

Supplementary Table 5. Ingenuity pathway analysis (IPA) of differentially expressed genes (DEGs).

Top-five IPA results for the 179 up-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-6 tumor versus matched benign prostatic tissue comparison in old patient group

Top Canonical Pathways	p-value	Overlap
Epithelial Adherens Junction Signaling	2.34E-04	4.6% 7/153
Atherosclerosis Signaling	4.89E-04	4.8% 6/124
FXR/RXR Activation	5.32E-04	4.8% 6/126
Hepatic Fibrosis/Hepatic Stellate Cell Activation	7.58E-04	3.8% 7/186
Top Diseases and Disorders	p-value range	Number of Genes
Cancer	4.94E-04 - 1.90E-13	175
Organismal Injury and Abnormalities	4.94E-04 - 1.90E-13	175
Gastrointestinal Disease	4.82E-04 - 1.04E-10	160
Dermatological Diseases and Conditions	3.74E-04 - 2.43E-10	122
Reproductive System Disease	4.94E-04 - 6.91E-08	115
Molecular and Cellular Functions	p-value range	Number of Genes
Cellular Assembly and Organization	4.29E-04 - 1.42E-05	42
Cell Cycle	1.89E-04 - 3.69E-05	7
Cellular Movement	3.77E-04 - 4.09E-05	13
Cellular Development	4.14E-04 - 7.54E-05	48
Cellular Growth and Proliferation	3.14E-04 - 7.54E-05	43
Physiological System Development and Function	p-value range	Number of Genes
Hair and Skin Development and Function	9.48E-06 - 9.48E-06	5
Skeletal and Muscular Development and Function	4.03E-04 - 1.15E-05	29
Organismal Development	4.90E-04 - 1.29E-05	54
Connective Tissue Development and Function	1.89E-04 - 3.35E-05	16
Tissue Development	4.03E-04 - 3.35E-05	33

Top-five IPA results for the 320 down-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-6 tumor versus matched benign prostatic tissue comparison in old patient group

Top Canonical Pathways	p-value	Overlap
Nicotine Degradation II	3.62E-05	10.8% 7/65
Nicotine Degradation III	1.36E-04	10.7% 6/56
Estrogen Biosynthesis	2.69E-04	12.2% 5/41
Bupropion Degradation	3.91E-04	16.0% 4/25
Human Embryonic Stem Cell Pluripotency	7.14E-04	5.9% 8/136

Top Diseases and Disorders	p-value range	Number of Genes
Cancer	2.20E-03 - 3.40E-14	297
Organismal Injury and Abnormalities	2.20E-03 - 3.40E-14	300
Dermatological Diseases and Conditions	1.73E-03 - 5.79E-12	220
Gastrointestinal Disease	1.87E-03 - 4.13E-10	271
Endocrine System Disorders	1.71E-03 - 3.86E-09	259
Molecular and Cellular Functions	p-value range	Number of Genes
Cellular Development	2.06E-03 - 2.14E-08	125
Cellular Movement	2.11E-03 - 1.81E-07	99
Cell Morphology	1.93E-03 - 6.16E-07	79
Cellular Assembly and Organization	1.93E-03 - 8.51E-06	72
Cellular Function and Maintenance	1.85E-03 - 8.51E-06	75
Physiological System Development and Function	p-value range	Number of Genes
Embryonic Development	2.05E-03 - 6.13E-14	88
Hair and Skin Development and Function	2.02E-03 - 6.13E-14	54
Organ Development	2.02E-03 - 6.13E-14	76
Organismal Development	2.12E-03 - 6.13E-14	124
Tissue Development	2.02E-03 - 6.13E-14	122

Top-five IPA results for the 192 up-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-6 tumor versus matched benign prostatic tissue in young patient group

