Presence of TMPRSS2-ERG is associated with alterations of the metabolic profile in human prostate cancer

Supplementary Materials

Supplementary Table S1: Sample distribution per patient in the main cohort classified as $\mathrm{ERG}_{\mathrm{low}}$, $\mathrm{ERG}_{\mathrm{intermediate}}$ and $\mathrm{ERG}_{\mathrm{high}}$

Patient	Benign	$\mathrm{ERG}_{\mathrm{low}}$	$\mathrm{ERG}_{\mathrm{intermediate}}$	$\mathrm{ERG}_{\mathrm{high}}$	Total
1	1	0	0	2	3
2	1	0	3	1	5
3	1	0	0	2	3
4	1	0	1	1	3
5	1	0	1	1	3
6	0	1	1	2	4
7	1	0	0	2	3
8	0	0	0	4	4
9	0	2	0	0	2
10	1	3	1	0	5
11	1	1	2	1	5
12	1	1	2	0	4
13	1	0	1	0	2
14	0	0	2	0	2
15	1	1	0	1	3
16	2	0	1	2	5
17	1	0	0	1	2
18	1	0	1	2	4
19	0	0	0	3	3
20	1	3	0	0	4
21	1	2	0	0	3
22	1	0	1	1	3
23	1	1	2	0	4
24	0	0	0	2	2
25	1	0	0	0	1
26	1	1	0	0	2
27	1	1	0	0	2
28	1	0	0	0	1
29	1	1	1	0	3
30	2	2	0	0	4
31	1	1	0	0	2
32	1	1	0	0	2

33	1	0	0	0	1
34	0	1	2	0	3
35	0	1	1	3	5
36	2	1	0	0	3
37	1	2	2	1	6
38	0	0	2	1	3
39	1	1	1	1	4
40	1	2	0	0	3
41	0	0	3	0	3
Total	34	30	31	34	129

Supplementary Table S2: Differences in levels of quantified metabolites in the main cohort comparing ERG_{high} samples to ERG_{low} samples

