Полнотранскриптомный анализ опухоли молочной железы в процессе неоадъювантной химиотерапии: связь с ответом на предоперационную химиотерапию. Дополнительный материал

М.К. Ибрагимова[1, 2], М.М. Цыганов[1], Н.В. Литвяков[1, 3]

[1]ФГБНУ «Томский национальный исследовательский медицинский центр Российской академии наук»; Россия, 634009 Томск, Кооперативный пер., 5;
[2]ФГАОУ ВО «Национальный исследовательский Томский государственный университет»; Россия, 634050 Томск, проспект Ленина, 36;
[3]Северский биофизический научный центр Федерального медико-биологического агентства России; Россия, 636039 Северск, Коммунистический проспект, 87

Whole transcriptome analysis of breast tumors during neoadjuvant chemotherapy: association with response to preoperative chemotherapy. Additional material

M.K. Ibragimova[1, 2], M.M. Tsyganov[1], N.V. Litviakov[1, 3]

[1]Cancer Research Institute, Tomsk National Research Medical Center of the Russian Academy of Sciences; 5 Kooperativny St., Tomsk 634009, Russia;
[2]Tomsk State University; 36 Lenin Prospekt, Tomsk 634050, Russia;
[3]Seversk Biophysical Research Center of the Federal Medical and Biological Agency; 87 Kommunistichesky Prospekt, Seversk 636039, Russia

Таблица 2. *Сигнальные клеточные пути, активность которых статистически значимо отличается при сравнении экспрессионного профиля пациенток при проведении неоадъювантной химиотерапии*

Table 2. *Signaling pathways whose activity differed significantly between patients during neoadjuvant chemotherapy when comparing their expression profiles*

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	**Down-гены** Down-regulated genes	**Количество down-генов, шт.** Number of down-regulated genes, pcs.	***p***
Malignant pleural mesothelioma	20	*EZH2*	1	*IGF1, WIF1, IL6, MET, HBEGF, NLRP3, PAK3, PDGFD, IGF2, CDH6, TEK, NTRK2, FGF10, ANGPT1, FGF14, SFRP1, ROR1, ADAMTS1, SELE*	19	0,001269
VEGFA/VEGFR2	18	–	0	*PRKD1, PTPRZ1, KL, PTGS2, EGR1, NR4A3, SELE, ADAMTS1, HBEGF, S1PR1, LDB2, DLL4, SLC2A14, CCRL2, SEMA6D, CYR61, TMOD1, TUBA1C*	18	0,010526
Orexin receptor pathway	16	*RARA, SPP1*	2	*PDE11A, FOS, LIPE, CGA, PRKD1, ADIPOQ, NR4A3, EGR1, EGR2, HBEGF, FOSB, IL6, SELE, IL1B*	14	0,000001
PI3K/Akt	16	*SPP1, MYB*	2	*COL1A2, RELN, COL1A1, FGF10, ANGPT1, FGF14, IGF1, IGF2, PDGFD, MET, TEK, LPAR4, IL6, NTRK2*	14	0,003203
Focal adhesion: PI3K/Akt/mTOR	16	*SPP1, COL11A1*	2	*COL1A2, RELN, COL1A1, FGF10, ANGPT1, FGF14, IGF1, PDGFD, MET, TEK, LPAR4, PPARGC1A, PFKFB1, LIPE*	14	0,000754
Nuclear receptors meta-pathway	15	–	0	*SPRY1, HBEGF, CES1, PPARGC1A, PDK4, RGS2, PTGS2, IL1B, MGAM, EGR1, NRG1, SLC2A12, SLC2A14, GSTM5, SLC6A16*	15	0,004732

Продолжение табл. 2
Continuation of table 2

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	**Down-гены** Down-regulated genes	**Количество down-генов, шт.** Number of down-regulated genes, pcs.	***p***
PodNet: protein-protein interactions in the podocyte	14	*ADCY1, SPP1, RARA*	3	*WIF1, TRPC6, PTGS2, CLIC5, ANGPT1, IGF1, NTRK3, NRN1, NRXN1, MAGI2, MET*	11	0,006865
Spinal cord injury	13	–	0	*AQP1, PTPRZ1, ZFP36, IL1B, IL6, FOS, EGR1, SLIT1, SLIT2, IL1R1, SELP, TACR1, PTGS2*	13	0,000001
Myometrial relaxation and contraction	12	*ADCY1*	1	*IGFBP6, FOS, RGS2, IL6, RGS1, IL1B, PRKD1, ATF3, ADCY4, IGFBP1, PKIA*	11	0,000125
MAPK	11	–	0	*RASGRP4, DUSP1, IL1R1, FOS, IL1B, NTRK2, CACNA2D3, CACNB2, CACNA1H, FGF10, FGF14*	11	0,020764
Sudden infant death syndrome susceptibility	10	*MYB*	1	*TACR1, MAOA, PPARGC1A, VIPR2, IL6, EGR1, NTRK2, SCN4B, IL1B*	9	0,002201
Endothelin pathway	10	–	0	*PTGS2, PLCB1,COL1A1, IL1B, COL1A2, IL6, FOS, EGR1, TCF4, ADIPOQ*	10	0,010055
Circadian rhythm genes	10	*ADCY1, EZH2*	2	*EGR1, ADIPOQ, PER3, NTRK3, IL6, PROX1, PPARGC1A, SIK1*	8	0,011824
Focal adhesion	9	*SPP1*	1	*COL1A1, PDGFD, MET, RELN, PAK3, FIGF, COL1A2, IGF1*	8	0,039641
Neuroinflammation and glutamatergic signaling	8	*ADCY1*	1	*IL6, IL1R1, IL1B, GRIA4, PLCB1, IGF1, FOS*	7	0,009951
Development of ureteric collection system	8	*RARA*	1	*GPC3, FOXC1, BMP5, SHH, SPRY1, SLIT2, FREM1*	7	0,000041
NRF2	8	–	0	*SLC2A14, CES1, SLC2A12, NRG1, EGR1, HBEGF, GSTM5, SLC6A16*	8	0,011219
Hair follicle development: cytodifferentiation – part 3 of 3	8	–	0	*FOS, WIF1, SFRP1, DSG1, CD34, FOSB, EGR2, TCF4*	8	0,000741
Adipogenesis	8	*RARA*	1	*IGF1, ADIPOQ, IL6, PPARGC1A, FRZB, EGR2, LIPE*	7	0,006782
Calcium regulation in cardiac cells	7	*ADCY1*	1	*ADCY4, RGS1, KCNB1, PRKD1, PKIA, RGS2*	6	0,045663
Overview of proinflammatory and profibrotic mediators	7	*SPP1, CXCL11*	2	*IL6, IL1B, IL33, XCL2, PPBP*	5	0,021501
AXL	7	*MKI67*	1	*NLRP3, NRG1, MITF, MET, IL1B, COL1A1*	6	0,017823
Hematopoietic stem cell differentiation	7	*MYB*	1	*FOS, CD34, FOSB, PRDM5, IL6, IL1B*	6	0,003377
Hippo signaling regulation	6	–	0	*CDH6, GNAL, PLCB1, MET, TEK, NTRK2*	6	0,017823
Lung fibrosis	6	*SPP1*	1	*IL6, ELN, IL1B, CMA1, IGF1*	5	0,002303
G protein signaling	6	*ADCY1*	1	*ADCY4, PDE1A, GNAL, PRKD1, AKAP12*	5	0,013402

Продолжение табл. 2
Continuation of table 2

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	**Down-гены** Down-regulated genes	**Количество down-генов, шт.** Number of down-regulated genes, pcs.	***p***
Corticotropin-releasing hormone signaling	6	–	0	*CRHBP, CACNA1H, FOS, FOSB, TCF4, CASP12*	6	0,015504
Prostaglandin synthesis and regulation	5	–	0	*PTGFR, PTGS2, HPGDS, MITF, PPARGC1A*	5	0,002778
Hypertrophy model	5	–	0	*IL1R1, NR4A3, ATF3, CYR61, HBEGF*	5	0,000049
EGFR tyrosine kinase inhibitor resistance	5	–	0	*NRG1, IGF1, PDGFD, IL6, MET*	5	0,034230
Hippo-merlin signaling dysregulation	5	–	0	*CDH6, MET, TEK, NTRK2, PAK3*	5	0,049261
IL-1 and megakaryocytes in obesity	5	–	0	*IL1R1, IL1B, NLRP3, FCER1A, HBEGF*	5	0,000126
Galanin receptor	4	–	0	*FOS, IL6, ADIPOQ, PPARGC1A*	4	0,000888
Phosphodiesterases in neuronal function	4	*ADCY1*	1	*ADCY4, PDE11A, PDE1A*	3	0,025605
BMP signaling in eyelid development	4	–	0	*FGF10, SHH, SFRP1, FOXC1*	4	0,000731
Photodynamic therapy-induced NF-κB survival signaling	4	–	0	*IL1B, IL6, PTGS2, SELE*	4	0,006153
Pre-implantation embryo	4	–	0	*NR3C2, EGR1, ZFP36, FOSB*	4	0,036098
Pluripotent stem cell differentiation	4	–	0	*SHH, IGF1, FGF10, IL6*	4	0,018462
Prostaglandin signaling	3	–	0	*IL6, IL1B, NLRP3*	3	0,032075
PPAR β/δ	3	–	0	*PDK4, PTGS2, IL1B*	3	0,013674
PPAR-γ	3	–	0	*PTGS2, ADIPOQ, IL1B*	3	0,049230
Angiotensin II receptor type 1	3	–	0	*PDGFD, COL1A1, COL1A2*	3	0,020802
GPR143 in melanocytes and retinal pigment epithelium cells	3	–	0	*ADCY4, PLCB1, MITF*	3	0,027251
COVID-19 adverse outcome	3	–	0	*IL1B, TMPRSS2, IL6*	3	0,003538
GDNF/RET signaling axis	3	–	0	*SPRY1, FOXC1, SLIT2*	3	0,012152
FBXL10 enhancement of MAP/ERK signaling in diffuse large B-cell lymphoma	3	*EZH2, HIST1H3F, H2AFX*	3	–	0	0,037314
Inflammatory response pathway	3	–	0	*COL1A1, COL1A2, IL5RA*	3	0,032075
Signal transduction through IL1R	3	–	0	*IL6, IL1R1, IL1B*	3	0,032075

Продолжение табл. 2
Continuation of table 2

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	**Down-гены** Down-regulated genes	**Количество down-генов, шт.** Number of down-regulated genes, pcs.	***p***
Extracellular vesicles in the crosstalk of cardiac cells	3	*SPP1*	1	*IL6, IGF1*	2	0,012152
Oxidative stress response	3	–	0	*FOS, XDH, MAOA*	3	0,032075
Ethanol effects on histone modifications	3	–	0	*ADH1B, ADH1C, ALDH1A2*	3	0,027251
Photodynamic therapy-induced HIF-1 survival signaling	3	–	0	*PTGS2, ANGPT1, IGFBP1*	3	0,042961
Photodynamic therapy-induced NFE2L2 (NRF2) survival signaling	3	–	0	*ABCG2, FOS, CES1*	3	0,012152
Transcription factor regulation in adipogenesis	3	–	0	*ADIPOQ, PPARGC1A, IL6*	3	0,010733
Sleep regulation	3	–	0	*FOS, IL6, PER3*	3	0,045936
Gastric cancer network 1	3	*CENPF, UBE2C, TPX2*	3	–	0	0,022847
Irinotecan	3	–	0	*CES1, BCHE, ABCG2*	3	0,002295
Serotonin transporter activity	3	–	0	*IL1B, MAOA, IL1R1*	3	0,001366
ACE inhibitor	2	–	0	*CMA1, NR3C2*	2	0,049230
ACE inhibitor pathway – for workshop	2	–	0	*CMA1, NR3C2*	2	0,029840
Activation of NLRP3 inflammasome by SARS-CoV-2	2	–	0	*NLRP3, IL1B*	2	0,017949
Cells and molecules involved in local acute inflammatory response	2	–	0	*IL6, SELP*	2	0,049230
PTF1A related regulatory pathway	2	–	0	*PROX1, FGF10*	2	0,021634
Nanomaterial-induced inflammasome activation	2	–	0	*IL1B, NLRP3*	2	0,014561
Fatty acid omega-oxidation	2	–	0	*ADH1C, ADH1B*	2	0,039072
miR-targeted genes in muscle cell	2	–	0	*MET, ABCG2*	2	0,014557
miR-targeted genes in lymphocytes	2	–	0	*ABCG2, MET*	2	0,002547

Окончание табл. 2
The end of table 2

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	**Down-гены** Down-regulated genes	**Количество down-генов, шт.** Number of down-regulated genes, pcs.	***p***
Effects of nitric oxide	2	–	0	*AOX1, XDH*	2	0,011485
Phase I biotransformations, non P450	2	–	0	*PON3, CES1*	2	0,011485
Anti-inflammatory response favouring Leishmania parasite infection	1	–	0	*IL6*	1	0,034617
G alpha(s) signaling events	1	–	0	*GNAL*	1	0,000094
TCF dependent signaling in response to WNT	1	–	0	*WIF1*	1	0,016382
Fc epsilon receptor signaling	1	–	0	*FOS*	1	0,035004
Glycosaminoglycan metabolism	1	–	0	*UST*	1	0,001332
miR-targeted genes in epithelium	1	–	0	*MET*	1	0,007992

Таблица 3. *Уровень экспрессии дифференциально экспрессирующихся генов в опухоли молочной железы до лечения в зависимости от ответа на неоадъювантную химиотерапию*

Table 3. *Pretreatment expression of differentially expressed genes in breast cancer depending on patients' response to neoadjuvant chemotherapy*

