

Silesian University of Technology



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**MOLECULAR MECHANISMS OF
TUMOR CELL RESISTANCE
TO THE FGFR KINASE INHIBITOR**

DOCTORAL DISSERTATION

Doctoral dissertation performed under the supervision of

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Supplementary Materials

LUNG - over-representation analysis (ORA)

Table S1. The list of significant pathways from ORA analysis performed based on the Lung gene set selected with the PREDICT pipeline.

No	Pathway ID	Description	Gene count	q value
1	R-HSA-168142	Toll Like Receptor 10 (TLR10) Cascade	2	0.013
2	R-HSA-168176	Toll Like Receptor 5 (TLR5) Cascade	2	0.013
3	R-HSA-975871	MyD88 cascade initiated on plasma membrane	2	0.013
4	R-HSA-975138	TRAF6 mediated induction of NFkB and MAP kinases upon TLR7/8 or 9 activation	2	0.013
5	R-HSA-975155	MyD88 dependent cascade initiated on endosome	2	0.013
6	R-HSA-168181	Toll Like Receptor 7/8 (TLR7/8) Cascade	2	0.013
7	R-HSA-168138	Toll Like Receptor 9 (TLR9) Cascade	2	0.013
8	R-HSA-166058	MyD88:MAL(TIRAP) cascade initiated on plasma membrane	2	0.013
9	R-HSA-168188	Toll Like Receptor TLR6:TLR2 Cascade	2	0.013
10	R-HSA-168179	Toll Like Receptor TLR1:TLR2 Cascade	2	0.013
11	R-HSA-181438	Toll Like Receptor 2 (TLR2) Cascade	2	0.013
12	R-HSA-166016	Toll Like Receptor 4 (TLR4) Cascade	2	0.019
13	R-HSA-168898	Toll-like Receptor Cascades	2	0.024
14	R-HSA-5661231	Metallothioneins bind metals	1	0.029
15	R-HSA-5660526	Response to metal ions	1	0.032
16	R-HSA-975110	TRAF6 mediated IRF7 activation in TLR7/8 or 9 signaling	1	0.032
17	R-HSA-210993	Tie2 Signaling	1	0.034
18	R-HSA-5603041	IRAK4 deficiency (TLR2/4)	1	0.034
19	R-HSA-881907	Gastrin-CREB signalling pathway via PKC and MAPK	1	0.034
20	R-HSA-198753	ERK/MAPK targets	1	0.040
21	R-HSA-171319	Telomere Extension By Telomerase	1	0.040
22	R-HSA-156588	Glucuronidation	1	0.040
23	R-HSA-3238698	WNT ligand biogenesis and trafficking	1	0.040
24	R-HSA-186763	Downstream signal transduction	1	0.040
25	R-HSA-442742	CREB1 phosphorylation through NMDA receptor-mediated activation of RAS signaling	1	0.040
26	R-HSA-450282	MAPK targets/ Nuclear events mediated by MAP kinases	1	0.040
27	R-HSA-5260271	Diseases of Immune System	1	0.040
28	R-HSA-5602358	Diseases associated with the TLR signaling cascade	1	0.040
29	R-HSA-5579029	Metabolic disorders of biological oxidation enzymes	1	0.042
30	R-HSA-1483166	Synthesis of PA	1	0.047
31	R-HSA-8853659	RET signaling	1	0.047
32	R-HSA-9696273	RND1 GTPase cycle	1	0.047
33	R-HSA-1433557	Signaling by SCF-KIT	1	0.047
34	R-HSA-425397	Transport of vitamins, nucleosides, and related molecules	1	0.047
35	R-HSA-437239	Recycling pathway of L1	1	0.048
36	R-HSA-1227986	Signaling by ERBB2	1	0.050
37	R-HSA-180786	Extension of Telomeres	1	0.050

LUNG - gene set enrichment analysis (GSEA)

Table S2. The list of significant pathways from GSEA analysis performed based on the Lung DEGs (differentially expressed genes) data set.

No	Patway ID	Description	Gene count	q value
1	R-HSA-5661231	Metallothioneins bind metals	6	0.018
2	R-HSA-5660526	Response to metal ions	6	0.018
3	R-HSA-6805567	Keratinization	16	0.040

STOMACH - gene set enrichment analysis (GSEA)

Table S3. The list of significant pathways from GSEA analysis performed based on the Stomach DEGs (differentially expressed genes) data set.

No	Pathway ID	Description	Gene count	q value
1	R-HSA-2555396	Mitotic Metaphase and Anaphase	106	9.321E-09
2	R-HSA-6791226	Major pathway of rRNA processing in the nucleolus and cytosol	71	9.321E-09
3	R-HSA-68877	Mitotic Prometaphase	97	9.321E-09
4	R-HSA-68882	Mitotic Anaphase	105	9.321E-09
5	R-HSA-68886	M Phase	166	9.321E-09
6	R-HSA-69620	Cell Cycle Checkpoints	140	9.321E-09
7	R-HSA-72163	mRNA Splicing - Major Pathway	89	9.321E-09
8	R-HSA-72172	mRNA Splicing	92	9.321E-09
9	R-HSA-72203	Processing of Capped Intron-Containing Pre-mRNA	117	9.321E-09
10	R-HSA-72312	rRNA processing	78	9.321E-09
11	R-HSA-72766	Translation	129	9.321E-09
12	R-HSA-8868773	rRNA processing in the nucleus and cytosol	73	9.321E-09
13	R-HSA-141424	Amplification of signal from the kinetochores	54	9.321E-09
14	R-HSA-141444	Amplification of signal from unattached kinetochores via a MAD2 inhibitory signal	54	9.321E-09
15	R-HSA-168273	Influenza Viral RNA Transcription and Replication	62	3.608E-08
16	R-HSA-168255	Influenza Infection	69	6.748E-08
17	R-HSA-69242	S Phase	62	1.711E-07
18	R-HSA-2500257	Resolution of Sister Chromatid Cohesion	65	1.711E-07
19	R-HSA-69618	Mitotic Spindle Checkpoint	60	3.070E-07
20	R-HSA-927802	Nonsense-Mediated Decay (NMD)	65	4.174E-07
21	R-HSA-975957	Nonsense Mediated Decay (NMD) enhanced by the Exon Junction Complex (EJC)	65	4.174E-07
22	R-HSA-73894	DNA Repair	123	8.480E-07
23	R-HSA-2467813	Separation of Sister Chromatids	84	1.297E-06
24	R-HSA-69306	DNA Replication	58	1.415E-06
25	R-HSA-69206	G1/S Transition	53	1.470E-06
26	R-HSA-72706	GTP hydrolysis and joining of the 60S ribosomal subunit	45	1.534E-06
27	R-HSA-453279	Mitotic G1 phase and G1/S transition	56	1.780E-06
28	R-HSA-72613	Eukaryotic Translation Initiation	47	1.780E-06
29	R-HSA-72737	Cap-dependent Translation Initiation	47	1.780E-06
30	R-HSA-69481	G2/M Checkpoints	72	3.110E-06
31	R-HSA-1799339	SRP-dependent cotranslational protein targeting to membrane	43	4.088E-06
32	R-HSA-156827	L13a-mediated translational silencing of Ceruloplasmin expression	43	5.476E-06
33	R-HSA-975956	Nonsense Mediated Decay (NMD) independent of the Exon Junction Complex (EJC)	53	5.588E-06
34	R-HSA-192823	Viral mRNA Translation	34	7.229E-06
35	R-HSA-9648025	EML4 and NUDC in mitotic spindle formation	59	8.018E-06
36	R-HSA-72689	Formation of a pool of free 40S subunits	39	9.609E-06
37	R-HSA-5685942	HDR through Homologous Recombination (HRR)	33	1.138E-05
38	R-HSA-1428517	The citric acid (TCA) cycle and respiratory electron transport	80	1.170E-05
39	R-HSA-69239	Synthesis of DNA	49	1.230E-05
40	R-HSA-5693532	DNA Double-Strand Break Repair	70	1.404E-05
41	R-HSA-5368287	Mitochondrial translation	39	1.404E-05