Top Canonical Pathways	p-value	Overlap
Atherosclerosis Signaling	9.54E-05	5.6% 7/124
Granulocyte Adhesion and Diapedesis	1.56E-04	4.5% 8/179
Bladder Cancer Signaling	1.85E-04	6.2% 6/97
Agranulocyte Adhesion and Diapedesis	2.51E-04	4.2% 8/192
Inhibition of Matrix Metalloproteases	3.34E-04	10.3% 4/39
Top Diseases and Disorders	p-value range	Number of Genes
Dermatological Diseases and Conditions	1.48E-03 - 2.55E-11	129
Organismal Injury and Abnormalities	1.80E-03 - 2.55E-11	187
Cancer	1.76E-03 - 3.32E-11	185
Gastrointestinal Disease	1.80E-03 - 3.21E-09	169
Immunological Disease	1.71E-03 - 1.31E-07	51
Molecular and Cellular Functions	p-value range	Number of Genes
Cellular Movement	2.41E-04 - 1.01E-08	51
Cell Death and Survival	1.00E-04 - 1.09E-07	54

Carbohydrate Metabolism	2.38E-04 - 6.63E-06	16
Small Molecule Biochemistry	2.00E-04 - 6.63E-06	8
Cellular Assembly and Organization	1.00E-04 - 7.14E-06	29
Physiological System Development and Function	p-value range	Number of Genes
Cell-mediated Immune Response	1.52E-03 - 2.50E-07	11
Hematological Development and Function	1.71E-03 - 2.50E-07	38
Immune Cell Trafficking	1.71E-03 - 2.50E-07	33
Tissue Morphology	1.48E-03 - 1.68E-06	59
Organismal Development	1.54E-03 - 5.51E-06	56

Top-five IPA results for the 322 down-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-6 tumor versus matched benign prostatic tissue in young patient group

Top Canonical Pathways	p-value	Overlap
Nicotine Degradation III	1.40E-04	10.7% 6/56
Estrogen Biosynthesis	2.77E-04	12.2% 5/41
Nicotine Degradation II	3.21E-04	9.2% 6/65
Bupropion Degradation	4.00E-04	16.0% 4/25
Amyotrophic Lateral Sclerosis Signaling	5.03E-04	7.1% 7/98
Top Diseases and Disorders	p-value range	Number of Genes
Cancer	4.32E-03 - 1.08E-13	302
Organismal Injury and Abnormalities	4.32E-03 - 1.08E-13	304
Dermatological Diseases and Conditions	3.77E-03 - 2.61E-10	219
Gastrointestinal Disease	3.85E-03 - 7.57E-10	273
Endocrine System Disorders	3.84E-03 - 1.04E-07	258
Molecular and Cellular Functions	p-value range	Number of Genes
Cellular Assembly and Organization	4.03E-03 - 1.98E-07	68
Cell-To-Cell Signaling and Interaction	2.91E-03 - 3.32E-07	49
Cellular Development	4.03E-03 - 9.00E-07	104
Lipid Metabolism	4.03E-03 - 5.09E-06	47
Molecular Transport	4.03E-03 - 5.09E-06	76
Physiological System Development and Function	p-value range	Number of Genes
Embryonic Development	4.04E-03 - 1.18E-08	88
Hair and Skin Development and Function	2.93E-03 - 1.18E-08	31
Organ Development	2.40E-03 - 1.18E-08	69
Organismal Development	4.08E-03 - 1.18E-08	128
Tissue Development	4.26E-03 - 1.18E-08	113

Top-five IPA results for the 107 up-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-7 tumor versus matched benign prostatic tissue in old patient group

Top Canonical Pathways	p-value	Overlap
SPINK1 Pancreatic Cancer Pathway	1.89E-04	6.7% 4/60
GDP-L-fucose Biosynthesis I (from GDP-Dmannose)	9.45E-03	50.0% 1/2
Intrinsic Prothrombin Activation Pathway	1.69E-02	4.8% 2/42
Neuroprotective Role of THOP1 in Alzheimer's Disease	1.78E-02	2.6% 3/116
LPS/IL-1 Mediated Inhibition of RXR Function	2.20E-02	1.8% 4/224
Top Diseases and Disorders	p-value range	Number of Genes
Cancer	3.61E-03 - 5.78E-10	104
Organismal Injury and Abnormalities	3.61E-03 - 5.78E-10	104
Gastrointestinal Disease	3.49E-03 - 5.97E-09	98
Reproductive System Disease	3.61E-03 - 3.34E-06	68
Renal and Urological Disease	3.61E-03 - 7.60E-05	11
Molecular and Cellular Functions	p-value range	Number of Genes
Cellular Movement	8.89E-04 - 8.89E-04	5
Cellular Development	1.42E-03 - 1.42E-03	8
Cellular Growth and Proliferation	1.42E-03 - 1.42E-03	8
Carbohydrate Metabolism	2.81E-03 - 1.95E-03	6
Nucleic Acid Metabolism	1.95E-03 - 1.95E-03	2
Physiological System Development and Function	p-value range	Number of Genes
Organ Development	3.50E-03 - 7.83E-04	8
Tissue Morphology	3.24E-03 - 2.81E-03	5
Embryonic Development	3.50E-03 - 3.24E-03	7
Organismal Development	3.50E-03 - 3.24E-03	7
Nervous System Development and Function	3.61E-03 - 3.50E-03	7