Ген Gene	**Полная и частичная регрессия** Full and partial regression	**Стабилизация и прогрессирование** Stabilization and progression	**Диапазон изменения** Fold Change	***p***	**FDR *p***
ADAMDEC1	680,3 ± 2,8	87,4 ± 2,3	–7,77	3,13E–09	6,09E–06
MMP9	1370,0 ± 3,1	266,9 ± 2,8	–5,12	6,39E–07	0,0003
GZMK	1234,7 ± 3,3	247,3 ± 3,4	–5,01	0,0006	0,034
CXCL13	487,8 ± 4,9	99,7 ± 2,4	–4,9	1,62E–06	0,0006
PXMP4	385,3 ± 3,3	86,2 ± 2,8	–4,48	0,0008	0,0382
LAX1	477,7 ± 3,5	111,4 ± 2,6	–4,27	0,0004	0,0253
TMEM53	290,0 ± 3,5	68,6 ± 3,0	–4,23	0,0007	0,036
LRRIQ1	335,5 ± 2,6	81,0 ± 3,2	–4,16	0,0008	0,0387
ZDBF2	390,7 ± 2,0	94,4 ± 2,1	–4,14	1,90E–06	0,0007
COQ4	548,7 ± 2,0	142,0 ± 1,6	–3,88	6,94E–11	4,96E–07
NAGA	226,0 ± 2,0	58,1 ± 2,3	–3,88	4,63E–05	0,0062
BEX5	310,8 ± 2,6	84,4 ± 2,8	–3,68	0,0003	0,0225
GYPC	1152,1 ± 1,8	315,2 ± 1,9	–3,67	3,63E–07	0,0002

Продолжение табл. 3
Continuation of table 3

Ген Gene	Полная и частичная регрессия Full and partial regression	Стабилизация и прогрессирование Stabilization and progression	Диапазон изменения Fold Change	*p*	FDR *p*
CD84	1128,4 ± 2,8	310,8 ± 2,5	–3,63	0,0002	0,0195
PKIG	1089,9 ± 2,1	304,4 ± 1,9	–3,58	1,45E–05	0,0028
SEMA4A	996,0 ± 2,0	280,1 ± 1,9	–3,57	1,09E–06	0,0005
UBD	2856,4 ± 3,7	814,6 ± 3,1	–3,51	0,0009	0,0423
KIF5C	221,3 ± 2,4	63,6 ± 1,9	–3,5	8,10E–07	0,0004
MGST1	324,0 ± 3,1	94,4 ± 2,4	–3,43	0,0003	0,0204
LCP2	584,1 ± 2,2	171,3 ± 2,0	–3,41	0,0003	0,0212
ZBTB34	330,8 ± 1,7	97,0 ± 2,0	–3,4	9,59E–09	1,29E–05
MLXIP	1418,4 ± 2,1	418,8 ± 2,0	–3,4	3,29E–06	0,0011
TNFRSF9	508,5 ± 2,9	149,1 ± 2,4	–3,4	0,0005	0,0286
SAMD3	114,6 ± 2,4	34,1 ± 1,9	–3,38	1,72E–07	0,0001
NCKAP1L	342,5 ± 2,0	104,0 ± 2,0	–3,29	1,41E–07	0,0001
TRIM14	1618,0 ± 1,6	505,0 ± 1,7	–3,21	2,75E–09	5,89E–06
MTRNR2L6	556,4 ± 1,5	173,6 ± 2,3	–3,2	8,26E–05	0,0092
PLEKHA2	352,1 ± 1,9	111,4 ± 2,3	–3,15	0,0003	0,0225
TOR4A	471,1 ± 1,3	153,3 ± 1,4	–3,06	1,65E–19	3,54E–15
OR10Q1	108,4 ± 1,5	35,8 ± 1,3	–3,02	2,11E–14	2,27E–10
U2AF2	2091,0 ± 2,1	694,6 ± 2,3	–3,02	0,0008	0,039
PGM2L1	487,8 ± 1,7	162,0 ± 2,0	–3	3,67E–06	0,0011
SGSH	237,2 ± 1,5	80,4 ± 1,7	–2,94	1,80E–06	0,0007
GBP2	1305,2 ± 2,3	445,7 ± 1,7	–2,93	0,0001	0,0119
ZNF676	407,3 ± 2,4	140,1 ± 1,4	–2,92	7,50E–06	0,0018
ALOX5	78,2 ± 1,7	26,9 ± 1,5	–2,9	2,09E–09	5,59E–06
SMAD1	522,8 ± 1,5	183,5 ± 1,6	–2,86	4,93E–08	4,80E–05
NFU1	2486,7 ± 1,8	873,1 ± 1,9	–2,85	5,88E–06	0,0016
IL15	250,7 ± 1,8	88,6 ± 1,9	–2,83	8,98E–06	0,002
KANSL1	1278,3 ± 1,9	451,9 ± 1,9	–2,83	3,05E–05	0,0044
SCN7A	83,3 ± 1,8	29,7 ± 2,0	–2,82	0,0006	0,0317
FAM105A	229,1 ± 1,9	81,6 ± 1,7	–2,81	3,13E–07	0,0002
TM4SF18	1370,0 ± 2,6	491,1 ± 2,4	–2,79	0,0011	0,0483
CXADR	235,6 ± 2,2	84,4 ± 1,9	–2,78	0,0004	0,0255
VNN1	163,1 ± 1,6	58,9 ± 1,4	–2,76	1,19E–05	0,0025
RGL1	942,3 ± 2,0	347,3 ± 1,8	–2,72	2,44E–05	0,0039
ZNF268	643,6 ± 2,6	237,2 ± 1,8	–2,71	0,0006	0,0319

Продолжение табл. 3
Continuation of table 3

Ген Gene	Полная и частичная регрессия Full and partial regression	Стабилизация и прогрессирование Stabilization and progression	Диапазон изменения Fold Change	*p*	FDR *p*
C15orf39	183,5 ± 1,5	69,1 ± 1,5	–2,67	2,39E–09	5,70E–06
CCSER1	240,5 ± 1,9	89,9 ± 1,9	–2,67	0,0002	0,0158
TRPC3	103,3 ± 1,9	39,1 ± 1,9	–2,64	5,69E–05	0,0073
CCDC74B	439,6 ± 2,3	166,6 ± 2,3	–2,64	0,0003	0,0227
CELF2	1136,2 ± 2,3	445,7 ± 2,2	–2,56	0,0006	0,0343
CRTC2	2005,9 ± 2,2	786,9 ± 2,2	–2,55	0,0002	0,0146
ATP6V0A4	159,8 ± 2,9	63,1 ± 1,7	–2,53	0,001	0,045
GAA	803,4 ± 1,8	319,6 ± 1,5	–2,52	1,08E–07	8,61E–05
XCL2	90,5 ± 2,0	36,0 ± 2,1	–2,52	0,0011	0,0477
TIAF1	505,0 ± 2,0	202,3 ± 2,1	–2,5	8,11E–05	0,0091
SLFN12	1184,4 ± 2,2	477,7 ± 1,7	–2,49	0,0002	0,0186
LMAN2L	199,5 ± 1,8	81,0 ± 1,7	–2,46	2,82E–05	0,0042
CSTF2	143,0 ± 1,6	58,1 ± 1,7	–2,46	3,20E–05	0,0046
APOBEC3F	259,6 ± 2,4	105,4 ± 2,1	–2,46	0,0011	0,0479
ARSJ	117,0 ± 2,1	47,8 ± 1,8	–2,45	3,60E–05	0,005
ACSL5	1217,7 ± 2,2	498,0 ± 1,6	–2,45	5,69E–05	0,0073
PYHIN1	410,1 ± 2,6	167,7 ± 1,8	–2,45	0,0009	0,0428
TLR4	1136,2 ± 2,2	464,6 ± 1,8	–2,44	0,0001	0,0119
FAM84B	176,1 ± 2,3	72,5 ± 1,9	–2,43	0,001	0,0451
STOX2	398,9 ± 2,2	164,3 ± 1,9	–2,42	5,03E–05	0,0066
CLEC7A	181,0 ± 2,4	75,1 ± 1,7	–2,42	0,0001	0,0107
R3HDM1	71,5 ± 2,0	29,4 ± 1,7	–2,42	0,0002	0,0162
XRN1	855,1 ± 1,6	354,6 ± 1,6	–2,41	0,0001	0,0107
LRRC69	222,9 ± 1,8	93,7 ± 1,7	–2,39	2,20E–06	0,0008
GSPT2	484,4 ± 1,6	202,3 ± 1,9	–2,39	3,60E–06	0,0011
TTI2	719,1 ± 2,1	300,2 ± 1,8	–2,39	0,0004	0,0262
ZMAT3	82,1 ± 1,7	34,5 ± 1,5	–2,37	9,78E–08	8,06E–05
C11orf71	192,7 ± 1,5	81,6 ± 1,4	–2,36	5,18E–08	4,81E–05
ZNF595	2556,6 ± 1,7	1097,5 ± 2,3	–2,34	0,0002	0,0155
FAM175B	6338,8 ± 1,9	2702,4 ± 2,2	–2,34	0,0004	0,0266
GNL1	191,3 ± 1,7	82,1 ± 1,6	–2,33	0,0001	0,0135
TBXAS1	369,6 ± 2,0	158,7 ± 1,7	–2,33	0,001	0,045
NBPF19	4451,3 ± 2,0	1924,1 ± 1,7	–2,31	0,0012	0,0495
STAP1	121,9 ± 2,6	53,1 ± 1,6	–2,3	7,36E–05	0,0086
SIK3	282,1 ± 1,9	122,8 ± 1,5	–2,3	0,0003	0,02

Продолжение табл. 3
Continuation of table 3

Ген Gene	Полная и частичная регрессия Full and partial regression	Стабилизация и прогрессирование Stabilization and progression	Диапазон изменения Fold Change	*p*	FDR *p*
HLA-A	1897,7 ± 2,0	826,0 ± 2,3	–2,3	0,0004	0,0247
GALR3	91,8 ± 1,5	40,2 ± 1,4	–2,29	5,28E–10	2,27E–06
STX11	120,3 ± 1,7	52,7 ± 1,7	–2,28	9,43E–05	0,01
ADAT1	477,7 ± 1,8	210,8 ± 1,6	–2,28	0,0001	0,0138
MAPK13	144,0 ± 1,4	63,1 ± 1,4	–2,27	4,51E–06	0,0013
SLC9A6	843,4 ± 1,7	372,2 ± 1,7	–2,27	9,88E–06	0,0022
YBX3	6793,8 ± 2,3	2998,4 ± 2,1	–2,27	0,001	0,0444
ZNF175	424,6 ± 2,1	190,0 ± 1,8	–2,25	7,66E–05	0,0089
CYP4F11	131,6 ± 2,7	59,3 ± 1,6	–2,21	0,0002	0,0168
YPEL2	474,4 ± 2,1	215,3 ± 2,0	–2,21	0,0009	0,0417
CRYGS	471,1 ± 2,3	212,3 ± 2,1	–2,21	0,0011	0,0479
CACNB2	192,7 ± 1,9	87,4 ± 1,3	–2,2	2,14E–05	0,0036
MAP3K7CL	187,4 ± 1,9	85,0 ± 1,6	–2,2	2,38E–05	0,0039
MTRNR2L7	300,2 ± 1,7	136,2 ± 1,8	–2,2	5,70E–05	0,0073
SAMD15	143,0 ± 2,1	64,9 ± 2,0	–2,2	7,97E–05	0,009
ANKRD29	213,8 ± 1,8	97,7 ± 1,7	–2,2	0,0004	0,0255
TRUB2	132,5 ± 2,0	60,1 ± 1,9	–2,2	0,0004	0,0266
COMMD9	113,8 ± 1,8	52,0 ± 1,4	–2,19	2,58E–07	0,0002
KLHDC7A	42,2 ± 1,8	19,3 ± 1,4	–2,19	5,05E–06	0,0014
FAM122C	256,0 ± 1,6	117,0 ± 1,4	–2,19	9,71E–06	0,0022
TRMT12	188,7 ± 1,8	86,2 ± 1,8	–2,19	0,0007	0,0361
RGMB	247,3 ± 1,5	113,0 ± 1,9	–2,19	0,0008	0,0386
PRIM2	242,2 ± 1,7	110,7 ± 1,7	–2,18	7,26E–07	0,0004
SEMA3B	259,6 ± 1,5	118,6 ± 1,7	–2,18	7,10E–06	0,0018
ZCWPW2	117,0 ± 1,4	54,2 ± 1,5	–2,16	2,21E–07	0,0001
CSRNP1	90,5 ± 1,9	41,9 ± 1,2	–2,15	3,07E–07	0,0002
YPEL1	53,1 ± 1,3	24,8 ± 1,9	–2,15	0,0001	0,0134
KSR1	652,6 ± 1,7	304,4 ± 1,4	–2,14	2,88E–06	0,001
GATAD2A	70,0 ± 1,7	32,7 ± 1,4	–2,14	9,24E–05	0,0099
TRANK1	133,4 ± 1,7	62,2 ± 1,7	–2,14	0,0001	0,0107
CTIF	81,0 ± 1,5	38,3 ± 1,5	–2,12	2,38E–06	0,0008
MALL	315,2 ± 1,9	149,1 ± 1,6	–2,12	7,41E–06	0,0018
LMNB2	107,6 ± 1,6	50,9 ± 1,6	–2,12	0,0002	0,0191
MRPL57	661,7 ± 1,9	310,8 ± 1,7	–2,12	0,0008	0,0382
CIPC	639,1 ± 1,9	302,3 ± 2,0	–2,12	0,001	0,0449

