX7C;NDUFA6;MAPK10;MAPK13;UQCRC1;COX5A;NDUFA10;NDUFA7;NDUFAB1;MAP3K5;ADIPOR1;NDUFA12;MLXIPL;NDUFV1;NDUFV2;COX6A1;P3R3URF-PIK3R3
Endocrine system	hsa04917	Prolactin signaling pathway	42/3285	8,93E+09	62	BCL2;VCAM1;IL1A;PRKCD;MAPK14;KRAS;NRAS;TGFB2;CCND1;VEGFA;CDKN1B;COL3A1;COL4A1;COL1A2;TGFB2;RELA;PIK3R1;CDC42;CASP3;MAPK9;PRKCE;AKT2;ICAM1;TGFB1;NFKB1;AKT1;SMAD2;JAK2;STAT1;AKT3;STAT3;AGT;COL4A5;DIAPH1;EGR1;F3;FN1;IL1B;SMAD3;SMAD4;SERPINE1;PIK3CA;PIK3CB;PLCG1;PLCG2;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;RAC1;STAT5B;VEGFC;NOX4;PLCE1;CYBB;PIK3R3;COL4A6;MAPK10;MAPK13;PLCB1;P3R3URF-PIK3R3
Folding, sorting and degradation	hsa03018	RNA degradation	45/3285	0.0001	72	E2F1;CREB1;MAP2K1;LDLR;ADCY9;RAP1B;E2F3;CDK6;RB1;CCND1;CDKN1A;CDKN1B;SP1;ADCY6;EGFR;GNAI3;DVL2;CCNE1;APC;GNAI2;CDK2;WNT10B;ADCY3;AGT;ARNT;ATF4;CAMK2G;ATF2;ATF6B;CTNBNB1;DVL3;GNAI1;GNAQ;GSK3B;ITPR1;ITPR2;KCNA4;KCNK2;KMT2A;PRKACA;PRKACB;MAPK1;MAPK3;RAP1A;RBBP5;WNT2;WNT9A;FZD5;FZD3;KMT2D;FZD4;FZD6;FZD8;CCNE2;CREB3;LEF1;NCEH1;FH;CACNA1D;USP8;TCF7L2;ADCY5;PDE8A;ITPR3;KCNK3;WNT2B;BRAF;DVL1;PLCB1;ADCY1;CREB3L1;CACNA1C
Neurodegenerative disease	hsa05020	Prion disease	129/3285	0.0001	67	ALDH9A1;SIRT1;SCD;MAPK14;CCND1;PPARA;IKKBK;RELA;IRAK1;TRAF6;CASP3;MAPK9;AKT2;FOXO3;TBK1;NFKB1;AKT1;AKT3;ACACB;ADH5;ALDH3A2;C3;C5;CHUK;CPT1A;CTNBNB1;FABP1;CXCL1;CXCL2;CXCL3;GSK3B;IL1B;MYD88;PRKAA1;PRKAA2;PRKAB1;PRKAB2;MAPK8;MAP2K6;MAP2K4;TRA2B;SREBF1;MAP3K7;TRAF3;TRA2A;NOX4;IRAK4;LEF1;ADIPOR2;SCD5;IL17RC;TAB3;ALDH1B1;PRKAG2;TNFRSF1A;ACOX3;CPT1C;TCF7L2;ALDH7A1;MAPK10;MAPK13;RIPK1;FASN;MAP3K5;ADIPOR1;MAP2K7;ACACA
Transport and catabolism	hsa04142	Lysosome	69/3285	0.0001	50	RHOG;SEPTIN2;ARPC1B;PTK2;CAV1;DNM2;PIK3R1;CDC42;GAB1;CRKL;MET;CDH1;ACTB;CLTA;CLTB;CLTC;CRK;CTNNA1;CTNBNB1;CTTN;FN1;ILK;ITGB1;PIK3CA;PIK3CB;PXN;RAC1;WASF1;ARPC5;ARPC3;ACTR3;ACTR2;WASF2;CD2AP;DNM3;ARHGEF26;SHC3;ARPC5L;ELMO1;ACTR3B;PIK3R3;CTNNA3;BCAR1;ARPC1A;DOCK1;WASL;SEPTIN11;SEPTIN6;SEPTIN3;P3R3URF-PIK3R3
Cellular community - eukaryotes	hsa04540	Gap junction	51/3285	0.0001	26	ADCY9;ATP6V0E1;TJP1;ATP6V1B2;ACTB;ADCY3;ATP6V1A;ATP6V1C1;ATP6V1E1;ATP6V0A1;ATP6AP1;PLCG1;PLCG2;PRKACA;PRKACB;PRKCA;SLC12A2;ATP6V0D1;ATP6V1G1;KDELRL2;SEC61A1;ARF1;ATP6V0C;ATP6V0A2;ATP6V1D;ERO1A
Cancer: specific types	hsa05221	Acute myeloid leukemia	40/3285	0.0001	43	ADAM17;MAPK14;ATP6V0E1;TJP1;IKKBK;EGFR;F11R;RELA;CDC42;CASP3;PAK1;MAPK9;MET;ATP6V1B2;NFKB1;ADAM10;ATP6V1A;ATP6V1C1;ATP6V1E1;ATP6V0A1;ATP6AP1;CHUK;CSK;CXCL1;CXCL2;CXCL3;PLCG1;PLCG2;MAPK8;PTPRZ1;RAC1;MAP2K4;ATP6V0D1;ATP6V1G1;GIT1;LYN;ATP6V0C;JAM3;MAPK10;MAPK13;NOD1;ATP6V0A2;ATP6V1D
Infectious disease: bacterial	hsa05130	Pathogenic Escherichia coli infection	98/3285	0.0001	98	FOS;ARF6;MYO1C;SEC24C;TUBB;TUBB2A;MAPK14;TUBA1A;MYO10;ARPC1B;TJP1;BAK1;IKKBK;RELA;CASP7;CDC42;IRAK1;TRAF6;CASP3;PAK1;MAPK9;ABL1;ROCK2;NFKB1;SEC24D;ACTB;CASP4;CHUK;CLDN7;LPAR1;CTTN;GAPDH;IL1B;IL1R1;ITGB1;MYO1B;MYD88;MYO1D;MYO1E;MYO5A;MYO5B;MYO6;NCL;PAK2;PAK3;MAPK1;MAPK3;MAPK8;RAB1A;RAC1;ROCK1;MAP3K7;TM6IM6;NCK2;TNFRSF10B;TNFRSF10A;WASF1;CLDN12;CLDN1;ABCF2;ARPC5;ARPC3;ACTR3;ACTR2;WASF2;TUBA1B;TUBB4B;SEC24B;GNA13;NCKAP1;SEC24A;WASF3;TMED10;ARHGEF12;IRAK4;TUBA8;ARPC5L;TAB3;OCLN;ABI1;ARF1;CYFIP2;ACTR3B;TNFRSF1A;NCK1;ARPC1A;F2R;MAPK10;MAPK13;RIPK1;WASL;MYH10;ARHGEF11;MYO5C;BAIAP2L1;WIPF2;RPS3;ABCF2-H2BK1
Endocrine system	hsa04914	Progesterone-mediated oocyte maturation	59/3285	0.0001	130	BCL2;ATM;ARF6;MTOR;HK2;UBB;PRKCD;SEPTIN2;H3C4;MAPK14;FBXW11;ARPC1B;PTK2;CD44;IKKBK;EGFR;TLN1;RELA;PIK3R1;CDC42;TRAF6;MAPK9;CRKL;PRKCE;RPTOR;AKT2;FOXO3;ROCK2;TBK1;NFKB1;AKT1;BTRC;AKT3;ACTB;ACTN4;ACTN1;BNIP3;C3;CAPN2;CASP4;CHUK;CRK;DIAPH1;CTTN;GSK3B;HK1;IL1B;IL1R1;ILK;ITGB1;ITPR1;ITPR2;MDM2;MYD88;PIK3C3;PIK3CA;PIK3CB;PLCG1;

						PLCG2;MAPK1;MAPK3;MAPK8;PXN;RAC1;ROCK1;RPS6KB1;MAP3K7;UBC;UBE2D1;UBE2D3;UBE2N;UBE2V1;UBE2V2;CUL1;BECN1;SQSTM1;WASF1;ATG12;ARPC5;ARPC3;ACTR3;ACTR2;WASF2;CALCOCO2;TNIP1;RRAGB;RBCK1;RRAGA;MALT1;CBX3;FBNP1;PIK3R4;PLCE1;RRAGC;MAP1LC3B;ARPC5L;TLN2;MAP1LC3A;TIFA;TAB3;ARF1;FBNP1L;TRAF5;UBA52;ELMO1;ACTR3B;U2AF1L4;TNFRSF1A;PIK3R3;RPS27A;BCAR1;ARPC1A;DOCK1;ITPR3;MAPK10;MAPK13;VDAC1;RIPK1;WASL;ATG5;NOD1;SKP1;RBX1;PLCB1;H3-5;STING1;SEPTIN11;SEPTIN6;SEPTIN3;P3R3URF-PIK3R3
Cell growth and death	hsa04115	p53 signaling pathway	43/3285	0.0001	132	BCL2;RHOG;HSP90B1;MAP2K1;FOS;ARF6;DYNC1LI2;KPNA1;KPNA4;TUBB;TUBB2A;MAPK14;TUBA1A;ARPC1B;BAK1;MYC;IKBKB;DNM2;PODXL;RELA;FYCO1;CASP7;CDC42;IRAK1;TRAF6;CASP3;PAK1;MAPK9;RAF1;AKT2;ROCK2;RHOB;NFKB1;AKT1;ACBD3;AKT3;ACTB;BIRC2;CASP4;CHUK;CTNNB1;DYNC1H1;FLNA;GAPDH;HSP90AA1;HSP90AB1;IL1B;KIF5A;KIF5B;KIF5C;KLC1;KPNA3;MYD88;MYO6;PAK3;PIK3C2A;PIK3C2B;PIK3C3;PIK3CA;PIK3CB;MAPK1;MAPK3;MAPK8;MAP2K6;RAB5A;RAB5C;RAC1;RALA;MAP2K4;MAP3K7;TNFRSF10B;TNFRSF10A;GCC2;ARPC5;ARPC3;ACTR3;ACTR2;TUBA1B;TUBB4B;EXOC5;NCKAP1;WASF3;EXOC7;ARHGEF26;IRAK4;DCTN4;LEF1;TUBA8;ARL8B;EXOC2;VPS18;EXOC4;VPS33A;AHNAK;DYNC2H1;ARPC5L;DCTN5;KLC4;AHNAK2;TAB3;ABI1;ARF1;CYFIP2;ELMO1;ACTR3B;TNFRSF1A;DCTN1;TCF7L2;ARPC1A;RAB9A;DYNC1I2;MAPK10;MAPK13;PTPRC;RIPK1;WASL;RAB7A;NOD1;DCTN2;DYNLT1;DYNLT3;SKP1;FBXO22;FHOD1;DYNLRB1;PLEKHM1;ACTR10;MAP2K7;SNX33;RPS3;GSDMD;DYNLL2
Signal transduction	hsa04370	VEGF signaling pathway	36/3285	0.0002	75	RHOG;MAP2K1;FOS;ARF6;RPS6KA3;MAPK14;ARPC1B;PTK2;IKBKB;RELA;PIK3R1;CDC42;IRAK1;TRAF6;MAPK9;CRKL;AKT2;ROCK2;TBK1;NFKB1;AKT1;AKT3;ACTB;CHUK;CRK;PTK2B;FN1;GNAQ;GSK3B;IL1B;ITGA4;ITGB1;LIMK1;MYD88;NFATC2;NFATC3;PIK3CA;PIK3CB;PLCG1;PKN2;MAPK1;MAPK3;MAPK8;MAP2K6;PXN;RAC1;ROCK1;MAP2K4;MAP3K7;ARHGEF7;GIT2;ARPC5;ARPC3;ACTR3;ACTR2;WASF2;ARHGEF12;RPS6KA6;IRAK4;ARHGEF28;ARPC5L;CD4;RPS6KA1;ELMO1;ACTR3B;PIK3R3;BCAR1;ARPC1A;DOCK1;MAPK10;MAPK13;WASL;WIPF2;MAP2K7;P3R3URF-PIK3R3
Chromosome	hsa03082	ATP-dependent chromatin remodeling	61/3285	0.0002	51	FOS;IFNGR1;MAPK14;TGFB2;IKBKB;TGFB2;GNAI3;RELA;PIK3R1;IRAK1;TRAF6;MAPK9;AKT2;PPP2R2A;GNAI2;TGFB1;NFKB1;AKT1;SMAD2;AKT3;C3;CALR;CHUK;GNAI1;GNAQ;IL1B;MYD88;SERPINE1;PIK3CA;PIK3CB;PPP2R2B;PPP2R1A;PPP2R1B;PPP2R2C;MAPK1;MAPK3;MAPK8;MAP2K4;IRAK4;PPP2R2D;TNFRSF1A;PIK3R3;PPP2R2B;GNAI;PPP2CA;MAPK10;MAPK13;PLCB1;GNAO1;ADCY1;P3R3URF-PIK3R3
Development and regeneration	hsa04380	Osteoclast differentiation	72/3285	0.0003	55	BCL2;LDLR;XIAP;HSPA1B;IFNGR1;MAPK14;LAMC2;LAMC1;IKBKB;TGFB2;GNAI3;RELA;IRAK1;TRAF6;CASP3;MAPK9;AKT2;JAK1;GNAI2;NFKB1;AKT1;JAK2;STAT1;AKT3;STAT3;BIRC2;CHUK;GNAI1;HLA-DRB5;HSPA1L;ITGA6;ITGB1;LAMA3;LAMA5;LAMB1;MYD88;PDPK1;MAPK1;MAPK3;MAPK8;MAP2K6;MAP3K7;TYK2;IRAK4;IL10RB;LAMA2;ALOX5;TNFRSF1A;MAPK10;MAPK13;BAD;HSPA8;GNAO1;LAMB2;PIK3R6
Cellular community - eukaryotes	hsa04530	Tight junction	83/3285	0.0003	85	E2F1;MAP2K1;LDLR;E2F3;CDK6;KRAS;NRAS;RB1;CCND1;PPARA;CDKN1A;APAF1;BAK1;MYC;IKBKB;SOCS3;EGFR;ARAF;RELA;RNAI;PIK3R1;TRAF6;CASP3;RAF1;AKT2;PPP2R2A;JAK1;YWHAZ;TBK1;NFKB1;AKT1;CDK2;STAT1;AKT3;STAT3;CHUK;CLDN7;CTNNB1;EIF2S1;GRB2;GSK3B;IFIT1;IFNAR1;IFNAR2;EIF3E;MX2;OAS2;PIK3CA;PIK3CB;PPP2CB;PPP2R1A;PPP2R1B;PPP2R2C;MAPK1;MAPK3;SOS2;TLR3;TRAF3;TYK2;YWHAE;YWHAG;YWHAB;PIAS1;CLDN12;CLDN1;EIF2AK3;IRF9;YWHQ;EIF2AK1;PPP2R2D;MAVS;OCLN;CXCL10;EIF2AK4;TNFRSF1A;PIK3R3;PPP2R2B;PPP2CA;YWHAB;RIPK1;BAD;BRAF;SOS1;RIGI;P3R3URF-PIK3R3
Endocrine system	hsa04915	Estrogen signaling pathway	70/3285	0.0003	93	BCL2;E2F1;CREB1;MAP2K1;FOS;DDX3X;EP300;MAPK14;E2F3;KRAS;NRAS;TGFB2;RB1;CDKN1A;APAF1;MYC;IKBKB;TGFB2;ARAF;RELA;PIK3R1;IRAK1;TRAF6;CASP3;CCNE1;MAPK9;RAF1;AKT2;JAK1;YWHAZ;TBK1;CCNA2;TGFB1;NFKB1;AKT1;JAK2;CDK2;STAT1;AKT3;STAT3;BIRC5;ATF4;ATP6A1;CHUK;ATF2;CREBBP;ATF6B;DDB1;DDB2;EGR3;PTK2B;GRB2;HSPG2;IFNAR1;SMAD3;SMAD4;MAP3K1;MYD88;NFATC2;NFATC3;PIK3CA;PIK3CB;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;MAP2K6;MAP2K4;SOS2;STAT5B;MAP3K7;TLR3;TRAF3;TYK2;CCNE2;CREB3;YWHQ;IRAK4;MAVS;IFIH1;PIK3R3;VDAC3;MAPK10;MAPK13;YWHAB;BAD;BRAF;SOS1;CREB3L1;MAP2K7;RIGI;P3R3URF-PIK3R3
Nervous system	hsa04723	Retrograde endocannabinoid signaling	74/3285	0.0004	67	BCL2;FOS;HSPA1B;IL1A;CDK6;ADAR;CCND1;CDKN1B;APAF1;BAK1;IKBKB;RELA;PIK3R1;IRAK1;TRAF6;CASP3;CCNE1;MAPK9;AKT2;JAK1;TBK1;NFKB1;AKT1;CDK2;STAT1;AKT3;STAT3;CHUK;CSNK2A1;CSNK2A2;EIF2S1;GSK3B;HSPA1L;IFNAR1;IFNAR2;IL1B;CD46;MX2;MYD88;OAS2;PIK3CA;PIK3CB;MAPK8;MAPK3;MAP3K7;TNFAIP3;TRAF3;TYK2;CCNE2;EIF2AK3;IRF9;EIF2AK1;IRAK4;MAVS;IFIH1;RCHY1;EIF2AK4;PIK3R3;RAB9A;CSNK2B;MAPK10;BAD;HSPA8;CBLB;RACK1;RIGI;P3R3URF-PIK3R3
Nervous system	hsa04724	Glutamatergic synapse	60/3285	0.0004	117	E2F1;CREB1;MAP2K1;ADCY9;MTOR;MAPK14;E2F3;CDK6;KRAS;NRAS;RB1;PTK2;CCND1;CDKN1A;VEGFA;IL6R;SP1;BAK1;MYC;IKBKB;ADCY6;EGFR;GNAI3;RELA;PIK3R1;CASP3;CRKL;RAF1;PTGS2;ITGB3;AKT2;JAK1;ROCK2;TBK1;GNAI2;NFKB1;AKT1;PPP3CA;AKT3;STAT3;ADCY3;ATF4;B2M;CALM1;CALM2;CALM3;CALR;CHUK;ATF2;ATF6B;CRK;CTNNB1;PTK2B;GNAI1;GNAQ;GNB1;GNB2;GRB2;PDIA3;GSK3B;HLA-A;IL1B;IL1R1;ITGAV;ITPR1;ITPR2;MDM2;NFATC2;NFATC3;PDGFRA;PIK3CA;PIK3CB;PPP3R1;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;MAP2K6;PXN;RAC1;RHEB;ROCK1;RPS6KB1;SOS2;TSC1;CREB3;GNA13;AKAP13;ARHGEF12;GNB4;GNG7;IL10RB;TSC2;PTGER4;TRAF5;TNFRSF1A;PIK3R3;PPP3CB;BCAR1;ADC

						Y5;PPP3CC;HLA-C;ITPR3;MAPK13;RIPK1;HLA-B;HLA-E;SOS1;ARHGEF11;PLCB1;GNAO1;ADCY1;CREB3L1;STING1;P3R3URF-PIK3R3
Cardiovascular disease	hsa05417	Lipid and atherosclerosis	101/3285	0.0005	76	MAP2K1;EP300;IFNGR1;IL1A;KPNA1;KPNA2;CDK6;ADAR;APAF1;BAK1;IKKBK;SOCS3;RELA;RNASEL;PIK3R1;CASP3;RAF1;AKT2;JAK1;TBK1;ICAM1;NFKB1;AKT1;JAK2;STAT1;AKT3;ACTB;SLC25A6;CHUK;CREBBP;EIF2S1;HLA-DRB5;DNAJB1;IFNAR1;IFNAR2;IL1B;KPNA5;MX2;MYD88;NUP98;OAS2;PIK3CA;PIK3CB;PRKCA;PRKCB;MAPK1;MAPK3;DNAJC3;TLR3;TRAF3;TYK2;XPO1;TNFRSF10B;TNFRSF10A;CALCOCO2;IRF9;HNRNPUL1;KPNA6;NXT1;IRAK4;MAVS;IFIH1;IL33;CXCL10;PLG;TNFRSF1A;NXF1;PIK3R3;SLC25A4;SLC25A5;VDAC1;RAB11B;PRSS3;RIGI;P3R3URF-PIK3R3;PRSS2
Neurodegenerative disease	hsa05012	Parkinson disease	123/3285	0.0005	177	E2F1;CREB1;MAP2K1;ATM;CSNK1A1;EP300;MTOR;SPP1;PPP2R5E;PTEN;PALSI;NOTCH1;LAMC2;CDK6;THBS1;KRAS;NRAS;RB1;LAMC1;ATP6V0E1;PTK2;CCND1;CDKN1A;VEGFA;CDKN1B;BAK1;COL4A1;COL1A2;IKKBK;EGFR;DVL2;RELA;PIK3R1;CDC42;NOTCH3;NOTCH2;CASP3;CCNE1;RBL1;RAF1;PTGS2;APC;ITGB3;AKT2;ITGB4;PPP2R2A;ATP6V1B2;JAG1;JAK1;TBK1;CCNA2;NFKB1;AKT1;RELN;CDK2;STAT1;AKT3;WNT10B;ATP6V1A;ATP6V1C1;ATP6V1E1;ATP6V0A1;ATP6AP1;CHD4;CHUK;COL4A5;COL6A1;CREBBP;CTNNB1;DLG1;DLG2;DVL3;FN1;GRB2;GSK3B;HDAC1;HLA-A;TNC;IFNAR1;IFNAR2;RBPJ;ITGA6;ITGA2;ITGA3;ITGA4;ITGA9;ITGAV;ITGB1;ITGB5;ITGB8;LAMA3;LAMA5;LAMB1;LLGL2;MDM2;MX2;PIK3CA;PIK3CB;PKM;PPP2CB;PPP2R1A;PPP2R1B;PPP2R2C;PPP2R3A;PPP2R5A;PPP2R5C;PRKACA;PRKACB;PRKCI;MAPK1;MAPK3;PSEN1;PXN;RHEB;RPS6KB1;SOS2;TLR3;TRAF3;TSC1;TYK2;UBE3A;WNT2;WNT9A;FZD5;FZD3;FZD4;FZD6;FZD8;ATP6V0D1;CCNE2;MAGI1;TBPL1;ATP6V1G1;IRF9;CREB3;ITGA11;UBR4;HEY1;HEY2;PPP2R3C;PPP2R2D;MAML2;TNXB;LAMA2;TSC2;VWF;PTGER4;TNFRSF1A;TUBG1;PIK3R3;PPP2R2B;ITGA7;TCF7L2;ATR;PARD3;ATP6V0C;COL4A6;HLA-C;NFX1;PPP2CA;TNR;WNT2B;BAD;COL6A3;DVL1;HLA-B;HLA-E;SOS1;PPP2R5D;ATP6V0A2;SCRIB;ATP6V1D;MAML3;CREB3L1;LAMB2;PATJ;P3R3URF-PIK3R3
Substance dependence	hsa05031	Amphetamine addiction	39/3285	0.0005	128	E2F1;ETS1;CREB1;MAP2K1;FOS;ATM;MAP3K3;ADCY9;XIAP;EP300;RAN;TRRAP;KAT2B;ELK4;PTEN;E2F3;KRAS;NRAS;TGFB2;RB1;CCND1;CDKN1A;MYC;IKKBK;ADCY6;TGFB2;TLN1;RELA;PIK3R1;CCNE1;MAPK9;ZFP36;AKT2;JAK1;CCNA2;ICAM1;TGFB1;NFKB1;AKT1;SMAD2;PPP3CA;CDK2;AKT3;ADCY3;SLC25A6;ATF4;B2M;BUB1B;CALR;CDC20;CDC27;CHUK;ATF2;CREBBP;ATF6B;DLG1;EGRI;ETS2;KAT2A;HLA-A;HLA-DRB5;IL1R1;ITGB2;LTBR;MAD2L1;SMAD3;SMAD4;MAP3K1;NFATC2;NFATC3;NFYB;PIK3CA;PIK3CB;PPP3R1;PRKACA;PRKACB;MAPK1;MAPK3;MAPK8;RELB;MAP2K4;SRF;STAT5B;XPO1;RANBP3;CDC23;NRP1;CCNE2;BUB3;TBPL1;ESPL1;CREB3;ANAPC13;ANAPC15;ANAPC7;VAC14;CRTC3;TLN2;ANAPC16;CCNB2;CD4;CANX;TNFRSF1A;CDC16;PIK3R3;ITGAL;VDAC3;PPP3CB;SLC25A4;SLC25A5;ATR;ADCY5;KAT5;IL15RA;PPP3CC;HLA-C;MAPK10;VDAC1;GPS2;FOSL1;HLA-B;HLA-E;SLC2A1;ADCY1;CREB3L1;CRTC2;PTTG1;P3R3URF-PIK3R3
Endocrine system	hsa04929	GnRH secretion	37/3285	0.0006	104	E2F1;CREB1;MAP2K1;FOS;EP300;MTOR;IFNGR1;UBB;MAPK14;E2F3;CDK6;KRAS;NRAS;RB1;PREX1;CCND1;CDKN1A;VEGFA;BAK1;MYC;IKKBK;RELA;PIK3R1;CASP3;MAPK9;HIF1A;RAF1;PTGS2;ZFP36;AKT2;JAK1;TBK1;ICAM1;NFKB1;AKT1;PPP3CA;JAK2;STAT1;AKT3;STAT3;C3;CALM1;CALM2;CALM3;CHUK;CREBBP;CTNNB1;FGF2;GNB1;GNB2;CXCL1;CXCL2;CXCL3;GSK3B;HLA-A;IFNAR1;IFNAR2;IL6ST;ITPR1;ITPR2;NFATC2;NFATC3;PIK3C3;PIK3CA;PIK3CB;PLCG1;PLCG2;PPP3R1;MAPK1;MAPK3;MAPK8;MAP2K6;RAC1;MAP2K4;TLR3;TRAF3;TYK2;UBC;BECN1;MAPKAPK2;IRF9;LEF1;GNB4;ATG3;MAP1LC3B;MAP1LC3A;GNG7;LYN;UBA52;TNFRSF1A;PIK3R3;RPS27A;PPP3CB;TCF7L2;PPP3CC;HLA-C;ITPR3;MAPK10;MAPK13;HLA-B;HLA-E;MAP2K7;PIK3R6;P3R3URF-PIK3R3
Cancer: overview	hsa05235	PD-L1 expression and PD-1 checkpoint pathway in cancer	48/3285	0.0007	82	BCL2;MTOR;IFNGR1;APAF1;BAK1;IKKBK;SOCS3;RELA;RNASEL;PIK3R1;IRAK1;TRAF6;CASP3;ITGB3;AKT2;JAK1;TBK1;NFKB1;AKT1;JAK2;STAT1;AKT3;BIRC2;B2M;C3;C5;CALR;CHUK;EIF2S1;PDIA3;HLA-A;HLA-DRB5;IFNAR1;IFNAR2;IL1B;MYD88;OAS2;PIK3CA;PIK3CB;POU2F1;POU2F2;PPP1CA;PPP1CB;PPP1CC;RHEB;SRSF1;SRSF2;SRSF4;SRSF5;SRSF6;SRSF7;SP100;MAP3K7;TLR3;TRAF3;TSC1;TYK2;EIF2AK3;IRF9;EIF2AK1;IRAK4;ZC3HAV1;MAVS;IFIH1;TSC2;EIF2AK4;TRAF5;TNFRSF1A;NXF1;PIK3R3;HLA-C;BAD;HCFC1;HLA-B;HLA-E;HCFC2;NECTIN2;SRSF8;DAXX;STING1;RIGI;P3R3URF-PIK3R3
Environmental adaptation	hsa04714	Thermogenesis	108/3285	0.0007	101	BCL2;E2F1;BCL2L1;MAPK14;E2F3;CDK6;RB1;CCND1;CDKN1A;CDKN1B;CD44;APAF1;BAK1;MYC;IKKBK;RELA;PIK3R1;IRAK1;TRAF6;CASP3;CCNE1;MAPK9;VIM;AKT2;JAK1;TBK1;CCNA2;ICAM1;NFKB1;AKT1;CDK2;STAT1;AKT3;STAT3;B2M;CALR;ENTPD1;CHUK;CR2;DDB2;GADD45A;PDIA3;HDAC1;HLA-A;HLA-DRB5;IFNAR1;IFNAR2;RBPJ;MDM2;MYD88;NEDD4;OAS2;PIK3CA;PIK3CB;PLCG2;MAPK8;MAP2K6;PSMC2;PSMC6;PSMD1;PSMD2;PSMD11;PSMD12;RAC1;RELB;MAP2K4;SKP2;MAP3K7;TNFAIP3;TRAF3;TYK2;USP7;SAP30;CCNE2;NCOR2;PSMD6;IRF9;SIN3A;IRAK4;POLK;MAVS;CXCL10;LYN;TRAF5;PIK3R3;ITGAL;HLA-C;MAPK10;MAPK13;PSMC3;PSMD3;PSMD13;RIPK1;CIR1;HLA-B;HLA-E;PSMD14;MAP2K7;PSMC5;RIGI;P3R3URF-PIK3R3
Endocrine system	hsa04926	Relaxin signaling pathway	65/3285	0.0007	110	BCL2;MAP2K1;FOS;ATM;MTOR;CUL5;MAPK14;FBXW11;KRAS;NRAS;PTK2;CFL2;BAK1;IKKBK;GNAI3;RELA;PIK3R1;IRAK1;TRAF6;CASP3;PAK1;MAPK9;CRKL;RAF1;AKT2;TBK1;GNAI2;NFKB1;AKT1;BTRC;PPP3CA;AKT3;AP1G1;B2M;CALM1;CALM2;CALM3;CALR;CCNB1;CDK1;CHUK;AP1S1;CRK;DDB1;PTK2B;GNAI1;GNAQ;GNB1;GNB2;PDIA3;HLA-A;ITPR1;ITPR2;LIMK1;MYD88;NFATC2;NFATC3;PAK2;PAK3;PIK3CA;PIK3CB;PLCG1;PLCG2;PPP3R1;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;MAP2K6;PXN;RAC1;