42	R-HSA-156902	Peptide chain elongation	48	1.900E-05
43	R-HSA-72764	Eukaryotic Translation Termination	51	1.959E-05
44	R-HSA-69002	DNA Replication Pre-Initiation	36	2.101E-05
45	R-HSA-72202	Transport of Mature Transcript to Cytoplasm	43	2.101E-05
46	R-HSA-5693579	Homologous DNA Pairing and Strand Exchange	24	2.319E-05
47	R-HSA-5368286	Mitochondrial translation initiation	37	2.802E-05
48	R-HSA-611105	Respiratory electron transport	60	2.876E-05
49	R-HSA-69190	DNA strand elongation	24	3.366E-05
50	R-HSA-73856	RNA Polymerase II Transcription Termination	36	4.112E-05
51	R-HSA-1474244	Extracellular matrix organization	105	4.112E-05
52	R-HSA-163200	Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins.	71	4.964E-05
53	R-HSA-68962	Activation of the pre-replicative complex	23	5.295E-05
54	R-HSA-9612973	Autophagy	46	5.448E-05
55	R-HSA-176187	Activation of ATR in response to replication stress	20	5.448E-05
56	R-HSA-5389840	Mitochondrial translation elongation	35	5.635E-05
57	R-HSA-1632852	Macroautophagy	42	7.072E-05
58	R-HSA-5663220	RHO GTPases Activate Formins	64	7.072E-05
59	R-HSA-5419276	Mitochondrial translation termination	36	7.393E-05
60	R-HSA-72187	mRNA 3'-end processing	30	7.505E-05
61	R-HSA-73886	Chromosome Maintenance	60	9.177E-05
62	R-HSA-5693616	Presynaptic phase of homologous DNA pairing and strand exchange	22	9.177E-05
63	R-HSA-191859	snRNP Assembly	29	9.537E-05
64	R-HSA-194441	Metabolism of non-coding RNA	29	9.537E-05
65	R-HSA-162594	Early Phase of HIV Life Cycle	8	0.0001
66	R-HSA-159236	Transport of Mature mRNA derived from an Intron-Containing Transcript	36	0.0002
67	R-HSA-159234	Transport of Mature mRNAs Derived from Intronless Transcripts	25	0.0002
68	R-HSA-5633007	Regulation of TP53 Activity	59	0.0002
69	R-HSA-5693538	Homology Directed Repair	59	0.0002
70	R-HSA-69186	Lagging Strand Synthesis	14	0.0002
71	R-HSA-2408557	Selenocysteine synthesis	34	0.0004
72	R-HSA-3700989	Transcriptional Regulation by TP53	116	0.0005
73	R-HSA-909733	Interferon alpha/beta signaling	16	0.0005
74	R-HSA-9007101	Rab regulation of trafficking	51	0.0005
75	R-HSA-156842	Eukaryotic Translation Elongation	51	0.0005
76	R-HSA-180786	Extension of Telomeres	28	0.0006
77	R-HSA-159231	Transport of Mature mRNA Derived from an Intronless Transcript	24	0.0008
78	R-HSA-1566948	Elastic fibre formation	20	0.0008
79	R-HSA-2980766	Nuclear Envelope Breakdown	30	0.0008
80	R-HSA-5685938	HDR through Single Strand Annealing (SSA)	20	0.0008
81	R-HSA-68867	Assembly of the pre-replicative complex	27	0.0010
82	R-HSA-8957275	Post-translational protein phosphorylation	38	0.0011
83	R-HSA-6804756	Regulation of TP53 Activity through Phosphorylation	41	0.0011
84	R-HSA-70326	Glucose metabolism	38	0.0011
85	R-HSA-4615885	SUMOylation of DNA replication proteins	29	0.0012
86	R-HSA-5693568	Resolution of D-loop Structures through Holliday Junction Intermediates	18	0.0012
87	R-HSA-72702	Ribosomal scanning and start codon recognition	23	0.0012
88	R-HSA-429958	mRNA decay by 3' to 5' exoribonuclease	7	0.0013
89	R-HSA-381426	Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Binding Proteins (IGFBPs)	42	0.0013
90	R-HSA-5693567	HDR through Homologous Recombination (HRR) or Single Strand Annealing (SSA)	54	0.0013
91	R-HSA-71403	Citric acid cycle (TCA cycle)	11	0.0013

92	R-HSA-69205	G1/S-Specific Transcription	16	0.0013
93	R-HSA-9675135	Diseases of DNA repair	20	0.0015
94	R-HSA-73933	Resolution of Abasic Sites (AP sites)	18	0.0015
95	R-HSA-6796648	TP53 Regulates Transcription of DNA Repair Genes	19	0.0015
96	R-HSA-5651801	PCNA-Dependent Long Patch Base Excision Repair	12	0.0015
97	R-HSA-72649	Translation initiation complex formation	22	0.0016
98	R-HSA-419408	Lysosphingolipid and LPA receptors	7	0.0019
99	R-HSA-376176	Signaling by ROBO receptors	64	0.0019
100	R-HSA-110373	Resolution of AP sites via the multiple-nucleotide patch replacement pathway	13	0.0022
101	R-HSA-162587	HIV Life Cycle	59	0.0022
102	R-HSA-9010553	Regulation of expression of SLITs and ROBOs	54	0.0024
103	R-HSA-180910	Vpr-mediated nuclear import of PICs	19	0.0024
104	R-HSA-191273	Cholesterol biosynthesis	16	0.0024
105	R-HSA-429914	Deadenylation-dependent mRNA decay	19	0.0025
106	R-HSA-5693537	Resolution of D-Loop Structures	18	0.0028
107	R-HSA-186712	Regulation of beta-cell development	20	0.0029
108	R-HSA-3301854	Nuclear Pore Complex (NPC) Disassembly	20	0.0029
109	R-HSA-6785807	Interleukin-4 and Interleukin-13 signaling	37	0.0029
110	R-HSA-177243	Interactions of Rev with host cellular proteins	19	0.0032
111	R-HSA-174417	Telomere C-strand (Lagging Strand) Synthesis	19	0.0032
112	R-HSA-72662	Activation of the mRNA upon binding of the cap-binding complex and eIFs, and subsequent binding to 43S	22	0.0032
113	R-HSA-162906	HIV Infection	76	0.0033
114	R-HSA-2129379	Molecules associated with elastic fibres	16	0.0036
115	R-HSA-159230	Transport of the SLBP Dependant Mature mRNA	20	0.0036
116	R-HSA-176033	Interactions of Vpr with host cellular proteins	20	0.0039
117	R-HSA-6790901	rRNA modification in the nucleus and cytosol	23	0.0046
118	R-HSA-174414	Processive synthesis on the C-strand of the telomere	12	0.0051
119	R-HSA-69183	Processive synthesis on the lagging strand	10	0.0052
120	R-HSA-2408522	Selenoamino acid metabolism	38	0.0056
121	R-HSA-180746	Nuclear import of Rev protein	17	0.0063
122	R-HSA-168276	NS1 Mediated Effects on Host Pathways	21	0.0064
123	R-HSA-73762	RNA Polymerase I Transcription Initiation	18	0.0065
124	R-HSA-72695	Formation of the ternary complex, and subsequently, the 43S complex	18	0.0066
125	R-HSA-168333	NEP/NS2 Interacts with the Cellular Export Machinery	17	0.0066
126	R-HSA-68949	Orc1 removal from chromatin	27	0.0066
127	R-HSA-1474228	Degradation of the extracellular matrix	32	0.0066
128	R-HSA-450531	Regulation of mRNA stability by proteins that bind AU-rich elements	28	0.0067
129	R-HSA-168271	Transport of Ribonucleoproteins into the Host Nucleus	17	0.0067
130	R-HSA-168274	Export of Viral Ribonucleoproteins from Nucleus	17	0.0070
131	R-HSA-210745	Regulation of gene expression in beta cells	10	0.0080
132	R-HSA-168325	Viral Messenger RNA Synthesis	23	0.0093
133	R-HSA-75067	Processing of Capped Intronless Pre-mRNA	16	0.0094
134	R-HSA-5696398	Nucleotide Excision Repair	44	0.0094
135	R-HSA-983712	Ion channel transport	66	0.0097
136	R-HSA-3108214	SUMOylation of DNA damage response and repair proteins	34	0.0097
137	R-HSA-113510	E2F mediated regulation of DNA replication	16	0.0099
138	R-HSA-8854214	TBC/RABGAPs	24	0.0106
139	R-HSA-9675136	Diseases of DNA Double-Strand Break Repair	15	0.0107
140	R-HSA-9701193	Defective HDR through Homologous Recombination (HRR) due to PALB2 loss of function	15	0.0107