Metabolites	Benign	ERG_{low}	$ERG_{intermediate}$	ERG_{high}	ERG_{high} vs ERG_{low} *p*-values	ERG_{high} vs ERG_{low} *p*-values*	*p*-trend**	Corrected for stromal content	Corrected for cancer content	Corrected for benign epithelial content	Corrected for luminal space content
	n = 34	*n* = 30	*n* = 31	*n* = 34							
	Concentrations mmoles/kg wet weight, median (IQR)	Concentrations mmoles/kg wet weight, median (IQR)	Concentrations mmoles/kg wet weight, median (IQR)	Concentrations mmoles/kg wet weight, median (IQR)							
Alanine	1.74 (1.32 to 2.09)	2.18 (1.75 to 2.79)	2.16 (1.65 to 2.57)	2.48 (1.78 to 2.85)	0.711	0.866	0.611	0.876	0.929	0.744	0.666
Choline	0.45 (0.28 to 0.61)	0.99 (0.59 to 1.43)	1.01 (0.65 to 1.68)	1.23 (0.89 to 1.51)	0.126	0.29	0.116	0.096	0.102	0.043	0.038
Citrate	8.45 (4.62 to 11.85)	9.44 (5.56 to 14.68)	6.74 (3.94 to 10.34)	3.91 (2.59 to 7.20)	< 0.001	< 0.001	< 0.001	5.60E-06	2.20E-05	6.10E-05	5.80E-05
Creatine	2.51 (1.97 to 3.06)	2.27 (1.65 to 2.70)	2.10 (1.82 to 2.55)	2.00 (1.64 to 2.54)	0.953	1	0.546	0.913	0.817	0.666	0.729
Ethm	0 (0 to 0.18)	0 (0 to 0)	0 (0 to 0.15)	0.01 (0 to 0.31)	0.49	0.663	0.043	0.421	0.352	0.238	0.326
Glucose	0.78 (0.47 to 1.25)	0.15 (0.00 to 0.63)	0.00 (0.00 to 0.43)	0.00 (0.00 to 0.07)	0.008	0.061	0.007	0.012	0.021	0.014	6.40E-03
Glutamate	2.73 (2.42 to 3.53)	4.60 (4.02 to 6.11)	4.75 (3.55 to 6.88)	5.98 (4.26 to 7.79)	0.139	0.291	0.101	0.133	0.244	0.116	0.049
Glutamine	2.05 (1.58 to 2.35)	2.57 (2.27 to 3.41)	2.82 (2.14 to 3.50)	3.05 (2.61 to 3.70)	0.422	0.647	0.12	0.485	0.281	0.413	0.3
Glycine	1.55 (1.28 to 1.98)	1.99 (1.68 to 2.78)	2.51 (1.98 to 3.18)	2.90 (1.93 to 3.65)	0.023	0.115	0.008	5.70E-03	1.00E-02	6.10E-03	4.00E-03
GPC	0.41 (0.25 to 0.50)	0.76 (0.49 to 1.28)	0.73 (0.43 to 1.41)	0.90 (0.60 to 1.17)	1	1	0.865	0.72	0.563	0.823	0.653
GPE	0.23 (0 to 0.43)	0.17 (0 to 0.55)	0.03 (0 to 0.51)	0 (0 to 0.72)	0.999	1	0.94	0.913	0.862	0.909	0.831
Isoleucine	0.09 (0 to 0.12)	0.17 (0.03 to 0.24)	0.15 (0.06 to 0.29)	0.19 (0.11 to 0.31)	0.097	0.248	0.138	0.024	0.014	0.022	0.05
Lactate	13.93 (10.35 to 16.54)	21.92 (16.52 to 25.63)	20.52 (13.61to 26.41)	17.34 (15.69 to 22.01)	0.34	0.602	0.166	0.148	0.134	0.178	0.174
Leucine	0.24 (0.16 to 0.36)	0.38 (0.30 to 0.60)	0.46 (0.32 to 0.70)	0.51 (0.37 to 0.70)	0.715	0.866	0.168	0.746	0.788	0.598	0.668
Myo-inositol	9.06 (8.01 to 10.67)	10.03 (6.92 to 11.67)	9.13 (7.16 to 12.66)	8.97 (7.23 to 10.56)	0.49	0.663	0.294	0.373	0.431	0.454	0.475
PCh	0.32 (0.16 to 0.60)	0.61 (0.33 to 0.91)	0.63 (0.43 to 1.17)	0.96 (0.64 to 1.36)	0.067	0.248	0.005	0.017	0.027	0.026	0.018
PE	1.73 (1.09 to 2.59)	2.33 (1.46 to 3.51)	2.57 (1.67 to 4.14)	2.86 (2.33 to 3.79)	0.087	0.248	0.032	0.02	0.029	0.042	0.045
Putrescine	0.44 (0 to 1.34)	0.12 (0 to 0.67)	0.06 (0 to 0.30)	0 (0 to 0.10)	0.025	0.115	0.003	2.20E-03	4.00E-03	7.70E-03	6.40E-03
Scyllo-inositol	0.33 (0.25 to 0.56)	0.39 (0.31 to 0.59)	0.50 (0.37 to 0.63)	0.47 (0.37 to 0.61)	0.087	0.248	0.438	4.50E-03	5.50E-03	0.029	0.067
Spermine	1.69 (0.90 to 2.71)	2.10 (1.20 to 3.19)	1.23 (0.79 to 2.02)	0.89 (0.45 to 1.40)	< 0.001	< 0.001	< 0.001	7.20E-06	3.10E-05	9.90E-05	7.00E-05
Succinate	0.37 (0.30 to 0.47)	0.60 (0.43 to 0 .74)	0.62 (0.44 to 0.89)	0.63 (0.49 to 0.88)	0.412	0.647	0.446	0.401	0.433	0.247	0.181
Taurine	5.74 (3.98 to 6.27)	5.39 (3.90 to 6.96)	4.84 (3.48 to 7.09)	4.26 (3.28 to 5.54)	0.168	0.322	0.097	0.117	0.167	0.14	0.071
Valine	0.21 (0.18 to 0.29)	0.35 (0.27 to 0.50)	0.39 (0.22 to 0.49)	0.39 (0.26 to 0.53)	0.972	1	0.666	0.975	0.983	0.847	0.999

Ethm: Ethanolamine, GPC: Glycerophosphocholine, GPE: Glycerophosphoethanolamine, PCh: Phosphocholine, PE: Phosphoethanolamine.
*Benjamini-Hochberg adjusted values, **trend across increasing ERG groups (not including benign samples).