						RPS6KB1;MAP3K7;WEE1;CUL4B;CUL4A;CUL1;RNF7;PAK4;SAMHD1;IRAK4;GNB4;CCNB2;GNG7;CD4;TRAF5;TNFRSF1A;PIK3R3;PPP3CB;ATR;PPP3CC;HLA-C;ITPR3;MAPK10;MAPK13;RIPK1;BAD;HLA-B;HLA-E;SKP1;RBX1;GNAO1;MAP2K7;AP1G2;DCAF1;PAK5;ELOC;STING1;P3R3URF-PIK3R3
Cardiovascular disease	hsa05418	Fluid shear stress and atherosclerosis	70/3285	0.0007	182	MAP2K1;ADAM17;CSNK1A1;MTOR;IL1A;ULK1;ATG2B;TUBB;TUBB2A;CSF1;TUBA1A;KRAS;NRAS;APAF1;IRS1;IKKB;IRS2;DVL2;ARAF;RELA;CASP7;PIK3R1;CASP3;MAPK9;APP;RAF1;PTGS2;APC;AKT2;NFKB1;AKT1;SNCA;PPP3CA;AKT3;WNT10B;ADAM10;SLC25A6;APBB1;ATF4;ATP2A2;CALM1;CALM2;CALM3;CAPN2;CHUK;COX7B;COX8A;CSNK2A1;CSNK2A2;CTNNB1;DVL3;EIF2S1;GAPDH;GNAQ;GRIN2A;GRM5;GSK3B;HSD17B10;IDE;IL1B;INSR;ITPR1;ITPR2;KIF5A;KIF5B;KIF5C;KLC1;LRP1;LRP6;MAPT;NDUFA4;NDUFA9;NDUFB1;NDUFB5;NDUFS4;PIK3C3;PIK3CA;PIK3CB;PPP3R1;MAPK1;MAPK3;MAPK8;PSEN1;PSMB5;PSMC2;PSMC6;PSMD1;PSMD2;PSMD11;PSMD12;RYYR3;UQCRC2;WNT2;WNT9A;FZD5;FZD3;FZD4;FZD6;FZD8;BECN1;CDK5R1;EIF2AK3;ULK2;RB1CC1;PSMD6;RTN3;TUBA1B;TUBB4B;ATF6;SLC39A14;SLC39A6;PIK3R4;NOX4;TUBA8;SLC39A9;CHRFAM7A;KLC4;CYBB;CACNA1D;TNFRSF1A;UQCRH;PSMA4;PIK3R3;SLC39A13;VDAC3;PPP3CB;ATG13;SLC25A4;SLC25A5;NDUFA2;UQCRB;NDUFS1;NDUFC2;PPP3CC;CSNK2B;ERN1;COX7C;ITPR3;NDUFA6;MAPK10;PSMA3;PSMB1;PSMB2;PSMC3;PSMD3;PSMD13;UQCRC1;VDAC1;WNT2B;COX5A;ATP2A1;BAD;BRAF;DVL1;NDUFA10;NDUFA7;NDUFAB1;PSMD14;MAP3K5;GRIN1;BACE2;PLCB1;AMBRA1;NDUFA12;MAP2K7;NDUFV1;NDUFV2;COX6A1;PSMC5;PSMA7;GRIN2B;ATP5F1A;ATP5MC2;ATP5MC3;ATP5F1B;ATP5PB;ATP5F1E;CACNA1C;ATP5PO;ATP5PD;PSMB3;P3R3URF-PIK3R3
Signal transduction	hsa04310	Wnt signaling pathway	83/3285	0.0008	123	UBB;TUBB;TUBB2A;TUBA1A;APAF1;GNAI3;CASP3;MAPK9;GNAI2;SNCA;SLC25A6;ATF4;CALM1;CALM2;CALM3;CAMK2G;COX7B;COX8A;DRD1;EIF2S1;GNAI1;HSPA5;ITPR1;ITPR2;KIF5A;KIF5B;KIF5C;KLC1;MAOA;MAPT;NDUFA4;NDUFA9;NDUFB1;NDUFB5;NDUFS4;PLCG1;PRKACA;PRKACB;MAPK8;PSMB5;PSMC2;PSMC6;PSMD1;PSMD2;PSMD11;PSMD12;RYYR3;SOD1;UBC;UBE2G1;UBE2L3;UQCRC2;EIF2AK3;KEAP1;PSMD6;MFN2;TUBA1B;TUBB4B;ATF6;SLC39A14;SLC39A6;UBE2J1;TUBA8;SLC39A9;KLC4;LRRK2;MAOB;UBA52;UQCRH;PSMA4;SLC39A13;RPS27A;VDAC3;GNAL;SLC25A4;SLC25A5;NDUFA2;ADCY5;UQCRB;NDUFS1;NDUFC2;ERN1;COX7C;ITPR3;NDUFA6;MAPK10;PSMA3;PSMB1;PSMB2;PSMC3;PSMD3;PSMD13;UBA1;UBE2G2;UQCRC1;VDAC1;UCHL1;UBE2L6;COX5A;NDUFA10;NDUFA7;NDUFAB1;PSMD14;MAP3K5;NDUFA12;PINK1;MFN1;NDUFV1;NDUFV2;COX6A1;PSMC5;PSMA7;ATP5F1A;ATP5MC2;ATP5MC3;SEPTIN5;DAXX;ATP5F1B;ATP5PB;ATP5F1E;ATP5PO;ATP5PD;PSMB3
Endocrine system	hsa04912	GnRH signaling pathway	49/3285	0.0008	176	GRIA2;BCL2;CAT;MTOR;FUS;ULK1;CHMP2B;ATG2B;NDC1;TUBB;TUBB2A;SMC R8;MAPK14;TUBA1A;POM121;APAF1;CASP3;TBK1;ERBB4;PPP3CA;ANXA11;AC TB;ANXA7;ATF4;COX7B;COX8A;EIF2S1;GLE1;GRIA1;GRIN2A;HNRNP A1;HNRN PA2B1;HSPA5;KIF5A;KIF5B;KIF5C;KLC1;NCBP1;NDUFA4;NDUFA9;NDUFB1;ND UFB5;NDUFS4;NEFH;NUP98;PIK3C3;PPP3R1;MAP2K6;PSMB5;PSMC2;PSMC6;PS MD1;PSMD2;PSMD11;PSMD12;RAB1A;RAB5A;RAC1;SRSF7;SOD1;TPR;UQCRC2; VCP;NUP214;BECN1;DNAH11;SQSTM1;EIF2AK3;NUP155;ULK2;RB1CC1;PSMD6; FIG4;NUP153;TUBA1B;TUBB4B;NUP50;ATXN2L;ATF6;SETX;NUP210;NUP160;TA RDBP;NXT1;UBQLN2;UBQLN1;PIK3R4;DCTN4;TUBA8;NUP54;UBQLN4;NUP107; DERL1;SPG11;MAP1LC3B;SEH1L;DNAL1;DCTN5;MAP1LC3A;KLC4;C9orf72;HNR NPA3;GPX8;GPX1;TNFRSF1A;NXF1;UQCRH;PSMA4;DCTN1;PPP3CB;ATG13;NRG 2;NDUFA2;VAPB;SLC1A2;UQCRB;NDUFS1;NDUFC2;PPP3CC;DNAH9;ERN1;COX 7C;GPX3;ITPR3;NDUFA6;NUP88;MAPK13;PSMA3;PSMB1;PSMB2;PSMC3;PSMD3; PSMD13;UQCRC1;VDAC1;COX5A;BAD;NDUFA10;NDUFA7;NDUFAB1;PSMD14; MAP3K5;RANBP2;DCTN2;GRIN1;NUP205;NUP188;AMBRA1;NUP133;WDR41;AC TR10;NDUFA12;NUP37;TOMM40L;PINK1;DNAH17;CHCHD10;NDUFV1;NDUFV2; COX6A1;PSMC5;PSMA7;GRIN2B;NUP58;POM121C;NEFL;ATP5F1A;ATP5MC2;AT P5MC3;DAXX;ATP5F1B;ATP5PB;ATP5F1E;ATP5PO;ATP5PD;PSMB3
Endocrine system	hsa04922	Glucagon signaling pathway	55/3285	0.0008	145	GRIA2;RCOR1;CREB1;EP300;MTOR;MAP3K10;ULK1;ATG2B;TUBB;TUBB2A;TFA M;TUBA1A;POLR2K;APAF1;SPI1;CASP3;MAPK9;REST;PPARG;AP2M1;AP2A1;AP2 B1;SLC25A6;CACNA1B;AP2S1;CLTA;CLTB;CLTC;COX7B;COX8A;CREBBP;GNAQ ;GRIA1;GRM5;HTT;HDAC1;ITPR1;KIF5A;KIF5B;KIF5C;KLC1;NDUFA4;NDUFA9;N DUFB1;NDUFB5;NDUFS4;NRF1;PIK3C3;POLR2B;POLR2C;POLR2D;POLR2E;POL R2H;MAPK8;PSMB5;PSMC2;PSMC6;PSMD1;PSMD2;PSMD11;PSMD12;SLC1A3;SO D1;TAF4;TAF4B;TGM2;UQCRC2;BECN1;DNAH11;TBPL1;ULK2;RB1CC1;PSMD6;T UBA1B;TUBB4B;CREB3;SIN3A;PIK3R4;DCTN4;TUBA8;DNAL1;DCTN5;KLC4;GP X8;GPX1;GRIA4;UQCRH;PSMA4;DCTN1;VDAC3;ATG13;SLC25A4;SLC25A 5;NDUFA2;SLC1A2;UQCRB;NDUFS1;NDUFC2;DNAH9;ERN1;COX7C;GPX3;KCNJ 10;NDUFA6;MAPK10;PSMA3;PSMB1;PSMB2;PSMC3;PSMD3;PSMD13;UQCRC1;V DAC1;COX5A;NDUFA10;NDUFA7;NDUFAB1;PSMD14;MAP3K5;DCTN2;GRIN1;PL CB1;AMBRA1;ACTR10;NDUFA12;CREB3L1;MAP2K7;DNAH17;NDUFV1;NDUFV2 ;COX6A1;PSMC5;PSMA7;GRIN2B;ATP5F1A;ATP5MC2;ATP5MC3;ATP5F1B;ATP5P B;ATP5F1E;ATP5PO;ATP5PD;PSMB3;SOD2
Global and overview maps	hsa01212	Fatty acid metabolism	33/3285	0.0008	86	GRIA2;MTOR;ULK1;ATG2B;SPI1;PIK3R1;ATXN1;MAPK9;AKT2;AKT1;RELN;AKT3 ;SLC25A6;ATP2A2;GNAQ;GRIA1;GRIN2A;GRM1;RBPJ;ITPR1;ITPR2;KCND3;NFY A;PIK3C3;PIK3CA;PIK3CB;PRKCA;PRKCB;MAPK8;PSMB5;PSMC2;PSMC6;PSMD 1;PSMD2;PSMD11;PSMD12;RORA;SPTBN2;VLDLR;BECN1;TBPL1;PUM1;ULK2;R B1CC1;PSMD6;NOP56;AFG3L2;ATXN2L;PUM2;ATXN10;PIK3R4;CACNA1A;GRIA 3;PSMA4;PIK3R3;ATXN3;VDAC3;ATXN1L;ATG13;SLC25A4;SLC25A5;KAT5;ERN1; ITPR3;MAPK10;PSMA3;PSMB1;PSMB2;PSMC3;PSMD3;PSMD13;VDAC1;FGF14;A

						TP2A1;KCNC3;PSMD14;MAP3K5;GRIN1;CIC;PLCB1;AMBRA1;PSMC5;PSMA7;GRIN2B;PSMB3;P3R3URF-PIK3R3
Substance dependence	hsa05032	Morphine addiction	48/3285	0.0009	129	CREB1;HSPA1B;IL1A;TUBB;TUBB2A;PRKCD;NOTCH1;MAPK14;TUBA1A;LAMC1;APAF1;CAV1;PIK3R1;CASP3;MAPK9;PPP3CA;NCAM1;SLC25A6;ATF4;C5;CACNA1B;COX7B;COX8A;ATF2;ATF6B;CSNK2A1;CSNK2A2;EGR1;EIF2S1;GRIN2A;GSK3B;HSPA1L;HSPA5;IL1B;ITPR1;ITPR2;KIF5A;KIF5B;KIF5C;KLC1;NCAM2;NDUFA4;NDUFA9;NDUFB1;NDUFB5;NDUFS4;PIK3CA;PIK3CB;PPP3R1;PRKACA;PRKACB;MAPK1;MAPK3;MAPK8;PSMB5;PSMC2;PSMC6;PSMD1;PSMD2;PSMD11;PSMD12;RAC1;RYR2;RYR3;SOD1;UQCRC2;EIF2AK3;PSMD6;TUBA1B;TUBB4B;CREB3;STIP1;TUBA8;KLC4;CYBB;CACNA1D;UQCRH;PSMA4;PIK3R3;VDAC3;PPP3CB;SLC25A4;SLC25A5;NDUFA2;UQCRB;NDUFS1;NDUFC2;PPP3CC;CSNK2B;COX7C;ITPR3;NDUFA6;MAPK10;MAPK13;PSMA3;PSMB1;PSMB2;PSMC3;PSMD3;PSMD13;UQCRC1;VDAC1;COX5A;BAD;NDUFA10;NDUFA7;NDUFAB1;PSMD14;HSPA8;GRIN1;NDUFA12;CREB3L1;NDUFV1;NDUFV2;COX6A1;PSMC5;PSMA7;GRIN2B;ATP5F1A;ATP5MC2;ATP5MC3;ATP5F1B;ATP5PB;ATP5F1E;CACNA1C;ATP5PO;ATP5PD;PSMB3;P3R3URF-PIK3R3
Environmental adaptation	hsa04710	Circadian rhythm	22/3285	0.001	233	GRIA2;BCL2;MAP2K1;CAT;CSNK1A1;MTOR;FUS;IL1A;MAP3K10;UBB;ULK1;CHMP2B;ATG2B;TUBB;TUBB2A;SMCR8;CSF1;MAPK14;TUBA1A;KRAS;NRAS;APAF1;BAK1;DVL2;ARAF;RELA;CASP7;CASP3;ATXN1;MAPK9;APP;RAF1;PTGS2;APC;TBK1;NFKB1;SNCA;PPP3CA;WNT10B;SLC25A6;ATF4;ATP2A2;CACNA1B;CALM1;CALM2;CALM3;CAMK2G;CAPN2;COX7B;COX8A;CSNK2A1;CSNK2A2;CTNNB1;DVL3;EIF2S1;GNAQ;GRIA1;GRIN2A;GRM1;GRM5;GSK3B;HSD17B10;HTT;HSPA5;IL1B;ITPR1;ITPR2;KIF5A;KIF5B;KIF5C;KLC1;LRP6;MAPT;NDUFA4;NDUFA9;NDUFB1;NDUFB5;NDUFS4;NEFH;PIK3C3;PLCG1;PPP3R1;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;MAP2K6;PSEN1;PSMB5;PSMC2;PSMC6;PSMD1;PSMD2;PSMD11;PSMD12;RAB1A;RAB5A;RAC1;RYR2;RYR3;SOD1;SPTBN2;UBC;UBE2G1;UBE2L3;UQCRC2;VCP;WNT2;WNT9A;FZD5;FZD3;FZD4;FZD6;FZD8;BECN1;DNAH11;CDK5R1;SQSTM1;EIF2AK3;ULK2;RB1CC1;PSMD6;FIG4;MFN2;TUBA1B;TUBB4B;ATXN2L;ATF6;TARDBP;PIK3R4;NOX4;DCTN4;UBE2J1;UBE2A;DERL1;SPG11;MAP1LC3B;DNAL1;DCTN5;MAP1LC3A;CHRFAM7A;KLC4;LRRK2;C9orf72;GPX8;GPX1;CYBB;CACNA1D;GRIA3;GRIA4;UBA52;TNFRSF1A;UQCRH;PSMA4;ATXN3;DCTN1;RPS27A;VDAC3;ATXN1L;PPP3CB;ATG13;SLC25A4;SLC25A5;NDUFA2;VAPB;UQCRB;NDUFS1;NDUFC2;PPP3CC;CSNK2B;DNAH9;ERN1;COX7C;GPX3;ITPR3;NDUFA6;MAPK10;MAPK13;PSMA3;PSMB1;PSMB2;PSMC3;PSMD3;PSMD13;UBA1;UBE2G2;UQCRC1;VDAC1;UCHL1;WNT2B;UBE2L6;COX5A;ATP2A1;BAD;BRAF;DVL1;NDUFA10;NDUFA7;NDUFAB1;PSMD14;MAP3K5;DCTN2;GRIN1;PLCB1;AMBRA1;WDR41;ACTR10;NDUFA12;TOMM40L;PINK1;MFN1;MAP2K7;DNAH17;NDUFV1;NDUFV2;COX6A1;PSMC5;PSMA7;GRIN2B;NEFL;ATP5F1A;ATP5MC2;ATP5MC3;SEPTIN5;DAXX;ATP5F1B;ATP5PB;ATP5F1E;CACNA1C;ATP5PO;ATP5PD;PSMB3
Transport and catabolism	hsa04136	Autophagy - other	21/3285	0.001	39	GRIA2;SIRT1;CREB1;FOS;PPP3CA;ATF4;CALM1;CALM2;CALM3;CAMK4;CAMK2G;ATF2;ATF6B;DRD1;GRIA1;GRIN2A;HDAC1;MAOA;PPP1CA;PPP1CB;PPP1CC;PPP3R1;PRKACA;PRKACB;PRKCA;PRKCB;CREB3;CACNA1D;GRIA3;GRIA4;MAOB;FOSB;PPP3CB;ADCY5;PPP3CC;GRIN1;CREB3L1;GRIN2B;CACNA1C
Environmental adaptation	hsa04713	Circadian entrainment	50/3285	0.001	48	ADCY9;ARRB2;GRK2;ADCY6;GNAI3;GNAI2;ADCY3;ARRB1;CACNA1B;DRD1;GABBR1;GABRA1;GABRB3;GNAI1;GNB1;GNB2;KCNJ9;PDE2A;PDE3B;PDE4D;PRKACA;PRKACB;PRKCA;PRKCB;GABBR2;GNB4;SLC32A1;GNB7;CACNA1A;GABRA2;GABRA4;GABRB2;GABRD;GABRG2;PDE1B;PDE1A;GRK4;ADCY5;PDE7A;PDE8A;KCNJ3;GRK5;GNAO1;ADCY1;GABRG1;GRK3;PDE10A
Cardiovascular disease	hsa05412	Arrhythmogenic right ventricular cardiomyopathy	45/3285	0.001	21	GRIA2;CACNA1B;GABRA1;GABRB3;GRIA1;GRIN2A;SLC17A6;CHRFAM7A;SLC32A1;CACNA1A;CHRN2B;GABRA2;GABRA4;GABRB2;GABRD;GABRG2;GRIA3;GRIA4;GRIN1;GABRG1;GRIN2B
Cancer: specific types	hsa05216	Thyroid cancer	23/3285	0.001	28	GOT1;DNMT3A;MTAP;DNMT1;AMD1;BCAT1;BCAT2;CTH;LDHA;LDHB;MAT1A;MAT2A;MDH1;SMS;AHCYL1;AHCYL2;PHGDH;PSAT1;ENOPH1;GOT1L1;MTR;AHCY;MR1;GCLM;GOT2;MDH2;APIP;SDSL
Infectious disease: viral	hsa05162	Measles	67/3285	0.002	26	ALDH9A1;ACAA2;HADHB;ACAT1;ALDH3A2;AUH;BCAT1;BCAT2;BCKDHB;DBT;DLD;HSD17B10;HADHA;HMGCS1;IVD;OXCT1;PCCA;PCCB;HIBADH;HMGCLL1;MCCC2;ALDH1B1;EHHADH;ALDH7A1;ALDH6A1;MMUT
Endocrine system	hsa04928	Parathyroid hormone synthesis, secretion and action	57/3285	0.002	42	ALDH9A1;KMT2E;SUV39H2;NSD2;PLOC3;EZH2;ACAT1;ALDH3A2;DLD;EZH1;HADHA;KMT2A;PLOC1;PLOC2;SUV39H1;KMT2D;SETD1B;ASH1L;KMT2C;PRDM16;SMYD3;COLGALT1;EHMT1;SMYD1;ALDH1B1;PRDM2;MECOM;SETDB1;EHHADH;ALDH7A1;AASS;SETD2;SETD1A;DHTKD1;NSD1;PHYKPL;SETMAR;KMT2B;KMT5B;KMT5A;KMT5C;NSD3
Signal transduction	hsa04024	cAMP signaling pathway	102/3285	0.002	39	PTEN;INPP5F;MTMR6;IMPA1;INPP5B;PIK3C2A;PIK3C2B;PIK3C3;PIK3CA;PIK3CB;PI4KB;PIP4K2A;PLCG1;PLCG2;SYNJ1;MTMR3;MTMR4;MINPP1;FIG4;CDIPT;SACM1L;PLCE1;INPP5K;PI4K2A;MTMR14;IPPK;PIP4K2C;IPMK;OCRL;INPP4B;PLCH1;INPP4A;ITPK1;PIKFYVE;MTMR1;MTMR7;ALDH6A1;PLCB1;PIP4K2B
Carbohydrate metabolism	hsa00562	Inositol phosphate metabolism	39/3285	0.002	7	PAPSS2;PAPSS1;SUOX;BPNT1;ETHE1;SQOR;BPNT2
Endocrine and metabolic disease	hsa04932	Non-alcoholic fatty liver disease	74/3285	0.002	52	CAT;HK2;GOT1;G6PD;ALDOA;ACAT1;ADH5;DLAT;DLD;GAPDH;GPI;HK1;IDH1;MDH1;ME1;OGDH;PCCA;PCCB;PFKP;PKM;PRPS1;PRPS2;TKT;RGN;PHGDH;PSAT1;ACSS1;GPT2;GOT1L1;CPS1;ENO1;ENO2;FH;PFKM;ACO2;ACOX3;GLYCTK;ME2;ESD;GOT2;ACO1;PGAM1;GLUD1;ALDH6A1;MDH2;TALDO1;GLUD2;SDSL;PGLS;PFKL;TKFC;MMUT