141	R-HSA-9704331	Defective HDR through Homologous Recombination Repair (HRR) due to PALB2 loss of BRCA1 binding function	15	0.0107
142	R-HSA-9704646	Defective HDR through Homologous Recombination Repair (HRR) due to PALB2 loss of BRCA2/RAD51/RAD51C binding function	15	0.0107
143	R-HSA-159227	Transport of the SLBP independent Mature mRNA	19	0.0107
144	R-HSA-9615933	Postmitotic nuclear pore complex (NPC) reformation	16	0.0109
145	R-HSA-76005	Response to elevated platelet cytosolic Ca ²⁺	46	0.0115
146	R-HSA-9639288	Amino acids regulate mTORC1	30	0.0115
147	R-HSA-170822	Regulation of Glucokinase by Glucokinase Regulatory Protein	18	0.0115
148	R-HSA-5619107	Defective TPR may confer susceptibility towards thyroid papillary carcinoma (TPC)	18	0.0115
149	R-HSA-9633012	Response of EIF2AK4 (GCN2) to amino acid deficiency	35	0.0116
150	R-HSA-5358606	Mismatch repair (MMR) directed by MSH2:MSH3 (MutSbeta)	7	0.0118
151	R-HSA-69091	Polymerase switching	10	0.0118
152	R-HSA-69109	Leading Strand Synthesis	10	0.0118
153	R-HSA-2426168	Activation of gene expression by SREBF (SREBP)	23	0.0118
154	R-HSA-72306	tRNA processing	36	0.0118
155	R-HSA-216083	Integrin cell surface interactions	30	0.0121
156	R-HSA-165054	Rev-mediated nuclear export of HIV RNA	18	0.0124
157	R-HSA-5693607	Processing of DNA double-strand break ends	42	0.0126
158	R-HSA-70171	Glycolysis	29	0.0126
159	R-HSA-442720	CREB1 phosphorylation through the activation of Adenylate Cyclase	6	0.0128
160	R-HSA-69473	G2/M DNA damage checkpoint	41	0.0137
161	R-HSA-114608	Platelet degranulation	45	0.0138
162	R-HSA-380972	Energy dependent regulation of mTOR by LKB1-AMPK	9	0.0138
163	R-HSA-71291	Metabolism of amino acids and derivatives	103	0.0138
164	R-HSA-157579	Telomere Maintenance	43	0.0138
165	R-HSA-1474290	Collagen formation	34	0.0144
166	R-HSA-69166	Removal of the Flap Intermediate	9	0.0149
167	R-HSA-69052	Switching of origins to a post-replicative state	32	0.0154
168	R-HSA-6799198	Complex I biogenesis	29	0.0154
169	R-HSA-5696399	Global Genome Nucleotide Excision Repair (GG-NER)	36	0.0160
170	R-HSA-913531	Interferon Signaling	49	0.0175
171	R-HSA-6784531	tRNA processing in the nucleus	27	0.0186
172	R-HSA-162909	Host Interactions of HIV factors	40	0.0186
173	R-HSA-163210	Formation of ATP by chemiosmotic coupling	14	0.0200
174	R-HSA-2514853	Condensation of Prometaphase Chromosomes	9	0.0202
175	R-HSA-5358565	Mismatch repair (MMR) directed by MSH2:MSH6 (MutSalpha)	8	0.0213
176	R-HSA-5693554	Resolution of D-loop Structures through Synthesis-Dependent Strand Annealing (SDSA)	16	0.0218
177	R-HSA-5696397	Gap-filling DNA repair synthesis and ligation in GG-NER	15	0.0218
178	R-HSA-6798695	Neutrophil degranulation	108	0.0219
179	R-HSA-3232142	SUMOylation of ubiquitylation proteins	21	0.0226
180	R-HSA-674695	RNA Polymerase II Pre-transcription Events	31	0.0232
181	R-HSA-9013418	RHOBTB2 GTPase cycle	17	0.0238
182	R-HSA-70895	Branched-chain amino acid catabolism	8	0.0239
183	R-HSA-1538133	G0 and Early G1	12	0.0243
184	R-HSA-77387	Insulin receptor recycling	17	0.0245
185	R-HSA-2990846	SUMOylation	61	0.0245
186	R-HSA-6804114	TP53 Regulates Transcription of Genes Involved in G2 Cell Cycle Arrest	12	0.0245
187	R-HSA-5358508	Mismatch Repair	8	0.0247
188	R-HSA-1592389	Activation of Matrix Metalloproteinases	10	0.0251
189	R-HSA-70263	Gluconeogenesis	13	0.0252

190	R-HSA-4551638	SUMOylation of chromatin organization proteins	35	0.0265
191	R-HSA-174437	Removal of the Flap Intermediate from the C-strand	10	0.0266
192	R-HSA-69275	G2/M Transition	65	0.0266
193	R-HSA-9706574	RHOBTB GTPase Cycle	13	0.0266
194	R-HSA-77595	Processing of Intronless Pre-mRNAs	10	0.0281
195	R-HSA-4570464	SUMOylation of RNA binding proteins	24	0.0291
196	R-HSA-6782210	Gap-filling DNA repair synthesis and ligation in TC-NER	25	0.0304
197	R-HSA-2206281	Mucopolysaccharidoses	5	0.0309
198	R-HSA-3108232	SUMO E3 ligases SUMOylate target proteins	58	0.0343
199	R-HSA-195258	RHO GTPase Effectors	88	0.0361
200	R-HSA-72165	mRNA Splicing - Minor Pathway	25	0.0370
201	R-HSA-176974	Unwinding of DNA	10	0.0374
202	R-HSA-917937	Iron uptake and transport	33	0.0374
203	R-HSA-4085377	SUMOylation of SUMOylation proteins	20	0.0374
204	R-HSA-176814	Activation of APC/C and APC/C:Cdc20 mediated degradation of mitotic proteins	30	0.0377
205	R-HSA-6805567	Keratinization	44	0.0394
206	R-HSA-139853	Elevation of cytosolic Ca ²⁺ levels	6	0.0399
207	R-HSA-2672351	Stimuli-sensing channels	38	0.0406
208	R-HSA-176409	APC/C:Cdc20 mediated degradation of mitotic proteins	29	0.0448
209	R-HSA-174143	APC/C-mediated degradation of cell cycle proteins	35	0.0448
210	R-HSA-453276	Regulation of mitotic cell cycle	35	0.0448
211	R-HSA-111931	PKA-mediated phosphorylation of CREB	7	0.0474
212	R-HSA-163615	PKA activation	6	0.0480
213	R-HSA-174178	APC/C:Cdh1 mediated degradation of Cdc20 and other APC/C:Cdh1 targeted proteins in late mitosis/early G1	27	0.0480
214	R-HSA-449147	Signaling by Interleukins	143	0.0482
215	R-HSA-198933	Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell	27	0.0482
216	R-HSA-68884	Mitotic Telophase/Cytokinesis	7	0.0492
217	R-HSA-6781827	Transcription-Coupled Nucleotide Excision Repair (TC-NER)	32	0.0495
218	R-HSA-3371571	HSF1-dependent transactivation	2	0.0496
219	R-HSA-209952	Peptide hormone biosynthesis	4	0.0499
220	R-HSA-917977	Transferrin endocytosis and recycling	20	0.0504

BLADDER - over-representation analysis (ORA)

Table S4. The list of significant pathways from ORA analysis performed based on the Bladder gene set selected with the PREDICT pipeline.

No	Pathway ID	Description	Gene count	q value
1	R-HSA-68882	Mitotic Anaphase	16	0.001
2	R-HSA-2555396	Mitotic Metaphase and Anaphase	16	0.001
3	R-HSA-389957	Prefoldin mediated transfer of substrate to CCT/TriC	6	0.001
4	R-HSA-389958	Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding	6	0.003
5	R-HSA-2995410	Nuclear Envelope (NE) Reassembly	8	0.005
6	R-HSA-68877	Mitotic Prometaphase	13	0.005
7	R-HSA-2500257	Resolution of Sister Chromatid Cohesion	10	0.005
8	R-HSA-389960	Formation of tubulin folding intermediates by CCT/TriC	5	0.005
9	R-HSA-68886	M Phase	19	0.007
10	R-HSA-390466	Chaperonin-mediated protein folding	8	0.011
11	R-HSA-180786	Extension of Telomeres	6	0.012
12	R-HSA-8854518	AURKA Activation by TPX2	7	0.012
13	R-HSA-391251	Protein folding	8	0.012
14	R-HSA-2980766	Nuclear Envelope Breakdown	6	0.012
15	R-HSA-2995383	Initiation of Nuclear Envelope (NE) Reformation	4	0.012
16	R-HSA-390471	Association of TriC/CCT with target proteins during biosynthesis	5	0.020
17	R-HSA-69275	G2/M Transition	11	0.020
18	R-HSA-390450	Folding of actin by CCT/TriC	3	0.020
19	R-HSA-453274	Mitotic G2-G2/M phases	11	0.020
20	R-HSA-171319	Telomere Extension By Telomerase	4	0.020
21	R-HSA-6790901	rRNA modification in the nucleus and cytosol	6	0.020
22	R-HSA-2565942	Regulation of PLK1 Activity at G2/M Transition	7	0.024
23	R-HSA-69273	Cyclin A/B1/B2 associated events during G2/M transition	4	0.025
24	R-HSA-9648025	EML4 and NUDC in mitotic spindle formation	8	0.025
25	R-HSA-6804756	Regulation of TP53 Activity through Phosphorylation	7	0.027
26	R-HSA-6791226	Major pathway of rRNA processing in the nucleolus and cytosol	10	0.032
27	R-HSA-69205	G1/S-Specific Transcription	4	0.033
28	R-HSA-6791312	TP53 Regulates Transcription of Cell Cycle Genes	5	0.033
29	R-HSA-2467813	Separation of Sister Chromatids	10	0.036
30	R-HSA-162594	Early Phase of HIV Life Cycle	3	0.036
31	R-HSA-162658	Golgi Cisternae Pericentriolar Stack Reorganization	3	0.036
32	R-HSA-8868773	rRNA processing in the nucleus and cytosol	10	0.038
33	R-HSA-69242	S Phase	9	0.038
34	R-HSA-8852276	The role of GTSE1 in G2/M progression after G2 checkpoint	6	0.041
35	R-HSA-5617833	Cilium Assembly	10	0.046
36	R-HSA-1362300	Transcription of E2F targets under negative control by p107 (RBL1) and p130 (RBL2) in complex with HDAC1	3	0.047
37	R-HSA-72312	rRNA processing	10	0.048

BLADDER - gene set enrichment analysis (GSEA)

Table S5. The list of significant pathways from GSEA analysis performed based on the Bladder DEGs (differentially expressed genes) data set.