Supplementary Table S3: Differences in levels of quantified metabolites in the main cohort, comparing all ERG groups to benign samples and ERG$_{low}$ to ERG$_{intermediate}$ and ERG$_{intermediate}$ to ERG$_{high}$

Metabolites	Benign vs ERG$_{low}$	Benign vs ERG$_{intermediate}$	Benign vs ERG$_{high}$	ERG$_{low}$ vs ERG$_{int}$	ERG$_{int}$ vs ERG$_{high}$
	***p*-value**	***p*-value**	***p*-value**	***p*-value**	***p*-value**
Alanine	2.80E–03	0.044	5.30E–03	0.728	0.779
Choline	9.70E–06	1.70E–07	8.70E–09	0.035	0.687
Citrate	0.334	0.099	1.30E–04	0.015	0.19
Creatine	0.692	0.995	0.342	0.282	0.518
Ethm	0.161	0.476	0.739	0.356	0.633
Glucose	5.40E–06	4.50E–11	1.40E–14	0.094	0.374
Glutamate	4.30E–09	7.00E–10	4.50E–13	0.15	0.239
Glutamine	6.80E–04	1.90E–03	1.30E–06	0.332	0.381
Glycine	6.30E–03	1.60E–04	2.10E–07	0.091	0.39
GPC	1.10E–09	2.20E–07	1.50E–06	0.32	0.316
GPE	0.986	0.604	0.84	0.601	0.945
Isoleucine	0.109	0.015	3.60E–04	0.254	0.177
Lactate	8.70E–08	6.00E–06	1.00E–04	0.881	0.386
Leucine	2.50E–04	2.80E–07	1.60E–05	0.719	0.847
Myo–inositol	0.286	0.222	0.751	0.927	0.327
PCh	9.00E–03	1.80E–06	1.00E–08	0.077	0.273
PE	1.60E–03	4.40E–06	2.90E–08	0.238	0.501
Putrescine	0.261	7.80E–03	5.70E–05	0.03	0.939
Scyllo–inositol	0.372	0.608	0.688	0.963	0.492
Spermine	0.118	0.201	3.80E–05	0.035	0.086
Succinate	0.016	0.019	4.70E–06	0.243	0.838
Taurine	0.796	0.489	0.104	0.827	0.035
Valine	0.065	0.152	0.02	0.764	0.359

Ethm: Ethanolamine, GPC: Glycerophosphocholine, GPE: Glycerophosphoethanolamine.
GSH: Glutathione, PCh:Phosphocholine, PE: Phosphoethanolamine.

Supplementary Table S4: Differences in levels of quantified metabolites in the validation cohort comparing TMPRSS2–ERG positive and negative patients

Metabolites	TMPRSS2:ERG negative	TMPRSS2:ERG positive	*p*-value	*p*-value*
	n = 33	*n* = 7		
	Concentrations mmoles/ kg wet weight (IQR)	Concentrations mmoles/kg wet weight (IQR)		
Alanine	2.51 (2.07 to 2.88)	2.13 (1.59 to 2.51)	0.202	0.721
Ascorbate	0.06 (0.00 to 0.06)	0.08 (0.00 to 0.22)	0.487	0.84
Choline	0.96 (0.79 to 1.19)	0.79 (0.40 to 0.99)	0.148	0.617
Citrate	6.74 (3.88 to 8.74)	3.05 (1.25 to 4.69)	0.013	0.263
Creatine	3.01 (2.61 to 3.51)	2.69 (2.14 to 3.66)	0.293	0.775
Ethm	0.22 (0.00 to 0.36)	0.00 (0.00 to 0.00)	0.088	0.55
Glucose	0.39 (0.00 to 0.77)	0.55 (0.00 to 1.56)	0.805	0.957
Glutamate	4.08 (3.12 to 4.62)	3.94 (3.45 to 4.64)	0.832	0.957
Glutamine	2.09 (1.61 to 2.47)	2.09 (1.78 to 2.55)	0.919	0.957
Glycine	2.37 (1.92 to 2.86)	2.41 (1.54 to 2.64)	0.857	0.957
GPC	0.90 (0.52 to 1.14)	0.85 (0.48 to 1.21)	0.905	0.957
GPE	0.13 (0.00 to 0.16)	0.18 (0.00 to 0.07)	0.099	0.55
GSH	0.84 (0.74 to 1.04)	0.86 (0.64 to 1.13)	0.898	0.957
Isoleucine	0.17 (0.09 to 0.25)	0.13 (0.08 to 0.16)	0.413	0.794
Lactate	16.01 (12.74 to 18.12)	15.92 (12.34 to 20.40)	0.959	0.959
Leucine	0.36 (0.22 to 0.47)	0.40 (0.27 to 0.38)	0.571	0.892
Myo–inositol	8.82 (7.31 to 10.05)	8.10 (7.09 to 8.90)	0.504	0.84
PCh	0.62 (0.31 to 0.81)	0.85 (0.63 to 0.98)	0.11	0.55
PE	2.34 (1.82 to 2.78)	2.68 (2.18 to 2.80)	0.282	0.775
Putrescine	0.17 (0.00 to 0.27)	0.06 (0.00 to 0.00)	0.348	0.791
Scyllo–inositol	0.60 (0.38 to 0.78)	0.48 (0.34 to 0.47)	0.381	0.794
Spermine	0.69 (0.38 to 0.81)	0.31 (0.10 to 0.52)	**0.021**	0.263
Succinate	0.54 (0.40 to 0.69)	0.46 (0.37 to 0.57)	0.31	0.775
Taurine	5.81 (4.83 to 7.06)	5.66 (5.16 to 6.80)	0.869	0.957
Valine	0.48 (0.41 to 0.50)	0.46 (0.39 to 0.49)	0.81	0.957