Продолжение табл. 3
Continuation of table 3

Ген Gene	Полная и частичная регрессия Full and partial regression	Стабилизация и прогрессирование Stabilization and progression	Диапазон изменения Fold Change	*p*	FDR *p*
MAP3K3	337,8 ± 1,7	160,9 ± 1,6	–2,11	2,48E–06	0,0009
ZNF594	333,1 ± 1,8	158,7 ± 1,5	–2,11	3,94E–05	0,0053
SLC27A4	477,7 ± 1,8	227,5 ± 1,8	–2,11	0,0003	0,0237
KIAA1958	533,7 ± 2,2	254,2 ± 2,1	–2,11	0,0008	0,0403
RASSF2	564,2 ± 2,1	266,9 ± 2,0	–2,11	0,001	0,0449
SLC25A46	519,1 ± 2,1	245,6 ± 1,8	–2,11	0,0011	0,0479
MBLAC2	200,9 ± 1,7	95,7 ± 1,2	–2,1	4,65E–10	2,27E–06
DYRK1B	548,7 ± 1,5	261,4 ± 1,4	–2,1	5,38E–08	4,81E–05
ATG16L1	477,7 ± 1,7	227,5 ± 1,8	–2,1	0,0002	0,0158
AGFG2	342,5 ± 1,9	163,1 ± 1,8	–2,1	0,0011	0,047
LRRC23	448,8 ± 1,6	215,3 ± 1,7	–2,09	0,0001	0,0106
CDK2AP1	154,3 ± 1,6	74,0 ± 1,9	–2,09	0,0002	0,0158
PKN1	897,6 ± 1,4	430,5 ± 1,9	–2,08	1,02E–06	0,0005
TAS2R3	141,0 ± 1,5	67,6 ± 1,8	–2,08	0,0003	0,02
METTL8	1978,2 ± 1,9	948,8 ± 1,7	–2,08	0,001	0,045
SLAMF8	377,4 ± 2,1	182,3 ± 1,7	–2,08	0,0011	0,0477
KLHL6	48,8 ± 1,5	23,6 ± 1,6	–2,07	7,79E–05	0,009
C22orf29	308,7 ± 1,8	149,1 ± 1,6	–2,07	8,61E–05	0,0095
DNAJC6	73,0 ± 2,0	35,5 ± 1,5	–2,07	0,0005	0,03
CYP4F3	140,1 ± 1,7	68,1 ± 1,4	–2,06	1,40E–05	0,0028
ESM1	424,6 ± 2,0	206,5 ± 1,7	–2,06	0,0005	0,0282
VPS52	401,7 ± 2,4	195,4 ± 2,1	–2,05	0,0004	0,0266
NF2	207,9 ± 1,8	101,8 ± 1,7	–2,05	0,0011	0,0482
BRPF1	178,5 ± 1,6	88,0 ± 1,4	–2,03	4,41E–06	0,0013
ALPL	45,9 ± 1,8	22,6 ± 1,4	–2,03	2,39E–05	0,0039
MICB	171,3 ± 2,0	84,4 ± 1,6	–2,03	0,0004	0,028
NFAM1	268,7 ± 1,4	133,4 ± 1,3	–2,02	9,25E–09	1,29E–05
TRIM21	584,1 ± 1,9	290,0 ± 1,6	–2,02	3,65E–05	0,005
DRAM1	290,0 ± 2,5	143,0 ± 1,9	–2,02	0,0011	0,047
GRAP2	82,1 ± 2,0	40,8 ± 1,7	–2,01	0,0002	0,0188
DYRK4	568,1 ± 1,6	282,1 ± 1,5	–2,01	0,0003	0,0204
ASB7	481,0 ± 1,7	238,9 ± 2,4	–2,01	0,0004	0,0266
SEMA6A	744,4 ± 1,9	372,2 ± 1,8	–2,01	0,0011	0,048
TMEM184A	200,9 ± 1,4	100,4 ± 1,4	–2	7,79E–06	0,0019
CCL4L2	127,1 ± 1,6	63,6 ± 1,6	–2	8,97E–05	0,0097

Окончание табл. 3
The end of table 3

Ген Gene	Полная и частичная регрессия Full and partial regression	Стабилизация и прогрессирование Stabilization and progression	Диапазон изменения Fold Change	*p*	FDR *p*
ISPD	79,3 ± 2,2	39,7 ± 1,5	–2	0,0007	0,036
POTEH	82,1 ± 1,8	165,4 ± 1,6	2,01	0,0012	0,0489
NTNG2	97,0 ± 1,6	196,7 ± 1,2	2,03	1,37E–05	0,0027
PTPRH	129,8 ± 1,6	263,2 ± 1,5	2,03	7,95E–05	0,009
WI2-2373I1.2	84,4 ± 1,7	171,3 ± 1,6	2,03	0,0011	0,0464
HOXB13	25,6 ± 1,5	52,0 ± 1,6	2,04	0,0007	0,037
AUNIP	132,5 ± 1,5	272,5 ± 1,6	2,06	3,20E–08	3,43E–05
TIGD3	78,8 ± 1,8	166,6 ± 1,7	2,13	6,90E–05	0,0085
ST3GAL3	263,2 ± 1,5	572,1 ± 1,9	2,17	2,04E–05	0,0035
RSPH1	75,6 ± 1,7	166,6 ± 1,5	2,2	6,57E–05	0,0081
C3orf49	39,9 ± 1,7	93,7 ± 1,5	2,35	0,0005	0,0297
ZNF671	56,9 ± 1,7	134,4 ± 1,4	2,37	8,73E–05	0,0095
CD1D	222,9 ± 1,62,2	560,3 ± 1,7	2,51	1,66E–05	0,003
EML5	29,0 ±	76,1 ± 1,7	2,63	0,0002	0,0194

Примечание. FDR – false discovery rate (частота ложных открытий).
Note. *FDR – false discovery rate.*

Таблица 4. *Сигнальные клеточные пути, активность которых статистически значимо различается при сравнении экспрессионного профиля пациенток с наличием/отсутствием объективного ответа на неоадъювантную химиотерапию до лечения*

Table 4. *Signaling pathways whose activity differed significantly between patients with and without objective response to neoadjuvant chemotherapy according to their pretreatment expression profiles*

Сигнальный путь Signaling pathway	Всего генов, шт. Total genes, pcs.	Up-гены Up-regulated genes	Количество up-генов, шт. Number of up-regulated genes, pcs.	*p*
Overview of proinflammatory and profibrotic mediators	5	*IL15, MMP9, CCL4L2, XCL2, CXCL13*	5	0,005244
Opioid receptor pathway annotation	4	*TLR4, MMP9, CACNB2, CELF2*	4	0,005414
Fatty acid transporters	2	*SLC27A4, ACSL5*	2	0,010026
Extracellular vesicles in the crosstalk of cardiac cells	2	*TLR4, MMP9*	2	0,016126
Eicosanoid synthesis	2	*ALOX5, TBXAS1*	2	0,018912
Angiogenesis	2	*SMAD1, MMP9*	2	0,020375
Biosynthesis of electrophilic omega-3 PUFA oxo-derivatives	1	*ALOX5*	1	0,025253
miRNA degrading enzymes	1	*XRN1*	1	0,025253
Biosynthesis of DPA-derived SPMs	1	*ALOX5*	1	0,033528
Kinase-mediated control of CRTC2 and HDAC4/5/7 subcellular localization and activity	2	*CRTC2, SIK3*	2	0,033655

Окончание табл. 4
The end of table 4

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	***p***
T-cell receptor	3	*LCP2, GRAP2, TNFRSF9*	3	0,043621
Neovascularisation processes	2	*MMP9, SMAD1*	2	0,047342
Vitamin B6-dependent and responsive disorders	1	*ALPL*	1	0,049871
Synthesis of wybutosine at G37 of tRNA (Phe)	1	*TRMT12*	1	0,049871
Biosynthesis of EPA-derived SPMs	1	*ALOX5*	1	0,057939

Таблица 5. *Сигнальные клеточные пути, активность которых статистически значимо различается при сравнении экспрессионного профиля пациенток с наличием объективного ответа на неоадъювантную химиотерапию до и после лечения*

Table 5. *Signaling pathways whose activity differed significantly between pre- and post-treatment expression profiles in patients with objective response to neoadjuvant chemotherapy*

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes,	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	**Количество down-генов, шт.** Number of down-regulated genes, pcs.	***p***
VEGFA/VEGFR2	32	*ACACB, SMARCA2, PRKD1, NRP1, PTPRZ1, FOXO1, TXNIP, RHOJ, KL, JUN, PTGS2, EGR1, NR4A2, NR4A3, SELE, MEF2C, ADAMTS1, HBEGF, ERG, S1PR1, LMO2, LDB2, DLL4, SLC2A14, SEMA6D, ADAMTS9, IGFBP3, CSRP2, CYR61, HTRA1, HYOU1, TMOD1*	32	0	0,000090
Nuclear receptors meta-pathway	31	*SPRY1, SDPR, HBEGF, CES1, SRGN, PDK4, RGS2, CBR1, GPX3, PTGS2, TXNRD3, IL1B, JUN, EGR1, SNAI2, CES4A, SLC2A4, TNS4, NRG1, KAT2B, SLC2A12, GSTP1, TGFBR3, SLC2A14, SLC2A3, SRPX2, FOXO1, GSTM5, SLC5A1, SLC6A16*	30	1	0,000000
Focal adhesion: PI3K/Akt/mTOR	27	*COL1A2, IL3RA, RELN, COL5A2, LAMB2, THBS4, PTEN, LAMA2, COL1A1, GHR, FGF10, FGF14, FGF7, IGF1, PDGFD, KDR, KIT, MET, PDGFRA, TEK, GNG7, RPTOR, FOXO1, CREB5, SLC2A4, SLC2A3, EPAS1*	27	0	0,000007
PI3K/Akt	25	*COL1A2, IL3RA, RELN, LAMB2, THBS4, PTEN, LAMA2, COL1A1, GHR, FGF10, FGF14, FGF7, IGF1, IGF2, PDGFD, KDR, KIT, MET, PDGFRA, TEK, GNG7, RPTOR, CREB5, IL6, NTRK2*	25	0	0,000409
Orexin receptor pathway	23	*PDE11A, LAMA2, SLC2A4, FOS, FOXO1, GNAI1, CGA, PRKD1, ADIPOQ, PLD1, HOMER1, NR4A3, EGR1, EGR2, HBEGF, NOG, DCLK1, ID3, FOSB, COX7A1, IL6, SELE, IL1B*	23	0	0,000000
Network map of SARS-CoV-2	22	*TMPRSS2, FOS, EGR1, PTGS2, JUN, DUSP1, IL6, IL1B, VPS11, RPTOR, SELP, IGFBP3, TRO, HBB, C1S, C1R, CD14, CFI, CCL15, SAA2*	20	2	0,000422

Продолжение табл. 5
Continuation of table 5

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes,	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	**Количество down-генов, шт.** Number of down-regulated genes, pcs.	***p***
PodNet: protein-protein interactions in the podocyte	21	*TRPC6, RAB4B, ANGPTL2, EPAS1, PTGS2, PLA2R1, CDH3, CLIC5, IGF1, NRN1, LAMB2, NRXN1, KDR, KHDRBS3, MAGI2, NRP1, MET, IGFBP3, ARHGAP24, TAGLN*	20	1	0,002258
Focal adhesion	18	*PDGFRA, COL1A1, THBS4, LAMA2, PDGFD, MET, KDR, RELN, PAK3, JUN, FIGF, MYLK, LAMB2, PTEN, COL1A2, COL5A2, IGF1, CAV2*	18	0	0,000178
Myometrial relaxation and contraction	16	*IGFBP6, FOS, RGS2, JUN, GNG7, IL6, CNN1, RGS1, CNN2,IL1B, PRKD1, ATF3, ADCY4, IGFBP1, IGFBP3, GUCY1A3*	16	0	0,000100
NRF2	16	*GPX3, SLC2A14, CBR1, GSTP1, CES1, CES4A, SLC2A12, NRG1, EGR1, SLC2A4, HBEGF, SLC2A3, TXNRD3, GSTM5, SLC5A1, SLC6A16*	16	0	0,000035
Endothelin	14	*PTGS2, PLCB1, COL1A1, IL1B, WWTR1, TNS1, COL1A2, EDNRB, JUN, IL6, FOS, EGR1, ADIPOQ, LEPR*	14	0	0,009788
Circadian rhythm genes	14	*JUN, EGR1, ADIPOQ, PER3, HOMER1, KLF9, IL6, ID3, PROX1, PTGDS, SIK1, NLGN1, PTEN*	13	1	0,017644
Sudden infant death syndrome susceptibility	13	*TACR1, MEF2C, PLP1, JUN, ADCYAP1R1, HTR2A, IL6, EGR1, NTRK2, KCNJ8, SCN4B, IL1B*	12	1	0,003663
Complement system in neuronal development and plasticity	13	*CX3CR1, PROS1, AXL, C1R, C7, CFD, PLSCR4, SERPING1, FCN1, C1S, CFI, CLU, MASP1*	13	0	0,000096
AXL	12	*NRG1, CAV2, AXL, CD36, KDR, JUN, MET, FOXO1, IL1B, COL1A1, SNAI2*	11	1	0,006681
Spinal cord injury	12	*LGALS3, AQP1, PTPRZ1, IL1B, IL6, FOS, EGR1, SLIT2, IL1R1, SELP, TACR1, PTGS2*	12	0	0,000716
Adipogenesis	12	*IGF1, ID3, DLK1, MEF2C, SLC2A4, ADIPOQ, IL6, LIFR, FRZB, EGR2, EPAS1, WWTR1*	12	0	0,001919
Burn wound healing	11	*IL6, COL1A2, CNN2, COL1A1, TAGLN, SNAI2, KDR, PECAM1, IL1B, ELN, CD248*	11	0	0,002074
TGF-β	11	*SIK1, ZEB2, ZFYVE9, ATF3, MET, JUN, FOS, MEF2C, COL1A2, TGFBR3, FOSB*	11	0	0,007060
Regulation of actin cytoskeleton	10	*CHRM3, FGF10, MRAS, FGF7, FGF14, PIK3C2G, MYLK, PAK3, CD14, PDGFRA*	10	0	0,041280
Neuroinflammation and glutamatergic signaling	10	*IL6, TGFBR3, IL1R1, IL1B, GRIA3, GRIA4, PLCB1, SLC2A3, IGF1, FOS*	10	0	0,030420
EGFR tyrosine kinase inhibitor resistance	10	*AXL, PDGFRA, PTEN, NRG1, IGF1, PDGFD, IL6, MET, KDR, MRAS*	10	0	0,000672
G protein	10	*PDE7B, GNAZ, ADCY4, GNAI1, PDE1A, PDE1C, GNAL, PRKD1, AKAP12, GNG7*	10	0	0,001249
Glucocorticoid receptor	10	*JUN, PTGS2, RGS2, SNAI2, SPRY1, TGFBR3, SRGN, SDPR, TNS4*	9	1	0,000153