No	Pathway ID	Description	Gene count	q value
1	R-HSA-1236978	Cross-presentation of soluble exogenous antigens (endosomes)	36	8.123E-10
2	R-HSA-1268020	Mitochondrial protein import	45	8.123E-10
3	R-HSA-141424	Amplification of signal from the kinetochores	55	8.123E-10
4	R-HSA-141444	Amplification of signal from unattached kinetochores via a MAD2 inhibitory signal	55	8.123EG-10
5	R-HSA-1428517	The citric acid (TCA) cycle and respiratory electron transport	88	8.123E-10
6	R-HSA-156827	L13a-mediated translational silencing of Ceruloplasmin expression	90	8.123E-10
7	R-HSA-156842	Eukaryotic Translation Elongation	77	8.123E-10
8	R-HSA-156902	Peptide chain elongation	75	8.123E-10
9	R-HSA-157579	Telomere Maintenance	60	8.123E-10
10	R-HSA-162587	HIV Life Cycle	68	8.123E-10
11	R-HSA-162599	Late Phase of HIV Life Cycle	72	8.123E-10
12	R-HSA-162906	HIV Infection	128	8.123E-10
13	R-HSA-162909	Host Interactions of HIV factors	86	8.123E-10
14	R-HSA-163200	Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins.	70	8.123E-10
15	R-HSA-168255	Influenza Infection	126	8.123E-10
16	R-HSA-168273	Influenza Viral RNA Transcription and Replication	112	8.123E-10
17	R-HSA-169911	Regulation of Apoptosis	38	8.123E-10
18	R-HSA-174084	Autodegradation of Cdh1 by Cdh1:APC/C	46	8.123E-10
19	R-HSA-174113	SCF-beta-TrCP mediated degradation of Emi1	40	8.123E-10
20	R-HSA-174143	APC/C-mediated degradation of cell cycle proteins	64	8.123E-10
21	R-HSA-174154	APC/C:Cdc20 mediated degradation of Securin	49	8.123E-10
22	R-HSA-174178	APC/C:Cdh1 mediated degradation of Cdc20 and other APC/C:Cdh1 targeted proteins in late mitosis/early G1	55	8.123E-10
23	R-HSA-174184	Cdc20:Phospho-APC/C mediated degradation of Cyclin A	52	8.123E-10
24	R-HSA-176187	Activation of ATR in response to replication stress	33	8.123E-10
25	R-HSA-176408	Regulation of APC/C activators between G1/S and early anaphase	56	8.123E-10
26	R-HSA-176409	APC/C:Cdc20 mediated degradation of mitotic proteins	55	8.123E-10
27	R-HSA-176814	Activation of APC/C and APC/C:Cdc20 mediated degradation of mitotic proteins	56	8.123E-10
28	R-HSA-179419	APC:Cdc20 mediated degradation of cell cycle proteins prior to satisfaction of the cell cycle checkpoint	53	8.123E-10
29	R-HSA-1799339	SRP-dependent cotranslational protein targeting to membrane	90	8.123E-10
30	R-HSA-180534	Vpu mediated degradation of CD4	38	8.123E-10
31	R-HSA-180585	Vif-mediated degradation of APOBEC3G	40	8.123E-10
32	R-HSA-180786	Extension of Telomeres	37	8.123E-10
33	R-HSA-187577	SCF(Skp2)-mediated degradation of p27/p21	44	8.123E-10
34	R-HSA-191859	snRNP Assembly	42	8.123E-10
35	R-HSA-192823	Viral mRNA Translation	74	8.123E-10
36	R-HSA-194441	Metabolism of non-coding RNA	42	8.123E-10
37	R-HSA-211733	Regulation of activated PAK-2p34 by proteasome mediated degradation	38	8.123E-10
38	R-HSA-2408522	Selenoamino acid metabolism	84	8.123E-10
39	R-HSA-2408557	Selenocysteine synthesis	76	8.123E-10

40	R-HSA-2467813	Separation of Sister Chromatids	114	8.123E-10
41	R-HSA-2500257	Resolution of Sister Chromatid Cohesion	68	8.123E-10
42	R-HSA-2555396	Mitotic Metaphase and Anaphase	137	8.123E-10
43	R-HSA-349425	Autodegradation of the E3 ubiquitin ligase COP1	38	8.123E-10
44	R-HSA-376176	Signaling by ROBO receptors	120	8.123E-10
45	R-HSA-450408	AUF1 (hnRNP D0) binds and destabilizes mRNA	41	8.123E-10
46	R-HSA-450531	Regulation of mRNA stability by proteins that bind AU-rich elements	54	8.123E-10
47	R-HSA-453274	Mitotic G2-G2/M phases	94	8.123E-10
48	R-HSA-453276	Regulation of mitotic cell cycle	64	8.123E-10
49	R-HSA-453279	Mitotic G1 phase and G1/S transition	93	8.123E-10
50	R-HSA-4615885	SUMOylation of DNA replication proteins	38	8.123E-10
51	R-HSA-5362768	Hh mutants are degraded by ERAD	40	8.123E-10
52	R-HSA-5368286	Mitochondrial translation initiation	74	8.123E-10
53	R-HSA-5368287	Mitochondrial translation	73	8.123E-10
54	R-HSA-5389840	Mitochondrial translation elongation	73	8.123E-10
55	R-HSA-5419276	Mitochondrial translation termination	73	8.123E-10
56	R-HSA-5607761	Dectin-1 mediated noncanonical NF-kB signaling	40	8.123E-10
57	R-HSA-5610780	Degradation of GLI1 by the proteasome	40	8.123E-10
58	R-HSA-5610785	GLI3 is processed to GLI3R by the proteasome	40	8.123E-10
59	R-HSA-5658442	Regulation of RAS by GAPs	44	8.123E-10
60	R-HSA-5663220	RHO GTPases Activate Formins	65	8.123E-10
61	R-HSA-5676590	NIK-->noncanonical NF-kB signaling	40	8.123E-10
62	R-HSA-611105	Respiratory electron transport	59	8.123E-10
63	R-HSA-6784531	tRNA processing in the nucleus	43	8.123E-10
64	R-HSA-6790901	rRNA modification in the nucleus and cytosol	47	8.123E-10
65	R-HSA-6791226	Major pathway of rRNA processing in the nucleolus and cytosol	142	8.123E-10
66	R-HSA-68827	CDT1 association with the CDC6:ORC:origin complex	46	8.123E-10
67	R-HSA-68867	Assembly of the pre-replicative complex	55	8.123E-10
68	R-HSA-68877	Mitotic Prometaphase	93	8.123E-10
69	R-HSA-68882	Mitotic Anaphase	136	8.123E-10
70	R-HSA-68886	M Phase	206	8.123E-10
71	R-HSA-68949	Orc1 removal from chromatin	55	8.123E-10
72	R-HSA-68962	Activation of the pre-replicative complex	30	8.123E-10
73	R-HSA-69002	DNA Replication Pre-Initiation	69	8.123E-10
74	R-HSA-69017	CDK-mediated phosphorylation and removal of Cdc6	52	8.123E-10
75	R-HSA-69052	Switching of origins to a post-replicative state	66	8.123E-10
76	R-HSA-69202	Cyclin E associated events during G1/S transition	51	8.123E-10
77	R-HSA-69206	G1/S Transition	91	8.123E-10
78	R-HSA-69239	Synthesis of DNA	90	8.123E-10
79	R-HSA-69242	S Phase	108	8.123E-10
80	R-HSA-69275	G2/M Transition	92	8.123E-10
81	R-HSA-69306	DNA Replication	96	8.123E-10
82	R-HSA-69481	G2/M Checkpoints	99	8.123E-10
83	R-HSA-69601	Ubiquitin Mediated Degradation of Phosphorylated Cdc25A	40	8.123E-10
84	R-HSA-69610	p53-Independent DNA Damage Response	40	8.123E-10
85	R-HSA-69613	p53-Independent G1/S DNA damage checkpoint	40	8.123E-10
86	R-HSA-69615	G1/S DNA Damage Checkpoints	44	8.123E-10
87	R-HSA-69618	Mitotic Spindle Checkpoint	71	8.123E-10
88	R-HSA-69620	Cell Cycle Checkpoints	168	8.123E-10
89	R-HSA-69656	Cyclin A:Cdk2-associated events at S phase entry	52	8.123E-10
90	R-HSA-72163	mRNA Splicing - Major Pathway	116	8.123E-10
91	R-HSA-72172	mRNA Splicing	117	8.123E-10