Top-five IPA results for the 195 down-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-7 tumor versus matched benign prostatic tissue in old patient group

Top Canonical Pathways	p-value	Overlap
Hepatic Fibrosis / Hepatic Stellate Cell Activation	4.16E-05	4.8% 9/186
PCP pathway	2.00E-04	8.2% 5/61
PXR/RXR Activation	2.70E-04	7.7% 5/65

LPS/IL-1 Mediated Inhibition of RXR Function	8.57E-04	3.6% 8/224
Glutathione Redox Reactions I	1.19E-03	12.5% 3/24
Top Diseases and Disorders	p-value range	Number of Genes
Cancer	9.63E-04 - 2.49E-11	187
Organismal Injury and Abnormalities	9.63E-04 - 2.49E-11	190
Reproductive System Disease	9.63E-04 - 5.69E-09	142
Skeletal and Muscular Disorders	9.30E-04 - 1.46E-08	78
Dermatological Diseases and Conditions	9.17E-04 - 4.67E-08	141
Molecular and Cellular Functions	p-value range	Number of Genes
Cellular Development	9.04E-04 - 4.69E-09	86
Cell Death and Survival	6.53E-04 - 8.87E-08	84
Cell Morphology	7.57E-04 - 1.27E-07	63
Cellular Assembly and Organization	9.66E-04 - 1.27E-07	56
Cellular Function and Maintenance	7.79E-04 - 1.27E-07	49
Physiological System Development and Function	p-value range	Number of Genes
Embryonic Development	9.04E-04 - 4.19E-10	83
Organismal Development	9.30E-04 - 4.19E-10	107
Hair and Skin Development and Function	3.76E-04 - 1.00E-09	29
Organ Development	8.59E-04 - 1.00E-09	73
Tissue Development	9.30E-04 - 1.00E-09	101

Top-five IPA results for the 131 up-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-7 tumor versus matched benign prostatic tissue in young patient group

Top Canonical Pathways	p-value	Overlap
Agranulocyte Adhesion and Diapedesis	1.71E-05	4.2% 8/192
Granulocyte Adhesion and Diapedesis	8.71E-05	3.9% 7/179
Atherosclerosis Signaling	8.82E-05	4.8% 6/124
Inhibition of Matrix Metalloproteases	1.51E-03	7.7% 3/39
Bladder Cancer Signaling	2.50E-03	4.1% 4/97
Top Diseases and Disorders	p-value range	Number of Genes
Cancer	2.42E-04 - 9.63E-11	127
Organismal Injury and Abnormalities	2.42E-04 - 9.63E-11	129
Gastrointestinal Disease	2.39E-04 - 1.20E-08	117
Immunological Disease	2.39E-04 - 3.19E-08	41
Reproductive System Disease	2.37E-04 - 1.10E-07	91
Molecular and Cellular Functions	p-value range	Number of Genes
Cellular Movement	2.41E-04 - 1.01E-08	51

Cell Death and Survival	1.00E-04 - 1.09E-07	54
Carbohydrate Metabolism	2.38E-04 - 6.63E-06	16
Small Molecule Biochemistry	2.00E-04 - 6.63E-06	8
Cellular Assembly and Organization	1.00E-04 - 7.14E-06	29
Physiological System Development and Function	p-value range	Number of Genes
Tissue Morphology	2.37E-04 - 2.62E-06	39
Hematological Development and Function	2.41E-04 - 3.16E-06	26
Immune Cell Trafficking	2.41E-04 - 3.16E-06	24
Cardiovascular Development and Function	2.12E-04 - 5.60E-06	23
Organismal Development	2.00E-04 - 5.60E-06	39