Cell growth and death	hsa04216	Ferroptosis	25/3285	0.002	33	SCD;ACAA2;HADHB;ELOVL1;ACAT1;CPT1A;CPT2;ACSL1;ACSL3;ACSL4;HADH A;FADS1;PPT1;SCP2;ELOVL4;PPT2;FADS2;ACSL6;HSD17B12;ACSL5;ELOVL2;ELOVL5;ELOVL6;SCD5;ELOVL7;CBR4;ACOX3;CPT1C;EHHADH;FASN;OXSM;HACD3;ACACA
Cardiovascular disease	hsa05415	Diabetic cardiomyopathy	93/3285	0.002	36	GOT1;ALDOA;ASS1;ASNS;BCAT1;BCAT2;CTH;GAPDH;IDH1;MAT1A;MAT2A;PFKP;PKM;PRPS1;PRPS2;ALDH18A1;TKT;PHGDH;PYCR2;PSAT1;GPT2;GOT1L1;CPS1;ENO1;ENO2;MTR;PFKM;ACO2;GOT2;ACO1;PGAM1;TALDO1;SDSL;ACY1;PFKL;ABHD14A-ACY1
Excretory system	hsa04960	Aldosterone-regulated sodium reabsorption	23/3285	0.002	29	MAN1A2;GANAB;B4GALT1;MAN2A1;DAD1;DPAGT1;STT3A;MAN2A2;RPN1;RPN2;MOGS;DPM1;ALG3;MGAT4A;DOLK;MAN1C1;ALG8;ALG9;MAGT1;ALG2;ALG10B;MGAT4B;ALG11;ALG13;MGAT2;MGAT5;OSTC;KRTCAP2;MGAT4C
Immune system	hsa04611	Platelet activation	61/3285	0.002	16	ACAA2;HADHB;ELOVL1;HADHA;PPT1;ELOVL4;PPT2;ACOT7;HSD17B12;ELOVL2;ELOVL5;ELOVL6;ELOVL7;ACOT4;MBLAC2;HACD3
Infectious disease: parasitic	hsa05145	Toxoplasmosis	55/3285	0.003	22	ALDH9A1;ACAA2;HADHB;ACAT1;ADH5;ALDH3A2;CPT1A;CPT2;ECI1;ACSL1;ACSL3;ACSL4;HADHA;ECI2;ACSL6;ACSL5;CYP2U1;ALDH1B1;ACOX3;CPT1C;EHHADH;ALDH7A1
Endocrine and metabolic disease	hsa04930	Type II diabetes mellitus	27/3285	0.003	32	ALDH9A1;LCLAT1;PLPP3;ALDH3A2;PNLIP;ABHD16A;DGAT1;DGKI;LIPG;AKR1A1;AGPAT1;MGLL;AGPAT5;AGK;AGPAT3;AGPAT4;PNPLA2;DGKH;ALDH1B1;MBOAT1;DGKG;GLYCTK;ALDH7A1;DGKE;DGKB;MBOAT2;PNLIPRP1;PLPP5;GPAT3;PLPP1;TKFC;GPAT4
Immune system	hsa04625	C-type lectin receptor signaling pathway	52/3285	0.003	17	SCD;ELOVL1;BAAT;FADS1;SCP2;ELOVL4;FADS2;ACOT7;HSD17B12;ELOVL2;ELOVL5;ELOVL6;SCD5;ELOVL7;ACOT4;ACOX3;HACD3
Infectious disease: parasitic	hsa05142	Chagas disease	51/3285	0.003	100	LBR;ELN;THBS1;NID1;SDC4;TPM4;LMNB1;COL3A1;COL4A1;COL1A2;FBN1;TLN1;VIM;ITGB3;ITGB4;FBN2;ATP1A2;ANK2;ACTB;ACTN2;ATP1A1;ATP1B1;ATP1B2;CAPZA1;COL4A5;COL5A1;COL5A2;COL6A1;DAG1;DIAPH1;DSC2;DSG2;DSP;FHL2;FLNC;FN1;HSPG2;ITGA6;ITGA2;ITGA3;ITGA4;ITGA9;ITGAV;ITGB1;ITGB5;ITGB8;JUP;PKP2;PLEC;SGCB;SNTB2;SPTAN1;SPTBN1;SPTBN2;ZYX;MYO1;PDLIM1;SDC3;PDLIM5;ITGA11;DAAM1;SYNE2;SYNE1;SUN1;DAAM2;ANKRD1;TMOD2;COL5A3;DIAPH3;TLN2;OBSCN;FBN3;COL27A1;FMNL2;XIRP2;SYNE3;SYNPO2;AGRN;ENO1;ENO2;LAMA2;VCAN;DTNA;ATP1B4;ITGA7;ANK3;NEB;TMOD1;COL4A6;DCN;DES;SDC2;TTN;COL6A3;FMNL1;MYH10;NRAP;FBLN1;DIAPH2;FMN2
Signaling molecules and interaction	hsa04512	ECM-receptor interaction	45/3285	0.003	61	SIRT1;CREB1;ADCY9;CAT;MTOR;IGF1R;ULK1;EIF4E2;KRAS;NRAS;SES1;IRS1;ADCY6;IRS2;RELA;PIK3R1;RPTOR;AKT2;FOXO3;PPARG;NFKB1;AKT1;AKT3;ADCY3;ATF4;CAMK4;ATF2;ATF6B;EIF4E;INSR;PIK3CA;PIK3CB;PRKAA1;PRKAA2;PRKAB1;PRKAB2;PRKACA;PRKACB;RHEB;RPS6KB1;TSC1;KL;RB1CC1;CREB3;APPL1;ADIPOR2;EHMT1;SES2;SES3;IGF1;TSC2;PRKAG2;PIK3R3;ATG13;ADCY5;ATG5;ADIPOR1;ADCY1;CREB3L1;SOD2;P3R3URF-PIK3R3
Nervous system	hsa04727	GABAergic synapse	45/3285	0.003	40	SIRT1;ADCY9;CAT;MTOR;HSPA1B;IGF1R;KRAS;NRAS;IRS1;ADCY6;IRS2;PIK3R1;RPTOR;AKT2;FOXO3;AKT1;AKT3;ADCY3;HDAC1;HSPA1L;INSR;PIK3CA;PIK3CB;PRKAA1;PRKAA2;PRKAB1;PRKAB2;PRKACA;PRKACB;RPS6KB1;SOD1;IGF1;PRKAG2;PIK3R3;ADCY5;ATG5;HSPA8;ADCY1;SOD2;P3R3URF-PIK3R3
Endocrine system	hsa04916	Melanogenesis	50/3285	0.004	81	BCL2;CREB1;ATP2B1;ADCY9;PPP2R5E;MAPK14;TPM4;ADCY6;GNAI3;AKT2;PPP2R2A;GNAI2;AKT1;AKT3;ATP1A2;ADCY3;AGT;ATF4;ATP1A1;ATP1B1;ATP1B2;ATP2A2;ATP2B4;CACNA2D1;CACNB2;CACNB4;CALM1;CALM2;CALM3;CAMK2G;ATF2;ATF6B;GNAI1;GNAQ;KCNK2;PPP1CA;PPP1CB;PPP1CC;PPP2CB;PPP2R1A;PPP2R1B;PPP2R2C;PPP2R3A;PPP2R5A;PPP2R5C;PRKACA;PRKACB;PRKCA;MAPK1;MAPK3;RYR2;SCN1B;SCN4B;SLC9A1;CREB3;RAPGEF4;BVES;PPP2R3C;PPP2R2D;CACNG8;CACNA2D4;ADRA1B;CACNA1D;ATP2B2;ATP2B3;CACNA2D2;SLC8A1;PPP2R2B;ATP1B4;ADCY5;CREM;PPP2CA;MAPK13;ATP2A1;PPP2R5D;PLCB1;CACNA2D3;ADCY1;CREB3L1;PIK3R6;CACNA1C
Endocrine and metabolic disease	hsa04934	Cushing syndrome	72/3285	0.004	112	BMPR2;UNC5B;KRAS;NRAS;PTK2;CFL2;GNAI3;PIK3R1;CDC42;PAK1;ABL1;RAF1;MET;RASA1;EFNB1;ROCK2;GNAI2;PPP3CA;BMPR1B;ROBO1;LRRCA4;EFNA5;CAMK2G;DCC;DPYSL2;EFNA1;EFNB2;EPHA2;EPHA4;EPHA5;EPHA7;EPHB4;GNAI1;GSK3B;ILK;ITGB1;L1CAM;ABLIM1;LIMK1;NEO1;NFATC2;NFATC3;PAK2;PAK3;PDPK1;PIK3CA;PIK3CB;PLCG1;PLCG2;PLXNA1;PLXNA2;PPP3R1;PRKCA;MAPK1;MAPK3;RAC1;ROCK1;TRPC1;SEMA3B;FZD3;NCK2;NRP1;SEMA5A;PLXNC1;PAK4;SEMA6B;SEMA4D;SEMA4B;SEMA3C;NTNG1;ARHGEF12;SRGAP2;PLXNB2;SH1;SEMA4C;ENAH;DPYSL5;SEMA3G;RGMA;SRGAP1;NTN4;SSH2;PLXNA4;BOC;UNC5D;PTCH1;SRGAP3;EPHA6;PIK3R3;PPP3CB;SEMA7A;PARD3;NCK1;SEMA4A;SEMA6D;SEMA4G;PPP3CC;SLIT1;SEMA3F;SEMA4F;SLIT2;EPHA3;SEMA3A;TRPC5;LRIG2;ABLIM3;SEMA6A;LRRCA4;UNC5A;SEMA3D;PAK5;P3R3URF-PIK3R3
Nervous system	hsa04725	Cholinergic synapse	56/3285	0.004	72	CREB1;MAP2K1;FOS;CYLD;IFNGR1;IL1A;TNFRSF11B;TNFSF11;CSF1;MAPK14;TGFB2;IKBKB;MITF;SOCS3;TGFB2;RELA;PIK3R1;TRAF6;MAPK9;ITGB3;AKT2;JAK1;PPARG;TGFB1;NFKB1;AKT1;PPP3CA;STAT1;AKT3;ATP2A2;CAMK4;CHUK;FHL2;GRB2;IFNAR1;IFNAR2;IL1B;IL1R1;ITPR1;ITPR2;NFATC2;PIK3CA;PIK3CB;PLCG2;PPP3R1;MAPK1;MAPK3;MAPK8;MAP2K6;RAC1;RELB;MAP3K7;TYK2;SQSTM1;GAB2;IRF9;SIRPA;TMEM64;TNFRSF1A;FOSB;PIK3R3;PPP3CB;PPP3CC;ITPR3;MAPK10;MAPK13;TEC;ATP2A1;FOSL2;FOSL1;MAP2K7;P3R3URF-PIK3R3
Cancer: overview	hsa05208	Chemical carcinogenesis - reactive	100/3285	0.005	36	ADCY9;KCNJ2;ADCY6;GNAI3;GNAI2;ATP1A2;ACTB;ADCY3;ATP1A1;ATP1B1;ATP1B2;CA2;CALM1;CALM2;CALM3;CAMK2G;GNAI1;GNAQ;HRH2;ITPR1;ITPR2;KCNK2;PRKACA;PRKACB;PRKCA;PRKCB;SLC9A1;MYLK4;SSTR2;ATP1B4;ADCY5;ITPR3;KCNJ10;PLCB1;ADCY1;KCNK10

		oxygen species				
Endocrine and metabolic disease	hsa04936	Alcoholic liver disease	67/3285	0.005	83	MAP2K1;MTOR;HK2;EIF4E2;KRAS;NRAS;GYS1;IRS1;IKBKB;SOCS3;IRS2;ARAF;PHKB;PIK3R1;MAPK9;CRKL;RAF1;RPTOR;AKT2;AKT1;AKT3;ACACB;CALM1;CALM2;CALM3;CRK;EIF4E;FLOT2;MKNK2;GRB2;GSK3B;HK1;INSR;PDE3B;PDPK1;PHKA2;PIK3CA;PIK3CB;PPP1CA;PPP1CB;PPP1CC;PPP1R3C;PPP1R3D;PRKAA1;PRKAA2;PRKAB1;PRKAB2;PRKACA;PRKACB;PRKAR1A;PRKAR2A;PRKAR2B;PRKCI;MAPK1;MAPK3;MAPK8;PTPRF;PYGB;PYGL;RHEB;RPS6KB1;SOS2;SREBF1;TSC1;FLOT1;EXOC7;SHC3;PPP1R3B;SOCS4;TSC2;SORBS1;PRKAG2;PIK3R3;MAPK10;FASN;BAD;BRAF;SOS1;CBLB;LIPE;PPP1R3E;ACACA;P3R3URF-PIK3R3
Excretory system	hsa04961	Endocrine and other factor-regulated calcium reabsorption	29/3285	0.005	49	MAP2K1;MAP3K3;ADCY9;PRKCD;MAPK14;KRAS;NRAS;ADCY6;EGFR;CDC42;MAPK9;RAF1;ADCY3;ATF4;CALM1;CALM2;CALM3;CAMK2G;EGR1;PTK2B;GNAQ;GRB2;ITPR1;ITPR2;MAP3K1;MAP3K4;PLA2G4A;PLD1;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;MAP2K6;MAP2K4;SOS2;MAP3K2;CACNA1D;ADCY5;ITPR3;MAPK10;MAPK13;SOS1;PLCB1;ADCY1;MAP2K7;CACNA1C
Signal transduction	hsa04072	Phospholipase D signaling pathway	69/3285	0.005	59	MAP2K1;ADCY9;IGF1R;RPS6KA3;CPEB4;MAPK14;KRAS;ADCY6;GNAI3;ARAF;PIK3R1;MAPK9;RAF1;AKT2;CDC25B;CCNA2;GNAI2;AKT1;CDK2;AKT3;ADCY3;UBI1;CCNB1;CDK1;CDC27;GNAI1;HSP90AA1;HSP90AB1;MAD2L1;PDE3B;PGR;PIK3CA;PIK3CB;PRKACA;PRKACB;MAPK1;MAPK3;MAPK8;AURKA;CDC23;CPEB3;ANAPC13;ANAPC15;RPS6KA6;ANAPC7;ANAPC16;CPEB2;CCNB2;IGF1;RPS6KA1;CDC16;PIK3R3;ADCY5;MAPK10;MAPK13;BRAF;STK10;ADCY1;P3R3URF-PIK3R3
Infectious disease: viral	hsa05168	Herpes simplex virus 1 infection	82/3285	0.006	70	ESR1;BCL2;NCOA3;HSP90B1;CREB1;MAP2K1;FOS;ADCY9;HSPA1B;PRKCD;KRAS;NRAS;NCOA2;SP1;ADCY6;EGFR;GNAI3;PIK3R1;RAF1;AKT2;GNAI2;AKT1;AKT3;ADCY3;ATF4;CALM1;CALM2;CALM3;ATF2;ATF6B;CTSD;FKBP5;GABBR1;GNAI1;GNAQ;GRB2;GRM1;HSPA1L;HSP90AA1;HSP90AB1;ITPR1;ITPR2;KCNJ9;KRT10;PGR;PIK3CA;PIK3CB;PRKACA;PRKACB;MAPK1;MAPK3;SOS2;GABBR2;GREB1;CREB3;SHC3;PIK3R3;ADCY5;FKBP4;ITPR3;KCNJ3;NCOA1;SOS1;HSPA8;PLCB1;GNAO1;ADCY1;CREB3L1;GPER1;P3R3URF-PIK3R3
Lipid metabolism	hsa01040	Biosynthesis of unsaturated fatty acids	17/3285	0.006	50	CREB1;MAP2K1;ADCY9;EP300;KIT;KRAS;NRAS;ADCY6;MITF;GNAI3;DVL2;RAF1;GNAI2;WNT10B;ADCY3;CALM1;CALM2;CALM3;CAMK2G;CREBBP;CTNNB1;DVL3;GNAI1;GNAQ;GSK3B;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;WNT2;WNT9A;FZD5;FZD3;FZD4;FZD6;FZD8;CREB3;LEF1;EDNRB;KITLG;TCF7L2;ADCY5;WNT2B;DVL1;PLCB1;GNAO1;ADCY1;CREB3L1
Nervous system	hsa04721	Synaptic vesicle cycle	40/3285	0.006	42	ESR1;MAP2K1;FOS;TNFSF11;MAPK14;KRAS;NRAS;CCND1;SOCS5;SOCS3;RELA;PIK3R1;MAPK9;RAF1;AKT2;FOXO3;NFKB1;AKT1;JAK2;STAT1;AKT3;STAT3;CIS;H;GRB2;GSK3B;PIK3CA;PIK3CB;MAPK1;MAPK3;MAPK8;PRLR;SOS2;STAT5B;SOCS6;SHC3;SOCS4;PIK3R3;MAPK10;MAPK13;SOS1;SOCS7;P3R3URF-PIK3R3
Signal transduction	hsa04340	Hedgehog signaling pathway	30/3285	0.007	36	HSP90B1;CREB1;ADCY9;ADCY6;ATP1A2;ADCY3;ATF4;ATP1A1;ATP1B1;ATP1B2;ATF2;ATF6B;GNAQ;GSR;HSPA5;ITPR1;ITPR2;PRKACA;PRKACB;PRKCA;PRKCB;TTF1;CREB3;GPX8;GPX1;ALB;CANX;ATP1B4;ADCY5;GPX3;ITPR3;PAX8;LRP2;PLCB1;ADCY1;CREB3L1
Endocrine system	hsa04920	Adipocytokine signaling pathway	36/3285	0.007	78	ESR1;NCOA3;MAP2K1;EP300;MTOR;KAT2B;MED14;NOTCH1;KRAS;NRAS;NCOA2;CCND1;SLC16A10;MYC;PIK3R1;NOTCH3;NOTCH2;HIF1A;RAF1;ITGB3;AKT2;MED1;AKT1;STAT1;AKT3;ATP1A2;ACTB;ATP1A1;ATP1B1;ATP1B2;ATP2A2;CREBBP;CTNNB1;KAT2A;GSK3B;HDAC1;ITGAV;MDM2;PDPK1;PFKFB2;PFKP;PIK3CA;PIK3CB;PLCG1;PLCG2;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;RHEB;SLC9A1;THRB;TBC1D4;MED13;MED16;MED13L;SIN3A;MED4;PLCE1;MED12L;PDKM;TSC2;PIK3R3;ATP1B4;SLCO1C1;NCOR1;RCAN2;NCOA1;HDAC3;ATP2A1;BAD;MED12;SLC2A1;PLCB1;PFKL;P3R3URF-PIK3R3
Drug resistance: antineoplastic	hsa01524	Platinum drug resistance	38/3285	0.007	36	MTOR;PPARA;IRS1;IKBKB;SOCS3;IRS2;RELA;MAPK9;AKT2;NFKB1;AKT1;JAK2;AKT3;STAT3;ACACB;CHUK;CPT1A;ACSL1;ACSL3;ACSL4;LEPR;PRKAA1;PRKAA2;PRKAB1;PRKAB2;MAPK8;ACSL6;APPL1;ACSL5;ADIPOR2;PRKAG2;TNFRSF1A;CPT1C;MAPK10;SLC2A1;ADIPOR1
Amino acid metabolism	hsa00270	Cysteine and methionine metabolism	28/3285	0.008	80	MAP2K1;FOS;ADCY9;KCNJ2;KRAS;NRAS;CCND1;CDKN1A;ADCY6;EGFR;GNAI3;RAF1;PTGS2;ROCK2;GNAI2;PPP3CA;ACTB;ADCY3;CACNA2D1;CACNB2;CACNB4;CALM1;CALM2;CALM3;CAMK4;CAMK2G;EEF2;GNAI1;GNAQ;GUCY1A2;ITPR1;ITPR2;KCNJ9;MEF2C;NFATC2;NFATC3;PLA2G4A;PPP1CA;PPP1CB;PPP1CC;PPP3R1;PRKAA1;PRKAA2;PRKAB1;PRKAB2;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;MAP2K5;RGS2;ROCK1;RYR2;RYR3;EEF2K;PPP1R12C;CACNG8;CACNA2D4;CACNA1D;CACNA2D2;MYLK4;PRKAG2;PPP3CB;PPP1R12B;ADCY5;PPP3CC;ITPR3;KCNJ3;PLCB1;CACNA2D3;CAMK1D;GNAO1;MYL6;ADCY1;PIK3R6;GUCY1A1;GUCY1B1;CACNA1C
Information processing in viruses	hsa03250	Viral life cycle - HIV-1	33/3285	0.009	55	SIRT1;CREB1;EP300;PPARA;GYS1;PHKB;AKT2;AKT1;PPP3CA;AKT3;ACACB;ATF4;CALM1;CALM2;CALM3;CAMK2G;CPT1A;ATF2;CREBBP;GNAQ;PRMT1;ITPR1;ITPR2;LDHA;LDHB;PDE3B;PFKP;PHKA2;PKM;PPP3R1;PRKAA1;PRKAA2;PRKAB1;PRKAB2;PRKACA;PRKACB;PYGB;PYGL;CREB3;PFKM;PRKAG2;CPT1C;PPP3CB;PPP3CC;ITPR3;PGAM1;SLC2A1;SIK2;PLCB1;CREB3L1;CRTC2;PFKL;PPP4R3B;PPP4R3A;ACACA
Amino acid metabolism	hsa00280	Valine, leucine and isoleucine degradation	26/3285	0.01	35	CREB1;KCNJ2;ADCY6;GNAI3;GNAI2;PPP3CA;AGT;CALM1;CALM2;CALM3;GNAI1;GNAQ;GUCY1A2;ITPR1;ITPR2;KCNMA1;PDE3A;PDE3B;PPP3R1;PRKACA;PRKACB;CACNA1D;PDE1B;PTGER4;PDE1A;ADCYAP1;ADCYAP1R1;PPP3CB;ADCY5;PPP3CC;ITPR3;PLCB1;GUCY1A1;GUCY1B1;CACNA1C
Endocrine system	hsa04924	Renin secretion	35/3285	0.01	47	CREB1;ATP2B1;LDLR;ADCY9;ADCY6;PRKD2;PRKCE;ATP1A2;ADCY3;AGT;ATF1;ATF4;ATP1A1;ATP1B1;ATP1B2;ATP2B4;DAGLA;CALM1;CALM2;CALM3;CAMK4

						;CAMK2G;ATF2;ATF6B;GNAQ;ITPR1;ITPR2;PDE2A;PRKACA;PRKACB;PRKCA;PRKCB;CREB3;PRKD3;CACNA1D;ATP2B2;ATP2B3;ATP1B4;ADCY5;ITPR3;KCNK3;PLCB1;CAMK1D;ADCY1;CREB3L1;LIPE;CACNA1C
Glycan biosynthesis and metabolism	hsa00510	N-Glycan biosynthesis	29/3285	0.01	65	CREB1;MAP2K1;FOS;ADCY9;ARRB2;MAPK14;KRAS;NRAS;TGFB2;VEGFA;COL3A1;COL4A1;COL1A2;ADCY6;EGFR;GNAI3;RELA;PIK3R1;MAPK9;RAF1;AKT2;GNAI2;TGFB1;NFKB1;AKT1;SMAD2;AKT3;ADCY3;ARRB1;ATF4;COL4A5;ATF2;ATF6B;GNAI1;GNB1;GNB2;GRB2;PIK3CA;PIK3CB;PRKACA;PRKACB;PRKCA;MAPK1;MAPK3;MAPK8;MAP2K4;SOS2;VEGFC;CREB3;SHC3;GNB4;GNG7;EDNRB;PIK3R3;ADCY5;COL4A6;MAPK10;MAPK13;SOS1;PLCB1;GNAO1;ADCY1;CREB3L1;MAP2K7;P3R3URF-PIK3R3
Signal transduction	hsa04330	Notch signaling pathway	32/3285	0.01	57	BCL2;CREB1;MAP2K1;FOS;FGFR1;ADCY9;TNFSF11;ARRB2;MAFB;CDKN1A;SP1;ADCY6;EGFR;GNAI3;ARAF;RAF1;MMP16;GNAI2;MEF2D;WINK1;ADCY3;ARRB1;ATF4;ATF2;ATF6B;EGFR;GATA3;GNAI1;GNAQ;ITPR1;ITPR2;LRP6;MEF2A;MEF2C;PDE4D;PLD1;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;SGK1;KL;OXSR1;CREB3;GNAI3;AKAP13;WINK3;ADCY5;ITPR3;BRAF;STK39;ARHGEF11;PLCB1;ADCY1;CREB3L1
Endocrine system	hsa04925	Aldosterone synthesis and secretion	47/3285	0.01	37	MAP2K1;SPPI;ARRB2;KRAS;NRAS;HCN2;PIK3R1;RAF1;AKT2;AKT1;AKT3;ARRB1;GABBR1;GNAQ;ITPR1;ITPR2;KCNJ9;KCNN4;PIK3CA;PIK3CB;PRKCA;PRKCB;MAPK1;MAPK3;TRPC1;GABBR2;CACNA1D;PIK3R3;ITPR3;KCNJ3;KCNN3;TRPC5;PLCB1;HCN1;GPER1;CACNA1C;P3R3URF-PIK3R3
NA	hsa04820	Cytoskeleton in muscle cells	100/3285	0.01	74	CREB1;MAP2K1;FOS;ADCY9;EP300;MTOR;MAPK14;KRAS;NRAS;PTK2;IRS1;ADCY6;SOCS3;IRS2;GNAI3;PIK3R1;MAPK9;CRKL;RAF1;AKT2;GNAI2;AKT1;JAK2;STAT1;AKT3;STAT3;ADCY3;ATF4;ATF2;CREBBP;ATF6B;CRK;GNAI1;GNAQ;GRB2;GSK3B;ITPR1;ITPR2;MAP3K1;PIK3CA;PIK3CB;PLCG1;PLCG2;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;MAP2K6;MAP2K4;SOS2;STAT5B;CREB3;SHC3;MRAP2;IGF1;GHR;CACNA1D;SSTR1;SSTR2;PIK3R3;BCAR1;ADCY5;ITPR3;MAPK10;MAPK13;SOS1;PLCB1;ADCY1;CREB3L1;CACNA1C;P3R3URF-PIK3R3
Replication and repair	hsa03420	Nucleotide excision repair	32/3285	0.01	22	CREB1;PER2;CLOCK;FBXW11;BTOR;CRY2;CSNK1D;PRKAA1;PRKAA2;PRKAB1;PRKAB2;RORA;RORB;CUL1;BHLHE40;PER3;NR1D1;NR1D2;BHLHE41;PRKAG2;SKP1;RBX1
Signal transduction	hsa04392	Hippo signaling pathway - multiple species	17/3285	0.01	50	GRIA2;CREB1;FOS;ADCY9;PER2;ADCY6;GNAI3;GNAI2;ADCY3;CALM1;CALM2;CALM3;CAMK2G;GNAI1;GNAQ;GNB1;GNB2;GRIA1;GRIN2A;GUCY1A2;ITPR1;KCNJ9;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;RYR2;RYR3;PER3;GNB4;GNG7;CACNA1D;GRIA3;GRIA4;PRKG1;ADCYAP1;ADCYAP1R1;ADCY5;ITPR3;KCNJ3;GRIN1;PLCB1;GNAO1;ADCY1;GRIN2B;GUCY1A1;GUCY1B1;CACNA1C
Infectious disease: viral	hsa05164	Influenza A	76/3285	0.01	108	CREB1;FGFR1;ADCY9;MTOR;RPS6KA3;MAPK14;KRAS;NRAS;ADCY6;RPTOR;PPARG;ACTB;ADCY3;COX7B;COX8A;COX10;CPT1A;CPT2;ATF2;ACSL1;ACSL3;ACSL4;GRB2;NDUFA4;NDUFA9;NDUFB1;NDUFB5;NDUFS4;PRKAA1;PRKAA2;PRKAB1;PRKAB2;PRKACA;PRKACB;RHEB;RPS6KB1;SMARCA2;SMARCA4;SMARCB1;SMARCC1;SMARCC2;SMARCD1;SOS2;TSC1;UQCRC2;DPF3;ARID1A;CREB3;FRS2;MGLL;KDM1A;ACSL6;RPS6KA6;NDUFAF1;COA4;ACSL5;KDM3B;NDUFAF7;PNPLA2;PRDM16;NDUFAF2;TSC2;RPS6KA1;COA5;NDUFAF5;PRKAG2;UQCRIH;PRKG1;CPT1C;KDM3A;CNR1;NDUFA2;SIRT6;MLST8;ADCY5;UQCRC2;NDUFS1;NDUFC2;COX7C;NDUFA6;MAPK13;UQCRC1;COX5A;COX11;COX15;NDUFA10;NDUFA7;NDUFAF1;SOS1;MAP3K5;ZNF516;ARID1B;NDUFA12;ADCY1;CREB3L1;NDUFV1;NDUFV2;COX6A1;LIPE;COA7;ATP5F1A;ATP5MC2;ATP5MC3;ATP5F1B;ATP5PB;ATP5F1E;ATP5PO;ATP5PD
Cancer: overview	hsa05207	Chemical carcinogenesis - receptor activation	93/3285	0.01	23	KRAS;IRS1;PIK3R1;ATP1A2;ATP1A1;ATP1B1;ATP1B2;SFN;INSR;NR3C2;PDPK1;PIK3CA;PIK3CB;PRKCA;PRKCB;MAPK1;MAPK3;SGK1;NEDD4L;IGF1;PIK3R3;ATP1B4;P3R3URF-PIK3R3
Replication and repair	hsa03030	DNA replication	20/3285	0.01	29	ESR1;ATP2B1;ADCY9;ADCY6;DNM2;AP2M1;ATP1A2;AP2A1;AP2B1;ATP1A1;ATP1B1;ATP1B2;ATP2B4;AP2S1;CLTA;CLTB;CLTC;GNAQ;PRKACA;PRKACB;PRKCA;PRKCB;KL;DNM3;ATP2B2;ATP2B3;SLC8A1;ATP1B4;PLCB1
Immune system	hsa04664	Fc epsilon RI signaling pathway	34/3285	0.01	23	CREB1;ADCY9;DYNC1L12;ADCY6;ADCY3;DYNC1H1;NSF;PRKACA;PRKACB;RAB5A;RAB5C;CREB3;DCTN4;DYNC2H1;DCTN5;DCTN1;DYNC1I2;AQP4;RAB11B;AQP3;DCTN2;CREB3L1;DYNLL2
Cancer: specific types	hsa05219	Bladder cancer	22/3285	0.02	82	MAP2K1;ADCY9;RAP1B;CCL22;ARRB2;PRKCD;GRK2;KRAS;NRAS;PREX1;PTK2;IKKB;ADCY6;GNAI3;RELA;PIK3R1;CDC42;PAK1;CRKL;RAF1;AKT2;FOXO3;ROCK2;GNAI2;NFKB1;AKT1;JAK2;STAT1;AKT3;STAT3;ADCY3;ARRB1;CHUK;CRK;PTK2B;GNAI1;GNAQ;GNB1;GNB2;GRB2;CXCL1;CXCL2;CXCL3;GSK3B;PIK3CA;PIK3CB;PLCG1;PLCG2;PRKACA;PRKACB;PRKCB;MAPK1;MAPK3;PXN;RAC1;RAPIA;ROCK1;CXCL5;SOS2;STAT5B;TIAM1;SHC3;GNB4;CXCL10;GNG7;LYN;GRK4;ELMO1;PIK3R3;BCAR1;PARD3;ADCY5;BAD;BRAF;GRK5;CXCL11;SOS1;PLCB1;ADCY1;PIK3R6;GRK3;P3R3URF-PIK3R3
Lipid metabolism	hsa00561	Glycerolipid metabolism	32/3285	0.02	61	ADCY9;RAP1B;ARHGAP35;MAPK14;COL3A1;COL1A2;ADCY6;TLN1;GNAI3;PIK3R1;ITGB3;AKT2;ROCK2;GNAI2;AKT1;AKT3;ACTB;ADCY3;GNAI1;GNAQ;GUCY1A2;ITGA2;ITGB1;ITPR1;ITPR2;PIK3CA;PIK3CB;PLA2G4A;PLCG2;PPP1C;PPP1CB;PPP1CC;PRKACA;PRKACB;PRKCI;MAPK1;MAPK3;RAPIA;ROCK1;STIM1;VAMP8;GNAI3;ARHGEF12;TLN2;LYN;VWF;MYLK4;PRKG1;PIK3R3;ADCY5;F2R;ITPR3;MAPK13;PLCB1;ADCY1;P2RY12;FERMT3;PIK3R6;GUCY1A1;GUCY1B1;P3R3URF-PIK3R3
Global and overview maps	hsa01230	Biosynthesis of amino acids	36/3285	0.02	52	CYLD;CCL22;PRKCD;MAPK14;KRAS;NRAS;IKKB;RELA;PIK3R1;PAK1;MAPK9;RAF1;PTGS2;AKT2;NFKB1;AKT1;PPP3CA;STAT1;AKT3;CALM1;CALM2;CALM3;CHUK;EGR3;IL1B;ITPR1;ITPR2;MDM2;NFATC2;NFATC3;PIK3CA;PIK3CB;PLCG2;PPP3R1;MAPK1;MAPK3;MAPK8;RELB;MAPKAPK2;IRF9;MALT1;ARHGEF12;MR