Продолжение табл. 5
Continuation of table 5

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes,	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	**Количество down-генов, шт.** Number of down-regulated genes, pcs.	***p***
Hair follicle development: cytodifferentiation – part 3 of 3	10	*S100A4, JUN, FOS, SFRP1, CD200, TP63, CD34, FOSB, EGR2, KLK7*	10	0	0,001249
JAK/STAT pathway	10	*FOS, JUN, FOXO1, IGF2, SOCS2, IL1B, GHR, LEPR, IGF1, ACACB*	10	0	0,003849
Complement and coagulation cascades	9	*CLU, TFPI, SERPING1, C1S, C7, CFI, C1R, PROS1, MASP1*	9	0	0,000199
Hippo-Merlin signaling dysregulation	9	*CDH3, KDR, KIT, MET, PDGFRA, TEK, NTRK2, SAV1, PAK3*	9	0	0,005094
Hippo signaling regulation pathways	9	*CDH3, GNAL, PLCB1, KDR, KIT, MET, PDGFRA, TEK, NTRK2*	9	0	0,006681
Embryonic stem cell pluripotency	9	*JUN, FGF10, PDGFRA, NOG, LIFR, FGF14, PTEN, FOS, FGF7*	9	0	0,018871
Dengue-2 interactions with complement and coagulation cascades	9	*CLU, TFPI, SERPING1, C1S, C7, CFI, C1R, PROS1, MASP1*	9	0	0,000226
Hematopoietic stem cell differentiation	9	*LMO2, FOS, CD34, FOSB, HLF, PRDM5, IL6, IL1B, MEF2C*	9	0	0,004419
Prostaglandin synthesis and regulation	8	*EDNRB, PTGFR, PTGS2, PTGDS, HPGDS, AKR1C3, CBR1, AKR1C2*	8	0	0,000156
Phosphodiesterases in neuronal function	8	*PDE1C, PDE3A, ADCY4, PDE7B, GUCY1B3, GUCY1A3, PDE11A, PDE1A*	8	0	0,000428
Copper homeostasis	8	*STEAP4, FOXO1, COMMD1, MT1B, MT1E, MT1H, JUN, PTEN*	8	0	0,000554
Cardiac progenitor differentiation	8	*KDR, KIT, PDGFRA, MEF2C, NOG, IGF2, IGF1, NRG1*	8	0	0,000428
miR-targeted genes in lymphocytes	8	*SUCLG2, MET, NRP1, KIT, HOXA5, AXL, PDE3A*	7	1	0,018150
Class A/1 (rhodopsin-like receptors)	7	*PTGFR, S1PR1, HRH1, CX3CR1, TACR1, P2RY14*	6	1	0,006387
Photodynamic therapy-induced AP-1 survival signaling	7	*PDGFRA, IL6, FOS, HBEGF, FGF7, JUN*	6	1	0,001536
MECP2 and associated Rett syndrome	7	*MEF2C, IGF2, IGF1, PTEN, GRIA3, GRIA4*	6	1	0,013662
Corticotropin-releasing hormone	7	*JUN, CRHBP, FOS, FOSB, NR4A2, GNAI1, GNAZ*	7	0	0,045656
Thyroid stimulating hormone	7	*EGR1, CGA, JUN, FOS, GNAI1, PLD1, PLCB1*	7	0	0,007472
Development of ureteric collection system	6	*FAT4, FOXC1, SPRY1, SLIT2, FREM1*	5	1	0,005856
Genes controlling nephrogenesis	6	*LAMB2, KDR, FOXC1, CD36, SLIT2*	5	1	0,001761

Продолжение табл. 5
Continuation of table 5

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes,	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	**Количество down-генов, шт.** Number of down-regulated genes, pcs.	***p***
Endochondral ossification with skeletal dysplasias	6	*IGF2, IGF1, MEF2C, ADAMTS5, ADAMTS1, DDR2*	6	0	0,025877
Endochondral ossification	6	*IGF2, IGF1, MEF2C, ADAMTS5, ADAMTS1, DDR2*	6	0	0,025877
PPAR	6	*CYP27A1, FABP7, CD36, ADIPOQ, FABP4, PLIN1*	6	0	0,029450
Lung fibrosis	6	*IL6, ELN, IL1B, CMA1, FGF7, IGF1*	6	0	0,022605
Sleep regulation	6	*FOS, HTR2A, IL6, PTGDS, NLGN1, PER3*	6	0	0,001761
Gastric cancer network 1	6	–	0	6	0,000394
Folate metabolism	6	*SAA4, SAA2, IL1B, HBB, HBA1, IL6*	6	0	0,035391
Vitamin B12 metabolism	6	*SAA4, SAA2, IL1B, IL6, HBA1, HBB*	6	0	0,008657
TGF-β receptor	5	*TGFBR3, NOG, ZFYVE9, JUN, FOS*	5	0	0,040427
Complement activation	5	*C1S, C1R, C7, MASP1, CFD*	5	0	0,001722
Hypertrophy model	5	*IL1R1, NR4A3, ATF3, CYR61, HBEGF*	5	0	0,000482
Familial partial lipodystrophy	5	*FABP4, PRRX1, KLF9, CIDEC, PLIN1*	5	0	0,005808
PPAR-γ pathway	5	*FABP4, PTGS2, ADIPOQ, CD36, IL1B*	5	0	0,002320
GDNF/RET signaling axis	5	*SPRY1, FOXC1, FAT4, SLIT2*	4	1	0,000959
Signal transduction through IL1R	5	*IL6, IRAK3, JUN, IL1R1, IL1B*	5	0	0,005096
Ethanol effects on histone modifications	5	*KAT2B, ADH1B, ADH1A, ADH1C, ALDH1A2*	5	0	0,003860
BMP signaling in eyelid development	5	*FGF10, SFRP1, DKK2, FOXC1, JUN*	5	0	0,000482
Pluripotent stem cell differentiation	5	*NOG, KIT, IGF1, FGF10, IL6*	5	0	0,024153
miR-targeted genes in epithelium	5	*KIT, MET, PHLDB2, NRP1*	4	1	0,037054
IL-1	5	*IL1B, IL1R1, PELI2, IRAK3, JUN*	5	0	0,040427
Galanin receptor pathway	4	*SLC2A4, FOS, IL6, ADIPOQ*	4	0	0,005231
Type I collagen synthesis in the context of osteogenesis imperfecta	4	*COL1A1, SERPINF1, COL1A2, P3H2*	4	0	0,025865
Eicosanoid metabolism via cyclooxygenases	4	*PTGS2, PTGDS, AKR1B1, PTGFR*	4	0	0,023347

Продолжение табл. 5
Continuation of table 5

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes,	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	**Количество down-генов, шт.** Number of down-regulated genes, pcs.	***p***
Factors and pathways affecting insulin-like growth factor-Akt signaling	4	*PLD1, PTEN, RPTOR, IGF1*	4	0	0,040826
Metallothioneins bind metals	4	*MT1H, MT1E, MT1M, MT1B*	4	0	0,006222
Photodynamic therapy-induced NF-κB survival signaling	4	*IL1B, IL6, PTGS2, SELE*	4	0	0,031371
Photodynamic therapy-induced HIF-1 survival signaling	4	*SLC2A3, PTGS2, IGFBP1, IGFBP3*	4	0	0,037514
Photodynamic therapy-induced NFE2L2 (NRF2) survival signaling	4	*GSTP1, JUN, FOS, CES1*	4	0	0,007330
Zinc homeostasis	4	*MT1B, MT1E, MT1H, MT1M*	4	0	0,037514
IL-1 and megakaryocytes in obesity	4	*IL1R1, IL1B, FCER1A, HBEGF*	4	0	0,008561
Complement cascade	4	*C7, CLU, SERPING1, CFI*	4	0	0,037415
ACE inhibitor pathway	3	*CTSG, CMA1, NR3C2*	3	0	0,019290
PPAR β/δ pathway	3	*PDK4, PTGS2, IL1B*	3	0	0,048115
Fatty acid transporters	3	*CD36, FABP4, FABP7*	3	0	0,022568
Angiotensin II receptor type 1 pathway	3	*COL1A1, PDGFD, COL1A2*	3	0	0,011147
ACE inhibitor pathway – for workshop	3	*CTSG, CMA1, NR3C2*	3	0	0,008985
COVID-19 adverse outcome pathway	3	*IL1B, TMPRSS2, IL6*	3	0	0,013582
PKC-γ calcium signaling pathway in ataxia	3	*PLCB1, GRIA3, GRIA4*	3	0	0,038496
Renin-angiotensin-aldosterone system	3	*CTSG, CMA1, CREB5*	3	0	0,022170
Cells and molecules involved in local acute inflammatory response	3	*C7, IL6, SELP*	3	0	0,019290
LTF danger signal response	3	*IL1B, IL6, CD14*	3	0	0,026128
Extracellular vesicles in the crosstalk of cardiac cells	3	*PTEN, IL6, IGF1*	3	0	0,043170

Продолжение табл. 5
Continuation of table 5

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes,	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	**Количество down-генов, шт.** Number of down-regulated genes, pcs.	***p***
PTF1A related regulatory	3	*PROX1, FGF10, KAT2B*	3	0	0,005457
Serotonin and anxiety-related events	3	*HTR2A, FOS, NLGN1*	3	0	0,008985
Olfactory receptor activity	3	*OR56B1, OR5P3, OR5P2*	3	0	0,001564
Fatty acid omega-oxidation	3	*ADH1C, ADH1B, ADH1A*	3	0	0,013582
Signaling by ROBO receptors	3	*NRP1, SLIT2*	2	1	0,020545
Mitotic G_2-G_2/M phases	3	*FBXL7*	1	2	0,038343
Benzo(a)pyrene metabolism	2	*AKR1C2, AKR1C3*	2	0	0,036313
Catalytic cycle of mammalian flavin-containing monooxygenases	2	*FMO2, FMO1*	2	0	0,011053
SARS-CoV-2 altering angiogenesis via NRP1	2	*NRP1, KDR*	2	0	0,016203
Conversion of angiotensinogen to angiotensin II	2	*CMA1, CTSG*	2	0	0,011053
Ciliary landscape	2	*RPGR, LCA5*	2	0	0,036946
Transcriptional regulation by RUNX1	2	*LGALS3, LIFR*	2	0	0,026581
Robo4 and VEGF signaling pathways crosstalk	2	*SLIT2, KDR*	2	0	0,016203
Leptin and adiponectin	2	*LEPR, ADIPOQ*	2	0	0,044373
Fc epsilon receptor signaling	2	*FOS, JUN*	2	0	0,004975
SARS-CoV-2 Infection	1	*TMPRSS2*	1	0	0,023320
SARS-CoV-1 Infection	1	*TMPRSS2*	1	0	0,049197
Anti-inflammatory response favouring Leishmania parasite infection	1	*IL6*	1	0	0,000868
G alpha(s) signaling events	1	*GNAL*	1	0	0,000000
Deubiquitination	1	*PTEN*	1	0	0,000010
IL-4 and IL-13 signaling	1	*PTGS2*	1	0	0,005436

Окончание табл. 5
End of table 5

Сигнальный путь Signaling pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены** Up-regulated genes,	**Количество up-генов, шт.** Number of up-regulated genes, pcs.	**Количество down-генов, шт.** Number of down-regulated genes, pcs.	***p***
Major pathway of rRNA processing in the nucleolus and cytosol	1	–	0	1	0,007935
Selenoamino acid metabolism	1	*SELP*	1	0	0,037148
HDR through homologous recombination or single strand annealing	1	–	0	1	0,049197
Regulation of lipid metabolism by PPARα	1	*RGL1*	1	0	0,033709
Degradation of the extracellular matrix	1	*CTSG*	1	0	0,032817
Mitotic Metaphase and Anaphase	1	–	0	1	0,007763
Glycosaminoglycan metabolism	1	*UST*	1	0	0,000003
PIP3 activates AKT signaling	1	*PTEN*	1	0	0,022923
TCR signaling	1	*PTEN*	1	0	0,015981
Mitotic G1 phase and G1/S transition	1	–	0	1	0,002599
Interferon alpha/beta signaling	1	*EGR1*	1	0	0,047930
Immunoregulatory interactions between lymphoid and non-lymphoid cells	1	*CD200*	1	0	0,000412