Top-five IPA results for the 212 down-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-7 tumor versus matched benign prostatic tissue in young patient group

Top Canonical Pathways	p-value	Overlap
Glutathione-mediated Detoxification	2.25E-04	12.5% 4/32
LPS/IL-1 Mediated Inhibition of RXR Function	2.88E-04	4.0% 9/224
PXR/RXR Activation	3.71E-04	7.7% 5/65
Histamine Degradation	5.10E-04	17.6% 3/17
Glutathione Redox Reactions I	1.45E-03	12.5% 3/24
Top Diseases and Disorders	p-value range	Number of Genes
Cancer	1.80E-03 - 9.91E-11	201
Organismal Injury and Abnormalities	1.83E-03 - 9.91E-11	204
Dermatological Diseases and Conditions	1.17E-03 - 1.99E-10	150
Gastrointestinal Disease	1.83E-03 - 6.99E-08	181
Reproductive System Disease	5.25E-04 - 2.80E-07	136
Molecular and Cellular Functions	p-value range	Number of Genes
Cellular Assembly and Organization	1.80E-03 - 4.84E-07	60
Cellular Function and Maintenance	1.30E-03 - 4.84E-07	56
Cell Morphology	1.80E-03 - 1.01E-06	59
Cell-To-Cell Signaling and Interaction	1.80E-03 - 1.36E-06	47
Cell Death and Survival	1.31E-03 - 1.38E-06	76
Physiological System Development and Function	p-value range	Number of Genes
Embryonic Development	1.81E-03 - 2.61E-09	61
Hair and Skin Development and Function	1.30E-03 - 2.61E-09	29
Organ Development	1.81E-03 - 2.61E-09	55
Organismal Development	1.84E-03 - 2.61E-09	94
Tissue Development	1.81E-03 - 2.61E-09	91

Top-five IPA results for the 384 up-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-8 tumor versus matched benign prostatic tissue in old patient group

Top Canonical Pathways	p-value	Overlap
Intrinsic Prothrombin Activation Pathway	7.07E-05	14.3% 6/42
D-mannose Degradation	1.69E-02	100.0% 1/1
Atherosclerosis Signaling	1.90E-02	4.8% 6/124
Fatty Acid Activation	1.97E-02	15.4% 2/13
Oleate Biosynthesis II (Animals)	1.97E-02	15.4% 2/13
Top Diseases and Disorders	p-value range	Number of Genes
Cancer	1.49E-02 - 1.67E-24	368
Organismal Injury and Abnormalities	1.56E-02 - 1.67E-24	371
Gastrointestinal Disease	1.39E-02 - 4.85E-19	335
Endocrine System Disorders	1.56E-02 - 1.12E-15	310
Dermatological Diseases and Conditions	1.36E-02 - 6.55E-10	229
Molecular and Cellular Functions	p-value range	Number of Genes
Cell Morphology	1.47E-02 - 6.40E-05	54
Cellular Assembly and Organization	1.47E-02 - 6.40E-05	68
Cellular Development	1.49E-02 - 6.40E-05	55
Cellular Function and Maintenance	1.42E-02 - 6.40E-05	64
Cellular Growth and Proliferation	1.49E-02 - 6.40E-05	47
Physiological System Development and Function	p-value range	Number of Genes
Nervous System Development and Function	1.52E-02 - 9.81E-07	93
Embryonic Development	1.52E-02 - 1.45E-06	83
Organ Development	1.49E-02 - 1.45E-06	54
Organismal Development	1.56E-02 - 1.45E-06	115
Tissue Development	1.49E-02 - 1.45E-06	85

Top-five IPA results for the 719 down-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-8 tumor versus matched benign prostatic tissue in old patient group

Top Canonical Pathways	p-value	Overlap
Human Embryonic Stem Cell Pluripotency	1.29E-08	14.7% 20/136
Hepatic Fibrosis / Hepatic Stellate Cell Activation	3.11E-08	12.4% 23/186
Axonal Guidance Signaling	1.59E-07	8.0% 39/487
Osteoarthritis Pathway	1.77E-05	9.4% 20/213
Clathrin-mediated Endocytosis Signaling	1.73E-04	8.8% 17/194
Top Diseases and Disorders	p-value range	Number of Genes