						AS;PIK3R3;PPP3CB;PPP3CC;ITPR3;MAPK10;MAPK13;KSR1;CBLB;P3R3URF-PIK3R3
Endocrine system	hsa04918	Thyroid hormone synthesis	36/3285	0.02	67	MAP2K1;FOS;PPP2R5E;MAPK14;KRAS;NRAS;IKBKB;MAP3K8;RELA;PIK3R1;CD42;PAK1;MAPK9;RAF1;AKT2;PPP2R2A;NFKB1;AKT1;PPP3CA;AKT3;CHUK;DLG1;GRB2;GSK3B;NFATC2;NFATC3;PAK2;PAK3;PDPK1;PIK3CA;PIK3CB;PLCG1;PPP2CB;PPP2R1A;PPP2R1B;PPP2R2C;PPP2R3A;PPP2R5A;PPP2R5C;PPP3R1;MAPK1;MAPK3;MAPK8;SOS2;MAP3K7;NCK2;PAK4;MALT1;PPP2R3C;PPP2R2D;CD4;PIK3R3;PPP2R2B;PPP3CB;NCK1;PPP3CC;PPP2CA;MAPK10;MAPK13;PTPRC;TEC;SOS1;PPP2R5D;MAP2K7;CBLB;PAK5;P3R3URF-PIK3R3
Infectious disease: bacterial	hsa05110	Vibrio cholerae infection	26/3285	0.02	34	MAP2K1;MAPK14;KRAS;NRAS;PIK3R1;MAPK9;RAF1;AKT2;AKT1;AKT3;GRB2;PDPK1;PIK3CA;PIK3CB;PLA2G4A;PLCG1;PLCG2;PRKCA;MAPK1;MAPK3;MAPK8;MAP2K6;RAC1;MAP2K4;SOS2;GAB2;LYN;ALOX5;PIK3R3;MAPK10;MAPK13;SOS1;MAP2K7;P3R3URF-PIK3R3
Lipid metabolism	hsa00062	Fatty acid elongation	16/3285	0.02	55	MAP2K1;ARF6;PRKCD;PLPP3;MYO10;ARPC1B;CFL2;DNM2;GSN;PIK3R1;CDC42;PAK1;CRKL;RAF1;PRKCE;AKT2;AKT1;AKT3;BIN1;CRK;LIMK1;PIK3CA;PIK3CB;PLA2G4A;PLCG1;PLCG2;PLD1;PRKCA;PRKCB;MAPK1;MAPK3;RAC1;RPS6KB1;ASAP2;WASF1;GAB2;ARPC5;ARPC3;ACTR3;ACTR2;WASF2;WASF3;ASAP1;MARCKSL1;ARPC5L;LYN;PLA2G6;ACTR3B;PIK3R3;ARPC1A;DOCK1;PTPRC;MARCKS;PLPP1;P3R3URF-PIK3R3
Excretory system	hsa04962	Vasopressin-regulated water reabsorption	23/3285	0.02	46	GRIA2;MAP2K1;EP300;RAP1B;RPS6KA3;KRAS;NRAS;ARAF;RAF1;PPP3CA;ATF4;CALM1;CALM2;CALM3;CAMK4;CAMK2G;CREBBP;GNAQ;GRIA1;GRIN2A;GRM1;GRM5;ITPR1;ITPR2;PPP1CA;PPP1CB;PPP1CC;PPP3R1;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;RAP1A;RPS6KA6;RPS6KA1;PPP3CB;PPP3CC;ITPR3;BRAF;GRIN1;PLCB1;ADCY1;GRIN2B;CACNA1C
Immune system	hsa04062	Chemokine signaling pathway	82/3285	0.03	40	STX2;ATP6V0E1;DNM2;ATP6V1B2;AP2M1;AP2A1;AP2B1;ATP6V1A;ATP6V1C1;ATP6V1E1;ATP6V0A1;CACNA1B;AP2S1;CLTA;CLTB;CLTC;NSF;RAB3A;SLC1A1;SLC1A3;SLC6A12;STX3;SYT1;ATP6V0D1;ATP6V1G1;UNC13B;UNC13A;DNM3;SLC17A6;SLC32A1;UNC13C;CACNA1A;CPLX2;STXBP1;RIMS1;SLC1A2;ATP6V0C;SLC6A1;ATP6V0A2;ATP6V1D
Digestive system	hsa04971	Gastric acid secretion	36/3285	0.03	72	BCL2;MAP2K1;MAP3K3;RAP1B;RPS6KA3;SORT1;PRKCD;MAPK14;KRAS;NRAS;IRS1;IKBKB;NTRK3;RELA;PIK3R1;CDC42;IRAK1;TRAF6;GAB1;MAPK9;CRKL;ABL1;RAF1;AKT2;FOXO3;NFKB1;AKT1;AKT3;ATF4;CALM1;CALM2;CALM3;CAMK4;CAMK2G;CRK;GRB2;GSK3B;MAP3K1;NTRK2;PDPK1;PIK3CA;PIK3CB;PLCG1;PLCG2;MAPK1;MAPK3;MAPK8;MAP2K5;PSEN1;RAC1;RAP1A;SOS2;YWHAE;MAPKAPK2;FRS2;PRDM4;RPS6KA6;IRAK4;SHC3;KIDINS220;MAGED1;RPS6KA1;PIK3R3;MAPK10;MAPK13;BAD;BRAF;SOS1;MAP3K5;ZNF274;MAP2K7;P3R3URF-PIK3R3
Signaling molecules and interaction	hsa04514	Cell adhesion molecules	69/3285	0.03	74	GRIA2;ADCY9;MAPK14;ADCY6;GNAI3;MAPK9;PTGS2;GNAI2;ADCY3;DAGLA;CACNA1B;GABRA1;GABRB3;GNAI1;GNAQ;GNB1;GNB2;GRIA1;GRM1;GRM5;ITPR1;ITPR2;KCNJ9;NDUFA4;NDUFA9;NDUFB1;NDUFB5;NDUFS4;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;MAPK8;MGLL;SLC17A6;GNB4;SLC32A1;GNG7;CACNA1A;CACNA1D;GABRA2;GABRA4;GABRB2;GABRD;GABRG2;GRIA3;GRIA4;NAPEPLD;CNR1;RIMS1;NDUFA2;ADCY5;NDUFS1;NDUFC2;FAAH;ITPR3;KCNJ3;NDUFA6;MAPK10;MAPK13;NDUFA10;NDUFA7;NDUFAB1;PLCB1;NDUFA12;ABHD6;GNAO1;ADCY1;GABRG1;NDUFV1;NDUFV2;CACNA1C
Global and overview maps	hsa01200	Carbon metabolism	52/3285	0.03	60	GRIA2;ADCY9;SLC38A2;GRK2;ADCY6;GNAI3;GNAI2;PPP3CA;ADCY3;GLS;GNAI1;GNAQ;GNB1;GNB2;GRIA1;GRIN2A;GRM1;GRM5;ITPR1;ITPR2;PLA2G4A;PLD1;PPP3R1;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;SLC1A1;SLC1A3;TRPC1;HOMER1;NCDN;SLC17A6;GNB4;SLC38A1;GNG7;CACNA1A;CACNA1D;GRIA3;GRIA4;GRIK3;DLGAP1;PPP3CB;SLC1A2;ADCY5;PPP3CC;ITPR3;KCNJ3;GRIN1;PLCB1;GNAO1;ADCY1;SHANK2;SHANK3;GRIN2B;LZTS3;GRK3;CACNA1C
Lipid metabolism	hsa00071	Fatty acid degradation	22/3285	0.03	56	BCL2;CREB1;MAP2K1;FOS;ADCY9;KCNJ2;KRAS;NRAS;ADCY6;GNAI3;PIK3R1;AKT2;GNAI2;AKT1;JAK2;AKT3;ADCY3;ATF4;CACNA1B;CAMK4;CAMK2G;GNAI1;GNAQ;GNB1;GNB2;ITPR1;ITPR2;KCNQ2;PIK3CA;PIK3CB;PRKACA;PRKACB;PRKCA;PRKCB;MAPK1;MAPK3;CREB3;GNB4;CHRFAM7A;GNG7;CACNA1A;CACNA1D;CHRN2;PIK3R3;KCNQ5;ADCY5;KCNQ3;ITPR3;KCNJ3;PLCB1;GNAO1;ADCY1;CREB3L1;PIK3R6;CACNA1C;P3R3URF-PIK3R3
Signal transduction	hsa04064	NF-kappa B signaling pathway	47/3285	0.04	45	ADCY9;SLC38A2;ADCY6;GNAI3;GNAI2;ADCY3;CACNA1B;GABBR1;GABRA1;GABRB3;GLS;GNAI1;GNB1;GNB2;NSF;PRKACA;PRKACB;PRKCA;PRKCB;SLC6A12;GABBR2;GABARAPL2;GNB4;SLC38A1;SLC32A1;GNG7;CACNA1A;CACNA1D;GABRA2;GABRA4;GABRB2;GABRD;GABRG2;GAD1;GAD2;GPHN;SLC12A5;ADCY5;SLC6A1;PLCL1;TRAK2;GNAO1;ADCY1;GABRG1;CACNA1C
Substance dependence	hsa05033	Nicotine addiction	21/3285	0.04	82	GRIA2;CREB1;FOS;ARRB2;PPP2R5E;CLOCK;MAPK14;GNAI3;MAPK9;AKT2;PPP2R2A;GNAI2;AKT1;PPP3CA;AKT3;ARRB1;ATF4;CACNA1B;CALM1;CALM2;CALM3;CAMK2G;COMT;ATF2;ATF6B;DRD1;GNAI1;GNAQ;GNB1;GNB2;GRIA1;GRIN2A;GSK3B;ITPR1;ITPR2;KCNJ9;KIF5A;KIF5B;KIF5C;MAOA;PPP1CA;PPP1CB;PPP1CC;PPP2CB;PPP2R1A;PPP2R1B;PPP2R2C;PPP2R3A;PPP2R5A;PPP2R5C;PRKACA;PRKACB;PRKCA;PRKCB;MAPK8;CREB3;PPP2R3C;PPP2R2D;GNB4;GNG7;CACNA1A;CACNA1D;GRIA3;GRIA4;MAOB;PPP2R2B;GNAL;PPP3CB;SCN1A;ADCY5;PPP3CC;ITPR3;KCNJ3;PPP2CA;MAPK10;MAPK13;PPP2R5D;PLCB1;GNAO1;CREB3L1;GRIN2B;CACNA1C

Supplementary Table S5. KEGG pathway enrichment of miR-181b target genes associated with schizophrenia. The table lists pathways significantly enriched for miR-181b targets that overlap with schizophrenia-related genes. Columns report the total number of miRNA target genes (n_miRNA_genes), total number of schizophrenia-related genes

(n_scz_genes), number of overlapping genes (n_overlap), the names of overlapping genes (Overlap_genes), and statistical significance values (p-value, FDR, and Bonferroni correction). Only pathways relevant to schizophrenia are shown.

hsa-miR-203a						
Subcategory	ID	Description	GeneRatio	p.adjust	Count	GeneSymbol
Cell growth and death	hsa04218	Cellular senescence	73/1882	1,25E+02	73	ABL1;E2F3;E2F1;CDK6;SMAD2;ATM;GSK3B;SMAD4;SMC1A;TTK;CCND1;CDKN1A;TGFB2;CDK4;CCND2;TP53;AURKB;YWHAZ;CCNA2;E2F2;PDS5A;PRKDC;ATRX;BUB1;CCNB1;CDK1;CDC6;CDC20;CDC25C;CREBBP;E2F4;EP300;MAD2L1;SMAD3;MCM2;MCM5;MCM6;MDM2;ORC4;ORC5;PPP2CB;PPP2R1A;PPP2R5A;PPP2R5C;SKP2;TFDP2;WEE1;YWHAG;YWHAH;CDC7;CUL1;CDC23;PKMYT1;SMC3;BUB3;TRIP13;STAG1;DBF4;YWHAQ;PDS5B;NIPBL;ANAPC15;CDT1;MAD2L1BP;MAD1L1;ATR;TGFB3;SKP1;CDC14C
Infectious disease: viral	hsa05163	Human cytomegalovirus infection	90/1882	5,04E+04	90	IGF1R;PPP1CB;PRKACB;CPEB4;MAPK14;SMC1A;FBXW11;ADCY6;MAP2K1;YWHAZ;BTRC;PPP3CA;MAPK11;ADCY9;AR;BUB1;CALM1;CALM2;CAMK2G;CCNB1;CDK1;CDC20;CDC25C;ITPR1;ITPR2;MAD2L1;PPP1CC;PPP2CB;PPP2R1A;PPP2R5A;PPP2R5C;PPP3R1;RPS6KA2;RPS6KA3;AURKA;YWHAG;YWHAH;CUL1;CDC23;PKMYT1;SMC3;YWHAQ;ANAPC15;CPEB2;MAD1L1;ADCY8;PPP3CB;PPP3CC;SKP1
Cell growth and death	hsa04110	Cell cycle	69/1882	8,44E+04	69	CDK6;ATM;PPM1D;PTEN;THBS1;CCND1;CDKN1A;SESN1;CDK4;PERP;CASP3;CCND2;TP53;BCL2L1;BBC3;CASP8;CCNB1;CCNG2;CDK1;MDM2;MDM4;SERPINE1;PMAIP1;RRM2;RRM2B;SHISA5;SESN3;RCHY1;GORAB;ATR;COP1
Cancer: overview	hsa05205	Proteoglycans in cancer	82/1882	1,35E+05	82	JUN;MAPK9;AKT2;FOS;ATM;BIRC5;PIK3CA;MAPK8;TNF;TUBA1A;KRAS;NRAS;DFFB;RELA;PIK3R1;CASP3;BCL2L1;TP53;CTSC;MAP2K1;HRAS;AKT1;AKT3;BCL2L1;BBC3;PARP4;BIRC2;BIRC3;XIAP;ATF4;CASP8;DDIT3;EIF2S1;ITPR1;ITPR2;NFKBIA;PMAIP1;TUBA1B;LMNB2;NOL3;MAP3K5;CASP2;DAXX;MCL1
Endocrine and metabolic disease	hsa04931	Insulin resistance	52/1882	3,72E+05	52	MAPK9;BIRC5;MAPK8;CASP3;BCL2L1;BCL2L1;BBC3;BIRC2;BIRC3;XIAP;CASP8;PMAIP1;BIRC6
Signal transduction	hsa04152	AMPK signaling pathway	56/1882	3,82E+05	56	PRNP;ALOX15;NCOA4;TP53;SLC7A11;ACSL1;FTL;PCBP1;SLC3A2;TFRCC;VDAC2;SLC39A14;PCBP2;VDAC3;SLC40A1
Cancer: specific types	hsa05210	Colorectal cancer	44/1882	7,32E+05	44	E2F3;E2F1;CDK6;AKT2;SMAD2;ATM;IL6;PIK3CA;PPP1CB;CXCL8;PTEN;MAPK14;FBXW11;KRAS;NRAS;ZFP36L2;CCND1;CDKN1A;HIPK3;TGFB2;CDK4;RELA;PIK3R1;SIRT1;CCND2;TP53;MAP2K1;FOXO1;CCNA2;HRAS;TGFB1;AKT1;BTRC;PPP3CA;E2F2;AKT3;MAPK11;SLC25A6;CALM1;CALM2;CCNB1;CDK1;E2F4;EIF4EBP1;FOXM1;MTOR;ITPR1;ITPR2;SMAD3;MDM2;MYBL2;NBN;NFATC2;NFATC3;SERPINE1;PPID;PPP1CC;PPP3R1;MAP2K3;RAD1;RAD9A;RHEB;VDAC2;MAPKAPK2;HIPK2;MCU;HIPK1;RBBP4;VDAC3;PPP3CB;ATR;PPP3CC;TGFB3
Signal transduction	hsa04010	MAPK signaling pathway	106/1882	8,22E+05	106	AKT2;ROCK2;FGF2;PIK3CA;PPP1CB;PIP5K1A;ENAH;SPATA13;SRC;KRAS;NRAS;MYH9;PIK3R1;PAK1;APC;ITGB4;MAP2K1;FGFR1;HRAS;AKT1;ITGA5;AKT3;CHRM3;CRK;DIAPH1;LPA1;FN1;GNA12;ITGA6;ITGA1;ITGA3;ITGB8;MSN;PPP1R12A;PAK2;PFN2;PIP4K2A;PPP1CC;PXN;RAC1;RAC2;ROCK1;SOS2;ITGA10;ARHGEF7;WASF1;ARPC5;ACTR3;AB12;WASF2;GNA13;NCKAP1;ARHGEF12;SSH1;PIP4K2C;CYFIP2;MYL12B;PPP1R12B;PIKFYVE;ARPC1A;FGF18;WASL;SOS1;ARPC2;GNG12;MYL5;PIP4K2B;CYRIB
Infectious disease: viral	hsa05166	Human T-cell leukemia virus 1 infection	85/1882	8,62E+05	85	KIF2A;KIF5B;KIF1C;KIF13A;DYNLT1;TPM1;TUBA1A;MYO10;TPM4;MYH9;TUBB6;ACTR1A;KIF1A;CAPZA1;CAPZA2;DNAH5;DYNCH1;DYNCH1L2;KIF5C;KLC1;KIF11;KIFC1;MYO1C;MYO5A;MYO5B;MYO6;MYO9A;KIF20B;KIF14;KIF20A;DNAL4;TUBA1B;DCTN6;KIFAP3;KIF1B;KIF4A;DYNCH2H1;KIF18A;HOOK3;KLC4;TUBB2B;TUBG1;MYL12B;DNAH6;KIF3B;DYNLRB1;ACTR10;MYO5C;KIF12;KIF18B;TNNT1;MYL5;DYNL2
Endocrine and metabolic disease	hsa04933	AGE-RAGE signaling pathway in diabetic complications	48/1882	1,21E+06	48	VEGFA;CAV1;JUN;MAPK9;MET;AKT2;SHC1;ROCK2;RAPGEF1;GSK3B;IGF1R;PIK3CA;PPP1CB;PRKCA;MAPK8;RAP1A;PIP5K1A;THBS2;PTEN;SRC;ERBB2;THBS1;LAMC1;CCND1;COL4A1;PIK3R1;PAK1;CCND2;ITGB4;MAP2K1;HRAS;AKT1;ITGA5;AKT3;BIRC2;BIRC3;XIAP;ARHGAP5;COL4A4;COL4A5;COL6A1;CRK;DIAPH1;ELK1;EMP1;FLNA;FLNB;FN1;TNC;ITGA6;ITGA1;ITGA3;ITGB8;LAMA3;LAMB1;PPP1R12A;PAK2;PPP1CC;PXN;RAC1;RAC2;ROCK1;SOS2;ZYX;ITGA10;TLN2;MYL12B;PPP1R12B;EMP2;TNR;COL6A3;SOS1;SHC2;LAMB2;MYL5
Infectious disease: viral	hsa05161	Hepatitis B	66/1882	3,35E+06	66	SNAI2;MET;CDH1;ROCK2;IGF1R;SMAD4;RAP1A;SNAI1;PDCD10;SMURF2;SRC;ERBB2;TJP1;CTNND1;FGFR1;TGFB1;ACPI;CREBBP;CSNK2A1;EP300;INSR;SMAD3;PTPN1;PTPRF;PTPRJ;RAC1;RAC2;ROCK1;TCF7;WASF1;WASF2;LEF1;HEG1;SORBS1;MYL12B;TCF7L2;SMURF1;WASL;MYL5;CSNK2A3;NECTIN2;ARHGAP29
Chromosome	hsa03083	Polycomb repressive complex	41/1882	4,36E+06	41	TJP2;JUN;MAPK9;ROCK2;PRKACB;MAPK8;RAP1A;PARD6B;SRC;ERBB2;TUBA1A;MYH9;CCND1;TJP1;RUNX1;CDK4;PRKCE;PPP2R2A;CFTR;DLG1;DLG2;DLG3;HSPA4;MAP3K1;RAB8A;MSN;NEDD4;PPP2CB;PPP2R1A;PRKAA1;PRKAA2;PRKAB2;PRKAG1;RAC1;ROCK1;SYMPK;YBX3;MPDZ;ARPC5;ACTR3;TUBA1B;NEDD4L;AMOTL2;RAPGEF6;RAP2C;TJAP1;OCLN;PRKCZ;PPP2R2B;MYL12B;ARPC1A;CLDN3;ARPC2;MAP3K5