92	R-HSA-72202	Transport of Mature Transcript to Cytoplasm	50	8.123E-10
93	R-HSA-72203	Processing of Capped Intron-Containing Pre-mRNA	155	8.123E-10
94	R-HSA-72306	tRNA processing	73	8.123E-10
95	R-HSA-72312	rRNA processing	156	8.123E-10
96	R-HSA-72613	Eukaryotic Translation Initiation	97	8.123E-10
97	R-HSA-72649	Translation initiation complex formation	44	8.123E-10
98	R-HSA-72662	Activation of the mRNA upon binding of the cap-binding complex and eIFs, and subsequent binding to 43S	44	8.123E-10
99	R-HSA-72689	Formation of a pool of free 40S subunits	83	8.123E-10
100	R-HSA-72702	Ribosomal scanning and start codon recognition	45	8.123E-10
101	R-HSA-72706	GTP hydrolysis and joining of the 60S ribosomal subunit	92	8.123E-10
102	R-HSA-72737	Cap-dependent Translation Initiation	97	8.123E-10
103	R-HSA-72764	Eukaryotic Translation Termination	78	8.123E-10
104	R-HSA-72766	Translation	206	8.123E-10
105	R-HSA-73886	Chromosome Maintenance	79	8.123E-10
106	R-HSA-73894	DNA Repair	138	8.123E-10
107	R-HSA-75815	Ubiquitin-dependent degradation of Cyclin D	40	8.123E-10
108	R-HSA-8852276	The role of GTSE1 in G2/M progression after G2 checkpoint	51	8.123E-10
109	R-HSA-8854050	FBXL7 down-regulates AURKA during mitotic entry and in early mitosis	40	8.123E-10
110	R-HSA-8868773	rRNA processing in the nucleus and cytosol	150	8.123E-10
111	R-HSA-8932339	ROS sensing by NFE2L2	43	8.123E-10
112	R-HSA-8941858	Regulation of RUNX3 expression and activity	38	8.123E-10
113	R-HSA-9010553	Regulation of expression of SLITs and ROBOs	113	8.123E-10
114	R-HSA-927802	Nonsense-Mediated Decay (NMD)	85	8.123E-10
115	R-HSA-9604323	Negative regulation of NOTCH4 signaling	38	8.123E-10
116	R-HSA-9633012	Response of EIF2AK4 (GCN2) to amino acid deficiency	78	8.123E-10
117	R-HSA-9648025	EML4 and NUDC in mitotic spindle formation	67	8.123E-10
118	R-HSA-9707587	Regulation of HMOX1 expression and activity	43	8.123E-10
119	R-HSA-975956	Nonsense Mediated Decay (NMD) independent of the Exon Junction Complex (EJC)	79	8.123E-10
120	R-HSA-975957	Nonsense Mediated Decay (NMD) enhanced by the Exon Junction Complex (EJC)	85	8.123E-10
121	R-HSA-69563	p53-Dependent G1 DNA Damage Response	42	9.698E-10
122	R-HSA-69580	p53-Dependent G1/S DNA damage checkpoint	42	9.698E-10
123	R-HSA-351202	Metabolism of polyamines	41	1.307E-09
124	R-HSA-168325	Viral Messenger RNA Synthesis	37	2.268E-09
125	R-HSA-5610783	Degradation of GLI2 by the proteasome	40	2.584E-09
126	R-HSA-72165	mRNA Splicing - Minor Pathway	37	3.120E-09
127	R-HSA-69190	DNA strand elongation	30	3.745E-09
128	R-HSA-69541	Stabilization of p53	38	4.124E-09
129	R-HSA-159236	Transport of Mature mRNA derived from an Intron-Containing Transcript	45	4.509E-09
130	R-HSA-4641257	Degradation of AXIN	38	4.648E-09
131	R-HSA-2871837	FCERI mediated NF-kB activation	43	6.938E-09
132	R-HSA-72695	Formation of the ternary complex, and subsequently, the 43S complex	40	6.966E-09
133	R-HSA-177243	Interactions of Rev with host cellular proteins	32	7.737E-09
134	R-HSA-5696398	Nucleotide Excision Repair	52	8.062E-09
135	R-HSA-5693532	DNA Double-Strand Break Repair	70	8.398E-09
136	R-HSA-350562	Regulation of ornithine decarboxylase (ODC)	38	1.253E-08
137	R-HSA-5689603	UCH proteinases	53	1.257E-08
138	R-HSA-6781827	Transcription-Coupled Nucleotide Excision Repair (TC-NER)	40	1.340E-08

139	R-HSA-1236974	ER-Phagosome pathway	47	1.633E-08
140	R-HSA-4641258	Degradation of DVL	40	2.190E-08
141	R-HSA-159234	Transport of Mature mRNAs Derived from Intronless Transcripts	32	2.461E-08
142	R-HSA-1168372	Downstream signaling events of B Cell Receptor (BCR)	44	2.524E-08
143	R-HSA-5387390	Hh mutants abrogate ligand secretion	40	2.639E-08
144	R-HSA-1234176	Oxygen-dependent proline hydroxylation of Hypoxia-inducible Factor Alpha	42	2.844E-08
145	R-HSA-5678895	Defective CFTR causes cystic fibrosis	40	3.536E-08
146	R-HSA-202424	Downstream TCR signaling	46	3.748E-08
147	R-HSA-5633007	Regulation of TP53 Activity	56	3.936E-08
148	R-HSA-165054	Rev-mediated nuclear export of HIV RNA	30	4.461E-08
149	R-HSA-68875	Mitotic Prophase	67	4.495E-08
150	R-HSA-3700989	Transcriptional Regulation by TP53	115	5.238E-08
151	R-HSA-159231	Transport of Mature mRNA Derived from an Intronless Transcript	31	5.283E-08
152	R-HSA-180910	Vpr-mediated nuclear import of PICs	28	5.436E-08
153	R-HSA-176033	Interactions of Vpr with host cellular proteins	29	5.669E-08
154	R-HSA-5693538	Homology Directed Repair	64	6.304E-08
155	R-HSA-180746	Nuclear import of Rev protein	29	6.327E-08
156	R-HSA-9020702	Interleukin-1 signaling	51	7.940E-08
157	R-HSA-71291	Metabolism of amino acids and derivatives	151	8.457E-08
158	R-HSA-6782210	Gap-filling DNA repair synthesis and ligation in TC-NER	35	9.154E-08
159	R-HSA-159230	Transport of the SLBP Dependant Mature mRNA	29	9.683E-08
160	R-HSA-8939902	Regulation of RUNX2 expression and activity	41	9.957E-08
161	R-HSA-168274	Export of Viral Ribonucleoproteins from Nucleus	28	1.051E-07
162	R-HSA-5358346	Hedgehog ligand biogenesis	41	1.209E-07
163	R-HSA-6804756	Regulation of TP53 Activity through Phosphorylation	42	1.424E-07
164	R-HSA-195258	RHO GTPase Effectors	100	1.484E-07
165	R-HSA-3301854	Nuclear Pore Complex (NPC) Disassembly	29	1.798E-07
166	R-HSA-70326	Glucose metabolism	46	1.808E-07
167	R-HSA-167172	Transcription of the HIV genome	33	2.128E-07
168	R-HSA-9013694	Signaling by NOTCH4	39	2.129E-07
169	R-HSA-4608870	Asymmetric localization of PCP proteins	39	2.156E-07
170	R-HSA-446652	Interleukin-1 family signaling	54	2.159E-07
171	R-HSA-8948751	Regulation of PTEN stability and activity	40	2.159E-07
172	R-HSA-159227	Transport of the SLBP independent Mature mRNA	28	2.205E-07
173	R-HSA-3371453	Regulation of HSF1-mediated heat shock response	39	2.407E-07
174	R-HSA-4085377	SUMOylation of SUMOylation proteins	29	2.648E-07
175	R-HSA-1169091	Activation of NF-kappaB in B cells	39	3.059E-07
176	R-HSA-3371556	Cellular response to heat stress	43	3.196E-07
177	R-HSA-1236975	Antigen processing-Cross presentation	48	3.331E-07
178	R-HSA-674695	RNA Polymerase II Pre-transcription Events	37	3.638E-07
179	R-HSA-70171	Glycolysis	39	3.924E-07
180	R-HSA-168271	Transport of Ribonucleoproteins into the Host Nucleus	27	4.759E-07
181	R-HSA-1234174	Cellular response to hypoxia	44	5.075E-07
182	R-HSA-168333	NEP/NS2 Interacts with the Cellular Export Machinery	27	5.114E-07
183	R-HSA-5693567	HDR through Homologous Recombination (HRR) or Single Strand Annealing (SSA)	60	5.282E-07
184	R-HSA-2980766	Nuclear Envelope Breakdown	35	6.153E-07
185	R-HSA-6782135	Dual incision in TC-NER	34	6.336E-07
186	R-HSA-5621481	C-type lectin receptors (CLRs)	54	6.424E-07
187	R-HSA-73856	RNA Polymerase II Transcription Termination	36	6.656E-07
188	R-HSA-5578749	Transcriptional regulation by small RNAs	56	7.389E-07
189	R-HSA-3232142	SUMOylation of ubiquitylation proteins	30	7.470E-07