Ethm: Ethanolamine, GPC: Glycerophosphocholine, GPE: Glycerophosphoethanolamine, GSH: Glutathione, PCh: Phosphocholine, PE: Phosphoethanolamine *Benjamini-Hochberg corrected for multiple testing.

Supplementary Table S5: Differences in expression levels of key metabolic genes comparing ERG_{high} and ERG_{low} in the main cohort, including estimated means and adjusted for benign epithelia, stroma, cancer and luminal space

Gene	Estimated/predicted means med 95 % CI		*p*-value	*p*-value*	Adjusted for benign epithelial content	Adjusted for stromal content	Adjusted for cancer content	Adjusted for luminal space content
	ERG_{low}	ERG_{high}						
ACACA	9.81 (9.67, 9.94)	10.10 (9.97, 10.24)	9.80E–04	0.003	2.50E–03	1.50E–03	3.10E–03	4.70E–04
ACO1	9.71 (9.61, 9.82)	9.40 (9.30, 9.51)	2.50E–06	6.09E–05	6.30E–06	6.00E–06	1.40E–05	2.60E–06
ACO2	8.06 (7.97, 8.15)	7.93 (7.85, 8.02)	0.036	0.065	0.031	0.013	0.014	0.046
ACSL1			0.683	0.683	0.715	0.593	0.606	0.64
ACSL3	10.78 (10.59, 10.97)	11.07 (10.88, 11.26)	5.80E–03	0.014	1.40E–03	4.80E–03	1.50E–03	8.80E–03
ACSL4	7.08 (6.95, 7.22)	6.82 (6.69, 6.95)	3.80E–03	0.010	6.90E–03	6.20E–03	0.012	4.00E–03
ACSL5	6.20 (5.85, 6.55)	6.67 (6.33, 7.01)	0.045	0.073	0.021	0.035	0.018	0.045
ACSL6			0.264	0.320	0.312	0.209	0.247	0.171
AGXT1			0.155	0.208	0.193	0.215	0.255	0.139
ALDOA	9.33 (9.15, 9.50)	8.79 (8.62, 8.96)	1.40E–05	1.89E–04	2.40E–05	2.20E–05	4.80E–05	1.90E–05
ALDOB	6.03 (5.85, 6.20)	6.37 (6.20, 6.55)	3.40E–03	0.009	3.40E–03	6.50E–03	8.40E–03	9.70E–04
ALDOC			0.38	0.420	0.43	0.546	0.636	0.311
AMD1	6.93 (6.73, 7.13)	7.28 (7.08, 7.48)	3.40E–03	0.009	1.70E–03	4.50E–03	2.80E–03	2.70E–03
CHKA	8.10 (7.99, 8.21)	8.42 (8.32, 8.53)	1.60E–05	1.89E–04	2.70E–05	2.00E–05	3.10E–05	2.50E–05
CS			0.148	0.203	0.175	0.144	0.161	0.12
DLD	7.83 (7.71, 7.94)	7.59 (7.47, 7.71)	3.40E–04	0.001	6.10E–04	4.60E–04	7.70E–04	8.40E–04
DLST			0.132	0.189	0.115	0.074	0.054	0.14
ENO1	11.39 (11.29, 11.49)	11.64 (11.55, 11.74)	8.10E–05	4.78E–04	1.70E–04	1.20E–04	2.10E–04	9.90E–05
FASN	11.62 (11.36, 11.87)	11.98 (11.72, 12.23)	0.015	0.030	0.014	0.017	0.015	6.80E–03
FH			0.549	0.567	0.58	0.365	0.361	0.853
G6PD	6.95 (6.86, 7.04)	7.08 (6.99, 7.17)	0.033	0.061	0.037	0.044	0.053	0.028
GAPDH			0.285	0.339	0.33	0.392	0.446	0.181
GPI			0.652	0.663	0.75	0.818	0.906	0.559
HK1			0.06	0.095	0.057	0.033	0.033	0.063
HK2			0.241	0.298	0.053	0.121	0.025	0.344
IDH1			0.324	0.378	0.415	0.323	0.394	0.157
IDH2			0.191	0.241	0.164	0.231	0.215	0.15
IDH3A			0.338	0.380	0.322	0.281	0.253	0.404
IDH3B	8.92 (8.84, 8.99)	8.74 (8.67, 8.82)	3.70E–04	0.001	4.40E–04	5.70E–04	6.90E–04	4.10E–04
IDH3G			0.119	0.179	0.179	0.17	0.279	0.081
LDHA			0.178	0.229	0.223	0.258	0.315	0.239
LDHB	9.41 (9.13, 9.68)	8.77 (8.50, 9.05)	1.90E–04	9.21E–04	4.00E–04	2.80E–04	5.20E–04	3.00E–06
MDH1	10.33 (10.22, 10.45)	10.19 (10.07, 10.30)	0.041	0.068	0.036	0.082	0.079	7.30E–03
MDH2	11.93 (11.86, 12.00)	12.10 (12.03, 12.16)	4.00E–05	3.60E–04	2.60E–05	6.90E–05	6.10E–05	2.80E–05