Cellular community - eukaryotes	hsa04550	Signaling pathways regulating pluripotency of stem cells	60/1882	4,36E+06	60	GNAS;PRKACB;PRKCA;HTR2A;SRC;TUBA1A;KRAS;NRAS;TJP1;ADCY6;GNAI3;TUBB6;MAP2K1;HRAS;ADCY9;CDK1;LPAR1;GNAI1;GNAQ;GRM1;GRM5;GUCY1A2;ITPR1;ITPR2;SOS2;TUBA1B;MAP3K2;TUBB2B;ADCY8;SOS1;PLCB1
Infectious disease: bacterial	hsa05132	Salmonella infection	90/1882	4,77E+06	90	HOXA1;BMI1;AKT2;SMAD2;ACVR2B;BMPR1A;DLX5;FGF2;GSK3B;IGF1R;LIFR;SMAD4;SMAD9;PAX6;PIK3CA;PCGF6;FZD2;MAPK14;KRAS;NRAS;BMPR2;DVL2;PCGF5;ID2;JARID2;PIK3R1;APC;JAK1;MAP2K1;FGFR1;HRAS;AKT1;BMPR1B;JAK2;AKT3;MAPK11;STAT3;ACVR1;ACVR2A;ZFXH3;DVL3;ID4;IL6ST;INHBB;SMAD3;SKIL;TBX3;TCF7;WNT7B;FZD5;FZD3;KAT6A;FZD4;FZD7;PCGF3;RIF1;ACVR1C;BMP4;COMMD3-BMI1;WNT3
Endocrine system	hsa04910	Insulin signaling pathway	58/1882	4,77E+06	58	E2F1;JUN;MAPK9;TBK1;MAPK8;SMURF2;SRC;KRAS;NRAS;SP1;MITF;RELA;RHOT1;HIF1A;TP53;HRAS;BCL2L1;ATF4;CSNK2A1;EIF2S1;RAB5A;RAB5B;VCP;ULK1;TAX1BP1;MFN2;USP15;HUWE1;CALCOCO2;CITED2;ATG9A;NLRX1;UBA52;SMURF1;RAB7A;NBR1;MON1B;SAMM50;FUNDNC1;CSNK2A3
Signal transduction	hsa04071	Sphingolipid signaling pathway	53/1882	4,90E+06	53	IRS1;MAPK9;AKT2;TBK1;IGF1R;PIK3CA;PRKACB;MAPK8;UVRAG;SH3GLB1;PTEN;KRAS;NRAS;HMGB1;IRS2;PIK3R1;HIF1A;MAP2K1;HRAS;AKT1;AKT3;BCL2L1;EIF2S1;MTOR;ITPR1;LAMP1;LAMP2;RAB8A;PPP2CB;PRKAA1;PRKAA2;RHEB;RPS6KB1;ULK1;VAMP8;TAX1BP1;MTMR3;SNAP29;RB1CC1;CALCOCO2;RRAGB;CAMKK2;RRAGA;VPS39;DAPK2;GORASP2;PIK3R4;ZFYVE1;ATG2B;BIRC6;RRAGD;RRAGC;VPS33A;ATG9A;RAB39B;SMCR8;UBA52;RAB7A;NBR1;WDFY3;ATG2A;WIPI1;EPG5;GORASP1;DAPK3;RUBCN
Endocrine system	hsa04935	Growth hormone synthesis, secretion and action	53/1882	4,90E+06	53	CAV1;SMAD2;IGF1R;KIF5B;PIP5K1A;SNX4;RNF41;ASAP1;SH3GLB1;RAB22A;SMURF2;PARD6B;CCR5;PLD2;SRC;DNM2;VPS45;IGF2R;HRAS;TGFBF1;RAB11FIP1;AP2B1;ARF6;CAPZA1;CAPZA2;CLTA;CLTC;DAB2;HSPA1L;KIF5C;SMAD3;MDM2;RAB8A;NEDD4;RAB5A;RAB5B;SH3GL1;SNX1;TFRC;STAM;GBF1;RABEP1;VPS4B;ARPC5;ACTR3;STAMBP;RAB10;RAB31;NEDD4L;SNX12;VPS36;VPS35;SNX6;VPS37B;MVB12A;VPS37A;ZFYVE27;PRKCZ;CHMP1A;ARFGAP3;EPS15;RAB35;ARPC1A;SMURF1;WASL;ARRB2;RAB7A;CBL;ARPC2;ARFGEF2;HSPA8;ACAP2;PSD3;VPS29;VTA1;ARFGAP1;VPS26B;WIPF2;WASHC3
Folding, sorting and degradation	hsa04120	Ubiquitin mediated proteolysis	59/1882	4,90E+06	59	CREB1;CALR;DUSP5;ALOX15;MAPK14;SLC16A1;THBS1;MERTK;DNMT3A;ADAM9;CASP3;SIRT1;HIF1A;PTGS2;ABCA1;MAP2K1;CEBPB;JAK2;ADAM17;MAPK11;ATP11A;ADAM10;ARG2;ARNT;ATP2A2;CAMK2G;CD47;CPT1A;CRK;MFG8;NFATC2;NFATC3;ODC1;PBX1;RAB5A;RAB5B;RAC1;MAPKAPK2;ATP8A1;ATP11B;VPS39;VPS8;GULP1;RAB14;TMEM30A;VPS33A;SIRPA;PTGER4;PPARD;DUSP4;BSG;RAB7A;SLC2A1;PLA2G15;XKR7
Folding, sorting and degradation	hsa04141	Protein processing in endoplasmic reticulum	67/1882	7,01E+06	67	VEGFA;JUN;MAPK9;MET;AKT2;FOS;DUSP5;FGF2;IGF1R;MYD88;PRKACB;PRKCA;MAPK8;RAP1A;RASA2;TNF;MAP3K13;MAPK14;ERBB2;KRAS;NRAS;EFNA3;TGFB2;RELA;CASP3;PAK1;RASA1;TP53;MAX;MAP2K1;ERBB4;FGFR1;HRAS;TGFBF1;AKT1;PPP3CA;AKT3;MAPK11;MAP3K3;EFNA5;ATF4;CACNA2D1;CACNB4;ATF2;CRK;DDIT3;DUSP1;EFNA1;EPHA2;ELK1;EREG;FLNA;GNA12;MKNK2;HSPA1L;IL1B;INSR;MEF2C;MAP3K1;MAP3K4;MAP3K9;NF1;NFATC3;NRTN;NTRK2;PAK2;PPP3R1;MAP2K3;PTPRR;MAP4K2;RAC1;RAC2;RPS6KA2;RPS6KA3;MAP2K4;SOS2;SRF;STK3;TGFA;MAPKAPK3;MAP4K3;RPS6KA4;RPS6KA5;MAPKAPK2;MAP3K2;TAB2;TAOK1;KITLG;PPM1B;MECOM;PPP3CB;MAP4K4;PPP3CC;DUSP4;ELK4;TGFB3;MAPKAPK5;FGF18;ARRB2;SOS1;MAP3K5;HSPA8;TAOK3;CACNA2D3;GNG12;DAXX
Endocrine system	hsa04926	Relaxin signaling pathway	55/1882	7,01E+06	55	ABL1;JUN;MAPK9;AKT2;SHC1;GSK3B;PIK3CA;PRKCA;MAPK8;SRC;ERBB2;KRAS;NRAS;CDKN1A;PIK3R1;PAK1;MAP2K1;ERBB4;HRAS;AKT1;AKT3;CAMK2G;CRK;HBEGF;EIF4EBP1;ELK1;EREG;MTOR;PAK2;PLCG2;RPS6KB1;MAP2K4;SOS2;TGFA;CBL;SOS1;SHC2
Infectious disease: viral	hsa05167	Kaposi sarcoma-associated herpesvirus infection	74/1882	7,10E+06	74	ABL1;VEGFA;MAPK9;MET;AKT2;SHC1;TBK1;FGF2;IGF1R;PIK3CA;PRKACB;PRKCA;MAPK8;RGL2;RAP1A;RASA2;RASAL2;EXOC2;PLD2;KRAS;NRAS;EFNA3;RELA;PIK3R1;PAK1;RASA1;MAP2K1;FGFR1;HRAS;AKT1;AKT3;BCL2L1;EFNA5;ARF6;CALM1;CALM2;EFNA1;EPHA2;ELK1;ETS2;GNB1;GNG5;INSR;NF1;NTRK2;PAK2;PLCG2;RAB5A;RAB5B;RAC1;RAC2;RALGDS;REL;SOS2;TGFA;SHOC2;RASSF1;PLCE1;RALGAPB;GNB4;PLA2G10;KITLG;FGF18;GNG11;SOS1;RALBP1;SHC2;GNG12;KSR2;GRIN2B;PLAAT3
Transport and catabolism	hsa04140	Autophagy - animal	66/1882	9,68E+05	66	VEGFA;MET;AKT2;CDH1;FGF2;GNAS;RAPGEF1;IGF1R;PIK3CA;PRKCA;RAP1A;ENAH;PARD6B;SRC;MAPK14;THBS1;KRAS;NRAS;EFNA3;ADCY6;GNAI3;CTNND1;PIK3R1;ADORA2B;MAP2K1;FGFR1;HRAS;AKT1;AKT3;MAPK11;EFNA5;ADCY9;CALM1;CALM2;CRK;LPAR1;EFNA1;EPHA2;GNAI1;GNAQ;INSR;PFN2;MAP2K3;RAC1;RAC2;RALGDS;RAP1GAP;DOCK4;RAPGEF4;PLCE1;RAPGEF6;TLN2;KITLG;PRKCZ;ADCY8;FGF18;PLCB1;GRIN2B
Cancer: specific types	hsa05212	Pancreatic cancer	38/1882	9,68E+06	38	IRS1;CREB1;AKT2;ROCK2;EDNRA;NPPC;PPP1CB;ADCY6;IRS2;GNAI3;PRKCE;ATP2B1;MAP2K1;AKT1;MEF2D;PPP3CA;AKT3;ATP1A2;ADCY9;ADRA2A;SLC25A6;ATF4;ATP1A1;ATP1B1;ATP2A2;CALM1;CALM2;ATF2;GNAI2;GNAI1;GNAQ;GUCY1A2;INSR;ITPR1;ITPR2;MEF2A;MEF2C;P

						PP1R12A;NFATC2;NFATC3;PPP1CC;PPP3R1;ROCK1;SRF;VDAC2;GNA13;CREB3L2;ADCY8;VDAC3;PPP3CB;PPP3CC;PLCB1;CREB3L1;CREB3L4
Aging	hsa04211	Longevity regulating pathway	42/1882	1,26E+07	42	VEGFA;AKT2;IGF1R;IL6;PIK3CA;PRKCA;EGLN1;LDHA;ERBB2;CDKN1A;RELA;PIK3R1;HIF1A;MAP2K1;AKT1;AKT3;STAT3;ARNT;CAMK2G;CREBBP;EDN1;EIF4EBP1;EP300;EPAS1;MTOR;GAPDH;MKNK2;HK2;INSR;SERPINE1;PDHA1;PFKP;PLCG2;RPS6;RPS6KB1;TFRC;SLC2A1;PGK2
Cellular community - eukaryotes	hsa04510	Focal adhesion	75/1882	1,41E+07	75	IRS1;MAPK9;AKT2;ATM;IGF1R;IL6;SMAD4;PIK3CA;MAPK8;PTEN;G6P C1;SOD2;MAPK14;BCL6;KRAS;NRAS;CCND1;CDKN1A;SGK3;IRS2;TGF B2;PIK3R1;SIRT1;BCL2L11;CCND2;MAP2K1;FOXO1;HRAS;TGFBF1;AK T1;AKT3;MAPK11;STAT3;CCNB1;CCNG2;CREBBP;EP300;FOXG1;GRM1 ;INSR;SMAD3;MDM2;PCK2;PRKAA1;PRKAA2;PRKAB2;PRKAG1;SKP2; SOS2;USP7;PLK4;PLK2;TGFB3;SOS1;C8orf44-SGK3
Signal transduction	hsa04068	FoxO signaling pathway	55/1882	1,44E+07	55	PIK3CA;PRKCA;PIP5K1A;PI4K2B;IPMK;PTEN;PIK3R1;INPP1;CALM1; CALM2;ITPR1;ITPR2;PIK3C2A;PIK3C2B;PIP4K2A;PLCG2;DGKZ;CDS2; MTMR3;SACM1L;PLCE1;IPPK;PIP4K2C;DGKH;OCRL;IP6K1;INPP4B;IT PK1;IP6K3;PIKFYVE;MTMR2;MTMR1;PLCB1;PIP5K2;PIP4K2B;PIP4P1; BPNT2
Cancer: specific types	hsa05225	Hepatocellular carcinoma	65/1882	2,73E+07	65	MAPK9;AKT2;ROCK2;PIK3CA;PRKCA;MAPK8;TNF;PLD2;PTEN;MAPK 14;KRAS;NRAS;GNAI3;RELA;SGPL1;PIK3R1;PRKCE;TP53;PPP2R2A;M AP2K1;HRAS;AKT1;AKT3;MAPK11;GNAI2;GNAI1;GNAQ;ABCC1;PPP2 CB;PPP2R1A;PPP2R3A;PPP2R5A;PPP2R5C;RAC1;RAC2;ROCK1;DEGS1; SPTLC1;GNAI3;PPP2R3B;CERS2;CERS4;SGPP1;SGMS2;SPTSSA;CERS6; SGMS1;PRKCZ;PPP2R2B;S1PR2;MAP3K5;PLCB1;SGPP2
Drug resistance: antineoplastic	hsa01522	Endocrine resistance	44/1882	3,04E+07	44	AKT2;SHC1;GNAS;PIK3CA;PRKCA;PIP5K1A;SYK;PLD2;CXCL8;KRAS; NRAS;ADCY6;DNM2;PIK3R1;MAP2K1;HRAS;AKT1;AKT3;ADCY9;ARF 6;LPAR1;MTOR;GNAI2;GRM1;GRM5;INSR;PLCG2;RALGDS;RHEB;SOS 2;DGKZ;GNAI3;RAPGEF4;AGPAT5;DGKH;KITLG;ADCY8;SOS1;SHC2;P LCB1;PLPP2;PLPP3
Cellular community - eukaryotes	hsa04520	Adherens junction	42/1882	3,45E+07	42	IRS1;AKT2;GSK3B;IGF1R;PIK3CA;PRKCA;TNF;FZD2;PTEN;KRAS;NRA S;DVL2;PIK3R1;MAP2K1;HRAS;AKT1;AKT3;ATP6V1A;ATP6V1C1;DVL 3;EIF4B;EIF4EBP1;MTOR;GRB10;INSR;LRP6;PRKAA1;PRKAA2;RHEB; RPS6;RPS6KA2;RPS6KA3;RPS6KB1;SKP2;SLC3A2;SOS2;WNT7B;FZD5; FZD3;SLC7A5;FZD4;FZD7;ULK1;ATP6V1F;RRAGB;RRAGA;CAB39;RRA GD;RRAGC;CAB39L;SEH1L;FNIP1;RICTOR;SOS1;FNIP2;WNT3
Infectious disease: viral	hsa05165	Human papillomavirus infection	108/1882	3,50E+07	108	CDK6;VEGFA;IRS1;MET;CREB1;AKT2;FGF2;GSK3B;IGF1R;IL6;IL7;PIK 3CA;PRKCA;SYK;THBS2;PTEN;G6PC1;ERBB2;THBS1;KRAS;NRAS;LA MC1;CCND1;CDKN1A;GYS1;SGK3;COL4A1;EFNA3;CDK4;RELA;PIK3R 1;BCL2L11;BRCA1;CCND2;TP53;ITGB4;PPP2R2A;JAK1;MAP2K1;YWH AZ;ERBB4;FGFR1;HRAS;AKT1;JAK2;ITGA5;AKT3;OSMR;BCL2L1;EFN A5;ATF4;COL4A4;COL4A5;COL6A1;ATF2;LPAR1;EFNA1;EPHA2;EIF4B; EIF4EBP1;EREG;FN1;MTOR;GNB1;GNG5;HSP90AA1;TNC;INSR;ITGA6; ITGA1;ITGA3;ITGB8;LAMA3;LAMB1;MDM2;NRTN;NTRK2;PCK2;PPP2 CB;PPP2R1A;PPP2R3A;PPP2R5A;PPP2R5C;PRKAA1;PRKAA2;PKN1;RA C1;RHEB;RPS6;RPS6KB1;SOS2;TGFA;YWHAG;YWHAH;ITGA10;YWHA Q;PPP2R3B;GNB4;CREB3L2;KITLG;PPP2R2B;TNR;FGF18;GNG11;COL6 A3;SOS1;GNG12;CREB3L1;CREB3L4;LAMB2;MCL1;C8orf44-SGK3
Infectious disease: viral	hsa05170	Human immunodeficiency virus 1 infection	76/1882	5,13E+07	76	IRS1;CREB1;AKT2;IGF1R;PIK3CA;G6PC1;CCND1;GYS1;IRS2;PIK3R1;SI RT1;PPP2R2A;FOXO1;CCNA2;AKT1;AKT3;ELAVL1;CFTR;CPT1A;EEF2; EIF4EBP1;MTOR;HNF4A;INSR;RAB8A;PCK2;PFKFB4;PFKP;PPP2CB;PP P2R1A;PPP2R3A;PPP2R5A;PPP2R5C;PRKAA1;PRKAA2;PRKAB2;PRKA G1;RAB2A;RHEB;RPS6KB1;SCD;ULK1;CAMKK2;RAB10;PPP2R3B;RAB 14;CAB39;CREB3L2;SCD5;CAB39L;PPP2R2B;FASN;ADIPOR1;CREB3L1; CREB3L4;ACACA
Cancer: specific types	hsa05219	Bladder cancer	24/1882	6,50E+07	24	JUN;MAPK9;ROCK2;GSK3B;SMAD4;PRKACB;PRKCA;MAPK8;WIF1;PR ICKLE2;FZD2;CXXC4;FBXW11;CCND1;DVL2;SIRT1;CCND2;APC;TP53; BTRC;PPP3CA;CAMK2G;CREBBP;CSNK1A1;CSNK2A1;CTBP2;DVL3;E P300;GPC4;PRICKLE3;LRP6;SMAD3;NFATC2;NFATC3;ROR1;PPP3R1;PS EN1;RAC1;RAC2;TCF7;WNT7B;FZD5;FZD3;FZD4;FZD7;CUL1;DAAM1; FRAT2;LEF1;LGR4;TBL1XR1;VANGL1;ZNF3;PPP3CB;TCF7L2;PPARD; PPP3CC;SKP1;PLCB1;CSNK2A3;WNT3
Nervous system	hsa04728	Dopaminergic synapse	53/1882	6,83E+07	53	GAS1;GSK3B;PRKACB;CUL3;SMURF2;FBXW11;CCND1;SUFU;GLI1;CC ND2;BTRC;CSNK1A1;CSNK1G3;EVC;CUL1;CDON;SPOPL;GLI3;SMURF 1;ARRB2;MOSMO
Signal transduction	hsa04390	Hippo signaling pathway	60/1882	7,69E+07	60	SMAD2;ACVR2B;BMPR1A;SMAD4;SMAD9;TNF;SMURF2;GREM1;THB S1;BMPR2;SP1;TGFB2;ID2;TGFBF1;BMPR1B;ACVR1;ACVR2A;CREBBP ;E2F4;EP300;ID4;INHBB;LTBP1;SMAD3;NEO1;PPP2CB;PPP2R1A;ROCK 1;RPS6KB1;SKIL;TFRC;TGIF1;CUL1;LEMD3;ACVR1C;NCOR1;SMURF1; BMP4;DCN;TGFB3;FST;SKP1
Cancer: specific types	hsa05215	Prostate cancer	45/1882	9,09E+07	45	VEGFA;AKT2;PIK3CA;PRKCA;SRC;MAPK14;KRAS;NRAS;PIK3R1;PTG S2;MAP2K1;HRAS;AKT1;PPP3CA;AKT3;MAPK11;NFATC2;PLCG2;PPP3 R1;PXN;RAC1;RAC2;MAPKAPK3;MAPKAPK2;PPP3CB;PPP3CC;SHC2
Cancer: specific types	hsa05220	Chronic myeloid leukemia	36/1882	9,11E+07	36	AKT2;CDH1;SMAD2;SMAD4;PRKACB;KRAS;NRAS;CCND1;ADCY6;GN AI3;PRKCE;MAP2K1;HRAS;TGFBF1;AKT1;MEF2D;AKT3;ADCY9;CAL M1;CALM2;EGR1;MTOR;GNAI1;GNAQ;GNB1;GNG5;ITPR1;ITPR2;SMA D3;MEF2A;MEF2C;SERPINE1;PRKAA1;PRKAA2;PRKAB2;PRKAG1;RPS 6;RPS6KB1;RYY2;GNAI3;PIK3R4;GNB4;ADCY8;GNG11;PLCB1;GNG12

Endocrine system	hsa04922	Glucagon signaling pathway	45/1882	1,20E+08	45	SNAI2;CDH1;SMAD2;BIRC5;BMPIR1A;GSK3B;SMAD4;PPP1CB;PARD6B;FZD2;FBXW11;LATS2;CCND1;BMPR2;TGFB2;TEAD1;DVL2;ID2;CCND2;APC;PPP2R2A;YAP1;YWHAZ;TGFBRI1;BTRC;BMPIR1B;BIRC3;BIRC2;BIRC3;DLG1;DLG2;DLG3;DVL3;SMAD3;SERPINE1;PPP1CC;PPP2CB;PPP2R1A;STK3;TCF7;WNT7B;YWHAG;YWHAH;FZD5;FZD3;FZD4;FZD7;TEAD2;LIMD1;DLG5;YWHAQ;RASSF1;WWTR1;LEF1;PRKCZ;PPP2R2B;TCF7L2;BMP4;TGFB3;WNT3
Signal transduction	hsa04151	PI3K-Akt signaling pathway	112/1882	2,50E+08	112	SOCS3;JUN;MAPK9;CREB1;AKT2;FOS;IL6;PIK3CA;MAPK8;TNF;MAPK14;RELA;PIK3R1;CASP3;PTGS2;MAP2K1;CEBPB;AKT1;ADAM17;AKT3;MAPK11;BIRC2;BIRC3;XIAP;ATF4;CASP8;ATF2;EDN1;CXCL2;IL1B;JUNB;MMP14;NFKBIA;MAP2K3;CXCL5;MAP2K4;RPS6KA4;RPS6KA5;TAB2;CREB3L2;TAB3;DNM1L;MAP3K5;CREB3L1;CREB3L4
Neurodegenerative disease	hsa05010	Alzheimer disease	119/1882	2,72E+08	119	THBS2;THBS1;LAMC1;CD44;COL4A1;ITGB4;ITGA5;CD47;COL4A4;COL4A5;COL6A1;DAG1;FN1;HMMR;HSPG2;TNC;ITGA6;ITGA1;ITGA3;ITGB8;LAMA3;LAMB1;SDC1;ITGA10;FRAS1;FREM2;TNFR;COL6A3;SV2A;LAMB2
Infectious disease: bacterial	hsa05131	Shigellosis	84/1882	3,02E+08	84	BCL7A;ARID1A;ARID2;ACTL6A;CHD4;BPTF;SMARCA1;SMARCC1;SMARCD1;YY1;CDK2AP1;BAZ1B;MORF4L2;CDK2AP2;ZNHIT1;BRD8;MORF4L1;BAZ2B;RSF1;MBD3;CHRA1;GATAD2A;INO80D;PBRM1;GATAD2B;EP400;MEAF6;ACTR5;PHF6;RBBP4;SRCAP;BAZ2A;EPC2;ARID1B;INO80;MTA3;BICRAL;MACROH2A2;H2AC6
Endocrine system	hsa04919	Thyroid hormone signaling pathway	48/1882	4,67E+08	48	BMI1;FOXK2;PCGF6;LCOR;FOXK1;PHF19;PCGF5;ASXL2;CBX7;JARID2;EZH2;AURKB;MAX;CREBBP;EP300;SCML1;UBE2D2;UBE2D3;YY1;USP7;CBX4;PCGF3;SCML2;MTF2;KDM2A;MGA;RYBP;CBX6;SUZ12;BCOR;TEX10;MBD5;PHC3;L3MBTL3;RBBP4;FBRSL1;COMMD3-BMI1;HCFC1;SKP1;ASXL1;OGT
Signal transduction	hsa04012	ErbB signaling pathway	37/1882	7,00E+08	37	BTG1;HSPD1;BTG2;DDX6;HSPA9;CNOT4;PFKP;EXOSC10;PABPC4;TOB2;XRN2;EDC4;PABPC1;EDC3;PNPT1;DCP2;PATL1;PAN2;CNOT2;CNOT3;CNOT1;EXOSC5;EXOSC6;CNOT6L;DCP1A;TENT4B
Drug resistance: antineoplastic	hsa01521	EGFR tyrosine kinase inhibitor resistance	35/1882	8,34E+08	35	SOCS3;FBXW7;CUL3;SMURF2;FBXW11;UBE2I;BRCA1;BTRC;RHOBTB1;BIRC2;BIRC3;XIAP;CDC20;DDB1;MDM2;MAP3K1;MID1;NEDD4;SKP2;UBE2B;UBE2D2;UBE2D3;UBE2E1;UBE2G1;UBE2H;UBE3A;CUL5;CUL4B;CUL4A;CUL1;PIAS1;CDC23;HERC3;TRIP12;RNF7;UBE3C;UBA2;HUWE1;UBE4B;NEDD4L;ANAPC15;UBE2S;UBR5;UBE2J1;UBA6;BIRC6;UBE3B;KLHL13;UBE2Q2;RCHY1;UBA52;SMURF1;UBE2A;CBL;SKP1;PRPF19;PIAS4;KLHL9;COP1
Neurodegenerative disease	hsa05022	Pathways of neurodegeneration - multiple diseases	139/1882	8,92E+08	139	MAPK9;CALR;MAPK8;SEC63;UBXN2A;DNAJC1;MAN1A1;DAD1;SEC24D;ATF4;DDIT3;EIF2S1;PDIA3;DNAJA1;HSPA1L;HSPA5;HSP90AA1;DNAJB1;NFE2L2;RAD23B;RPN2;SSR1;SSR3;SEC62;UBE2D2;UBE2D3;UBE2G1;VCP;WFS1;MOGS;CUL1;PDIA4;SEC24C;EDEM1;UBE4B;SEC24B;SEC23A;HYOU1;MAN1A2;SEC61B;TRAM1;UBQLN2;UBQLN1;UBE2J1;DNAJC10;SEC61A2;YOD1;NPLOC4;SAR1A;DERL1;RNF5;PRKCSH;DERL3;CANX;BAG1;SSR2;RAD23A;MAP3K5;HSPA8;SKP1;MBTPS2;TRAM1L1;BCAP31;STT3B;ERO1A;MARCHF6;EDEM2
Endocrine system	hsa04917	Prolactin signaling pathway	32/1882	1,04E+09	32	RAN;IPO7;NUP50;SUMO1;PNN;UBE2I;EEF1A2;TNPO1;CSE1L;EEF1A1;KPNA1;KPNA3;KPNA4;NUP98;XPO1;NUP214;NUP155;NUP153;SRRM1;IPO8;NUP210;NUP160;KPNA6;NUP62;AHCTF1;UPF2;TNPO2;IPO11;TMEM33;THOC2;XPO4;THOC7;SEH1L;SUMO2;IPO5;RANBP2;RNPS1;NUP133;NUP37;THOC3;NUP85;NUP58
Development and regeneration	hsa04360	Axon guidance	64/1882	1,10E+09	64	PPP1CB;MSI2;WDR82;PNN;PPP2R2A;CSTF3;GSPT1;PPP1CC;PPP2CB;PPP2R1A;PPP2R3A;PPP2R5A;PPP2R5C;SYMPK;RNMT;PABPC4;SMG7;SRRM1;HBS1L;PAPOLA;CPSF6;SMG1;CSTF2T;TARDBP;UPF2;PABPC1;PPP2R3B;CPSF1;WDR33;FIP1L1;PPP2R2B;ETF1;RNPS1;PCF11;CPSF2
Immune system	hsa04625	C-type lectin receptor signaling pathway	42/1882	1,23E+09	42	ZEB1;BMI1;MET;ATM;RUNX2;IGF1R;IL6;SIX1;BCL11B;CXCL8;BCL6;DX5;CDKN1A;SP1;HMG2A;RUNX1;MITF;RELA;ID2;RUNX1T1;CCND2;TP53;MAX;FOXO1;CCNA2;CEBPB;BMP2K;ETV6;BCL2L1;BIRC2;BIRC3;CCNT1;CCNT2;DDIT3;FUT8;MDM2;MEF2C;KMT2A;MLLT3;PBX1;PBX3;CDK14;REL;NR4A3;TAF15;SUPT3H;KLF3;ZBTB16;NCOR1;COMMD3-BMI1;CD40;ELK4;TSPAN7;NSD2;H3-5;TMPSR2
Cancer: specific types	hsa05224	Breast cancer	54/1882	1,33E+09	54	CDK6;JUN;CREB1;PIK3CA;PRKACB;RASA2;CCR5;SYK;SRC;KRAS;NRAS;CCND1;CDKN1A;GTF2B;CDK4;RELA;GTF2H1;PIK3R1;CASP3;CCND2;TP53;JAK1;YWHAZ;CCNA2;HRAS;STAT3;ATF4;C3;CASP8;CDK1;CD20;CHD4;ATF2;CREBBP;DDB1;DDX3X;DLG1;EGR3;EP300;GTF2A1;IL6ST;MDM2;NFKBIA;PMAIP1;PXN;RAC1;REL;SKP2;SRF;UBE3A;YWHAG;YWHAH;USP7;MAPKAPK2;IRF9;YWHAQ;UBR4;SND1;MRPS18B;CREB3L2;MAD1L1;HDAC7;VDAC3;POLB;HDAC3;CREB3L1;CREB3L4;H2BC8
Signal transduction	hsa04310	Wnt signaling pathway	61/1882	1,35E+09	61	VEGFA;CAV1;MET;AKT2;ROCK2;SMAD2;FGF2;IGF1R;PIK3CA;PPP1CB;PRKACB;PRKCA;TNF;FZD2;SRC;MAPK14;ERBB2;THBS1;KRAS;NRAS;TIMP3;DDX5;PDCD4;CCND1;ESR1;CDKN1A;CD44;HOXD10;TGFB2;TFAP4;PIK3R1;CASP3;PAK1;HIF1A;TP53;MAP2K1;ERBB4;FGFR1;HRAS;AKT1;ITGA5;AKT3;MAPK11;STAT3;CAMK2G;HBEGF;EIF4B;ELK1;FLNA;FN1;MTOR;HSPG2;ITPR1;ITPR2;MDM2;MSN;PPP1R12A;PLCG2;PPP1C;PXN;RAC1;ROCK1;RPS6;RPS6KB1;SDC1;SOS2;WNT7B;FZD5;FZD3;FZD4;FZD7;FRS2;ARHGEF12;DROSHA;PLCE1;ANK1;PPP1R12B;DCN;SDC2;CBL;SOS1;WNT3