190	R-HSA-2454202	Fc epsilon receptor (FCERI) signaling	51	7.504E-07
191	R-HSA-109581	Apoptosis	67	7.846E-07
192	R-HSA-5668541	TNFR2 non-canonical NF-kB pathway	45	8.182E-07
193	R-HSA-9615933	Postmitotic nuclear pore complex (NPC) reformation	23	8.200E-07
194	R-HSA-69205	G1/S-Specific Transcription	22	8.729E-07
195	R-HSA-2995410	Nuclear Envelope (NE) Reassembly	37	1.057E-06
196	R-HSA-6799198	Complex I biogenesis	37	1.068E-06
197	R-HSA-5689880	Ub-specific processing proteases	73	1.081E-06
198	R-HSA-9707564	Cytoprotection by HMOX1	54	1.149E-06
199	R-HSA-5607764	CLEC7A (Dectin-1) signaling	46	1.156E-06
200	R-HSA-170822	Regulation of Glucokinase by Glucokinase Regulatory Protein	25	1.273E-06
201	R-HSA-5619107	Defective TPR may confer susceptibility towards thyroid papillary carcinoma (TPC)	25	1.273E-06
202	R-HSA-5688426	Deubiquitination	90	1.374E-06
203	R-HSA-6807505	RNA polymerase II transcribes snRNA genes	48	1.535E-06
204	R-HSA-6782315	tRNA modification in the nucleus and cytosol	27	1.615E-06
205	R-HSA-202403	TCR signaling	49	1.663E-06
206	R-HSA-8939236	RUNX1 regulates transcription of genes involved in differentiation of HSCs	57	1.751E-06
207	R-HSA-8949613	Cristae formation	22	1.888E-06
208	R-HSA-5685942	HDR through Homologous Recombination (HRR)	34	2.062E-06
209	R-HSA-211859	Biological oxidations	70	2.494E-06
210	R-HSA-168276	NS1 Mediated Effects on Host Pathways	30	2.730E-06
211	R-HSA-5687128	MAPK6/MAPK4 signaling	46	2.803E-06
212	R-HSA-195253	Degradation of beta-catenin by the destruction complex	43	3.399E-06
213	R-HSA-167161	HIV Transcription Initiation	24	4.504E-06
214	R-HSA-167162	RNA Polymerase II HIV Promoter Escape	24	4.504E-06
215	R-HSA-73776	RNA Polymerase II Promoter Escape	24	4.504E-06
216	R-HSA-73779	RNA Polymerase II Transcription Pre-Initiation And Promoter Opening	24	4.504E-06
217	R-HSA-75953	RNA Polymerase II Transcription Initiation	24	4.504E-06
218	R-HSA-76042	RNA Polymerase II Transcription Initiation And Promoter Clearance	24	4.504E-06
219	R-HSA-113510	E2F mediated regulation of DNA replication	16	7.091E-06
220	R-HSA-5693607	Processing of DNA double-strand break ends	46	7.331E-06
221	R-HSA-389957	Prefoldin mediated transfer of substrate to CCT/TriC	16	8.185E-06
222	R-HSA-69273	Cyclin A/B1/B2 associated events during G2/M transition	16	8.752E-06
223	R-HSA-389958	Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding	17	9.089E-06
224	R-HSA-5619084	ABC transporter disorders	40	1.066E-05
225	R-HSA-1169410	Antiviral mechanism by IFN-stimulated genes	38	1.122E-05
226	R-HSA-8878166	Transcriptional regulation by RUNX2	53	1.256E-05
227	R-HSA-5632684	Hedgehog 'on' state	44	1.282E-05
228	R-HSA-6781823	Formation of TC-NER Pre-Incision Complex	30	1.479E-05
229	R-HSA-174417	Telomere C-strand (Lagging Strand) Synthesis	25	1.507E-05
230	R-HSA-5696399	Global Genome Nucleotide Excision Repair (GG-NER)	37	1.595E-05
231	R-HSA-9711097	Cellular response to starvation	80	1.708E-05
232	R-HSA-211000	Gene Silencing by RNA	61	1.757E-05
233	R-HSA-5357801	Programmed Cell Death	71	1.808E-05
234	R-HSA-167169	HIV Transcription Elongation	25	1.962E-05
235	R-HSA-167200	Formation of HIV-1 elongation complex containing HIV-1 Tat	25	1.962E-05
236	R-HSA-167246	Tat-mediated elongation of the HIV-1 transcript	25	1.962E-05
237	R-HSA-69186	Lagging Strand Synthesis	18	1.968E-05
238	R-HSA-69473	G2/M DNA damage checkpoint	42	2.123E-05
239	R-HSA-176974	Unwinding of DNA	13	2.366E-05
240	R-HSA-112382	Formation of RNA Pol II elongation complex	29	2.690E-05

241	R-HSA-75955	RNA Polymerase II Transcription Elongation	29	2.690E-05
242	R-HSA-4086400	PCP/CE pathway	44	2.992E-05
243	R-HSA-5693579	Homologous DNA Pairing and Strand Exchange	29	3.015E-05
244	R-HSA-167152	Formation of HIV elongation complex in the absence of HIV Tat	26	3.039E-05
245	R-HSA-15869	Metabolism of nucleotides	38	3.917E-05
246	R-HSA-6796648	TP53 Regulates Transcription of DNA Repair Genes	29	5.643E-05
247	R-HSA-8951664	Neddylation	74	5.924E-05
248	R-HSA-110373	Resolution of AP sites via the multiple-nucleotide patch replacement pathway	20	6.026E-05
249	R-HSA-171319	Telomere Extension By Telomerase	17	6.306E-05
250	R-HSA-8878159	Transcriptional regulation by RUNX3	43	6.415E-05
251	R-HSA-5693616	Presynaptic phase of homologous DNA pairing and strand exchange	23	7.042E-05
252	R-HSA-162594	Early Phase of HIV Life Cycle	11	8.629E-05
253	R-HSA-212165	Epigenetic regulation of gene expression	55	8.751E-05
254	R-HSA-1169408	ISG15 antiviral mechanism	33	8.751E-05
255	R-HSA-73863	RNA Polymerase I Transcription Termination	17	8.925E-05
256	R-HSA-9609690	HCMV Early Events	55	0.0001
257	R-HSA-201681	TCF dependent signaling in response to WNT	78	0.0001
258	R-HSA-5619115	Disorders of transmembrane transporters	72	0.0001
259	R-HSA-75067	Processing of Capped Intronless Pre-mRNA	18	0.0001
260	R-HSA-5651801	PCNA-Dependent Long Patch Base Excision Repair	17	0.0001
261	R-HSA-167238	Pausing and recovery of Tat-mediated HIV elongation	22	0.0001
262	R-HSA-167243	Tat-mediated HIV elongation arrest and recovery	22	0.0001
263	R-HSA-1538133	G0 and Early G1	19	0.0001
264	R-HSA-167287	HIV elongation arrest and recovery	23	0.0001
265	R-HSA-167290	Pausing and recovery of HIV elongation	23	0.0001
266	R-HSA-983705	Signaling by the B Cell Receptor (BCR)	46	0.0001
267	R-HSA-606279	Deposition of new CENPA-containing nucleosomes at the centromere	34	0.0001
268	R-HSA-774815	Nucleosome assembly	34	0.0001
269	R-HSA-429958	mRNA decay by 3' to 5' exoribonuclease	12	0.0002
270	R-HSA-72187	mRNA 3'-end processing	28	0.0002
271	R-HSA-156711	Polo-like kinase mediated events	11	0.0002
272	R-HSA-2995383	Initiation of Nuclear Envelope (NE) Reformation	11	0.0002
273	R-HSA-68689	CDC6 association with the ORC:origin complex	12	0.0002
274	R-HSA-8878171	Transcriptional regulation by RUNX1	75	0.0002
275	R-HSA-389960	Formation of tubulin folding intermediates by CCT/Tric	14	0.0003
276	R-HSA-72086	mRNA Capping	18	0.0003
277	R-HSA-5684996	MAPK1/MAPK3 signaling	83	0.0003
278	R-HSA-2514853	Condensation of Prometaphase Chromosomes	12	0.0003
279	R-HSA-8978868	Fatty acid metabolism	57	0.0003
280	R-HSA-380320	Recruitment of NuMA to mitotic centrosomes	33	0.0003
281	R-HSA-5610787	Hedgehog 'off' state	45	0.0003
282	R-HSA-5673001	RAF/MAP kinase cascade	81	0.0003
283	R-HSA-6807070	PTEN Regulation	49	0.0004
284	R-HSA-75035	Chk1/Chk2(Cds1) mediated inactivation of Cyclin B:Cdk1 complex	10	0.0004
285	R-HSA-983712	Ion channel transport	57	0.0004
286	R-HSA-9609507	Protein localization	57	0.0004
287	R-HSA-69183	Processive synthesis on the lagging strand	14	0.0004
288	R-HSA-69091	Polymerase switching	12	0.0004
289	R-HSA-69109	Leading Strand Synthesis	12	0.0004
290	R-HSA-6791312	TP53 Regulates Transcription of Cell Cycle Genes	20	0.0004
291	R-HSA-113418	Formation of the Early Elongation Complex	18	0.0004