NPY	10.93 (10.18, 11.68)	13.24 (12.50, 13.98)	2.90E–06	6.09E–05	1.60E–06	3.30E–06	2.10E–06	6.10E–06
OAZ			0.17	0.223	0.177	0.174	0.091	0.587
ODC	10.75 (10.49, 11.01)	11.12 (10.85, 11.38)	0.012	0.024	0.013	0.032	0.04	7.50E–03
OGDH			0.075	0.115	0.056	0.092	0.079	0.071
OGDHL	6.13 (5.94, 6.32)	7.48 (7.29, 7.66)	7.70E–29	4.85E–27	2.50E–33	2.10E–28	2.80E–30	5.90E–28
PDHA	8.55 (8.47, 8.62)	8.69 (8.62, 8.76)	7.90E–03	0.018	0.011	9.70E–03	0.014	8.90E–03
PDHB			0.448	0.487	0.479	0.384	0.418	0.424
PGD	8.41 (8.29, 8.53)	8.66 (8.54, 8.77)	2.80E–04	0.001	4.30E–04	6.20E–04	1.20E–03	5.70E–04
PGK1	10.36 (10.23, 10.50)	10.04 (9.91, 10.17)	7.70E–05	4.78E–04	1.00E–04	6.10E–05	9.50E–05	3.40E–05
PGLS	8.69 (8.58, 8.79)	8.94 (8.84, 9.04)	9.10E–05	4.78E–04	1.80E–04	2.20E–04	4.40E–04	1.70E–05
PGLS	8.69 (8.59, 8.79)	8.94 (8.84, 9.04)	9.10E–05	4.78E–04	1.80E–04	2.20E–04	4.40E–04	1.70E–05
PGM1	9.56 (9.40, 9.73)	9.19 (9.03, 9.36)	1.10E–03	0.003	1.80E–03	1.70E–03	3.40E–03	1.20E–03
PKM2	9.20 (9.09, 9.31)	9.36 (9.26, 9.47)	0.027	0.052	0.027	0.028	0.027	0.025
RBKS	6.82 (6.73, 6.91)	7.05 (6.97, 7.14)	2.50E–04	0.001	6.10E–04	3.50E–04	8.10E–04	3.20E–04
RPE			0.335	0.380	0.332	0.244	0.24	0.443
RPIA	7.44 (7.30, 7.58)	7.62 (7.49, 7.76)	0.04	0.068	0.051	0.06	0.075	4.40E–03
SAT1	12.27 (12.12, 12.43)	12.64 (12.49, 12.80)	4.00E–04	0.001	1.30E–04	2.40E–04	9.80E–05	1.30E–03
SDHA	8.67 (8.59, 8.74)	8.55 (8.47, 8.62)	0.012	0.024	0.013	0.016	0.017	0.015
SDHB			0.548	0.567	0.492	0.528	0.584	0.609
SDHC			0.132	0.189	0.139	0.287	0.161	0.216
SDHD	7.59 (7.44, 7.75)	7.33 (7.17, 7.48)	0.011	0.024	0.012	0.013	0.311	6.50E–03
SHMT1	7.01 (6.9, 7.2)	7.31 (7.16, 7.46)	0.003	0.009	0.003	0.001	0.002	2.00E–03
SMOX	7.15 (6.86, 7.43)	7.75 (7.47, 8.03)	1.80E–05	1.89E–04	3.00E–05	2.50E–05	4.00E–05	1.10E–06
SMS	9.73 (9.46, 10.00)	9.37 (9.10, 9.64)	0.041	0.068	0.019	0.011	4.60E–03	0.067
SRM	8.06 (7.94, 8.19)	8.30 (8.17, 8.42)	6.20E–03	0.014	0.011	9.00E–03	0.015	5.20E–03
SUCLG			0.148	0.203	0.165	0.137	0.142	0.198
TALDO1			0.506	0.540	0.637	0.461	0.552	0.473
TKT	9.46 (9.31, 9.61)	9.86 (9.71, 10.01)	4.80E–05	3.78E–04	1.10E–04	1.00E–04	2.50E–04	6.20E–06