Nervous system	hsa04722	Neurotrophin signaling pathway	46/1882	1,54E+09	46	TP63;ABL1;E2F3;E2F1;CDK6;ZEB1;ZEB2;VEGFA;IRS1;BCL2L2;BMI1;MET;SHC1;ATM;PIK3CA;PRKCA;PTEN;TRIM71;ERBB2;TPM1;THBS1;KRAS;NRAS;TIMP3;PDCD4;CCND1;CDKN1A;SLC7A1;SOX4;CD44;BMPR2;IGF2BP1;DNMT3A;HOXD10;HMG2A;EFNA3;IRS2;TGFB2;UBE2I;PIK3R1;NOTCH2;CASP3;SIRT1;BCL2L11;EZH2;DICER1;BRCA1;VIM;PTGS2;PI3M1;CCND2;PRKCE;MMP16;APC;TP53;MAP2K1;FSCN1;DNMT1;HRAS;E2F2;ITGA5;FOXO1;STAT3;EFNA5;CDC25C;CREBBP;CRK;EFNA1;EP300;MTOR;GLS;TNC;MDM2;MDM4;ABCC1;PLCG2;ROCK1;SOS2;FZD3;RPS6KA5;RASSF1;COMMD3-BMI1;TNR;SOS1;WNT3;MCL1
Infectious disease: bacterial	hsa05135	Yersinia infection	51/1882	1,55E+09	51	E2F1;VEGFA;JUN;CREB1;AKT2;FOS;BIRC5;FGF2;GNAS;PIK3CA;PRKACB;PRKCA;GSTO2;SRC;BCL6;KRAS;NRAS;CCND1;ESR1;ADCY6;GNAI3;AHR;RELA;PIK3R1;NOTCH2;MAP2K1;HRAS;AKT1;JAK2;AKT3;STAT3;ADCY9;XIAP;AR;ARNT;ATF4;CDC6;ATF2;EIF4EBP1;MTOR;GNAI1;HSP90AA1;KPNA1;KPNA3;KPNA4;RPS6KA2;RPS6KA3;RPS6KB1;SOS2;KPNA6;CREB3L2;PAQR8;UGT1A6;ADCY8;FGF18;ARRB2;SOS1;PTGES3;UGT1A8;CREB3L1;CREB3L4;EPHX4
Cancer: specific types	hsa05211	Renal cell carcinoma	31/1882	2,07E+09	31	ABL1;VEGFA;JUN;MAPK9;MET;AKT2;FOS;PIK3CA;MAPK8;GSTO2;PLD2;PTEN;SOD2;SRC;MAPK14;KRAS;NRAS;AHR;RELA;PIK3R1;HIF1A;MAP2K1;HRAS;ACPI;AKT1;AKT3;MAPK11;SLC25A6;ARNT;AKR1C2;SLC26A2;NDUFA9;NDUFB2;NDUFB4;NDUFS4;NFE2L3;NFKBIA;PTPN1;TPRJ;RAC1;MAP2K4;SOS2;UQCRC2;VDAC2;AKR1C3;UQCRCQ;NQO1;UQCRC10;VDAC3;CBR1;UQCRC1;SOS1;MAP3K5;EPHX4;NDUFV2;COX6A1;ATP5F1A;ATP5MC2;ATP5MC3
Nervous system	hsa04720	Long-term potentiation	30/1882	2,18E+09	30	MET;AKT2;PIK3CA;PTEN;LDHA;G6PD;ERBB2;KRAS;NRAS;PIK3R1;HIF1A;TP53;MAP2K1;FGFR1;HRAS;AKT1;AKT3;MTOR;GLS;HK2;IDH1;PDHA1;PFKP;SLC1A5;SLC7A5;PGAM4;SLC2A1
Signal transduction	hsa04150	mTOR signaling pathway	56/1882	2,18E+09	56	SLC44A1;JUN;MAPK9;AKT2;FOS;PIK3CA;PRKCA;MAPK8;PIP5K1A;PLD2;GPCPD1;KRAS;NRAS;SP1;PIK3R1;HIF1A;MAP2K1;HRAS;AKT1;AKT3;EIF4EBP1;MTOR;PCYT1A;RAC1;RAC2;RALGDS;RHEB;RPS6KB1;SOS2;DGK2;WASF2;CHPT1;SLC44A2;DGKH;SOS1;PLPP2;PLPP3
Endocrine system	hsa04928	Parathyroid hormone synthesis, secretion and action	44/1882	2,45E+09	44	JUN;AKT2;FOS;STAT1;MYD88;PIK3CA;PTEN;MAPK14;KRAS;NRAS;RELA;PIK3R1;HIF1A;JAK1;MAP2K1;HRAS;AKT1;PPP3CA;JAK2;AKT3;MAPK11;MAP3K3;STAT3;CSNK2A1;MTOR;NFATC2;NFATC3;NFKBIA;PPP3R1;MAP2K3;RPS6KB1;PPP3CB;PPP3CC;CSNK2A3
Translation	hsa03013	Nucleocytoplasmic transport	42/1882	2,45E+09	42	JUN;MAPK9;AKT2;FOS;SMAD2;BIRC5;GSK3B;SMAD4;PIK3CA;MAPK8;KRAS;NRAS;CCND1;CDKN1A;TGFB2;MSH2;PIK3R1;CASP3;BCL2L11;APC;TP53;MAP2K1;HRAS;TGFB1;AKT1;AKT3;BBC3;ERBB2;MTOR;SMAD3;MLH1;PMAIP1;RAC1;RAC2;RALGDS;RPS6KB1;SOS2;TCF7;TGFA;APPL1;LEF1;TCF7L2;TGFB3;SOS1
Signal transduction	hsa04668	TNF signaling pathway	45/1882	2,67E+09	45	VEGFA;JUN;MET;AKT2;RAGEF1;PIK3CA;RAP1A;EGLN1;KRAS;NRAS;CDKN1A;TGFB2;PIK3R1;PAK1;HIF1A;MAP2K1;HRAS;AKT1;AKT3;ARNT;CREBBP;CRK;EP300;EPAS1;PAK2;RAC1;SOS2;TGFA;TGFB3;SOS1;SLC2A1
Cancer: overview	hsa05203	Viral carcinogenesis	68/1882	2,80E+09	68	E2F3;E2F1;CDK6;VEGFA;MAPK9;AKT2;SMAD2;STAT1;SMAD4;PIK3CA;MAPK8;PLD2;ERBB2;KRAS;CCND1;CDKN1A;TGFB2;CDK4;RELA;PIK3R1;TP53;JAK1;MAP2K1;TGFB1;AKT1;E2F2;AKT3;BCL2L1;STAT3;MTOR;SMAD3;RAC1;RAC2;RALGDS;RPS6KB1;TGFA;TGFB3;RALBP1
Aging	hsa04213	Longevity regulating pathway - multiple species	28/1882	3,42E+09	28	AKT2;CDH1;GSK3B;PIK3CA;PTEN;ERBB2;KRAS;NRAS;CCND1;CDKN1A;PIK3R1;APC;TP53;MAP2K1;HRAS;AKT1;AKT3;ELK1;MLH1;SOS2;TCF7;LEF1;TCF7L2;SOS1
Transport and catabolism	hsa04148	Efferocytosis	55/1882	3,57E+09	55	E2F3;E2F1;CDK6;AKT2;SHC1;IGF1R;PIK3CA;PRKCA;PTEN;KRAS;NRAS;CCND1;CDKN1A;CDK4;PIK3R1;TP53;MAP2K1;HRAS;AKT1;E2F2;AKT3;CALM1;CALM2;CAMK2G;MTOR;MDM2;PLCG2;SOS2;TGFA;SOS1;SHC2
Signal transduction	hsa04350	TGF-beta signaling pathway	42/1882	3,88E+09	42	E2F3;E2F1;ZEB1;CREB1;AKT2;GSK3B;IGF1R;PIK3CA;PTEN;ERBB2;KRAS;NRAS;CCND1;CDKN1A;RELA;PIK3R1;TP53;MAP2K1;FOXO1;FGFR1;HRAS;AKT1;E2F2;AKT3;KLK3;AR;ATF4;CREBBP;EP300;MTOR;GRM1;GRM5;HSP90AA1;MDM2;NFKBIA;SOS2;TCF7;TGFA;LEF1;CREB3L2;TCF7L2;SOS1;CREB3L1;CREB3L4;TMPRSS2
Endocrine system	hsa04912	GnRH signaling pathway	37/1882	4,44E+09	37	GSK3B;FZD2;CDKN1A;SUFU;DVL2;GLI1;APC;TP53;DVL3;TCF7;WNT7B;FZD5;FZD3;FZD4;FZD7;LEF1;GLI3;TCF7L2;BMP4;WNT3
Signal transduction	hsa04370	VEGF signaling pathway	27/1882	5,01E+09	27	E2F3;E2F1;CDK6;MET;AKT2;CDH1;FGF2;IGF1R;PIK3CA;PTEN;KRAS;NRAS;CCND1;CDKN1A;MITF;CDK4;PIK3R1;TP53;MAP2K1;FGFR1;HRAS;AKT1;E2F2;AKT3;MDM2;FGF18
Transport and catabolism	hsa04144	Endocytosis	79/1882	5,01E+09	79	E2F3;E2F1;VEGFA;CDH1;MMP1;CXCL8;SRC;ERBB2;THBS1;KRAS;NRAS;CCND1;CDKN1A;CDK4;TP53;MAP2K1;HRAS;E2F2;HBEGF;MDM2;RPS6KA5;RASSF1;DAPK2;DAPK3
Endocrine system	hsa04916	Melanogenesis	39/1882	5,64E+09	39	ABL1;E2F3;E2F1;CDK6;AKT2;SHC1;SMAD4;PIK3CA;KRAS;NRAS;CCND1;CDKN1A;RUNX1;TGFB2;CDK4;RELA;PIK3R1;TP53;MAP2K1;HRAS;TGFB1;AKT1;E2F2;AKT3;BCL2L1;CRK;CTBP2;SMAD3;MDM2;NFKBIA;SOS2;MECOM;TGFB3;CBL;SOS1;SHC2

Transport and catabolism	hsa04137	Mitophagy - animal	40/1882	6,29E+09	40	AKT2;PIK3CA;KRAS;NRAS;CCND1;RUNX1;RELA;PIK3R1;PIM1;RUNX1T1;MAP2K1;CCNA2;HRAS;AKT1;AKT3;STAT3;EIF4EBP1;MTOR;RPS6KB1;SOS2;TCF7;LEF1;ZBTB16;TCF7L2;PPARD;SOS1
Cancer: overview	hsa05231	Choline metabolism in cancer	38/1882	8,22E+09	38	E2F3;E2F1;CDK6;AKT2;PIK3CA;PTEN;LAMC1;CCND1;CDKN1A;COL4A1;CDK4;RELA;PIK3R1;CASP3;PTGS2;TP53;MAX;AKT1;E2F2;AKT3;BCL2L1;BIRC2;BIRC3;XIAP;COL4A4;COL4A5;FN1;ITGA6;ITGA3;LAMA3;LAMB1;NFKBIA;SKP2;CKS1B;LAMB2
Cell growth and death	hsa04114	Oocyte meiosis	49/1882	8,22E+09	49	E2F3;E2F1;CDK6;MET;AKT2;KIF5B;PIK3CA;PRKCA;ERBB2;KRAS;NRAS;CCND1;CDKN1A;CDK4;PIK3R1;TP53;MAP2K1;HRAS;AKT1;E2F2;AKT3;STAT3;KIF5C;PLCG2;SOS2;TGFA;RASSF1;SOS1
Cardiovascular disease	hsa05417	Lipid and atherosclerosis	69/1882	8,48E+08	69	E2F3;E2F1;CDK6;JUN;AKT2;SHC1;FOS;FGF2;GSK3B;IGF1R;PIK3CA;FZD2;PTEN;NCOA3;ERBB2;KRAS;NRAS;CCND1;ESR1;CDKN1A;SP1;DVL2;CDK4;PIK3R1;NOTCH2;BRCA1;APC;TP53;MAP2K1;FGFR1;HRAS;AKT1;E2F2;AKT3;CSNK1A1;DVL3;MTOR;LRP6;RPS6KB1;SOS2;TCF7;WNT7B;FZD5;FZD3;FZD4;FZD7;FRAT2;LEF1;TCF7L2;NCOA1;FGF18;SOS1;SHC2;WNT3
Cell growth and death	hsa04115	p53 signaling pathway	31/1882	8,57E+09	31	E2F3;E2F1;CDK6;MET;AKT2;SHC1;SMAD2;GSK3B;IGF1R;SMAD4;PIK3CA;PRKCA;ARID1A;ARID2;GSTO2;FZD2;PTEN;KRAS;NRAS;CCND1;CDKN1A;TGFB2;DVL2;CDK4;PIK3R1;APC;TP53;MAP2K1;HRAS;TGFB1;AKT1;E2F2;AKT3;BCL2L1;ACTL6A;CSNK1A1;DVL3;ELK1;MTOR;LRP6;SMAD3;NFE2L2;PLCG2;RPS6KB1;SMARCC1;SMARCD1;SOS2;TCF7;TGFA;TXNRD1;WNT7B;FZD5;FZD3;FZD4;FZD7;FRAT2;LEF1;PBRM1;NQO1;TCF7L2;TGFB3;SOS1;SHC2;ARID1B;WNT3
Cancer: specific types	hsa05214	Glioma	31/1882	0.0001157 89577646 665	31	E2F3;E2F1;MET;AKT2;SHC1;CDH1;SMAD2;FGF2;GSK3B;SMAD4;PIK3CA;FZD2;ERBB2;KRAS;NRAS;CCND1;CDKN1A;TGFB2;DVL2;PIK3R1;APC;TP53;MAP2K1;HRAS;TGFB1;AKT1;E2F2;AKT3;CSNK1A1;DVL3;MTOR;LRP6;SMAD3;MLH1;RPS6KB1;SOS2;TCF7;WNT7B;FZD5;FZD3;FZD4;FZD7;FRAT2;LEF1;TCF7L2;TGFB3;FGF18;SOS1;SHC2;WNT3
Cardiovascular disease	hsa05418	Fluid shear stress and atherosclerosis	49/1882	0.0001482 64014718 28	49	IRS1;MAPK9;AKT2;SMAD2;GSK3B;PIK3CA;PPP1CB;PRKCA;MAPK8;PTEN;G6PD;MAPK14;GYS1;SP1;TGFB2;RELA;PIK3R1;TGFB1;AKT1;AKT3;MAPK11;SLC25A6;ATP2A2;CAMK2G;MTOR;GAPDH;GFPT1;INSR;SMAD3;NDUFA9;NDUFB2;NDUFB4;NDUFS4;PDHA1;PPP1CC;RAC1;RAC2;RYR2;UQCRC2;VDAC2;TBC1D4;UQCRCQ;UQCRI0;PRKCZ;VDAC3;PDK3;TGFB3;UQCRC1;SLC2A1;PLCB1;NDUFV2;COX6A1;ATP5F1A;ATP5MC2;ATP5MC3
Signal transduction	hsa04070	Phosphatidylinositol signaling system	37/1882	0.0001504 27318817 738	37	JUN;MAPK9;AKT2;FOS;ROCK2;TBK1;MMP1;GSK3B;IL6;MYD88;PIK3CA;PRKCA;MAPK8;RAP1A;TNF;CXCL8;SOD2;SRC;MAPK14;HSPD1;KRAS;NRAS;RELA;PIK3R1;CASP3;ABCA1;TP53;HRAS;AKT1;PPP3CA;JAK2;AKT3;MAPK11;BCL2L1;STAT3;ATF4;CALM1;CALM2;CAMK2G;CASP8;DDIT3;EIF2S1;CXCL2;HSPA1L;HSPA4;HSPA5;HSP90AA1;IL1B;ITPR1;NFATC2;NFATC3;NFE2L2;NFKBIA;OLR1;POU2F1;PPP3R1;MAP2K3;RAC1;MAP2K4;VLDLR;TAB2;MIB1;PPP3CB;PPP3CC;CD40;MAP3K5;HSPA8;PLCB1;ERO1A
Endocrine system	hsa04915	Estrogen signaling pathway	48/1882	0.0001694 87521762 126	48	VEGFA;CAV1;JUN;MAPK9;AKT2;FOS;ACVR2B;BMP1A;NPPC;PIK3CA;MAPK8;TNF;SUMO1;GSTO2;SRC;MAPK14;BMP2;RELA;PIK3R1;ASS1;TP53;AKT1;BMP1B;AKT3;MAPK11;ACVR1;ACVR2A;CALM1;CALM2;DUSP1;EDN1;HSP90AA1;IL1B;MEF2A;MEF2C;NFE2L2;PRKAA1;PRKAA2;RAC1;RAC2;SDC1;MAP2K4;NQO1;SUMO2;PRKCZ;BMP4;SDC2;MAP3K5;PIAS4
Neurodegenerative disease	hsa05017	Spinocerebellar ataxia	49/1882	0.0002151 77162233 809	49	VEGFA;MET;AKT2;SHC1;FGF2;GSK3B;IGF1R;IL6;PIK3CA;PRKCA;PTEN;SRC;ERBB2;KRAS;NRAS;PIK3R1;BCL2L1;JAK1;MAP2K1;HRAS;AKT1;JAK2;AKT3;BCL2L1;STAT3;EIF4EBP1;MTOR;NF1;PLCG2;RPS6;RPS6KB1;SOS2;TGFA;SOS1;SHC2
Neurodegenerative disease	hsa05014	Amyotrophic lateral sclerosis	105/1882	0.0002304 25310484 642	105	E2F3;E2F1;JUN;MAPK9;AKT2;SHC1;FOS;GNAS;IGF1R;PIK3CA;PRKACB;MAPK8;SRC;MAPK14;NCOA3;ERBB2;KRAS;NRAS;CCND1;ESR1;CDKN1A;SP1;ADCY6;CDK4;PIK3R1;NOTCH2;TP53;MAP2K1;MED1;HRAS;AKT1;E2F2;AKT3;MAPK11;ADCY9;HBEGF;MTOR;MDM2;RPS6KB1;SOS2;ADCY8;NCOR1;SOS1;SHC2
Cancer: specific types	hsa05222	Small cell lung cancer	35/1882	0.0002498 59408107 688	35	AKT2;ATM;BIRC5;PIK3CA;TOP2A;GSTO2;ERBB2;CDKN1A;MSH2;PIK3R1;CASP3;BRCA1;TP53;AKT1;AKT3;BCL2L1;BBC3;BIRC2;BIRC3;XIAP;CASP8;SLC31A1;MDM2;MLH1;PMAIP1;REV3L;TOP2B;ERCC1;MAP3K5
Cancer: overview	hsa05235	PD-L1 expression and PD-1 checkpoint pathway in cancer	34/1882	0.0002867 09856901 883	34	SOCS3;IRS1;MAPK9;CREB1;AKT2;GSK3B;IL6;PIK3CA;PPP1CB;MAPK8;TNF;PTEN;G6PC1;GYS1;IRS2;RELA;PIK3R1;PRKCE;FOXO1;AKT1;AKT3;STAT3;CPT1A;MTOR;GFPT1;INSR;NFKBIA;PCK2;PPP1CC;PPP1R3C;PRKAA1;PRKAA2;PRKAB2;PRKAG1;PTPN1;PTPRF;PYGB;PYGL;RPS6KA2;RPS6KA3;RPS6KB1;TBC1D4;MLXIP;TRIB3;CREB3L2;PRKCZ;PPARGC1B;SLC2A1;CREB3L1;CREB3L4;OGT;OGA
Cancer: specific types	hsa05226	Gastric cancer	50/1882	0.0003144 61726715 167	50	SOCS3;IRS1;JUN;MAPK9;AKT2;FOS;GSK3B;IL6;PIK3CA;MAPK8;TNF;CXCL8;MAPK14;IRS2;RELA;PIK3R1;CASP3;BCL2L1;AKT1;AKT3;MAPK11;ATF4;CASP8;DDIT3;EIF2S1;IL1B;INSR;NDUFA9;NDUFB2;NDUFB4;NDUFS4;PRKAA1;PRKAA2;PRKAB2;PRKAG1;RAC1;UQCRC2;MLXIP;UQCRCQ;UQCRI0;UQCRC1;MAP3K5;ADIPOR1;GSK3A;NDUFV2;COX6A1
Signal transduction	hsa04022	cGMP-PKG signaling pathway	54/1882	0.0003422 53220800 316	54	VEGFA;JUN;MAPK9;AKT2;SMAD2;STAT1;IL6;SMAD4;PIK3CA;PRKCA;MAPK8;TNF;CXCL8;MAPK14;KRAS;NRAS;CCND1;COL4A1;TGFB2;CDK4;RELA;PIK3R1;CASP3;PIM1;PRKCE;FOXO1;HRAS;TGFB1;AKT1;JA