Таблица 6. *Сигнальные клеточные пути, активность которых статистически значимо отличается при сравнении экспрессионного профиля пациенток с отсутствием объективного ответа на неоадъювантную химиотерапию до и после лечения*

Table 6. *Signaling pathways whose activity differed significantly between pre- and post-treatment expression profiles in patients with no objective response to neoadjuvant chemotherapy*

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Olfactory receptor activity	168	168	*OR2W1, OR6C76, OR5H2, OR10H5, OR1F1, OR2H1, OR10C1, OR10A3, OR5V1, OR14J1, OR5T1, OR2B2, OR6C74, OR5AU1, OR10G3, OR10A2, OR4C46, OR5M10, OR13C5, OR6C70, OR8K3, OR10A4, OR56B1, OR1L6, OR5C1, OR4D2, OR6T1, OR2L8, OR5M8, OR7C2, OR2C1, OR10W1, OR13D1, OR5P3, OR2B3, OR7C1, OR2F1, OR7A10, OR5B3, OR4K5, OR2G2, OR51A4, OR52A5, OR51A2, OR4A5, OR52H1, OR2A12, OR8B2, OR2AG2, OR10H3, OR7D2, OR8B12, OR52I2, OR52D1, OR5AN1, OR1J1, OR2T8, OR52K2, OR4A16, OR5T2, OR4L1, OR52N2, OR5K2, OR10A6, OR4A15, OR4F4, OR1N2, OR6C68, OR9A2, OR10G7, OR1N1, OR13C3, OR2AK2, OR2J3, OR51I1, OR6B1, OR6C2, OR2A25, OR5B21, OR6X1, OR2A14, OR9G4, OR4N4, OR8H3, OR4A47, OR2V2, OR4F15, OR2D3, OR6V1, OR51E2, OR2D2, OR8D4, OR3A3, OR8K5, OR5M11, OR56A1, OR10K1, OR6K2, OR7A17, OR4C11, OR4C5, OR1D2, OR4K2, OR2S2, OR8J3, OR5I1, OR10J5, OR4N5, OR2M3, OR2T10, OR4F6, OR51B6, OR10H4, OR2C3, OR7G3, OR4C15, OR2AP1, OR1K1, OR4F17, OR10J3, OR2A2, OR2G6, OR5L2, OR2AE1, OR4X1, OR4D11, OR8B8, OR11H12, OR13J1, OR52B4, OR51M1, OR5AC2, OR51D1, OR5B17, OR2K2, OR5D13, OR13G1, OR52M1, OR2T27, OR51F2, OR8A1, OR8B4, OR5A1, OR5H1, OR10H1, OR5AK2, OR2Y1, OR51G1, OR1A2, OR52I1, OR4D10, OR51B5, OR1A1, OR2T3, OR52K1, OR51V1, OR13H1, OR14A16, OR10T2, OR10G8, OR9I1, OR2M2, OR10R2, OR8B3, OR52B6, OR56A4, OR5B2, OR6N1*	0	0,000000
GPCRs, class A rhodopsin-like	69	69	*GPR32, RRH, OR3A3, OR10H3, DRD2, OPRM1, CYSLTR2, HTR1F, OR7C1, OR5V1, MAS1L, GPR85, OR7C2, NTSR2, GPR15, OR8B8, OR7A17, CHRM2, HCRTR1, MTNR1A, OR2S2, OR10A4, TRHR, OR7A10, OR2W1, OR2B3, OR1D2, OR1F1, GPR68, GPR1, P2RY13, CCR3, OR2B2, DRD3, OR10H1, GPR45, CCRL2, OR1A1, OR2J3, OR5I1, NPY5R, OR2D2, ADRA1A, CHRM3, BRS3, CCR2, DRD5, OR1A2, NTSR1, AGTR2, CHRM1, OR2F1, HTR7, P2RY12, MAS1, MC5R, DRD1, GPR18, OPN1LW, BDKRB2, OR2C1, GPR83, NPY2R, HTR1D, OR6B1, CCR5, GPR12, CCR9, OR2H1*	0	0,000018
VEGFA/ VEGFR2	39	33	*BMX, PTK2, MYL2, PTPRZ1, MYH9, PLA2G5, NOS3, KL, SRF, NR4A3, SELE, EPS15, NOTCH4, MMRN2, FGD5, CCRL2, TRPC3, CYR61, DSC1, EIF3F, HBD, PBXIP1, PDE4DIP, PGD, SPIRE1, CNP, CSRP1, EPB41, FMNL3, MICAL2, RCN1, RPL39P5, TUBA1C*	6	0,000017
Focal adhesion: PI3K/Akt/ mTOR	35	33	*NOS3, TSC1, ITGAD, RELN, PTK2, ITGB2, COL4A6, PIK3CB, COL6A2, IL2RG, COL4A4, FGF12, FGF18, FGF6, FGF8, HGF, INS, PDGFD, TEK, OSM, PRL, CHRM1, CHRM2, LPAR5, LPAR4, GNG7, CAB39L, TCL1A, PPP2R3A, TCL1B, CREB3L3, CREB5, NOS1*	2	0,039121
Overview of pro-inflammatory and profibrotic mediators	32	32	*IFNK, IL13, IL36A, CXCL1, IL21, IFNA2, TSLP, IL1F10, IL19, OSM, IL9, IL7, IFNL1, IL3, IL27, IFNA1, IL11, IFNA5, IFNA6, IL33, IL36B, IL36G, IL17B, IFNA10, CCL4L2, CCL5, CCL8, CCL19, CCL26, CXCL5, CXCL6, PF4V1*	0	0,011330
Network map of SARS-CoV-2	30	27	*TMPRSS2, TLE1, TLE3, FOS, IRF9, CCR5, CXCL6, CXCL1, CCL8, CXCL5, VPS11, SELP, CFP, CCL26, CCL5, CRP, HP, IL33, APOL1, CASP5, IL7, IL13, HBD, IL9, IL18RAP, IL21, CD247*	3	0,048062
PodNet: protein-protein interactions in the podocyte	28	26	*SLC4A1, WIF1, MPZ, TLN2, KCNMA1, FRAS1, CLIC5, COL4A4, ANGPTL3, MYO1E, MYH9, SCEL, CRB2, PTK2, TCF21, CTNNA2, SMAD7, NRXN1, SULT1B1, PIK3CB, PAX2, CDK5, EGLN3, DDN, COL4A3, KIRREL3*	2	0,000853

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Alzheimer's disease	26	22	*PPP3R2, CACNA1S, GNAQ, PLCB1, ATP2A1, ATP2A3, ITPR2, NOS1, CDK5, INS, PIK3CB, GPR83, CHRNA7, NOX1, TUBA1C, TUBB2B, TUBB1, WNT2, WNT3, PSMB2, PSMC6, PSMC4*	4	0,003345
Class A/ 1 (rhodopsin-like receptors)	26	26	*NMS, OXER1, P2RY13, LPAR4, CCK, NPSR1, NPS, CCRL2, HCAR2, LPA, QRFPR, CCL19, PTGDR2, DRD2, HRH4, FPR2, CCR9, TRHR, TACR1, CYSLTR2, P2RY12, AGTR2, TSHR, GPR18, HCRTR1, ACKR2*	0	0,000000
MAPK	26	24	*SRF, LRRK2, PTPN7, FOS, CACNG3, PPP3R2, NTF4, NTF3, DUSP16, CACNG5, CACNA2D3, CACNA1A, CACNA1S, CACNB2, CACNB4, CACNA1I, CACNA1H, CACNA1G, FGF5, FGF6, FGF8, FGF12, FGF23, FGF18*	2	0,013557
Endothelin pathway	21	20	*KSR1, RGS3, CDH2, ABHD3, PLCB1, RUNX1, GNAQ, IL11, COL9A1, GATA4, NOS3, CXCL1, MCAM, FOS, EDN3, TCF4, PPP1R14A, MSN, PTK2, FLI1*	1	0,003268
IL-18	21	17	*IL18RAP, NOX1, IL13, CCL5, FOS, PTPRZ1, EPB41, CSN2, CCL19, GRM7, HCAR2, CNTN2, MYH7, NR0B2, GPAT4, APBA2, TGM2*	4	0,000034
Focal adhesion	18	17	*HGF, SHC3, COL4A4, VAV1, PDGFD, RELN, PAK3, COL6A2, PTK2, COL4A6, HCK, PIK3CB, STYK1, PTK6, PPP1R12C, MYL2, TLN2*	1	0,006194
miR-targeted genes in muscle cell	18	12	*NAT6, IGF2BP1, KPNA3, SRF, HSD17B12, PSAT1, CSRP1, RBMS1, MYO1E, GRIA2, ABCG2, LUZP1*	6	0,000000
miR-targeted genes in lymphocytes	18	11	*ABCG2, TNFRSF10A, CSRP1, TERT, IGF2BP1, PSAT1, KPNA3, LUZP1, MYO1E, HSD17B12, RBMS1*	7	0,000000
Epithelial to mesenchymal transition in colorectal cancer	16	16	*FOXQ1, NR2C2, NOTCH4, CDH2, CLDN4, CLDN6, CLDN14, CLDN17, CLDN22, COL4A3, COL4A4, COL4A6, WNT2, WNT3, WNT8B, PIK3CB*	0	0,039227
EGF/EGFR	15	11	*ARHGEF1, INPP5D, PTK6, NOS3, RPS6KA1, VAV1, FOS, EPS15, USP8, STAT5B, PTK2*	4	0,017497
Breast cancer	15	13	*FGF6, TCF7, FGF5, FGF23, FGF18, SHC3, NOTCH4, HES5, ESR2, FOS, FGF8, WNT2, WNT3*	2	0,035229
Ras signaling	15	14	*HTR7, TEK, GNG7, SHC3, RASAL1, PAK3, KSR1, PLA2G2C, PLA1A, PLA2G2A, PLA2G5, PLA2G2F, RGL1, PIK3CB*	1	0,003105
Insulin signaling	14	13	*SHC3, PRKCH, SRF, STXBP4, FOS, RRAD, PIK3CB, TSC1, RPS6KA1, RHOQ, FLOT2, SORBS1, PPP1R3A*	1	0,009323
Hepatitis B infection	14	13	*SLC10A1, PIK3CB, STAT4, STAT5B, FOS, CREB5, CREB3L3, TLR4, IFNA1, IFNA5, IFNA6, IFNA2, IFNA10*	1	0,024929
Nonalcoholic fatty liver disease	14	8	*PIK3CB, MLXIP, NDUFV3, NDUFA8, NDUFA12, INS, PPARA, SMAD7*	6	0,019916
Ectoderm differentiation	14	14	*PLCXD3, CLVS1, ANKS1B, KCNK10, MECP2, RHPN1, JAKMIP1, ELOVL4, ARHGAP15, SHH, CTNNA2, ZBTB16, PTPN13, ARHGAP10*	0	0,049807
Ciliary landscape	13	9	*SPATA7, MCM2, NUP88, USH1C, MSH2, BBS5, PSMC6, INTU, PSMC4*	4	0,000019
Sleep regulation	12	12	*NPY2R, NPS, ADA, CACNA1I, DRD3, TH, DRD1, FOS, CHRNB2, DRD2, CRH, HCRTR1*	0	0,013596

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Mesodermal commitment	12	11	*PARP8, ZIC2, T, TCF4, WNT3, C6orf201, PRKAR1A, SRF, FGF8, NFE2L2, ZIC3*	1	0,001793
Adipogenesis	12	11	*STAT5B, RETN, NDN, PPARA, CNTFR, OSM, INS, GATA4, GDF10, LPIN1, PCK1*	1	0,031041
Regulation of toll-like receptor signaling pathway	12	12	*IFNA10, CCL5, PELI2, PIK3CB, MBL2, IFNA2, TLR4, TLR7, IFNA1, IFNA5, IFNA6, FOS*	0	0,006670
Monoamine GPCRs	11	11	*DRD3, CHRM3, ADRA1A, DRD5, CHRM2, HTR1D, CHRM1, HTR7, DRD2, HTR1F, DRD1*	0	0,016088
22q11.2 copy number variation syndrome	11	11	*RELN, DRD2, GP5, ARVCF, AIFM3, P2RX6, TSKS, SRF, FGF8, SHH, ACTC1*	0	0,003141
Striated muscle contraction	11	10	*MYBPC1, TNNI1, MYOM1, MYL4, MYH6, TNNC2, MYL2, NEB, MYH8, TNNT3*	1	0,041934
Dopaminergic neurogenesis	11	11	*OTX2, GLI2, ALDH1A1, SLC6A3, EN1, TH, ASCL1, FGF8, NKX6–1, GLI1, SHH*	0	0,004684
Complement system	11	10	*SELE, CR2, CFHR1, SELP, C9, MBL2, CFP, CLEC4M, SELL, CRP*	1	0,005544
Alzheimer's disease and miRNA effects	11	9	*PPP3R2, CACNA1S, GNAQ, PLCB1, ATP2A1, ATP2A3, ITPR2, NOS1, CDK5*	2	0,003141
Burn wound healing	10	9	*TLR4, SCEL, IFNA2, SERPINH1, ELN, FOXE1, TLR7, HGF, AMBP*	1	0,039531
Fragile X syndrome	10	9	*PLCB1, ALDH5A1, GRIA1, GRIA2, SLC16A1, PIK3CB, TSC1, PRKAR1A, MECP2*	1	0,023356
Embryonic stem cell pluripotency pathways	10	10	*WNT3, SMAD7, FGF6, FGF18, WNT2, FGF23, FGF5, FGF12, FOS, FGF8*	0	0,029956
TGF-β signaling pathway	10	8	*DAB2, SMAD7, SIK1, ZFYVE9, TERT, FOS, PIAS2, PTK2*	2	0,004445
Farnesoid X receptor pathway	10	9	*NR1H4, UGT2B4, SLC10A1, CYP7A1, NR0B2, BAAT, CYP3A4, IP6K3, ABCB4*	1	0,000236
Senescence and autophagy in cancer	9	9	*SLC39A2, SERPINB2, ATG16L1, CD44, MAP1LC3C, CXCL1, UVRAG, INS, IL3*	0	0,014720
CCL18	9	8	*CDH2, PTK2, FOS, CCR3, CCR2, CCR5, CD44, ITGB2*	1	0,006762
Integrated breast cancer	9	6	*SMAD7, MSH6, TSC1, MSH2, RAD54L, CYP19A1*	3	0,000044
7q11.23 copy number variation syndrome	8	6	*CHRNA7, TCF4, CLDN4, WNT2, TRIM74, ELN*	2	0,006675
Acute viral myocarditis	8	6	*CCR5, PTCRA, TLR4, ITGB2, MYH6, CCR3*	2	0,036607
Ebola virus pathway in host	8	7	*CLEC4M, TLR4, MBL2, RAB9A, VPS11, EPS15, PIK3CB*	1	0,000414