TPI1	9.69 (9.52, 9.86)	9.30 (9.14, 9.47)	4.50E–04	0.001	7.60E–04	7.00E–04	1.10E–03	7.00E–04

ACACA: Acetyl-CoA carboxylase alpha, ACO1: Aconitase 1, ACO2: Aconitase 2, ACSL1: Acyl-CoA synthetase 1, ACSL3: Acyl-CoA synthetase 3, ACSL4: Acyl-CoA synthetase 4,ACSL5: Acyl-CoA synthetase 5, ACSL6: Acyl-CoA synthetase 6, AGXT1: Alanine-glyoxylate aminotransferase 1, ALDOA: Aldolase A, ALDOB: Aldolase B, ALDOC: Aldolase C,AMD1: Adenosylmethionine decarboxylase, CHKA: Choline kinase alpha, CS: Citrate synthase, DLD: Dihydrolipoamide dehydrogenase, DLST: Dihydrolipoamides–succinyltransferase, ENO1: Enolase 1, FASN: Fatty acid synthase, FH: Fumarate hydratase, G6PD: Glucose-6-phosphate dehydrogenase, GAPDH: Glyceraldehyde-3-phosphatedehydrogenase, GPI: Glucose-6-phosphate isomerase, HK1: Hexokinase 1, HK2: Hexokinase 2, IDH1: Isocitrate dehydrogenase 1, IDH2: Isocitrate dehydrogenase 2, IDH3A:Isocitrate dehydrogenase 3A, IDH3B: Isocitrate dehydrogenase 3B, IDH3G: Isocitrate dehydrogenase 3G, MDH1: Malate dehydrogenase 1, MDH2: Malate dehydrogenase 2, NPY:Neuropeptide Y, OAZ: Ornithine decarboxylase antizyme, ODC: Ornithine decarboxylase, OGDH: Oxoglutarate (alpha–ketoglutarate) dehydrogenase, OGDHL: Oxoglutarate dehydrogenase-like, PDHA: Pyruvate dehydrogenase alpha, PDHB: Pyruvate dehydrogenase beta, PGK1: Phosphoglycerate kinase, PGD: Phosphogluconate dehydrogenase, PGLS: 6-phosphogluconolactonase, PGM1: Phosphoglucomutase, PKM2: Pyruvate kinase, RBKS: Ribokinase, RPE: Ribulose-5-phosphate-3-epimerase, RPIA: Ribose 5-phosphate isomerase, SAT1: Spermidine/spermine-N1-acetyltransferase 1, SDHA: Succinate dehydrogenase complex, subunit A, SDHB: Succinate dehydrogenase complex, subunit B, SDHD: Succinate dehydrogenase complex, subunit D, SHMT1: Serine hydroxymethyltransferase 1, SMOX: Spermine oxidase, SMS: Spermine synthase, SRM: Spermidine synthase, SUCLG: Succinyl-CoA ligase, TALDO1: Transaldolase 1, TKT: Transketolase, TPI1: Triosephosphate isomerase 1. Since the gene expression values were log2 transformed, a difference in expression by one unit corresponds to a twofold mean change in probe intensities. *Benjamini–Hochberg corrected.