						K2;AKT3;MAPK11;STAT3;COL4A4;COL4A5;DIAPH1;EDN1;EGR1;FN1;IL1B;SMAD3;SERPINE1;PLCG2;RAC1;PLCE1;PRKCZ;TGFB3;PLCB1
Endocrine system	hsa04921	Oxytocin signaling pathway	51/1882	0.0003809 16789551 657	51	E2F3;E2F1;CDK6;CREB1;GNAS;GSK3B;PRKACB;RAP1A;FZD2;CCND1;CDKN1A;SP1;ADCY6;GNAI3;AHR;DVL2;CDK4;APC;MAP2K1;E2F2;ADCY9;ARNT;ATF4;CAMK2G;ATF2;DVL3;GNAI1;GNAQ;ITPR1;ITPR2;KMT2A;PBX1;TCF7;WNT7B;FZD5;FZD3;KMT2D;FZD4;FZD7;LEF1;CREB3L2;ADCY8;TCF7L2;PLCB1;CREB3L1;CREB3L4;WNT3
Drug resistance: antineoplastic	hsa01524	Platinum drug resistance	29/1882	0.0005718 80988166 797	29	MAPK9;AKT2;TBK1;GSK3B;IL6;MYD88;MAPK8;TNF;CXCL8;MAPK14;CCND1;ALDH9A1;RELA;CASP3;SIRT1;FOXO1;AKT1;AKT3;MAPK11;ACADVL;ADH5;C3;CASP8;CPT1A;CXCL2;IL1B;NFKBIA;PRKAA1;PRKAA2;PRKAB2;PRKAG1;MAP2K3;SCD;MAP2K4;TRA2B;TCF7;CAMKK2;TAB2;TRA2A;LEF1;SCD5;TAB3;TCF7L2;FASN;MAP3K5;ADIPOR1;ACACA
Signal transduction	hsa04014	Ras signaling pathway	71/1882	0.0006239 76904681 222	71	CAV1;MET;SHC1;CDH1;PIK3CA;SRC;DNM2;PIK3R1;ITGA5;CLTA;CLTC;CRK;FN1;PXN;RAC1;WASF1;ARPC5;ACTR3;WASF2;CD2AP;ARPC1A;WASL;CBL;ARPC2;SHC2;SEPTIN2;SEPTIN6;SEPTIN3
Cellular community - eukaryotes	hsa04530	Tight junction	54/1882	0.0006568 87851108 778	54	TJP2;GNAS;PRKACB;PRKCA;KCNQ1;TJP1;ADCY9;ATP6V1A;ATP6V1C1;CFTR;PLCG2;SLC12A2;ATP6V1F;PDIA4;KDELRL1;SEC61B;KDELRL2;SEC61A2;ATP6V0E2;ERO1A
Signal transduction	hsa04371	Apelin signaling pathway	46/1882	0.0008117 74714464 388	46	JUN;MAPK9;MET;MAPK8;CXCL8;SRC;MAPK14;TJP1;RELA;CASP3;PAK1;ADAM17;MAPK11;ADAM10;ATP6V1A;ATP6V1C1;HBEGF;CXCL2;NFKBIA;PLCG2;PTPRZ1;RAC1;MAP2K4;ATP6V1F;ATP6V0E2
Cancer: specific types	hsa05213	Endometrial cancer	24/1882	0.0008117 74714464 388	24	ABL1;JUN;MAPK9;FOS;ROCK2;IL6;MYD88;NCL;MAPK8;TNF;CXCL8;SRC;MAPK14;TUBA1A;MYO10;MYH9;TJP1;TUBB6;RELA;CASP3;PAK1;MAPK11;SEC24D;ARF6;CASP8;LPAR1;GAPDH;GNA12;IL1B;MYO1C;MYO5A;MYO5B;MYO6;NFKBIA;PAK2;RAC1;ROCK1;WASF1;SEC24C;ARPC5;ACTR3;WASF2;TUBA1B;SEC24B;GNA13;NCKAP1;TMED10;TAB2;ARHGEF12;TAB3;TUBB2B;OCLN;CYFIP2;ARPC1A;CLDN3;WASL;ARPC2;ARHGEF11;MYO5C;WIPF2
Endocrine and metabolic disease	hsa04936	Alcoholic liver disease	47/1882	0.0008117 74714464 388	47	JUN;MAPK9;AKT2;ROCK2;TBK1;ATM;GSK3B;MYD88;PIK3CA;MAPK8;TNF;CXCL8;SRC;MAPK14;FBXW11;CD44;RELA;PIK3R1;PRKCE;TP53;FOXO1;AKT1;BTRC;ITGA5;AKT3;MAPK11;BCL2L1;ARF6;C3;CAPNS1;CRK;DIAPH1;MTOR;HK2;IL1B;ITPR1;ITPR2;MDM2;NFKBIA;PFN2;PLCG2;PPID;PXN;RAC1;ROCK1;RPS6KB1;UBE2D2;UBE2D3;CUL1;BCL10;WASF1;RPS6KA5;ARPC5;ACTR3;WASF2;CALCOCO2;RRAGB;RRAGA;MALT1;GLMN;TAB2;TECPR1;PIK3R4;PLCE1;RRAGD;RRAGC;TLN2;TAB3;FNBP1L;UBA52;MYL12B;ARPC1A;WASL;ARPC2;SKP1;PLCB1;WIP1;GSK3A;MYL5;SEPTIN2;SEPTIN7;H3-5;SEPTIN6;SEPTIN3
Cancer: specific types	hsa05223	Non-small cell lung cancer	28/1882	0.0008117 74714464 388	28	FYCO1;JUN;MAPK9;AKT2;FOS;ROCK2;IL6;KIF5B;MYD88;PIK3CA;MAPK8;TNF;EXOC2;DYNLT1;CXCL8;MAPK14;TUBA1A;DNM2;TUBB6;PODXL;RELA;ACTR1A;CASP3;PAK1;MAP2K1;HRAS;RHOB;AKT1;AKT3;MAPK11;BIRC2;BIRC3;ARF6;CASP8;CSE1L;DYNC1H1;DYNC1L12;FLNA;GAPDH;HSP90AA1;IL1B;KIF5C;KLC1;KPN1A;KPN3A;KPN4;M6PR;MYO6;NFKBIA;PFN2;PIK3C2A;PIK3C2B;PKN1;MAP2K3;RAB5A;RAB5B;RAC1;MAP2K4;TCF7;GCC2;ARPC5;ACTR3;TUBA1B;EXOC5;DCTN6;NCKAP1;TAB2;EXOC7;VPS39;LEF1;ARL8B;VPS33A;AHNAK;DYNC2H1;KLC4;TAB3;TUBB2B;CYFIP2;MYL12B;TCF7L2;ARPC1A;S100A10;WASL;RAB7A;ARPC2;SKP1;DYNLRB1;ACTR10;MYL5;DYNLL2
Signal transduction	hsa04066	HIF-1 signaling pathway	38/1882	0.0008760 64530864 453	38	IL6;MYD88;TNF;CXCL8;HSPD1;RELA;CASP3;EEF1A2;C3;CASP8;EEF1A1;CXCL2;HSPA1L;IL1B;NFKBIA;VCP;HBS1L;SAR1A;HSPA8
Infectious disease: parasitic	hsa05142	Chagas disease	36/1882	0.0009659 88394888 381	36	JUN;MAPK9;AKT2;FOS;ROCK2;TBK1;GSK3B;IL6;MYD88;PIK3CA;MAPK8;TNF;PIP5K1A;ARHGEF28;CXCL8;SRC;MAPK14;RELA;PIK3R1;MAP2K1;AKT1;ITGA5;AKT3;MAPK11;ARF6;CRK;FN1;GNAQ;IL1B;NFATC2;NFATC3;NFKBIA;PKN1;MAP2K3;PXN;RAC1;RAC2;ROCK1;RPS6KA2;RPS6KA3;MAP2K4;ARHGEF7;ARPC5;ACTR3;WASF2;TAB2;ARHGEF12;ARPC1A;WASL;ARPC2;WIPF2
Immune system	hsa04660	T cell receptor signaling pathway	41/1882	0.0009711 23798276 974	41	JUN;MAPK9;AKT2;FOS;SMAD2;CALR;GNAS;IL6;MYD88;PIK3CA;MAPK8;TNF;CXCL8;MAPK14;TGFB2;GNAI3;RELA;PIK3R1;PPP2R2A;TGFB1;AKT1;AKT3;MAPK11;C3;CASP8;GNAI1;GNAQ;IL1B;NFKBIA;SERPIN E1;PPP2CB;PPP2R1A;MAP2K4;PPP2R2B;TGFB3;PLCB1
Cancer: overview	hsa05230	Central carbon metabolism in cancer	27/1882	0.0011799 87871429 95	27	MAPK9;AKT2;STAT1;MYD88;MAPK8;TNF;CCR5;MAPK14;LAMC1;TGF B2;GNAI3;RELA;CASP3;JAK1;AKT1;JAK2;AKT3;MAPK11;BCL2L1;STAT3;BIRC2;BIRC3;XIAP;CASP8;GNAI1;HSPA1L;ITGA6;LAMA3;LAMB1;NFKBIA;MAP2K3;TAB2;CD40;TGFB3;HSPA8;LAMB2
Cell motility	hsa04810	Regulation of actin cytoskeleton	68/1882	0.0013332 05220481 99	68	SOCS3;E2F3;E2F1;CDK6;AKT2;TBK1;STAT1;GSK3B;IFIT1;PIK3CA;TNF;KRAS;NRAS;CCND1;CDKN1A;CDK4;RELA;PIK3R1;CASP3;TP53;PPP2R2A;JAK1;MAP2K1;YWHAZ;HRAS;AKT1;E2F2;AKT3;STAT3;CASP8;EIF2S1;EIF3E;NFKBIA;PPP2CB;PPP2R1A;SOS2;YWHAG;YWHAB;PIAS1;IRF9;YWHAQ;EIF2AK1;OCLN;PPP2R2B;CLDN3;SOS1
Cancer: specific types	hsa05221	Acute myeloid leukemia	26/1882	0.0013335 06456431 89	26	E2F3;E2F1;JUN;MAPK9;CREB1;AKT2;FOS;TBK1;STAT1;BIRC5;IL6;SMA D4;MYD88;PIK3CA;PRKCA;MAPK8;TNF;CXCL8;SRC;MAPK14;KRAS;NRAS;CDKN1A;TGFB2;RELA;PIK3R1;CASP3;TP53;JAK1;MAP2K1;YWH AZ;CCNA2;HRAS;TGFB1;AKT1;E2F2;JAK2;AKT3;MAPK11;STAT3;ATF4;CASP8;ATF2;CREBBP;DDB1;DDX3X;EGR3;ELK1;EP300;HSPG2;SMA

						D3;MAP3K1;NFATC2;NFATC3;NFKBIA;MAP2K3;MAP2K4;SOS2;YWHQ;TAB2;CREB3L2;VDAC3;TGFB3;SOS1;CREB3L1;CREB3L4
Neurodegenerative disease	hsa05020	Prion disease	79/1882	0.0013335 0645643189	79	CDK6;JUN;MAPK9;AKT2;FOS;TBK1;STAT1;GSK3B;IL6;MYD88;PIK3CA;MAPK8;ADAR;CCND1;CDK4;RELA;PIK3R1;CASP3;CCND2;TP53;JAK1;AKT1;AKT3;BCL2L1;BBC3;STAT3;CASP8;CSNK2A1;EIF2S1;HSPA1L;IL1B;MSN;NFKBIA;IRF9;TAB2;EIF2AK1;RCHY1;HSPA8;CSNK2A3
Chromosome	hsa03082	ATP-dependent chromatin remodeling	39/1882	0.0015519 9726950791	39	E2F3;E2F1;CDK6;VEGFA;CREB1;AKT2;ROCK2;TBK1;CALR;GNAS;GSK3B;IL6;PIK3CA;PRKACB;PRKCA;TNF;CCR5;CXCL8;SRC;MAPK14;KRAS;NRAS;CCND1;CDKN1A;SP1;ADCY6;GNAI3;CDK4;RELA;PIK3R1;CASP3;PTGS2;TP53;JAK1;MAP2K1;HRAS;AKT1;PPP3CA;E2F2;AKT3;MAPK11;STAT3;ADCY9;ATF4;CALM1;CALM2;CASP8;ATF2;CRK;EIF4EBP1;ELK1;MTOR;GNAI2;GNAI1;GNAQ;GNB1;GNG5;PDIA3;IL1B;ITPR1;ITPR2;MDM2;NFATC2;NFATC3;NFKBIA;PPP3R1;PXN;RAC1;RAC2;RHEB;ROCK1;RPS6KB1;SOS2;GNA13;AKAP13;ARHGEF12;GNB4;CREB3L2;TAP2;PTGER4;ADCY8;PPP3CB;PPP3CC;GNG11;SOS1;ARHGEF11;PLCB1;GNG12;CREB3L1;CREB3L4
Cell growth and death	hsa04210	Apoptosis	44/1882	0.0017074 2796610434	44	E2F1;CDK6;VEGFA;CREB1;AKT2;TBK1;STAT1;ATM;GNAS;GSK3B;PIK3CA;PRKACB;TNF;PARD6B;FZD2;THBS2;PTEN;THBS1;KRAS;NRAS;LAMC1;CCND1;CDKN1A;COL4A1;DVL2;CDK4;RELA;PIK3R1;NOTCH2;CASP3;PTGS2;CCND2;APC;TP53;ITGB4;PPP2R2A;JAK1;MAP2K1;FOXO1;CCNA2;HRAS;AKT1;ITGA5;AKT3;ATP6V1A;ATP6V1C1;CASP8;CHD4;COL4A4;COL4A5;COL6A1;CREBBP;CSNK1A1;DLG1;DLG2;DLG3;DVL3;EIF4EBP1;EP300;FN1;MTOR;TNC;ITGA6;ITGA1;ITGA3;ITGB8;LAMA3;LAMB1;MDM2;PPP2CB;PPP2R1A;PPP2R3A;PPP2R5A;PPP2R5C;PSEN1;PXN;RHEB;RPS6KB1;SOS2;TCF7;UBE3A;WNT7B;FZD5;FZD3;FZD4;FZD7;ITGA10;ATP6V1F;IRF9;UBR4;PPP2R3B;CREB3L2;MAML2;PTGER4;PRKCZ;TUBG1;ATP6V0E2;PPP2R2B;TCF7L2;ATR;TNR;COL6A3;SOS1;CREB3L1;CREB3L4;BCAP31;LAMB2;WNT3
Glycan biosynthesis and metabolism	hsa00510	N-Glycan biosynthesis	22/1882	0.0017106 270157159	22	E2F3;E2F1;JUN;MAPK9;CREB1;AKT2;FOS;SMAD2;ATM;CALR;IL6;SMAD4;PIK3CA;PRKACB;MAPK8;RAN;TNF;PTEN;KRAS;NRAS;CCND1;CDKN1A;ADCY6;TGFB2;CDK4;RELA;PIK3R1;CCND2;TP53;JAK1;MAP2K1;CCNA2;HRAS;TGFB1;AKT1;PPP3CA;E2F2;AKT3;BCL2L1;MAP3K3;ADCY9;SLC25A6;XIAP;ATF4;CDC20;ATF2;CREBBP;DLG1;EGR1;ELK1;EP300;ETS2;MAD2L1;SMAD3;MAP3K1;NFATC2;NFATC3;NFKBIA;PPP3R1;MAP2K4;SRF;VDAC2;XPO1;CDC23;NRP1;BUB3;ANAPC15;CREB3L2;CRTC3;TLN2;MAD1L1;CANX;ADCY8;VDAC3;PPP3CB;ATR;PPP3CC;CD40;ELK4;MSX1;POLB;TGFB3;SLC2A1;CREB3L1;CREB3L4
Lipid metabolism	hsa00600	Sphingolipid metabolism	22/1882	0.0017106 270157159	22	E2F3;E2F1;CDK6;VEGFA;JUN;MAPK9;CREB1;AKT2;FOS;TBK1;STAT1;FGF2;GSK3B;IL6;PIK3CA;MAPK8;CCR5;SYK;CXCL8;SRC;MAPK14;KRAS;NRAS;PREX1;CCND1;CDKN1A;CDK4;RELA;PIK3R1;CASP3;HIF1A;PTGS2;TP53;JAK1;MAP2K1;HRAS;AKT1;PPP3CA;E2F2;JAK2;AKT3;MAPK11;STAT3;C3;CALM1;CALM2;CASP8;CREBBP;EP300;MTOR;GNB1;GNG5;CXCL2;IL6ST;ITPR1;ITPR2;NFATC2;NFATC3;NFKBIA;PLCG2;PPP3R1;RAC1;MAP2K4;TCF7;MAPKAPK2;IRF9;LEF1;GNB4;UBA52;PPP3CB;TCF7L2;PPP3CC;GNG11;GNG12
Translation	hsa03015	mRNA surveillance pathway	35/1882	0.0019268 6000405697	35	SOC3;AKT2;TBK1;STAT1;CALR;IL6;MYD88;PIK3CA;PPP1CB;TNF;SYK;SRC;RELA;PIK3R1;CASP3;TP53;JAK1;AKT1;JAK2;ITGA5;AKT3;BCL2L1;BIRC2;BIRC3;C3;CASP8;EIF2S1;EIF4EBP1;MTOR;PDIA3;IL1B;NFKBIA;POU2F1;PPP1CC;RHEB;SRSF1;SRSF2;SRSF6;SRSF7;SRPK1;EIF2B4;EIF2B5;IRF9;TAB2;EIF2AK1;ZC3HAV1;TAP2;HCFC1;NECTIN2;DAXX
Circulatory system	hsa04261	Adrenergic signaling in cardiomyocytes	48/1882	0.0019958 711670277	48	E2F3;E2F1;CDK6;JUN;MAPK9;AKT2;TBK1;STAT1;CALR;IL6;MYD88;PIK3CA;MAPK8;TNF;SYK;MAPK14;CCND1;CDKN1A;CD44;CDK4;RELA;PIK3R1;CASP3;BCL2L1;VIM;CCND2;TP53;JAK1;CCNA2;AKT1;E2F2;AKT3;MAPK11;STAT3;CASP8;PDIA3;MDM2;NEDD4;NFKBIA;PLCG2;MAP2K3;PSMC2;PSMC4;PSMD1;PSMD2;PSMD7;PSMD12;RAC1;MAP2K4;SKP2;USP7;NCOR2;IRF9;TAB2;TAP2;CD40;PSMD13
Infectious disease: bacterial	hsa05130	Pathogenic Escherichia coli infection	60/1882	0.0020665 173939389	60	JUN;MAPK9;AKT2;FOS;TBK1;ATM;CALR;MYD88;PIK3CA;PRKCA;MAPK8;TNF;CCR5;MAPK14;FBXW11;KRAS;NRAS;GNAI3;RELA;PIK3R1;CASP3;PAK1;MAP2K1;HRAS;AKT1;BTRC;PPP3CA;AKT3;MAPK11;BCL2L1;AP1G1;CALM1;CALM2;CASP8;CCNB1;CDK1;CDC25C;CRK;DDDB1;MTOR;GNAI1;GNAQ;GNB1;GNG5;PDIA3;ITPR1;ITPR2;NFATC2;NFATC3;NFKBIA;PAK2;PLCG2;PPP3R1;MAP2K3;PXN;RAC1;RAC2;RPS6KB1;WEI1;CUL5;CUL4B;CUL4A;CUL1;AP1S2;RNF7;TAB2;GNB4;AP1S3;TAP2;PPP3CB;ATR;PPP3CC;GNG11;SKP1;GNG12;DCAF1
Endocrine system	hsa04920	Adipocytokine signaling pathway	26/1882	0.0020665 173939389	26	IRS1;MAPK9;AKT2;GSK3B;IL6;KIF5B;PIK3CA;MAPK8;TNF;SLC39A9;FZD2;TUBA1A;KRAS;NRAS;BACE1;IRS2;TUBB6;DVL2;RELA;PIK3R1;CASP3;APP;PTGS2;APC;MAP2K1;HRAS;AKT1;PPP3CA;ADAM17;AKT3;ADAM10;SLC25A6;ATF4;ATP2A2;CALM1;CALM2;CASP8;CHRM3;CSNK1A1;CSNK2A1;DDIT3;DVL3;EIF2S1;MTOR;GAPDH;GNAQ;GRIN2D;GRM5;IL1B;INSR;ITPR1;ITPR2;KIF5C;KLC1;LRP6;NDUFA9;NDUFB2;NDUFB4;NDUFS4;PPID;PPP3R1;PSEN1;PSMB5;PSMC2;PSMC4;PSMD1;PSMD2;PSMD7;PSMD12;UQCRC2;VDAC2;WNT7B;FZD5;SLC39A7;FZD3;FZD4;FZD7;ULK1;RB1CC1;RTN3;TUBA1B;NCSTN;FRAT2;SLC39A14;SLC39A6;UQCRCQ;SLC39A1;PIK3R4;APH1A;ATG2B;RTN4;SLC39A10;APH1B;KLC4;MCU;TUBB2B;UQCRC10;PSMA4;VDAC3;PPP3CB;PPP3CC;PSMA3;PSMB2;PSMD13;UQCRC1;MAP3K5;BACE2;ATG2A;PLCB1;WIP1;PSMB6;

						NDUFV2;COX6A1;CSNK2A3;GRIN2B;WNT3;ATP5F1A;ATP5MC2;ATP5MC3
Infectious disease: bacterial	hsa05100	Bacterial invasion of epithelial cells	28/1882	0.0024244 82409134 72	28	MAPK9;GNAS;KIF5B;PRKACB;MAPK8;PARK7;SLC39A9;TUBA1A;GNAI3;TUBB6;CASP3;TP53;BCL2L1;SLC25A6;ATF4;CALM1;CALM2;CAMK2G;DDIT3;DUSP1;EIF2S1;GNAI1;HSPA5;ITPR1;ITPR2;KIF5C;KLC1;MAOA;NDUFA9;NDUFB2;NDUFB4;NDUFS4;NFE2L2;PSMB5;PSMC2;PSMC4;PSMD1;PSMD2;PSMD7;PSMD12;UBE2G1;UQCRC2;VDAC2;SLC39A7;MFN2;TRAP1;TUBA1B;SLC39A14;SLC39A6;UQCRCQ;SLC39A1;UBE2J1;SLC39A10;KLC4;MCU;TUBB2B;UQCRC10;UBA52;PSMA4;VDAC3;PSMA3;PSMB2;PSMD13;UQCRC1;MAP3K5;PSMB6;NDUFV2;COX6A1;ATP5F1A;ATP5MC2;ATP5MC3;DAXX
Global and overview maps	hsa01230	Biosynthesis of amino acids	27/1882	0.0028199 24565453 06	27	TBK1;KIF5B;TNF;NUP50;MAPK14;TUBA1A;MATR3;TUBB6;ACTR1A;CASP3;TP53;ERBB4;PPP3CA;MAPK11;BCL2L1;ATF4;DDIT3;DNAH5;EIF2S1;MTOR;GRIN2D;HNRNPA2B1;HSPA5;KIF5C;KLC1;RAB8A;NDUFA9;NDUFB2;NDUFB4;NDUFS4;NUP98;PFN2;PPP3R1;MAP2K3;PSMB5;PSMC2;PSMC4;PSMD1;PSMD2;PSMD7;PSMD12;RAB5A;RAC1;SRSF7;UQCRC2;VCP;NUP214;ULK1;NUP155;RB1CC1;FIG4;NUP153;DNAL4;SIGMAR1;TUBA1B;DCTN6;SETX;NUP210;NUP160;TARDBP;NUP62;UQCRCQ;UBQLN2;UBQLN1;PIK3R4;ATG2B;DERL1;SPG11;SEH1L;KLC4;MCU;RAB39B;SMCR8;HNRNPA3;TUBB2B;GPX8;ALS2;UQCRC10;PSMA4;PPP3CB;VAPB;SLC1A2;PPP3CC;DNAH6;PSMA3;PSMB2;PSMD13;UQCRC1;MAP3K5;RANBP2;ATG2A;WIP1;NUP133;ACTR10;NUP37;PSMB6;NDUFV2;COX6A1;NUP85;GRIN2B;NUP58;ATP5F1A;ATP5MC2;ATP5MC3;DAXX
Global and overview maps	hsa01212	Fatty acid metabolism	22/1882	0.0028414 95949907 9	22	MAPK9;CREB1;KIF5B;MAPK8;SOD2;TUBA1A;SP1;TUBB6;ACTR1A;CASP3;TP53;BBC3;AP2B1;SLC25A6;CASP8;CLTA;CLTC;CREBBP;DNAH5;EP300;MTOR;GNAQ;GRM5;ITPR1;KIF5C;KLC1;NDUFA9;NDUFB2;NDUFB4;NDUFS4;POLR2A;POLR2B;POLR2C;POLR2D;POLR2I;PSMB5;PSMC2;PSMC4;PSMD1;PSMD2;PSMD7;PSMD12;TAF4;TAF4B;UQCRC2;VDAC2;ULK1;RB1CC1;DNAL4;TUBA1B;DCTN6;UQCRCQ;PIK3R4;ATG2B;CREB3L2;KLC4;TUBB2B;GPX8;UQCRC10;PSMA4;VDAC3;SLC1A2;HIP1;DNAH6;PSMA3;PSMB2;PSMD13;UQCRC1;MAP3K5;ATG2A;PLCB1;WIP1;IFT57;ACTR10;CREB3L1;CREB3L4;PSMB6;NDUFV2;COX6A1;GRIN2B;ATP5F1A;ATP5MC2;ATP5MC3
Infectious disease: bacterial	hsa05110	Vibrio cholerae infection	20/1882	0.0037800 71463898 08	20	MAPK9;AKT2;NFYA;PIK3CA;PRKCA;MAPK8;GTF2B;SP1;PIK3R1;ATXN1;AKT1;AKT3;SLC25A6;ATP2A2;MTOR;GNAQ;GRIN2D;GRM1;ITPR1;ITPR2;PSMB5;PSMC2;PSMC4;PSMD1;PSMD2;PSMD7;PSMD12;TRPC3;VDAC2;VLDLR;ULK1;PUM1;RB1CC1;PIK3R4;ATG2B;MCU;PSMA4;VDAC3;ATXN1L;PSMA3;PSMB2;PSMD13;MAP3K5;ATG2A;CIC;PLCB1;WIP1;PSMB6;GRIN2B
Substance dependence	hsa05031	Amphetamine addiction	25/1882	0.0037800 71463898 08	25	CAV1;MAPK9;CREB1;GSK3B;IL6;KIF5B;PIK3CA;PRKACB;MAPK8;PRNP;TNF;MAPK14;TUBA1A;LAMC1;TUBB6;PIK3R1;CASP3;PPP3CA;MAPK11;SLC25A6;ATF4;ATF2;CSNK2A1;DDIT3;EGR1;EIF2S1;GRIN2D;HSPA1L;HSPA5;IL1B;ITPR1;ITPR2;KIF5C;KLC1;NCAM2;NDUFA9;NDUFB2;NDUFB4;NDUFS4;PPP3R1;PSMB5;PSMC2;PSMC4;PSMD1;PSMD2;PSMD7;PSMD12;RAC1;RAC2;RYR2;UQCRC2;VDAC2;TUBA1B;STIP1;UQCRCQ;CREB3L2;KLC4;MCU;TUBB2B;UQCRC10;PSMA4;VDAC3;PPP3CB;PPP3CC;PSMA3;PSMB2;PSMD13;UQCRC1;HSPA8;CREB3L1;CREB3L4;PSMB6;NDUFV2;COX6A1;CSNK2A3;GRIN2B;ATP5F1A;ATP5MC2;ATP5MC3
Cancer: specific types	hsa05218	Melanoma	26/1882	0.0040073 99612853 31	26	MAPK9;TBK1;GSK3B;IL6;KIF5B;PRKCA;MAPK8;PRNP;TNF;PARK7;FZD2;MAPK14;TUBA1A;KRAS;NRAS;TUBB6;DVL2;RELA;ACTR1A;CASP3;ATXN1;APP;PTGS2;APC;MAP2K1;HRAS;PPP3CA;MAPK11;BCL2L1;SLC25A6;ATF4;ATP2A2;CALM1;CALM2;CAMK2G;CASP8;CHRM3;CSNK1A1;CSNK2A1;DDIT3;DNAH5;DVL3;EIF2S1;MTOR;GNAQ;GRIN2D;GRM1;GRM5;HSPA5;IL1B;ITPR1;ITPR2;KIF5C;KLC1;LRP6;RAB8A;NDUFA9;NDUFB2;NDUFB4;NDUFS4;PPID;PPP3R1;MAP2K3;PSEN1;PSMB5;PSMC2;PSMC4;PSMD1;PSMD2;PSMD7;PSMD12;RAB5A;RAC1;RYR2;TRPC3;UBE2G1;UQCRC2;VCP;VDAC2;WNT7B;FZD5;FZD3;FZD4;FZD7;ULK1;RB1CC1;FIG4;MFN2;DNAL4;TRAP1;SIGMAR1;TUBA1B;DCTN6;FRAT2;TARDBP;UQCRCQ;PIK3R4;UBE2J1;ZFYE1;ATG2B;DERL1;SPG11;KLC4;MCU;RAB39B;SMCR8;TUBB2B;GPX8;ALS2;UQCRC10;UBA52;PSMA4;VDAC3;ATXN1L;PPP3CB;VAPB;HIP1;PPP3CC;DNAH6;PSMA3;PSMB2;PSMD13;UQCRC1;MAP3K5;ATG2A;PLCB1;WIP1;IFT57;ACTR10;PSMB6;NDUFV2;COX6A1;CSNK2A3;GRIN2B;WNT3;ATP5F1A;ATP5MC2;ATP5MC3;DAXX
Endocrine and metabolic disease	hsa04934	Cushing syndrome	47/1882	0.0040073 99612853 31	47	JUN;CREB1;FOS;GNAS;PPP1CB;PRKACB;PRKCA;SIRT1;PPP3CA;ATF4;CALM1;CALM2;CAMK2G;ATF2;GRIN2D;MAOA;PPP1CC;PPP3R1;CREB3L2;FOSB;PPP3CB;PPP3CC;CREB3L1;CREB3L4;GRIN2B
Cancer: overview	hsa05207	Chemical carcinogenesis - receptor activation	62/1882	0.0040485 08380223 12	62	NSD3;ALDH9A1;EZH2;ACAT2;KMT2A;PLOD1;PLOD2;KMT2D;SETD1B;ASH1L;KMT2E;KMT2C;PRDM2;MECOM;EHADH;AASS;SETD2;DHTKD1;NSD1;KMT2B;KMT5A;NSD2
Cellular community - eukaryotes	hsa04540	Gap junction	31/1882	0.0040640 58304520 26	31	PIK3CA;PIP5K1A;PI4K2B;IPMK;PTEN;INPPL1;PIK3C2A;PIK3C2B;PIP4K2A;PLCG2;MTMR3;FIG4;SACM1L;PLCE1;IPPK;PIP4K2C;OCRL;INPP4B;ITPK1;PIKFYVE;MTMR2;MTMR1;PLCB1;PIP4K2B
Cancer: overview	hsa05206	MicroRNAs in cancer	86/1882	0.0042918 21868595 29	86	HADHB;ACADL;ACADS;ACADVL;ACAT2;CPT1A;ACSL1;SCD;ELOVL4;FADS2;HSD17B12;ELOVL5;ELOVL6;SCD5;ACSF3;EHADH;FASN;OXSM;HACD1;HACD3;HACD2;ACACA