Cancer	3.34E-06 - 1.74E-31	683
Organismal Injury and Abnormalities	3.60E-06 - 1.74E-31	689
Dermatological Diseases and Conditions	1.82E-06 - 9.89E-29	504
Reproductive System Disease	3.34E-06 - 2.78E-26	497
Gastrointestinal Disease	3.60E-06 - 4.47E-21	617
Molecular and Cellular Functions	p-value range	Number of Genes
Cellular Movement	2.11E-06 - 9.21E-17	218
Cell-To-Cell Signaling and Interaction	1.90E-06 - 8.46E-14	144
Cellular Assembly and Organization	1.58E-06 - 8.46E-14	157
Cellular Development	3.67E-06 - 4.24E-12	259
Cellular Growth and Proliferation	2.68E-06 - 4.24E-12	245
Physiological System Development and Function	p-value range	Number of Genes
Organismal Development	3.51E-06 - 2.56E-18	338
Cardiovascular System Development and Function	3.69E-06 - 9.63E-18	179
Embryonic Development	2.34E-06 - 5.82E-15	233
Hair and Skin Development and Function	2.34E-06 - 5.82E-15	83
Organ Development	2.34E-06 - 5.82E-15	207

Top-five IPA results for the 279 up-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-8 tumor versus matched benign prostatic tissue in young patient group

Top Canonical Pathways	p-value	Overlap*
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	3.29E-04	10.2% 5/49
Atherosclerosis Signaling	8.63E-04	5.6% 7/124
Mitotic Roles of Polo-Like Kinase	1.30E-03	7.6% 5/66
Intrinsic Prothrombin Activation Pathway	1.72E-03	9.5% 4/42
Cell Cycle Control of Chromosomal Replication	4.94E-03	7.1% 4/56
Top Diseases and Disorders	p-value range	Number of Genes
Cancer	4.30E-03 - 9.30E-19	267
Organismal Injury and Abnormalities	4.30E-03 - 9.30E-19	268
Gastrointestinal Disease	4.00E-03 - 3.22E-15	246
Endocrine System Disorders	3.86E-03 - 2.47E-10	224
Hepatic System Disease	2.70E-03 - 3.95E-10	153
Molecular and Cellular Functions	p-value range	Number of Genes
Cell Cycle	4.00E-03 - 1.52E-11	49
Cellular Assembly and Organization	4.16E-03 - 5.10E-09	77
DNA Replication, Recombination, and Repair	2.42E-03 - 5.10E-09	29
Cell-To-Cell Signaling and Interaction	4.16E-03 - 9.56E-09	44

Cell Death and Survival	3.93E-03 - 2.99E-07	99
Physiological System Development and Function	p-value range	Number of Genes
Nervous System Development and Function	4.00E-03 - 6.47E-08	66
Tissue Morphology	3.58E-03 - 6.47E-08	35
Digestive System Development and Function	4.00E-03 - 6.23E-05	17
Embryonic Development	4.00E-03 - 6.23E-05	64
Endocrine System Development and Function	3.58E-03 - 6.23E-05	10

Top-five IPA results for the 392 down-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-8 tumor versus matched benign prostatic tissue in young patient group

Top Canonical Pathways	p-value	Overlap*
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	3.29E-04	10.2 % 5/49
Atherosclerosis Signaling	8.63E-04	5.6 % 7/124
Mitotic Roles of Polo-Like Kinase	1.30E-03	7.6 % 5/66
Intrinsic Prothrombin Activation Pathway	1.72E-03	9.5 % 4/42
Cell Cycle Control of Chromosomal Replication	4.94E-03	7.1 % 4/56
Top Diseases and Disorders	p-value range	Number of Genes
Cancer	4.30E-03 - 9.30E-19	267
Organismal Injury and Abnormalities	4.30E-03 - 9.30E-19	268
Gastrointestinal Disease	4.00E-03 - 3.22E-15	246
Endocrine System Disorders	3.86E-03 - 2.47E-10	224
Hepatic System Disease	2.70E-03 - 3.95E-10	153
Molecular and Cellular Functions	p-value range	Number of Genes
Cell Cycle	4.00E-03 - 1.52E-11	49
Cellular Assembly and Organization	4.16E-03 - 5.10E-09	77
DNA Replication, Recombination, and Repair	2.42E-03 - 5.10E-09	29
Cell-To-Cell Signaling and Interaction	4.16E-03 - 9.56E-09	44
Cell Death and Survival	3.93E-03 - 2.99E-07	99
Physiological System Development and Function	p-value range	Number of Genes
Nervous System Development and Function	4.00E-03 - 6.47E-08	66
Tissue Morphology	3.58E-03 - 6.47E-08	35
Digestive System Development and Function	4.00E-03 - 6.23E-05	17
Embryonic Development	4.00E-03 - 6.23E-05	64
Endocrine System Development and Function	3.58E-03 - 6.23E-05	10