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Plasma lipoprotein assembly, remodeling, and clearance	8	8	*CREB3L3, LIPC, HDLBP, APOA5, SAR1B, ANGPTL3, LPA, GPIHBP1*	0	0,009020
Angiopoietin-like protein 8 regulatory pathway	8	8	*PIK3CB, TSC1, SHC3, FLOT2, RHOQ, CYP3A4, CYP7A1, RPS6KA1*	0	0,000782
Allograft rejection	8	7	*CCL19, LRRK2, IL21, GNLY, IL13, GZMB, C9*	1	0,047886
miR-targeted genes in epithelium	8	5	*PSAT1, CSRP1, TERT, HSD17B12, MYO1E*	3	0,000000
ACE inhibitor	7	7	*NOS3, AGTR2, KNG1, CMA1, MAS1, NR3C2, BDKRB2*	0	0,011424
3q29 copy number variation syndrome	7	7	*HAMP, STAT5B, GRIA1, FNDC8, TM4SF19-TCTEX1D2, PIGZ, SENP5*	0	0,017194
AXL	7	6	*MSN, GLI2, VAV1, GLI1, CCR2, PTK2*	1	0,000439
Small cell lung cancer	7	6	*COL4A4, COL4A6, COL4A3, PTK2, PIK3CB, BIRC8*	1	0,017077
Transcriptional regulation by MECP2	7	7	*GRIA2, CRH, OPRM1, RBFOX1, FOXG1, LBR, MECP2*	0	0,000034
ncRNAs involved in Wnt signaling in hepatocellular carcinoma	7	6	*WNT2, WNT3, TCF7, NOTUM, WIF1, PORCN*	1	0,030411
lncRNA in canonical Wnt signaling and colorectal cancer	7	6	*WNT2, WNT3, TCF7, NOTUM, WIF1, PORCN*	1	0,017530
Visual phototransduction	7	7	*OPN1LW, SAG, ABCA4, RBP3, RPE65, AWAT2, RDH12*	0	0,017194
B cell receptor signaling pathway	7	6	*INPP5D, VAV1, RPS6KA1, TEC, PIP5K1B, CR2*	1	0,012860
Drug induction of bile acid pathway	7	7	*SLCO1B1, CYP3A4, SLC10A1, CYP7A1, BAAT, NR1H4, NR1I2*	0	0,011424
Androgen receptor network in prostate cancer	7	7	*HSD3B1, TMPRSS2, KLK3, KLK2, ACTL6B, HGF, FOS*	0	0,000745
Fatty acid omega-oxidation	7	7	*ADH1C, ALDH1A1, CYP3A4, ADH4, ADH1A, CYP4A11, CYP2A6*	0	0,005060
Signaling by ROBO receptors	7	7	*SLIT1, MSI1, LHX2, ETF1, DCC, ROBO3, HOXA2*	0	0,000000
Cell cycle	7	6	*MCM2, CCNB3, ANAPC10, YWHAG, SMC1B, WEE2*	1	0,001068
miRNA regulation of DNA damage response	7	4	*TP53AIP1, CDK5, PMAIP1, CCNB3*	3	0,017530
Non-genomic actions of 1,25 dihydroxyvitamin D3	6	5	*PLCB1, PRKCH, PIK3CB, RSAD2, TLR4*	1	0,019070

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Prader-Willi and Angelman syndrome	6	6	*GABRA5, GABRG3, NDN, NPAP1, DLX5, GABRR1*	0	0,024695
TCF dependent signaling in response to WNT	6	6	*PIP5K1B, USP34, TERT, USP8, WIF1, KMT2D*	0	0,000000
Regulation of lipid metabolism by PPARalpha	6	6	*PPARA, ABCB4, CYP7A1, APOA5, RGL1, CYP4A11*	0	0,000000
TNF-α	6	4	*NOXO1, NOX1, SELE, KSR1*	2	0,009895
Irinotecan pathway	6	6	*CYP3A4, BCHE, ABCC1, CYP3A5, ABCG2, SLCO1B1*	0	0,010082
Glioblastoma signaling pathways	6	5	*LPA, TSC1, PIK3CB, PRKCH, MSH6*	1	0,010204
IL-1 family signaling	6	6	*IL1RL1, IL18RAP, IL1F10, IL33, IL1RL2, IL1RAPL1*	0	0,000000
Immunoregulatory interactions between lymphoid and non-lymphoid cells	6	6	*KIR3DL2, SELL, KLRG1, CD200R1, KIR3DL1, KIR2DL1*	0	0,000000
Factors involved in megakaryocyte development and platelet production	6	6	*CDK5, HBG2, ITPK1, HBD, HBE1, HBG1*	0	0,000394
Cell surface interactions at the vascular wall	6	5	*TEK, SELE, INPP5D, FCAMR, SPN*	1	0,000000
Apoptotic execution phase	6	4	*BMX, PLEC, TJP2, PTK2*	2	0,000034
DNA damage response (only ATM dependent)	5	4	*WNT2, PIK3CB, PMAIP1, WNT3*	1	0,000697
ErbB signaling pathway	5	5	*PTK2, STAT5B, PAK3, SHC3, PIK3CB*	0	0,003826
SARS-CoV-2 innate immunity evasion and cell-specific immune response	5	5	*CXCL5, CXCL6, CXCL1, TLR7, CCL5*	0	0,019441
NGF-stimulated transcription	5	5	*RRAD, LYL1, SRF, CDK5, ASCL1*	0	0,010204
EGFR tyrosine kinase inhibitor resistance	5	4	*HGF, PDGFD, SHC3, PIK3CB*	1	0,007293
Melanoma	5	3	*GRM3, FOS, PIK3CB*	2	0,047665
Joubert syndrome	5	5	*TMEM17, PCNT, BBS5, SHH, B9D2*	0	0,026354

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Genes related to primary cilium development (based on CRISPR)	5	5	*TMEM17, BBS5, TTC23, WDR35, TTC21B*	0	0,000082
Keratinization	5	5	*SPINK9, IVL, LOR, KLK12, KLK5*	0	0,000356
Phase I – Functionalization of compounds	5	5	*CYP19A1, CYP21A2, CYP3A43, AADAC, SPN*	0	0,000154
Glycerophospholipid biosynthesis	5	5	*PLA1A, CHAT, ABHD3, AWAT2, LPCAT1*	0	0,000007
Glial cell differentiation	5	5	*GAP43, MBP, PLP1, CNP, MSN*	0	0,003732
Leptin signaling	5	3	*STAT5B, NOS3, PTK2*	2	0,019070
Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins	5	3	*NDUFA12, NDUFV3, COX19*	2	0,000002
Processing of capped intron-containing pre-mRNA	5	3	*U2AF2, YBX1, PPIE*	2	0,000000
IL-3, IL-5 and GM–CSF signaling	5	5	*IL5RA, CSF2RA, IL3, VAV1, TEC*	0	0,025971
Modulators of TCR signaling and T cell activation	4	4	*CD247, GRAP2, VAV1, SH2D1A*	0	0,037253
Overlap between signal transduction pathways contributing to LMNA laminopathies	4	4	*TCF7, TLE1, HES5, MAOA*	0	0,037907
Eicosanoid metabolism via cytochrome P450 monooxygenases (CYP) pathway	4	4	*EPHX2, CYP2C8, CYP4A11, PPARA*	0	0,041258
Head and neck squamous cell carcinoma	4	4	*TERT, PIK3CB, TSC1, NFE2L2*	0	0,010315
Pancreatic adenocarcinoma pathway	4	2	*PAK3, PIK3CB*	2	0,001271

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Non-small cell lung cancer	4	3	*PIK3CB, ALK, STAT5B*	1	0,014014
Gene and protein expression by JAK-STAT signaling after IL-12 stimulation	4	3	*CA1, SERPINB2, MSN*	1	0,010028
Glucose metabolism	4	4	*PCK1, GCKR, G6PC2, MAL*	0	0,000055
Activation of anterior HOX genes in hindbrain development during early embryogenesis	4	3	*HOXD3, PIAS2, HOXA2*	1	0,000001
TP53 regulates transcription of cell cycle genes	4	2	*NPM1, PLAGL1*	2	0,000891
TP53 regulates transcription of cell death genes	4	3	*PMAIP1, TP53AIP1, BCL2L14*	1	0,000035
Sphingolipid metabolism	4	4	*SUMF1, NEU2, ENPP7, NEU3*	0	0,000034
DAP12 interactions	4	4	*CD300E, KIR2DS5, NCR2, CD300LB*	0	0,027734
Host Interactions of HIV factors	4	3	*NPM1, HCK, APOBEC3G*	1	0,000000
Apoptosis	4	3	*PMAIP1, GZMB, IGF2*	1	0,001805
Retinoblastoma gene in cancer	4	2	*MSH6, HLTF*	2	0,001275
Histone modifications	4	2	*SETD4, SETD7*	2	0,027734
miR-targeted genes in squamous cell	4	1	*HSD17B12*	3	0,000000
L1CAM interactions	4	4	*L1CAM, CNTN2, GAP43, CNTN6*	0	0,000002
Intrinsic pathway for apoptosis	4	3	*GZMB, APIP, PMAIP1*	1	0,000439
Proteasome degradation	4	3	*PSMB2, PSMC6, PSMC4*	1	0,026936
Interferon type I signaling pathways	3	3	*STAT4, IRF9, VAV1*	0	0,019306
TGF-β receptor signaling	3	3	*ZFYVE9, SMAD7, FOS*	0	0,039577

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
NR1H2 and NR1H3-mediated signaling	3	3	*FABP6, ANGPTL3, PCK1*	0	0,000026
EGR2 and SOX10-mediated initiation of Schwann cell myelination	3	3	*MBP, MPZ, DRP2*	0	0,014166
Transcriptional regulation of granulopoiesis	3	3	*FLI1, RUNX1, GFI1*	0	0,000118
Extra-nuclear estrogen signaling	3	3	*SRF, PTK2, FOS*	0	0,000008
RNA pol II transcription – Initiation and elongation	3	1	*TAF4B*	2	0,000364
TGF-β receptor signaling in skeletal dysplasias	3	3	*ZFYVE9, SMAD7, FOS*	0	0,019354
Sumoylation of intracellular receptors	3	2	*NR3C2, PPARA*	1	0,000118
Signaling by PTK6	3	3	*LRRK2, PTK6, KHDRBS2*	0	0,000038
ESR-mediated signaling	3	1	*TLE3*	2	0,000000
Class B/2 (secretin family receptors)	3	3	*GHRHR, CRHBP, CRH*	0	0,000003
Transcriptional regulation by RUNX2	3	2	*SP7, IHH*	1	0,000085
miRNAs involvement in the immune response in sepsis	3	3	*TLR4, TLR7, GZMB*	0	0,009761
Genotoxicity	3	1	*SEMG2*	2	0,009602
Cilium assembly	3	3	*TTC21B, BBS5, WDR35*	0	0,000000
Signaling by MET	3	2	*USP8, PTK2*	1	0,000038
Transcriptional regulation by RUNX1	3	3	*RSPO3, ELF1, IL3*	0	0,000000
Deubiquitination	3	3	*USP13, USP9X, USP34*	0	0,000000
Antimicrobial peptides	3	3	*PI3, BPI, GNLY*	0	0,000942
IL-4 and IL-13 signaling	3	3	*IL13, IL2RG, MAOA*	0	0,000000

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
DNA IR-damage and cellular response via ATR	3	2	*MSH2, MCM2*	1	0,000793
IL-4 signaling pathway	3	3	*INPP5D, STAT5B, IL2RG*	0	0,027633
IL-20 family signaling	3	3	*IL22RA2, IL19, IFNL1*	0	0,027204
Pathways affected in adenoid cystic carcinoma	3	2	*CNTN6, MAML3*	1	0,009761
Metabolism of polyamines	3	3	*SPN, MRI1, AZIN1*	0	0,000057
Assembly of the primary cilium	3	3	*WDR35, TTC21B, BBS5*	0	0,000000
XBP1 (S) activates chaperone genes	3	2	*EDEM1, EXTL1*	1	0,000118
Mitochondrial biogenesis	3	0		3	0,000008
Hedgehog “on” state	3	3	*HHIP, GLI1, ULK3*	0	0,000001
EPH-Ephrin signaling	3	3	*NGEF, ARHGEF28, PTK2*	0	0,000000
Copper homeostasis	3	3	*STEAP1, MT3, MT4*	0	0,039577
Apoptosis-related network due to altered Notch3 in ovarian cancer	3	3	*PTK2, SMAD7, CARD14*	0	0,038151
Signaling by ERBB4	3	3	*GFAP, CSN2, MXD4*	0	0,000039
Signaling by NOTCH3	3	3	*HES5, PTCRA, YBX1*	0	0,000038
Diclofenac metabolic pathway	3	3	*CYP2C9, CYP2C8, CYP2C19*	0	0,031286
Cell differentiation – expanded index	3	3	*SRF, TLX2, PAX7*	0	0,006930
miR-targeted genes in leukocytes	3	1	*CSRP1*	2	0,000000
Angiogenesis overview	3	3	*TEK, BMX, NOS3*	0	0,006751
TCR signaling	3	3	*PTPN22, INPP5D, GRAP2*	0	0,000000
Mitotic G_2-G_2/M phases	3	0	–	3	0,000000