Infectious disease: parasitic	hsa05145	Toxoplasmosis	36/1882	0.0044886 65561447 67	36	PSAT1;ASS1;CS;ARG2;ASNS;CTH;GAPDH;IDH1;IDH3A;MAT1A;PAH;PFKP;PRPS1;PRPS2;PYCR1;RPE;SHMT2;TKT;PHGDH;MAT2B;ASL;MTR;PGAM4;ACO2;TALDO1;IDH3B;PGK2
Nervous system	hsa04725	Cholinergic synapse	37/1882	0.0045021 97690569 85	37	MAN2A1;MAN1A1;DAD1;DPAGT1;FUT8;MAN2A2;MGAT3;RPN2;ST6GAL1;MOGS;B4GALT3;DPM1;MAN1A2;DOLK;ALG5;ALG8;ALG9;MGAT4B;ALG11;DPM2;DPM3;STT3B
Signaling molecules and interaction	hsa04512	ECM-receptor interaction	30/1882	0.0046287 23065456 29	30	SGPL1;KDSR;GLB1;PSAP;UGCG;UGT8;DEGS1;B4GALT5;SPTLC1;CERS2;CERK;CERS4;SGPP1;SAMD8;SGMS2;CERS6;SGMS1;GM2A;B4GALNT1;SGPP2;PLPP2;PLPP3
Signal transduction	hsa04340	Hedgehog signaling pathway	21/1882	0.0051331 67150255 64	21	MYH9;DAG1;LAMP1;LAMP2;PCDH7;TFRC;NRP2;PCDH1
Infectious disease: bacterial	hsa05120	Epithelial cell signaling in Helicobacter pylori infection	25/1882	0.0055020 56614180 35	25	IRS1;CREB1;AKT2;IGF1R;PIK3CA;PRKACB;SOD2;KRAS;NRAS;SESN1;ADCY6;IRS2;RELA;PIK3R1;SIRT1;TP53;FOXO1;HRAS;AKT1;AKT3;ADCY9;ATF4;ATF2;EIF4EBP1;MTOR;INSR;PRKAA1;PRKAA2;PRKAB2;PRKAG1;RHEB;RPS6KB1;ULK1;RB1CC1;CAMKK2;APPL1;CREB3L2;SESN3;ADCY8;ADIPOR1;CREB3L1;CREB3L4
Neurodegenerative disease	hsa05016	Huntington disease	83/1882	0.0060688 03918019 83	83	IRS1;AKT2;IGF1R;PIK3CA;PRKACB;SOD2;KRAS;NRAS;ADCY6;IRS2;PIK3R1;SIRT1;FOXO1;HRAS;AKT1;AKT3;ADCY9;EIF4EBP2;MTOR;HSPA1L;INSR;PRKAA1;PRKAA2;PRKAB2;PRKAG1;RPS6KB1;ADCY8;HSPA8
Immune system	hsa04662	B cell receptor signaling pathway	30/1882	0.0066161 81157283 47	30	CREB1;AKT2;GNAS;PPP1CB;PRKACB;PRKCA;MAPK14;TPM1;KCNQ1;TPM4;ADCY6;GNAI3;ATP2B1;PPP2R2A;AKT1;AKT3;MAPK11;ATP1A2;ADCY9;ATF4;ATP1A1;ATP1B1;ATP2A2;CACNA2D1;CACNB4;CALM1;CALM2;CAMK2G;ATF2;GNAI1;GNAQ;PPP1CC;PPP2CB;PPP2R1A;PPP2R3A;PPP2R5A;PPP2R5C;RYR2;RPS6KA5;RAPGEF4;PPP2R3B;CREB3L2;ADCY8;PPP2R2B;PLCB1;CACNA2D3;CREB3L1;CREB3L4
Endocrine and metabolic disease	hsa04932	Non-alcoholic fatty liver disease	46/1882	0.0087005 53342175 15	46	ABL1;MET;ROCK2;GSK3B;PIK3CA;PRKCA;ENAH;SRGAP1;PARD6B;SEMA3D;SRC;KRAS;NRAS;BMPR2;EFNA3;GNAI3;PIK3R1;PAK1;RASA1;EFNB1;HRAS;PPP3CA;BMPR1B;LRRC4;EFNA5;CAMK2G;DPYSL2;EFNA1;EFNB2;EPHA2;EPHA4;GNAI1;ABLIM1;NEO1;NFATC2;NFATC3;PAK2;PLCG2;PPP3R1;RAC1;RAC2;ROCK1;TRPC3;FZD3;NRP1;PLXNC1;SEMA3C;ARHGEF12;SRGAP2;SSH1;SEMA4C;PLXNA3;PRKCZ;ABLIM2;PPP3CB;MYL12B;SEMA7A;SEMA4A;PPP3CC;EPHB2;EPHB3;ABLIM3;SEMA6A;MYL5
Excretory system	hsa04962	Vasopressin-regulated water reabsorption	17/1882	0.0091460 81963893 18	17	SOCS3;JUN;MAPK9;CREB1;AKT2;FOS;STAT1;PIK3CA;MAPK8;TNF;SYK;MAPK14;MITF;TGFB2;RELA;PIK3R1;JAK1;MAP2K1;TGFB1;AKT1;PPP3CA;AKT3;MAPK11;ATP2A2;IL1B;ITPR1;ITPR2;JUNB;NFATC2;NFKBIA;PLCG2;PPP3R1;RAC1;IRF9;LILRA1;TAB2;SIRPA;FOSB;PPP3CB;PPP3CC;FOSL2
Infectious disease: viral	hsa05169	Epstein-Barr virus infection	57/1882	0.0096469 57952160 6	57	KCNJ2;GNAS;PRKACB;PRKCA;KCNQ1;ADCY6;GNAI3;ATP1A2;ADCY9;ATP1A1;ATP1B1;CA2;CALM1;CALM2;CAMK2G;CFTR;CHRM3;GNAI1;GNAQ;ITPR1;ITPR2;ADCY8;PLCB1;SLC4A2
Folding, sorting and degradation	hsa03018	RNA degradation	26/1882	0.0102442 43049389 4	26	SOCS3;IRS1;MAPK9;AKT2;SHC1;RAPGEF1;GSK3B;PIK3CA;PPP1CB;PRKACB;MAPK8;G6PC1;KRAS;NRAS;GYS1;IRS2;PIK3R1;INPPL1;MAP2K1;FOXO1;HRAS;AKT1;AKT3;CALM1;CALM2;CRK;EIF4EBP1;ELK1;MTOR;MKNK2;HK2;INSR;PCK2;PPP1CC;PPP1R3C;PRKAA1;PRKAA2;PRKAB2;PRKAG1;PRKAR2A;PRKAR2B;PTPN1;PTPRF;PYGB;PYGL;RHEB;RPS6;RPS6KB1;SOS2;SOCS2;EXOC7;PRKCZ;SORBS1;FASN;CBL;SOS1;SHC2;ACACA
Environmental adaptation	hsa04710	Circadian rhythm	14/1882	0.0102442 43049389 4	14	JUN;MAPK9;GNAS;PRKACB;PRKCA;MAPK8;PLD2;SRC;MAPK14;KRAS;NRAS;ADCY6;MAP2K1;HRAS;MAPK11;MAP3K3;ADCY9;ATF4;CALM1;CALM2;CAMK2G;HBEGF;EGR1;ELK1;GNAQ;ITPR1;ITPR2;MAP3K1;MAP3K4;MMP14;MAP2K3;MAP2K4;SOS2;MAP3K2;ADCY8;SOS1;PLCB1
Amino acid metabolism	hsa00310	Lysine degradation	22/1882	0.0105761 80899353 9	22	MAPK9;AKT2;IGF1R;PIK3CA;PRKACB;MAPK8;CPEB4;MAPK14;KRAS;ADCY6;GNAI3;PIK3R1;MAP2K1;CCNA2;AKT1;AKT3;MAPK11;ADCY9;BUB1;CCNB1;CDK1;CDC25C;GNAI1;HSP90AA1;MAD2L1;RPS6KA2;RPS6KA3;AURKA;CDC23;PKMYT1;ANAPC15;CPEB2;MAD1L1;ADCY8
Cancer: overview	hsa05202	Transcriptional misregulation in cancer	56/1882	0.0107418 28109881 4	56	JUN;CREB1;AKT2;SHC1;FOS;GNAS;PIK3CA;PRKACB;SRC;NCOA3;KRAS;NRAS;NCOA2;ESR1;SP1;ADCY6;GNAI3;PIK3R1;MAP2K1;HRAS;AKT1;AKT3;ADCY9;ATF4;CALM1;CALM2;ATF2;HBEGF;FKBP5;GNAI1;GNAQ;GRM1;HSPA1L;HSP90AA1;ITPR1;ITPR2;SOS2;TGFA;CREB3L2;ADCY8;NCOA1;SOS1;HSPA8;SHC2;PLCB1;KRT24;CREB3L1;CREB3L4
Infectious disease: viral	hsa05160	Hepatitis C	46/1882	0.0107418 28109881 4	46	CREB1;GNAS;GSK3B;PRKACB;PRKCA;FZD2;KRAS;NRAS;ADCY6;MITF;GNAI3;DVL2;MAP2K1;HRAS;ADCY9;CALM1;CALM2;CAMK2G;CREBBP;DVL3;EDN1;EP300;GNAI1;GNAQ;TCF7;WNT7B;FZD5;FZD3;FZD4;FZD7;LEF1;CREB3L2;KITLG;ADCY8;TCF7L2;PLCB1;CREB3L1;CREB3L4;WNT3
Endocrine system	hsa04918	Thyroid hormone synthesis	25/1882	0.0116764 81817906 7	25	SOCS3;MAPK9;AKT2;SHC1;FOS;STAT1;GSK3B;PIK3CA;MAPK8;SOCS6;SRC;MAPK14;KRAS;NRAS;CCND1;ESR1;SOCS5;RELA;PIK3R1;CCND2;MAP2K1;HRAS;AKT1;JAK2;AKT3;MAPK11;STAT3;SOS2;SOCS2;SOS1;SHC2;SOCS7
Neurodegenerative disease	hsa05012	Parkinson disease	72/1882	0.0119315 47068951 4	72	CREB1;GNAS;PRKACB;PRKCA;ADCY6;ATP1A2;ADCY9;ATF4;ATP1A1;ATP1B1;ATF2;GNAQ;HSPA5;ITPR1;ITPR2;TTF2;PDIA4;CREB3L2;GPX8;ALB;CANX;ADCY8;PLCB1;CREB3L1;CREB3L4

Endocrine system	hsa04914	Progesterone-mediated oocyte maturation	34/1882	0.0123255 45395554 2	34	AKT2;STAT1;GSK3B;PIK3CA;PRKACB;PRKCA;SRC;NCOA3;KRAS;NRA S;NCOA2;CCND1;ESR1;DIO3;PIK3R1;NOTCH2;HIF1A;TP53;MAP2K1;F OXO1;MED1;HRAS;AKT1;AKT3;ATP1A2;ATP1A1;ATP1B1;ATP2A2;CRE BBP;EP300;MTOR;MDM2;PDK1;PLCG2;RHEB;TBC1D4;MED13;MED13L ;PLCE1;MED12L;NCOR1;BMP4;NCOA1;HDAC3;MED14;MED12;SLC2A1 ;PLCB1
Immune system	hsa04657	IL-17 signaling pathway	30/1882	0.0123255 45395554 2	30	SOCS3;IRS1;MAPK9;AKT2;MAPK8;TNF;G6PC1;IRS2;RELA;AKT1;JAK2; AKT3;STAT3;CPT1A;ACSL1;MTOR;NFKBIA;PCK2;PRKAA1;PRKAA2;P RKAB2;PRKAG1;CAMKK2;APPL1;SLC2A1;ADIPOR1
Immune system	hsa04666	Fc gamma R-mediated phagocytosis	31/1882	0.0123255 45395554 2	31	KCNJ2;JUN;FOS;ROCK2;GNAS;PPP1CB;PRKACB;PRKCA;SRC;KRAS;N RAS;CCND1;CDKN1A;ADCY6;GNAI3;PTGS2;MAP2K1;HRAS;PPP3CA;A DCY9;CACNA2D1;CACNB4;CALM1;CALM2;CAMK2G;EEF2;ELK1;GNA I1;GNAQ;GUCY1A2;ITPR1;ITPR2;MEF2C;PPP1R12A;NFATC2;NFATC3;P PP1CC;PPP3R1;PRKAA1;PRKAA2;PRKAB2;PRKAG1;ROCK1;RYR2;CA MKK2;ADCY8;PPP3CB;PPP1R12B;PPP3CC;PLCB1;CACNA2D3
Signal transduction	hsa04015	Rap1 signaling pathway	58/1882	0.0134839 06760555 5	58	CREB1;AKT2;GNAS;PRKACB;G6PC1;LDHA;GYS1;SIRT1;FOXO1;AKT1; PPP3CA;AKT3;ATF4;CALM1;CALM2;CAMK2G;CPT1A;ATF2;CREBBP;E P300;GNAQ;ITPR1;ITPR2;PCK2;PDHA1;PDK1;PPP3R1;PRKAA1;PRKAA 2;PRKAB2;PRKAG1;PYGB;PYGL;CREB3L2;SIK1;PGAM4;PPP3CB;PPP3 CC;SLC2A1;SIK2;PLCB1;CREB3L1;CREB3L4;PPP4R3A;ACACA
Cell growth and death	hsa04215	Apoptosis - multiple species	13/1882	0.0149654 91784857 1	13	KCNJ2;CREB1;EDNRA;GNAS;PRKACB;ADCY6;GNAI3;PPP3CA;CALM1 ;CALM2;EDN1;GNAI1;GNAQ;GUCY1A2;ITPR1;ITPR2;PPP3R1;PTGER4; PDE1A;ADCYAP1;PPP3CB;PPP3CC;PLCB1
Immune system	hsa04664	Fc epsilon RI signaling pathway	23/1882	0.0153954 98727761 3	23	VEGFA;JUN;MAPK9;CREB1;AKT2;SHC1;FOS;SMAD2;MMP1;GNAS;PIK 3CA;PRKACB;PRKCA;MAPK8;SRC;MAPK14;KRAS;NRAS;COL4A1;AD CY6;GNAI3;RELA;PIK3R1;MAP2K1;HRAS;TGFB1;AKT1;AKT3;MAPK 11;ADCY9;ATF4;COL4A4;COL4A5;ATF2;EDN1;GNAI1;GNB1;GNG5;NF KBIA;MAP2K4;SOS2;GNB4;CREB3L2;RLN1;PRKCZ;ADCY8;GNG11;AR RB2;RLN2;SOS1;SHC2;PLCB1;GNG12;CREB3L1;CREB3L4
Endocrine system	hsa04924	Renin secretion	23/1882	0.0153954 98727761 3	23	CREB1;FOS;RUNX2;GNAS;PRKACB;PRKCA;PLD2;CDKN1A;SP1;ADCY 6;GNAI3;MMP16;MAP2K1;NR4A2;FGFR1;MEF2D;WNK1;ADCY9;ATF4; ATF2;HBEGF;EGR1;GNA12;GNAI1;GNAQ;ITPR1;ITPR2;LRP6;MEF2A;M EF2C;MMP14;OXSR1;GNA13;MMP24;AKAP13;CREB3L2;PDE4B;ADCY8 ;ARRB2;STK39;ARHGEF11;PLCB1;CREB3L1;CREB3L4
Carbohydrate metabolism	hsa00562	Inositol phosphate metabolism	24/1882	0.0156785 08463031 8	24	SOCS3;IRS1;MAPK9;CREB1;AKT2;SHC1;FOS;STAT1;GNAS;GSK3B;PIK 3CA;PRKACB;PRKCA;MAPK8;MAPK14;KRAS;NRAS;ADCY6;IRS2;GNA I3;PIK3R1;MAP2K1;HRAS;AKT1;JAK2;AKT3;MAPK11;STAT3;ADCY9;A TF4;ATF2;CREBBP;CRK;EP300;MTOR;GNAI1;GNAQ;ITPR1;ITPR2;JUNB ;MAP3K1;PLCG2;MAP2K3;MAP2K4;SOS2;SOCS2;CREB3L2;ADCY8;SO S1;SHC2;PLCB1;CREB3L1;CREB3L4
Development and regeneration	hsa04380	Osteoclast differentiation	41/1882	0.0185373 08466906 4	41	CLOCK;CREB1;FBXL3;FBXW11;BTRC;NFIL3;PRKAA1;PRKAA2;PRKA B2;PRKAG1;CUL1;BHLHE40;NR1D2;SKP1
Infectious disease: viral	hsa05168	Herpes simplex virus 1 infection	50/1882	0.0205606 17122194	50	CREB1;GNAS;PRKACB;ADCY6;ADCY9;DYNC1H1;DYNC1L1;NSF;RA B5A;RAB5B;DCTN6;CREB3L2;DYNC2H1;VAMP2;CREB3L1;CREB3L4;D YNLL2
Signal transduction	hsa04072	Phospholipase D signaling pathway	42/1882	0.0228864 70535649 9	42	JUN;MAPK9;AKT2;STAT1;IL6;PIK3CA;MAPK8;TNF;SYK;SRC;MAPK14; KRAS;NRAS;RELA;PIK3R1;PAK1;PTGS2;HRAS;AKT1;PPP3CA;AKT3;M APK11;CALM1;CALM2;CASP8;EGR3;IL1B;ITPR1;ITPR2;MDM2;NFATC2 ;NFATC3;NFKBIA;PLCG2;PPP3R1;BCL10;MAPKAPK2;IRF9;MALT1;AR HGEF12;PPP3CB;PPP3CC
Cardiovascular disease	hsa05415	Diabetic cardiomyopathy	55/1882	0.0237341 54823462	55	JUN;MAPK9;FOS;TBK1;MMP1;GSK3B;IL6;MAPK8;TNF;CXCL8;MAPK1 4;RELA;CASP3;PTGS2;CEBPB;MAPK11;ELAVL1;CASP8;CXCL2;HSP90 AA1;IL1B;NFKBIA;MAPK6;CXCL5;SRSF1;TAB2;TAB3;MUC5B;FOSB;L CN2
Infectious disease: bacterial	hsa05134	Legionellosis	19/1882	0.0237757 63087922 1	19	JUN;MAPK9;AKT2;FOS;GSK3B;PIK3CA;MAPK8;TNF;MAPK14;KRAS;N RAS;CDK4;RELA;PIK3R1;PAK1;PPP2R2A;MAP2K1;HRAS;AKT1;PPP3C A;AKT3;MAPK11;DLG1;NFATC2;NFATC3;NFKBIA;PAK2;PPP2CB;PPP2R 1A;PPP2R3A;PPP2R5A;PPP2R5C;PPP3R1;SOS2;BCL10;MALT1;PPP2R3B; PPP2R2B;PPP3CB;PPP3CC;SOS1
Cell motility	hsa04814	Motor proteins	53/1882	0.0250260 77247774	53	JUN;AKT2;FOS;GSK3B;PIK3CA;SYK;KRAS;NRAS;RELA;PIK3R1;INPPL 1;MAP2K1;HRAS;AKT1;PPP3CA;AKT3;NFATC2;NFATC3;NFKBIA;PLCG 2;PPP3R1;RAC1;RAC2;SOS2;BCL10;MALT1;LILRA1;PPP3CB;PPP3CC;S OSI
NA	hsa03273	Virion - Lassa virus and SFTS virus	8/1882	0.0255522 24165667 1	8	MAPK9;AKT2;PIK3CA;PRKCA;MAPK8;TNF;SYK;MAPK14;KRAS;NRAS ;PIK3R1;MAP2K1;HRAS;AKT1;AKT3;MAPK11;PLCG2;MAP2K3;RAC1;R AC2;MAP2K4;SOS2;SOS1
Digestive system	hsa04971	Gastric acid secretion	24/1882	0.0255522 24165667 1	24	AKT2;PIK3CA;PRKCA;PIP5K1A;ASAP1;SYK;PLD2;MYO10;DNM2;PIK3 R1;PAK1;INPPL1;PRKCE;MAP2K1;AKT1;AKT3;ARF6;CRK;PLCG2;RAC 1;RAC2;RPS6KB1;WASF1;ARPC5;ACTR3;ARPC2;MARCKSL1;ARPC1A; ARPC2;PLPP2;PLPP3
Cell growth and death	hsa04216	Ferroptosis	15/1882	0.0295004 42536799 3	15	PPP1CB;PRKACB;PRKCA;RAP1A;KRAS;NRAS;MAP2K1;HRAS;PPP3CA ;ATF4;CALM1;CALM2;CAMK2G;CREBBP;EP300;GNAQ;GRIN2D;GRM1; GRM5;ITPR1;ITPR2;PPP1CC;PPP3R1;RPS6KA2;RPS6KA3;ADCY8;PPP3C B;PPP3CC;PLCB1;GRIN2B

Infectious disease: viral	hsa05162	Measles	39/1882	0.0301327 21574639 3	39	ABL1;IRS1;JUN;MAPK9;AKT2;SHC1;RAPGEF1;GSK3B;PIK3CA;MAPK8;RAP1A;MAPK14;KRAS;NRAS;RELA;PIK3R1;TP53;MAP2K1;HRAS;AKT1;AKT3;MAPK11;MAP3K3;ATF4;CALM1;CALM2;CAMK2G;CRK;MAP3K1;NFKBIA;NTRK2;PLCG2;PSEN1;RAC1;RPS6KA2;RPS6KA3;SOS2;RPS6KA5;MAPKAPK2;FRS2;PRDM4;MAGED1;SOS1;MAP3K5;SHC2;BEX3
Cancer: overview	hsa05208	Chemical carcinogenesis - reactive oxygen species	59/1882	0.0349728 67046951 1	59	KCNJ2;CREB1;AKT2;FOS;PIK3CA;PRKACB;PRKCA;KCNQ1;KRAS;NRAS;ADCY6;GNAI3;PIK3R1;MAP2K1;HRAS;AKT1;JAK2;AKT3;ADCY9;ATF4;CAMK2G;CHRM3;GNAI1;GNAQ;GNB1;GNG5;ITPR1;ITPR2;GNB4;CREB3L2;ADCY8;KCNQ3;GNG11;PLCB1;GNG12;CREB3L1;CREB3L4
Sensory system	hsa04750	Inflammatory mediator regulation of TRP channels	29/1882	0.0378262 38892585 4	29	CLOCK;MAPK9;CREB1;AKT2;FOS;GNAS;GSK3B;KIF5B;PPP1CB;PRKACB;PRKCA;MAPK8;MAPK14;GNAI3;PPP2R2A;AKT1;PPP3CA;AKT3;MAPK11;ATF4;CALM1;CALM2;CAMK2G;COMT;ATF2;GNAI1;GNAQ;GNB1;GNG5;ITPR1;ITPR2;KIF5C;MAOA;PPP1CC;PPP2CB;PPP2R1A;PPP2R3A;PPP2R5A;PPP2R5C;PPP2R3B;GNB4;CREB3L2;PPP2R2B;PPP3CB;PPP3CC;GNG11;ARRB2;PLCB1;GNG12;GSK3A;CREB3L1;CREB3L4;GRIN2B
Cancer: specific types	hsa05217	Basal cell carcinoma	20/1882	0.0408566 94963870 7	20	GNAS;IGF1R;PRKCA;KRAS;NRAS;GNAI3;MAP2K1;HRAS;GNAI2;GNAI1;GNAQ;GRM1;GUCY1A2;ITPR1;ITPR2;PPP2CB;PPP2R1A;GNAI3;PLCB1
Nervous system	hsa04730	Long-term depression	19/1882	0.0481832 87447987 8	19	MAPK9;GNAS;PIK3CA;PPP1CB;PRKACB;PRKCA;MAPK8;HTR2A;SRC;MAPK14;ADCY6;PIK3R1;PRKCE;MAPK11;ADCY9;CALM1;CALM2;CAMK2G;F2RL1;GNAQ;IL1B;ITPR1;ITPR2;PLCG2;PPP1CC;MAP2K3;PTGER4;ADCY8;PLCB1

Supplementary Table S6. KEGG pathway enrichment of miR-203a target genes associated with schizophrenia. The table lists pathways significantly enriched for miR-203a targets that overlap with schizophrenia-related genes. Columns report the total number of miRNA target genes (n_miRNA_genes), total number of schizophrenia-related genes (n_scz_genes), number of overlapping genes (n_overlap), the names of overlapping genes (Overlap_genes), and statistical significance values (p-value, FDR, and Bonferroni correction). Only pathways relevant to schizophrenia are shown.