292	R-HSA-167158	Formation of the HIV-1 Early Elongation Complex	18	0.0004
293	R-HSA-174411	Polymerase switching on the C-strand of the telomere	19	0.0004
294	R-HSA-429914	Deadenylation-dependent mRNA decay	24	0.0005
295	R-HSA-3858494	Beta-catenin independent WNT signaling	55	0.0005
296	R-HSA-69166	Removal of the Flap Intermediate	13	0.0005
297	R-HSA-110314	Recognition of DNA damage by PCNA-containing replication complex	20	0.0006
298	R-HSA-167160	RNA Pol II CTD phosphorylation and interaction with CE during HIV infection	17	0.0006
299	R-HSA-77075	RNA Pol II CTD phosphorylation and interaction with CE	17	0.0006
300	R-HSA-2565942	Regulation of PLK1 Activity at G2/M Transition	34	0.0007
301	R-HSA-390450	Folding of actin by CCT/TriC	10	0.0007
302	R-HSA-73762	RNA Polymerase I Transcription Initiation	22	0.0007
303	R-HSA-73893	DNA Damage Bypass	22	0.0007
304	R-HSA-195721	Signaling by WNT	96	0.0008
305	R-HSA-380270	Recruitment of mitotic centrosome proteins and complexes	31	0.0008
306	R-HSA-380287	Centrosome maturation	31	0.0008
307	R-HSA-5696397	Gap-filling DNA repair synthesis and ligation in GG-NER	17	0.0008
308	R-HSA-9687139	Aberrant regulation of mitotic cell cycle due to RB1 defects	24	0.0009
309	R-HSA-5683057	MAPK family signaling cascades	82	0.0009
310	R-HSA-4570464	SUMOylation of RNA binding proteins	30	0.0009
311	R-HSA-380972	Energy dependent regulation of mTOR by LKB1-AMPK	12	0.0010
312	R-HSA-2990846	SUMOylation	65	0.0010
313	R-HSA-76071	RNA Polymerase III Transcription Initiation From Type 3 Promoter	16	0.0010
314	R-HSA-163210	Formation of ATP by chemiosmotic coupling	17	0.0010
315	R-HSA-73933	Resolution of Abasic Sites (AP sites)	23	0.0011
316	R-HSA-8854518	AURKA Activation by TPX2	29	0.0011
317	R-HSA-156580	Phase II - Conjugation of compounds	34	0.0011
318	R-HSA-3108214	SUMOylation of DNA damage response and repair proteins	44	0.0011
319	R-HSA-8956320	Nucleobase biosynthesis	14	0.0013
320	R-HSA-73884	Base Excision Repair	40	0.0013
321	R-HSA-5250913	Positive epigenetic regulation of rRNA expression	42	0.0014
322	R-HSA-176412	Phosphorylation of the APC/C	15	0.0014
323	R-HSA-382556	ABC-family proteins mediated transport	45	0.0014
324	R-HSA-5685938	HDR through Single Strand Annealing (SSA)	20	0.0014
325	R-HSA-5696400	Dual Incision in GG-NER	20	0.0015
326	R-HSA-167242	Abortive elongation of HIV-1 transcript in the absence of Tat	17	0.0016
327	R-HSA-5250941	Negative epigenetic regulation of rRNA expression	40	0.0016
328	R-HSA-140342	Apoptosis induced DNA fragmentation	8	0.0016
329	R-HSA-6803529	FGFR2 alternative splicing	19	0.0017
330	R-HSA-179409	APC-Cdc20 mediated degradation of Nek2A	19	0.0019
331	R-HSA-77588	SLBP Dependent Processing of Replication-Dependent Histone Pre-mRNAs	12	0.0019
332	R-HSA-9711123	Cellular response to chemical stress	55	0.0020
333	R-HSA-449147	Signaling by Interleukins	110	0.0021
334	R-HSA-110313	Translesion synthesis by Y family DNA polymerases bypasses lesions on DNA template	21	0.0023
335	R-HSA-5663202	Diseases of signal transduction by growth factor receptors and second messengers	109	0.0024
336	R-HSA-189483	Heme degradation	10	0.0025
337	R-HSA-194068	Bile acid and bile salt metabolism	18	0.0025
338	R-HSA-73780	RNA Polymerase III Chain Elongation	11	0.0026
339	R-HSA-5693554	Resolution of D-loop Structures through Synthesis-Dependent Strand Annealing (SDSA)	17	0.0026

340	R-HSA-9018519	Estrogen-dependent gene expression	52	0.0026
341	R-HSA-9675126	Diseases of mitotic cell cycle	24	0.0026
342	R-HSA-74158	RNA Polymerase III Transcription	25	0.0026
343	R-HSA-749476	RNA Polymerase III Abortive And Retractive Initiation	25	0.0026
344	R-HSA-174048	APC/C:Cdc20 mediated degradation of Cyclin B	17	0.0027
345	R-HSA-983168	Antigen processing: Ubiquitination & Proteasome degradation	84	0.0028
346	R-HSA-8950505	Gene and protein expression by JAK-STAT signaling after Interleukin-12 stimulation	16	0.0029
347	R-HSA-5358351	Signaling by Hedgehog	54	0.0030
348	R-HSA-9609646	HCMV Infection	59	0.0033
349	R-HSA-141405	Inhibition of the proteolytic activity of APC/C required for the onset of anaphase by mitotic spindle checkpoint components	16	0.0033
350	R-HSA-141430	Inactivation of APC/C via direct inhibition of the APC/C complex	16	0.0033
351	R-HSA-427413	NoRC negatively regulates rRNA expression	39	0.0033
352	R-HSA-397014	Muscle contraction	72	0.0033
353	R-HSA-76046	RNA Polymerase III Transcription Initiation	22	0.0033
354	R-HSA-5656169	Termination of translesion DNA synthesis	17	0.0034
355	R-HSA-5620912	Anchoring of the basal body to the plasma membrane	32	0.0037
356	R-HSA-3108232	SUMO E3 ligases SUMOylate target proteins	62	0.0037
357	R-HSA-5250924	B-WICH complex positively regulates rRNA expression	37	0.0041
358	R-HSA-211945	Phase I - Functionalization of compounds	35	0.0041
359	R-HSA-73772	RNA Polymerase I Promoter Escape	35	0.0042
360	R-HSA-2299718	Condensation of Prophase Chromosomes	31	0.0043
361	R-HSA-1483257	Phospholipid metabolism	74	0.0047
362	R-HSA-1660499	Synthesis of PIPs at the plasma membrane	19	0.0048
363	R-HSA-211897	Cytochrome P450 - arranged by substrate type	21	0.0048
364	R-HSA-2672351	Stimuli-sensing channels	42	0.0050
365	R-HSA-73854	RNA Polymerase I Promoter Clearance	41	0.0050
366	R-HSA-157118	Signaling by NOTCH	81	0.0052
367	R-HSA-76066	RNA Polymerase III Transcription Initiation From Type 2 Promoter	12	0.0052
368	R-HSA-77595	Processing of Intronless Pre-mRNAs	17	0.0052
369	R-HSA-189445	Metabolism of porphyrins	12	0.0053
370	R-HSA-9013418	RHOBTB2 GTPase cycle	16	0.0054
371	R-HSA-193807	Synthesis of bile acids and bile salts via 27-hydroxycholesterol	9	0.0060
372	R-HSA-73864	RNA Polymerase I Transcription	41	0.0063
373	R-HSA-110312	Translesion synthesis by REV1	12	0.0064
374	R-HSA-111367	SLBP independent Processing of Histone Pre-mRNAs	11	0.0066
375	R-HSA-1362300	Transcription of E2F targets under negative control by p107 (RBL1) and p130 (RBL2) in complex with HDAC1	12	0.0066
376	R-HSA-5696394	DNA Damage Recognition in GG-NER	21	0.0069
377	R-HSA-202670	ERKs are inactivated	6	0.0071
378	R-HSA-1362277	Transcription of E2F targets under negative control by DREAM complex	14	0.0072
379	R-HSA-8876725	Protein methylation	14	0.0072
380	R-HSA-203927	MicroRNA (miRNA) biogenesis	16	0.0074
381	R-HSA-390466	Chaperonin-mediated protein folding	21	0.0080
382	R-HSA-380259	Loss of Nlp from mitotic centrosomes	27	0.0080
383	R-HSA-380284	Loss of proteins required for interphase microtubule organization from the centrosome	27	0.0080
384	R-HSA-162658	Golgi Cisternae Pericentriolar Stack Reorganization	6	0.0085
385	R-HSA-76061	RNA Polymerase III Transcription Initiation From Type 1 Promoter	12	0.0091
386	R-HSA-176407	Conversion from APC/C:Cdc20 to APC/C:Cdh1 in late anaphase	13	0.0092
387	R-HSA-73980	RNA Polymerase III Transcription Termination	17	0.0092