Top-five IPA results for the 162 up-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-8 tumor versus Gleason-6 tumor comparisons in old patient group

Top Canonical Pathways	p-value	Overlap
LXR/RXR Activation	1.16E-02	3.3% 4/121
Atherosclerosis Signaling	1.26E-02	3.2% 4/124
Inhibition of Matrix Metalloproteases	3.22E-02	5.1% 2/39
Role of hyperchemokine in the Pathogenesis of Influenza	3.86E-02	4.7% 2/43
Granulocyte Adhesion and Diapedesis	4.11E-02	2.2 % 4/179
Top Diseases and Disorders	p-value range	Number of Genes
Cancer	2.86E-02 - 8.42E-08	153
Organismal Injury and Abnormalities	2.86E-02 - 8.42E-08	155
Gastrointestinal Disease	2.30E-02 - 1.96E-06	138
Respiratory Disease	2.20E-02 - 9.45E-05	44
Dermatological Diseases and Conditions	2.15E-02 - 1.26E-04	95
Molecular and Cellular Functions	p-value range	Number of Genes
Cellular Development	2.86E-02 - 2.24E-04	36
Cellular Growth and Proliferation	2.86E-02 - 3.08E-04	25
Cellular Movement	1.44E-02 - 5.11E-04	5
Cell Morphology	2.86E-02 - 8.59E-04	24
Cellular Assembly and Organization	2.86E-02 - 8.59E-04	21
Physiological System Development and Function	p-value range	Number of Genes
Organismal Development	2.86E-02 - 2.32E-04	52
Embryonic Development	2.86E-02 - 2.69E-04	44
Nervous System Development and Function	2.86E-02 - 3.37E-04	42
Tissue Development	2.86E-02 - 3.37E-04	43
Organ Development	2.86E-02 - 4.15E-04	24

Top-five IPA results for the 211 down-regulated DEGs (Fold change > 2.0 and FDR < 0.05) identified from Gleason-8 tumor versus Gleason-6 tumor comparisons in old patient group

Top Canonical Pathways	p-value	Overlap
Axonal Guidance Signaling	1.98E-04	2.9 % 14/487
RhoA Signaling	1.03E-03	4.9 % 6/123
Cellular Effects of Sildenafil (Viagra)	1.43E-03	4.6 % 6/131
Agranulocyte Adhesion and Diapedesis	2.18E-03	3.6 % 7/192
Prostanoid Biosynthesis	2.97E-03	22.2 % 2/9

Top Diseases and Disorders	p-value range	Number of Genes
Cancer	7.76E-03 - 1.56E-16	198
Dermatological Diseases and Conditions	6.27E-03 - 1.56E-16	151
Organismal Injury and Abnormalities	8.13E-03 - 1.56E-16	201
Reproductive System Disease	7.27E-03 - 1.78E-09	143
Gastrointestinal Disease	7.92E-03 - 3.70E-09	181
Molecular and Cellular Functions	p-value range	Number of Genes
Cellular Assembly and Organization	5.27E-03 - 2.34E-09	20
Cellular Development	6.22E-03 - 3.60E-08	38
Cellular Growth and Proliferation	5.27E-03 - 3.60E-08	25
Cellular Movement	7.64E-03 - 6.36E-05	59
Cellular Compromise	1.75E-03 - 8.60E-05	8
Physiological System Development and Function	p-value range	Number of Genes
Skeletal and Muscular Development and Function	7.43E-03 - 2.56E-11	46
Organismal Development	7.43E-03 - 1.97E-08	85
Embryonic Development	7.43E-03 - 3.23E-08	59
Organ Development	7.43E-03 - 3.23E-08	51
Tissue Development	7.43E-03 - 3.23E-08	58