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Metabolism of water-soluble vitamins and cofactors	3	2	*GIF, ABCC1*	1	0,000082
Interferon alpha/beta signaling	3	2	*RSAD2, IRF9*	1	0,000000
Costimulation by the CD28 family	3	3	*GRAP2, PDCD1, VAV1*	0	0,000005
Circadian Clock	3	3	*NR1D1, SIK1, CRY2*	0	0,000005
ABC-family proteins mediated transport	3	3	*ABCB4, ABCA4, CFTR*	0	0,000003
MicroRNAs in cardiomyocyte hypertrophy	3	2	*PIK3CB, GATA4*	1	0,000026
AMP-activated protein kinase signaling	3	3	*ADRA1A, TSC1, PLCB1*	0	0,006930
Malignant pleural mesothelioma	2	1	*TSC1*	1	0,000002
Glycogen synthesis and degradation	2	1	*PPP2R3A*	1	0,037600
DNA repair pathways, full network	2	2	*MSH2, MSH6*	0	0,000000
1q21.1 copy number variation syndrome	2	1	*TJP2*	1	0,026291
G1 to S cell cycle control	2	2	*CREB3L3, MCM2*	0	0,001899
Fatty acyl-CoA biosynthesis	2	2	*ELOVL7, MAL*	0	0,015444
Ion channel transport	2	1	*SLC17A3*	1	0,000000
Cargo recognition for clathrin-mediated endocytosis	2	2	*VAMP7, DAB2*	0	0,000005
RNA polymerase I transcription	2	2	*TAF1A, POLR1B*	0	0,000040
Clathrin-mediated endocytosis	2	1	*EPS15*	1	0,000000
E3 ubiquitin ligases ubiquitinate target proteins	2	1	*HLTF*	1	0,000002
DNA IR-double strand breaks and cellular response via ATM	2	1	*CDK5*	1	0,006038

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Novel intracellular components of RIG-I-like receptor (RLR) pathway	2	2	*IFNA1, IFNK*	0	0,004077
Intra-Golgi and retrograde Golgi-to-ER traffic	2	1	*STX18*	1	0,000000
Cardiac conduction	2	1	*NOS1*	1	0,000000
TP53 Regulates Transcription of DNA Repair Genes	2	2	*MSH2, CDK12*	0	0,000018
Major pathway of rRNA processing in the nucleolus and cytosol	2	1	*BYSL*	1	0,000000
Cargo concentration in the ER	2	1	*GRIA1*	1	0,012537
Amyloid fiber formation	2	1	*USP9X*	1	0,000008
Hedgehog ligand biogenesis	2	2	*NOTUM, HHAT*	0	0,000004
RHO GTPases activate formins	2	2	*SRF, FMNL3*	0	0,000000
TP53 regulates metabolic genes	2	2	*TSC1, COX19*	0	0,000002
MTOR signaling	2	2	*SLC38A9, LAMTOR1*	0	0,018090
Hedgehog “off” state	2	2	*GLI1, GLI2*	0	0,000000
O-linked glycosylation	2	2	*GCNT3, CHST4*	0	0,000000
Transcriptional regulation of pluripotent stem cells	2	2	*ZIC3, PRDM14*	0	0,018378
Regulation of IGF transport and uptake by IGF binding proteins	2	2	*IGFALS, IGFBP1*	0	0,000000
Signaling by ERBB2	2	2	*PTK6, USP8*	0	0,000058
Toll-like receptor cascades	2	2	*BPI, TLR10*	0	0,037601
Degradation of the extracellular matrix	2	1	*CD44*	1	0,000000

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Activation of matrix metalloproteinases	2	1	*SPOCK3*	1	0,000018
Gamma carboxylation, hypusine formation and arylsulfatase activation	2	2	*SUMF1, FN3K*	0	0,000027
Transcriptional activity of SMAD2/SMAD3: SMAD4 heterotrimer	2	2	*USP9X, SMAD7*	0	0,000186
PI metabolism	2	2	*BMX, MTMR8*	0	0,000018
Signaling by the B cell receptor (BCR)	2	2	*VAV1, BCR*	0	0,000000
Signaling by TGF-beta receptor complex	2	1	*SMAD7*	1	0,000405
IL-2 family signaling	2	2	*IL2RG, IL21*	0	0,009006
Signaling by NOTCH4	2	2	*NOTCH4, HES5*	0	0,000000
Signaling by NOTCH2	2	2	*GZMB, HES5*	0	0,001294
Extracellular matrix organization	2	2	*DMP1, NRXN1*	0	0,000000
Meiotic recombination	2	2	*TEX15, PRDM9*	0	0,000619
ISG15 antiviral mechanism	2	1	*UBA7*	1	0,000038
Defensins	2	1	*CCR2*	1	0,000005
Elastic fibre formation	2	2	*LTBP4, ELN*	0	0,012856
Arachidonic acid metabolism	2	2	*ABCC1, ALOXE3*	0	0,002933
Interleukin-1 (IL1) structural pathway	2	1	*MBP*	1	0,012537
Integrated lung cancer pathway	2	2	*SH2D1A, FOS*	0	0,037601
TNF-related weak inducer of apoptosis (TWEAK) signaling pathway	2	2	*CCL5, TRIM63*	0	0,037600

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Cell differentiation – index	2	2	*SRF, TLX2*	0	0,004070
RANKL/RANK signaling pathway	2	2	*FOS, PTK2*	0	0,008694
Sterol regulatory element-binding proteins signaling	2	2	*LPIN1, SAR1B*	0	0,000599
Opioid signaling	2	2	*OPRM1, CDK5*	0	0,000000
IL-1 signaling pathway	2	1	*PELI2*	1	0,008694
Transport of vitamins, nucleosides, and related molecules	2	2	*SLC29A3, SLCO1B1*	0	0,027093
Post-translational modification: synthesis of GPI-anchored proteins	2	2	*PIGZ, GPLD1*	0	0,000000
Netrin-1 signaling	2	2	*DCC, PTK2*	0	0,000405
NCAM signaling for neurite out-growth	2	2	*PTK2, CNTN2*	0	0,000186
Kinesins	2	1	*KIF15*	1	0,012537
Interferon gamma signaling	2	0	–	2	0,000000
Integration of energy metabolism	2	2	*RAPGEF4, CHRM3*	0	0,000000
Cell junction organization	2	2	*PLEC, FBLIM1*	0	0,000001
Translation factors	2	2	*ETF1, EIF1AY*	0	0,018378
Vitamin A and carotenoid metabolism	1	1	*RPE65*	0	0,010499
SARS-CoV-2 Infection	1	1	*TMPRSS2*	0	0,000000
SARS-CoV-1 Infection	1	1	*TMPRSS2*	0	0,000000
Assembly and cell surface presentation of NMDA receptors	1	1	*GRIN3A*	0	0,022805
Anti-inflammatory response favouring Leishmania parasite infection	1	1	*MYH9*	0	0,000000

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
FOXO-mediated transcription of cell cycle genes	1	1	*FOXG1*	0	0,015444
DNA replication	1	1	*MCM2*	0	0,010256
Signaling by NTRK3 (TRKC)	1	0	–	1	0,033769
SUMOylation of transcription cofactors	1	1	*NPM1*	0	0,000000
p75 NTR receptor-mediated signaling	1	1	*MCF2*	0	0,000000
Peroxisomal protein import	1	1	*USP9X*	0	0,000010
Integrin signaling	1	1	*PTK2*	0	0,004589
COPII-mediated vesicle transport	1	1	*SAR1B*	0	0,000007
G alpha (12/13) signaling events	1	1	*ARHGEF1*	0	0,000024
Fibrin complement receptor 3 signaling pathway	1	1	*TLR4*	0	0,010256
RUNX1 regulates genes involved in megakaryocyte differentiation and platelet function	1	1	*NR4A3*	0	0,000002
Neddylation	1	0	–	1	0,000000
Deregulated CDK5 triggers multiple neurodegenerative pathways in Alzheimer's disease models	1	1	*CDK5*	0	0,010499
Phase II – Conjugation of compounds	1	1	*OPLAH*	0	0,000000
mRNA processing	1	1	*U2AF2*	0	0,000000
Regulation of mitotic cell cycle	1	0	–	1	0,000000
Cristae formation	1	1	*DNAJC11*	0	0,016095
Chromatin organization	1	0	–	1	0,000000

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Transcriptional regulation by the AP-2 (TFAP2) family of transcription factors	1	1	*NPM1*	0	0,000006
PTEN regulation	1	0	–	1	0,000000
Nucleobase catabolism	1	1	*NUDT15*	0	0,015286
miRNA regulation of prostate cancer signaling pathways	1	1	*TCF7*	0	0,006907
Oxidative damage response	1	1	*CR2*	0	0,015444
ATM signaling in development and disease	1	1	*CDK5*	0	0,004589
Factors and pathways affecting insulin-like growth factor (IGF1) – Akt signaling	1	1	*NEB*	0	0,023463
Retinoid metabolism and transport	1	1	*RBP2*	0	0,023463
RNA polymerase II transcribes snRNA genes	1	0	–	1	0,000002
Regulation of TP53 activity through methylation	1	1	*TTC5*	0	0,010499
Regulation of TP53 activity through acetylation	1	0	–	1	0,015444
Selenoamino acid metabolism	1	1	*SELP*	0	0,000000
Physico-chemical features and toxicity-associated pathways	1	1	*NOS1*	0	0,000177
Hepatitis C and hepatocellular carcinoma	1	1	*CD44*	0	0,001403
Photodynamic therapy-induced NF-kB survival signaling	1	1	*SELE*	0	0,034334

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Surfactant metabolism	1	1	*DMBT1*	0	0,001403
Trans-Golgi Network Vesicle Budding	1	1	*VAMP7*	0	0,000002
HDR through Homologous Recombination (HRR) or single strand annealing	1	1	*RTEL1*	0	0,000000
tRNA modification in the nucleus and cytosol	1	0	–	1	0,023463
Oxidative stress induced senescence	1	1	*FOS*	0	0,000000
Activated PKN1 stimulates transcription of AR (androgen receptor) regulated genes KLK2 and KLK3	1	1	*KDM4C*	0	0,002175
RHO GTPases activate PKNs	1	1	*PPP1R14A*	0	0,015286
BMAL1: CLOCK, NPAS2 activates circadian gene expression	1	1	*PPARA*	0	0,004924
RHO GTPases activate PAKs	1	1	*PAK3*	0	0,015444
Macroautophagy	1	1	*ATG16L1*	0	0,000003
Sumoylation of DNA damage response and repair proteins	1	0	–	1	0,000000
MAPK6/MAPK4 signaling	1	1	*IGF2BP1*	0	0,000000
miRNA targets in ECM and membrane receptors	1	1	*COL6A2*	0	0,007171
Detoxification of reactive oxygen species	1	0	–	1	0,004924
Cytosolic sensors of pathogen-associated DNA	1	1	*NLRC3*	0	0,000000
WNT ligand biogenesis and trafficking	1	1	*PORCN*	0	0,000288

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Syndecan interactions	1	0	–	1	0,004673
Pre-NOTCH expression and processing	1	1	*RUNX1*	0	0,000000
Binding and uptake of ligands by scavenger receptors	1	1	*SCARF1*	0	0,000000
Translocation of SLC2A4 (GLUT4) to the plasma membrane	1	1	*MYH9*	0	0,000403
Host interactions with influenza factors	1	0	–	1	0,004589
Citric acid cycle and respiratory electron transport	1	1	*MAL*	0	0,000134
Fc epsilon receptor (FCERI) signaling	1	1	*FOS*	0	0,000000
ATF4 activates genes in response to endoplasmic reticulum stress	1	1	*IGFBP1*	0	0,022805
Transcriptional regulation of white adipocyte differentiation	1	1	*PCK1*	0	0,000000
Insulin processing	1	1	*TMEM27*	0	0,010499
RAF/MAP kinase cascade	1	1	*PTPN7*	0	0,000000
Incretin synthesis, secretion, and inactivation	1	1	*GATA4*	0	0,033769
Cellular response to hypoxia	1	0	–	1	0,000001
Collagen biosynthesis and modifying enzymes	1	1	*SERPINH1*	0	0,000000
Signaling by NOTCH1	1	1	*HES5*	0	0,000000
Signaling by Hippo	1	1	*TJP2*	0	0,006907
Signaling by SCF-KIT	1	1	*VAV1*	0	0,000117