388	R-HSA-5655862	Translesion synthesis by POLK	12	0.0092
389	R-HSA-73817	Purine ribonucleoside monophosphate biosynthesis	12	0.0092
390	R-HSA-3371568	Attenuation phase	10	0.0092
391	R-HSA-2046104	alpha-linolenic (omega3) and linoleic (omega6) acid metabolism	5	0.0092
392	R-HSA-2046106	alpha-linolenic acid (ALA) metabolism	5	0.0092
393	R-HSA-9706574	RHOBTB GTPase Cycle	18	0.0093
394	R-HSA-4551638	SUMOylation of chromatin organization proteins	35	0.0094
395	R-HSA-170670	Adenylate cyclase inhibitory pathway	7	0.0094
396	R-HSA-983169	Class I MHC mediated antigen processing & presentation	96	0.0104
397	R-HSA-9663891	Selective autophagy	27	0.0104
398	R-HSA-9687136	Aberrant regulation of mitotic exit in cancer due to RB1 defects	14	0.0107
399	R-HSA-9709957	Sensory Perception	67	0.0114
400	R-HSA-113501	Inhibition of replication initiation of damaged DNA by RB1/E2F1	11	0.0117
401	R-HSA-977606	Regulation of Complement cascade	10	0.0117
402	R-HSA-174414	Processive synthesis on the C-strand of the telomere	14	0.0119
403	R-HSA-192105	Synthesis of bile acids and bile salts	15	0.0122
404	R-HSA-2465910	MASTL Facilitates Mitotic Progression	9	0.0122
405	R-HSA-156584	Cytosolic sulfonation of small molecules	13	0.0126
406	R-HSA-110320	Translesion Synthesis by POLH	14	0.0126
407	R-HSA-9617828	FOXO-mediated transcription of cell cycle genes	9	0.0130
408	R-HSA-8956321	Nucleotide salvage	8	0.0130
409	R-HSA-156590	Glutathione conjugation	17	0.0132
410	R-HSA-2206281	Mucopolysaccharidoses	7	0.0133
411	R-HSA-9007101	Rab regulation of trafficking	48	0.0135
412	R-HSA-1852241	Organelle biogenesis and maintenance	79	0.0142
413	R-HSA-450513	Tristetraprolin (TTP, ZFP36) binds and destabilizes mRNA	11	0.0143
414	R-HSA-5358606	Mismatch repair (MMR) directed by MSH2:MSH3 (MutSbeta)	10	0.0144
415	R-HSA-211958	Miscellaneous substrates	7	0.0147
416	R-HSA-9675136	Diseases of DNA Double-Strand Break Repair	15	0.0148
417	R-HSA-9701193	Defective HDR through Homologous Recombination (HRR) due to PALB2 loss of function	15	0.0148
418	R-HSA-9704331	Defective HDR through Homologous Recombination Repair (HRR) due to PALB2 loss of BRCA1 binding function	15	0.0148
419	R-HSA-9704646	Defective HDR through Homologous Recombination Repair (HRR) due to PALB2 loss of BRCA2/RAD51/RAD51C binding function	15	0.0148
420	R-HSA-8851708	Signaling by FGFR2 IIIa TM	15	0.0148
421	R-HSA-8868766	rRNA processing in the mitochondrion	8	0.0148
422	R-HSA-2559586	DNA Damage/Telomere Stress Induced Senescence	27	0.0173
423	R-HSA-425393	Transport of inorganic cations/anions and amino acids/oligopeptides	34	0.0178
424	R-HSA-391251	Protein folding	30	0.0179
425	R-HSA-1834949	Cytosolic sensors of pathogen-associated DNA	19	0.0182
426	R-HSA-379724	tRNA Aminoacylation	19	0.0183
427	R-HSA-8948216	Collagen chain trimerization	12	0.0183
428	R-HSA-525793	Myogenesis	13	0.0187
429	R-HSA-5656121	Translesion synthesis by POLI	12	0.0193
430	R-HSA-9610379	HCMV Late Events	48	0.0203
431	R-HSA-9670095	Inhibition of DNA recombination at telomere	28	0.0207
432	R-HSA-5358508	Mismatch Repair	12	0.0212
433	R-HSA-352230	Amino acid transport across the plasma membrane	14	0.0215
434	R-HSA-6804116	TP53 Regulates Transcription of Genes Involved in G1 Cell Cycle Arrest	9	0.0226
435	R-HSA-9033241	Peroxisomal protein import	23	0.0226
436	R-HSA-1500620	Meiosis	35	0.0227

437	R-HSA-6804114	TP53 Regulates Transcription of Genes Involved in G2 Cell Cycle Arrest	10	0.0229
438	R-HSA-3371511	HSF1 activation	10	0.0238
439	R-HSA-8939211	ESR-mediated signaling	64	0.0238
440	R-HSA-400206	Regulation of lipid metabolism by PPARalpha	31	0.0242
441	R-HSA-174437	Removal of the Flap Intermediate from the C-strand	12	0.0250
442	R-HSA-2559584	Formation of Senescence-Associated Heterochromatin Foci (SAHF)	6	0.0269
443	R-HSA-1660661	Sphingolipid de novo biosynthesis	14	0.0269
444	R-HSA-1483255	PI Metabolism	31	0.0273
445	R-HSA-425407	SLC-mediated transmembrane transport	64	0.0275
446	R-HSA-9662361	Sensory processing of sound by outer hair cells of the cochlea	25	0.0275
447	R-HSA-5601884	PIWI-interacting RNA (piRNA) biogenesis	15	0.0275
448	R-HSA-9675135	Diseases of DNA repair	19	0.0284
449	R-HSA-211981	Xenobiotics	6	0.0287
450	R-HSA-9613829	Chaperone Mediated Autophagy	8	0.0287
451	R-HSA-8949215	Mitochondrial calcium ion transport	17	0.0290
452	R-HSA-5358565	Mismatch repair (MMR) directed by MSH2:MSH6 (MutSalpha)	12	0.0297
453	R-HSA-450604	KSRP (KHSRP) binds and destabilizes mRNA	10	0.0298
454	R-HSA-6804757	Regulation of TP53 Degradation	17	0.0298
455	R-HSA-211979	Eicosanoids	9	0.0304
456	R-HSA-390471	Association of TriC/CCT with target proteins during biosynthesis	12	0.0307
457	R-HSA-6783310	Fanconi Anemia Pathway	19	0.0307
458	R-HSA-390918	Peroxisomal lipid metabolism	13	0.0318
459	R-HSA-5693537	Resolution of D-Loop Structures	17	0.0320
460	R-HSA-1592230	Mitochondrial biogenesis	37	0.0324
461	R-HSA-428157	Sphingolipid metabolism	21	0.0327
462	R-HSA-375165	NCAM signaling for neurite out-growth	30	0.0328
463	R-HSA-5205647	Mitophagy	12	0.0333
464	R-HSA-2559583	Cellular Senescence	56	0.0333
465	R-HSA-1989781	PPARA activates gene expression	21	0.0342
466	R-HSA-2022857	Keratan sulfate degradation	6	0.0346
467	R-HSA-71240	Tryptophan catabolism	8	0.0347
468	R-HSA-68884	Mitotic Telophase/Cytokinesis	9	0.0351
469	R-HSA-3214858	RMTs methylate histone arginines	35	0.0356
470	R-HSA-5675221	Negative regulation of MAPK pathway	17	0.0368
471	R-HSA-8852135	Protein ubiquitination	28	0.0369
472	R-HSA-3781860	Diseases associated with N-glycosylation of proteins	11	0.0374
473	R-HSA-186797	Signaling by PDGF	15	0.0374
474	R-HSA-9639288	Amino acids regulate mTORC1	18	0.0374
475	R-HSA-70263	Gluconeogenesis	15	0.0378
476	R-HSA-390247	Beta-oxidation of very long chain fatty acids	8	0.0379
477	R-HSA-9662360	Sensory processing of sound by inner hair cells of the cochlea	30	0.0379
478	R-HSA-1257604	PIP3 activates AKT signaling	68	0.0379
479	R-HSA-211935	Fatty acids	8	0.0382
480	R-HSA-5576891	Cardiac conduction	37	0.0416
481	R-HSA-193648	NRAGE signals death through JNK	31	0.0424
482	R-HSA-975634	Retinoid metabolism and transport	10	0.0425
483	R-HSA-428540	Activation of RAC1	9	0.0436
484	R-HSA-9013148	CDC42 GTPase cycle	77	0.0437
485	R-HSA-3371571	HSF1-dependent transactivation	11	0.0442
486	R-HSA-3371497	HSP90 chaperone cycle for steroid hormone receptors (SHR) in the presence of ligand	17	0.0448
487	R-HSA-5689901	Metalloprotease DUBs	20	0.0461

488	R-HSA-174430	Telomere C-strand synthesis initiation	10	0.0466
489	R-HSA-74217	Purine salvage	10	0.0496
490	R-HSA-2029485	Role of phospholipids in phagocytosis	14	0.0497
491	R-HSA-204998	Cell death signalling via NRAGE, NRIF and NADE	37	0.0499
492	R-HSA-77289	Mitochondrial Fatty Acid Beta-Oxidation	20	0.0504