Top-five IPA results for the 298 up-regulated DEGs (Fold change > 1.5 and FDR < 0.05) identified from Gleason-8 tumor versus Gleason-6 tumor comparison in young patient group

Top Canonical Pathways	p-value	Overlap*
Cyclins and Cell Cycle Regulation	9.30E-05	8.6 % 7/81
FXR/RXR Activation	1.37E-03	5.6 % 7/126
Mitotic Roles of Polo-Like Kinase	1.73E-03	7.6 % 5/66
LPS/IL-1 Mediated Inhibition of RXR Function*	2.87E-03	4.0 % 9/224
Apelin Liver Signaling Pathway	4.62E-03	11.5 % 3/26
Top Diseases and Disorders	p-value range	Number of Genes
Cancer	1.30E-02 - 5.89E-15	281
Organismal Injury and Abnormalities	1.31E-02 - 5.89E-15	282
Gastrointestinal Disease	1.31E-02 - 8.89E-09	246
Nutritional Disease	2.26E-03 - 4.48E-08	20
Renal and Urological Disease	7.17E-03 - 1.36E-07	57
Molecular and Cellular Functions	p-value range	Number of Genes
Cell Cycle	1.21E-02 - 1.27E-12	69
Cellular Assembly and Organization	1.11E-02 - 1.27E-12	66
DNA Replication, Recombination, and Repair	1.21E-02 - 1.27E-12	41

Cellular Development	1.21E-02 - 2.15E-05	76
Cellular Growth and Proliferation	1.24E-02 - 2.15E-05	76
Physiological System Development and Function	p-value range	Number of Genes
Embryonic Development	1.24E-02 - 4.28E-06	85
Organismal Development	1.31E-02 - 4.28E-06	90
Organismal Survival	3.43E-03 - 3.23E-05	77
Cardiovascular Development and Function	1.31E-02 - 1.03E-04	24
Connective Tissue Development and Function	1.21E-02 - 4.84E-04	45

*Endotoxin lipopolysaccharide (LPS), a major component of the outer membrane of Gram-negative bacteria, potently stimulates host innate immune response. LPS binds the CD14/TRL4/MD2 receptor complex, which promotes the secretion of pro-inflammatory cytokines (IL-1, TNF) in different cell types, but especially in macrophages.

Top-five IPA results for the 349 down-regulated DEGs (Fold change > 1.5 and FDR < 0.05) identified from Gleason-8 tumor versus Gleason-6 tumor comparison in young patient group

Top Canonical Pathways	p-value	Overlap*
Axonal Guidance Signaling	6.32E-05	4.1 % 20/487
Synaptic Long Term Depression	1.44E-04	5.9 % 11/187
Cellular Effects of Sildenafil (Viagra)	1.82E-04	6.9 % 9/131
Thrombin Signaling	3.77E-04	5.3 % 11/209
Signaling by Rho Family GTPases	3.83E-04	4.9 % 12/244
Top Diseases and Disorders	p-value range	Number of Genes
Cancer	2.32E-03 - 2.57E-20	330
Organismal Injury and Abnormalities	2.34E-03 - 2.57E-20	332
Reproductive System Disease	2.25E-03 - 3.67E-17	243
Gastrointestinal Disease	2.24E-03 - 1.86E-15	299
Dermatological Diseases and Conditions	1.05E-03 - 1.65E-13	223
Molecular and Cellular Functions	p-value range	Number of Genes
Cell-To-Cell Signaling and Interaction	2.13E-03 - 3.41E-05	37
Amino Acid Metabolism	2.02E-03 - 6.28E-05	15
Cell Death and Survival	1.36E-03 - 6.28E-05	9
Small Molecule Biochemistry	2.24E-03 - 6.28E-05	40
Cellular Movement	3.86E-04 - 8.48E-05	8
Physiological System Development and Function	p-value range	Number of Genes
Cardiovascular System Development and Function	2.01E-03 - 6.74E-08	57
Skeletal and Muscular System Development and Function	2.24E-03 - 1.26E-07	51
Respiratory System Development and Function	2.24E-03 - 4.00E-07	22
Organismal Development	2.31E-03 - 8.44E-07	135
Digestive System Development and Function	2.29E-03 - 2.26E-06	25

Highlighted yellow are immune related pathways, functions or diseases.