Продолжение табл. 6
Continuation of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
Influenza Infection	1	1	*IPO5*	0	0,000000
Iron uptake and transport	1	0	–	1	0,000010
Neurotoxicity of clostridium toxins	1	1	*VAMP1*	0	0,000078
HIV life cycle	1	0	–	1	0,000000
Aryl hydrocarbon receptor netpath	1	1	*NCOA7*	0	0,003179
PDGF pathway	1	1	*SRF*	0	0,015444
Endothelin pathways	1	1	*NPY*	0	0,022805
miR-targeted genes in adipocytes	1	1	*CSRP1*	0	0,015286
Unfolded protein response	1	1	*CREB3L3*	0	0,003179
tRNA aminoacylation	1	1	*VARS*	0	0,006880
Telomere maintenance	1	1	*TERT*	0	0,000288
Synthesis of DNA	1	1	*MCM2*	0	0,000000
Signaling by VEGF	1	1	*PTK2*	0	0,000000
Signaling by EGFR	1	0	–	1	0,000000
Signal amplification	1	1	*P2RY12*	0	0,023463
RNA polymerase II transcription	1	1	*MLLT3*	0	0,000000
Regulation of DNA replication	1	1	*MCM2*	0	0,000002
Regulation of apoptosis	1	1	*ARHGAP10*	0	0,000177
Protein folding	1	1	*TBCD*	0	0,000000
Platelet homeostasis	1	0	–	1	0,000003
Neurotransmitter release cycle	1	1	*CHAT*	0	0,002175
Mitotic G1 phase and G1/S transition	1	0	–	1	0,000000

Окончание табл. 6
End of table 6

Сигнальный путь Pathway	**Всего генов, шт.** Total genes, pcs.	**Up-гены, шт.** Up-regulated genes, pcs.	**Список up-генов** Up-regulated gene list	**Down-гены, шт.** Down-regulated genes, pcs.	***p***
MAPK targets/ Nuclear events mediated by MAP kinases	1	1	*FOS*	0	0,003074
Generic transcription pathway	1	0	–	1	0,000000
Gap junction trafficking and regulation	1	1	*DAB2*	0	0,015286
DNA damage bypass	1	1	*UBA7*	0	0,000055
Complement cascade	1	1	*CR2*	0	0,000000
miRNAs involved in DNA damage response	1	0	–	1	0,000288

Таблица 8. *Описание дифференциально экспрессирующихся генов и их характерные сигнальные пути у пациентов с наличием/отсутствием объективного ответа на неоадъювантную химиотерапию до и после лечения*

Table 8. *Description of differentially expressed genes and their typical signaling pathways in patients with/without objective response to neoadjuvant chemotherapy before and after treatment*

Ген Gene	**Описание** Description	**Сигнальный путь** Signaling pathway
ST3GAL3	ST3 beta-galactoside alpha-2,3-sialyltransferase 3	Synthesis of substrates in N-glycan biosynthesis, glycosaminoglycan metabolism, keratan sulfate/keratin metabolism, metabolism of proteins
ZFYVE9	Zinc finger, FYVE domain containing 9	Loss of function of SMAD2/3 in cancer, TGF-beta receptor signaling activates SMADs, HIV life cycle, Wnt/Hedgehog/Notch, SMAD signaling network
CYR61	Cysteine-rich, angiogenic inducer, 61	Adhesion, regulation of Wnt-mediated beta catenin signaling and target gene transcription
PLPPR4	Phospholipid phosphatase related 4	Peptide ligand-binding receptors, signaling by GPCR
CD1C	CD1c molecule	Hematopoietic stem cells and lineage-specific markers, innate immune system, immunoregulatory interactions between a lymphoid and a non-lymphoid cell
ATP1A2	ATPase, Na^+/K^+ transporting, alpha 2 polypeptide	Hepatic ABC transporters, transport of glucose and other sugars, bile salts and organic acids, metal ions and amine compounds
RGL1	Ral guanine nucleotide dissociation stimulator-like 1	Metabolism, Immune response antigen presentation by MHC class II, G-protein signaling – K-RAS regulation pathway
RGS1	Regulator of G-protein signaling 1	Signaling by GPCR, activation of GABAB receptors, MAPK-ERK pathway
CENPF	Centromere protein F	Cell cycle, mitotic, signaling by rho GTPases
SELP	Selectin P (granule membrane protein 140 kDa, antigen CD62)	Immune response IL-12 signaling pathway, IL4-mediated signaling events, amb2 Integrin signaling

Продолжение табл. 8
Continuation of table 8

Ген Gene	**Описание** Description	**Сигнальный путь** Signaling pathway
GSTM5	Glutathione S-transferase mu 5	Metapathway biotransformation, glutathione metabolism, NRF2 pathway
AKNAD1	AKNA domain containing 1	Нет данных No data
SELE	Selectin E	ATF-2 transcription factor network
VIT	Vitrin	Нет данных No data
B3GALT1	UDP-Gal: betaGlcNAc beta 1,3-galactosyltransferase 1	Ganglio sphingolipid metabolism
DHRS9	Dehydrogenase/reductase (SDR family) member 9	Signaling by retinoic acid, signaling by GPCR
MYO3B	Myosin IIIB	PAK pathway, RhoGDI pathway
NRXN1	Neurexin 1	MET promotes cell motility
TACR1	Tachykinin receptor 1	Signaling by GPCR, vesicle-mediated transport
ACVR1C	Activin A receptor type IC	Signaling by NODAL, human embryonic stem cell pluripotency, MAPK signaling pathway
PDE11A	Phosphodiesterase 11A	Signaling by GPCR
IL1RL1	Interleukin 1 receptor-like 1	IL-1 family signaling pathways, cytokine signaling in immune system
C2orf61	Chromosome 2 open reading frame 61	Нет данных No data
SYN2	Synapsin II	Neurotransmitter release cycle
CIDEC	Cell death-inducing DFFA-like effector C	Metabolism
PROS1	Protein S (alpha)	Innate immune system, collagen formation
BCHE	Butyrylcholinesterase	Metabolism, peptide hormone metabolism
CCDC39	Coiled-coil domain containing 39	Нет данных No data
PROL1	Proline rich, lacrimal 1	Нет данных No data
MMRN1	Multimerin 1	Response to elevated platelet cytosolic Ca^{2+}
ANK2	Ankyrin 2, neuronal	Vesicle-mediated transport, metabolism of proteins
MYOZ2	Myozenin 2	Нет данных
ADH1A; ADH1C	Alcohol dehydrogenase 1A/1C (class I), alpha polypeptide	Metapathway biotransformation, signaling by Retinoic Acid
NR3C2	Nuclear receptor subfamily 3, group C, member 2	Gene expression, nuclear receptor transcription pathway
MGARP	Mitochondria localized glutamic acid rich protein	Нет данных No data
FBXL7	F-box and leucine-rich repeat protein 7	Cell cycle, mitotic, innate immune system
GPX3	Glutathione peroxidase 3	Glutathione metabolism, metapathway biotransformation
KCNIP1	Kv channel interacting protein 1	Cardiac conduction

Продолжение табл. 8
Continuation of table 8

Ген Gene	Описание Description	Сигнальный путь Signaling pathway
CRHBP	Corticotropin releasing hormone binding protein	Corticotropin-releasing hormone signaling pathway, signaling by GPCR
FAM153C, FAM169A	Family with sequence similarity 153/169, member C/A,	Нет данных No data
NCOA7	Nuclear receptor coactivator 7	Aryl Hydrocarbon Receptor, AHR Pathway
HIST1H3F, HIST1H2BL	Histone cluster 1, H3f/H2bl	Activated PKN1 stimulates transcription of AR (androgen receptor) regulated genes KLK2 and KLK3, cell cycle, mitotic
CLIC5	Chloride intracellular channel 5	Hepatic ABC transporters
BMP5	Bone morphogenetic protein 5	TGF-β pathway, PEDF induced signaling, apoptotic pathways in synovial fibroblasts
PLAGL1	Pleiomorphic adenoma gene-like 1	Gene expression, TP53 Regulates Transcription of Cell Cycle Genes, Regulation of TP53 Activity
MLIP	Muscular LMNA-interacting protein	Нет данных No data
CREB5	cAMP responsive element binding protein 5	MFAP5-mediated ovarian cancer cell motility and invasiveness
IGFBP1	Insulin like growth factor binding protein 1	PERK regulates gene expression, metabolism of proteins, regulation of insulin-like growth factor (IGF) transport and uptake by Insulin-like growth factor binding proteins (IGFBPs)
ELN	Elastin	Integrin pathway, ERK signaling, phospholipase-C pathway
RUNDC3B	RUN domain containing 3B	Нет данных No data
PTPRZ1	Protein tyrosine phosphatase, receptor-type, Z polypeptide 1	PAK pathway
RELN	Reelin	Metabolism, integrin-mediated cell adhesion
ESYT2	Extended synaptotagmin-like protein 2	Metabolism
BHLHE22	Basic helix-loop-helix family, member e22	Нет данных No data
EBF2	Early B-cell factor 2	Нет данных No data
TEK	TEK tyrosine kinase, endothelial	RET signaling, GPCR pathway, nanog in mammalian ESC pluripotency, ERK signaling, Immune response IL-23 signaling pathway
GALNT12	Polypeptide N-acetylgalactosaminyltransferase 12	Metabolism of proteins
NR4A3	Nuclear receptor subfamily 4, group A, member 3	Gene expression, nuclear receptor transcription pathway
ZNF483	Zinc finger protein 483	Gene expression
FREM1	FRAS1 related extracellular matrix 1	Integrin pathway, ERK signaling
CNTNAP3	Contactin associated protein-like 3	Нет данных No data
PRUNE2	Prune homolog 2 (Drosophila)	Нет данных No data
XG	Xg blood group	Нет данных No data

Продолжение табл. 8
Continuation of table 8

Ген Gene	**Описание** Description	**Сигнальный путь** Signaling pathway
EGFL6	EGF-like-domain, multiple 6	Нет данных No data
CNKSR2	Connector enhancer of kinase suppressor of Ras 2	RET signaling, signaling by moderate kinase activity BRAF mutants, cytokine signaling in immune system
TCEAL7	Transcription elongation factor A (SII) – like 7	Нет данных No data
PLP1	Proteolipid protein 1	Glial Cell Differentiation
PAK3	p21 protein (Cdc42/Rac) – activated kinase 3	Integrin pathway, CD28 co-stimulation, ERK signaling
ALAS2	5-aminolevulinate synthase 2	Metabolism
ZC4H2	Zinc finger, C4H2 domain containing	Нет данных No data
SLC7A3	Solute carrier family 7 member 3	Amino acid transport across the plasma membrane
CHRDL1	Chordin-like 1	Signaling by BMP, signaling by GPCR
CAPN6	Calpain 6	Apoptosis pathway, B cell receptor signaling pathway, ERK signaling
GPC3	Glypican 3	mTOR signaling, development VEGF signaling via VEGFR2 – generic cascades
CACNB2	Calcium channel, voltage-dependent, beta 2 subunit	CCR5 pathway in macrophages, sweet taste signaling
ZNF365	Zinc finger protein 365	Нет данных No data
CDNF	Cerebral dopamine neurotrophic factor	Нет данных No data
MKI67	Marker of proliferation Ki-67	DNA damage, neuroscience
GSTP1	Glutathione S-transferase pi 1	Metapathway biotransformation, glutathione metabolism, acetaminophen pathway (therapeutic doses), pharmacokinetics, innate immune system
PDGFD	Platelet derived growth factor D	GPCR pathway, ERK signaling, nanog in mammalian ESC pluripotency
TREH	Trehalase	Metabolism
H2AFX	H2A histone family, member X	Activated PKN1 stimulates transcription of AR (androgen receptor) regulated genes KLK2 and KLK3, cell cycle, mitotic
OR56B1	Olfactory receptor, family 56, subfamily B, member 1	Signaling by GPCR
IGF2	Insulin-like growth factor 2	GPCR Pathway, ERK Signaling, Nanog in Mammalian ESC Pluripotency
HBG2, HBG1	Hemoglobin, gamma G; hemoglobin, gamma A	IL-2 pathway
KCNA1	Potassium channel, voltage gated shaker related subfamily A, member 1	Transmission across chemical synapses
CAPZA3	Capping protein (actin filament) muscle Z-line, alpha 3	Cell cycle, spindle assembly and chromosome separation
KCNMB4	Potassium channel subfamily M regulatory beta subunit 4	Response to elevated platelet cytosolic Ca^{2+}

Окончание табл. 8
End of table 8

Ген Gene	**Описание** Description	**Сигнальный путь** Signaling pathway
RERGL	RERG/RAS-like	Нет данных No data
KL	Klotho	RET signaling, PI3K/AKT activation, downstream signaling of activated FGFR2, Negative regulation of FGFR3 signaling
PELI2	Pellino E3 ubiquitin protein ligase family member 2	Activated TLR4 signalling, cytokine signaling in immune system, IL-1 signaling pathway
FOS	FBJ murine osteosarcoma viral oncogene homolog	Activated TLR4 signalling, IL-2 pathway, IL-1 family signaling pathways
CMA1	Chymase 1, mast cell	ACE inhibitor pathway, pharmacodynamics, metabolism of proteins, Matrix metalloproteinases
C17orf51	Chromosome 17 open reading frame 51	Нет данных No data
ZNF677	Zinc finger protein 677	Gene expression
LILRB5	Leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 5	Innate immune system, immunoregulatory interactions between a lymphoid and a non-lymphoid cell
TPX2	TPX2, microtubule-associated	Regulation of TP53 activity, cell cycle, mitotic gene expression
BPI	Bactericidal/permeability-increasing protein	Innate immune system, activated TLR4 signalling
KCNB1	Potassium channel, voltage gated Shab related subfamily B, member 1	Integration of energy metabolism, Metabolism
SIK1	Salt-inducible kinase 1	BMAL1-CLOCK, NPAS2 activates circadian gene expression, circadian rythm related genes
TMPRSS2	Transmembrane protease, serine 2	Regulation of Androgen receptor activity