Supplementary Table S6: Differences in expression levels of key metabolic genes comparing ERG_{high} and ERG_{low} in low Gleason (Gleason ≤ 3 + 4) samples in the main cohort, including estimated means and adjusted for benign epithelia, stroma, cancer and luminal space

Gene	Estimated/predicted means med 95 % CI		*p*-value	*p*-value*	Adjusted for benign epithelial content	Adjusted for stromal content	Adjusted for cancer content	Adjusted for luminal space content
	ERG_{low}	ERG_{high}						
ACACA	9.81 (9.64, 9.98)	10.19 (10.04, 10.33)	2.90E–04	0.001	0.247	0.55	0.355	0.22
ACO1	9.70 (9.58, 9.83)	9.47 (9.36, 9.58)	4.20E–03	0.010	0.016	0.026	8.90E–03	0.041
ACO2	8.12 (8.01, 8.23)	7.91 (7.81, 8.00)	2.80E–03	0.007	0.016	7.60E–04	4.40E–03	0.016
ACSL1	9.30 (8.99, 9.60)	8.86 (8.59, 9.13)	0.017	0.029	0.026	0.072	0.078	0.028
ACSL3			0.294	0.331	1.06E–01	0.062	6.00E–02	8.70E–02
ACSL4	7.18 (7.01, 7.35)	6.76 (6.62, 6.91)	1.80E–04	7.56E–04	0.552	0.647	0.615	0.617
ACSL5			0.248	0.284	6.40E–05	0.029	1.90E–04	2.10E–04
ACSL6			0.826	0.853	0.14	0.136	0.22	0.488
AGXT1			0.951	0.957	3.70E–07	4.40E–06	6.30E–07	4.30E–07
ALDOA	9.39 (9.14, 9.63)	8.74 (8.53, 8.94)	5.80E–05	3.32E–04	8.90E–03	0.022	0.015	0.015
ALDOB	6.06 (5.82, 6.30)	6.45 (6.25, 6.65)	0.014	0.025	2.00E–04	2.80E–04	5.20E–05	2.00E–05
ALDOC	7.43384 (7.29, 7.58)	7.05 (6.92, 7.19)	3.30E–06	2.97E–05	0.526	0.563	0.62	0.497
AMD1	6.93 (6.66, 7.21)	7.35 (7.11, 7.59)	0.013	0.024	3.70E–05	3.70E–05	2.40E–05	4.70E–05
CHKA			0.129	0.159	4.30E–03	6.20E–05	6.30E–05	1.10E–04
CS			0.638	0.681	4.10E–03	9.70E–03	5.50E–03	5.50E–03
DLD	7.89 (7.73, 8.04)	7.55 (7.41, 7.70)	2.00E–06	2.10E–05	1.40E–04	4.70E–04	1.70E–04	8.80E–05
DLST			0.321	0.355	1.10E–04	2.40E–13	3.70E–04	2.50E–11
ENO1	11.29 (11.15, 11.43)	11.63 (11.51, 11.74)	2.60E–04	0.001	1.50E–06	1.50E–11	8.70E–03	1.50E–06
FASN			0.066	0.099	1.30E–04	2.10E–03	2.90E–04	2.50E–04
FH			0.957	0.957	2.10E–03	3.20E–03	3.50E–03	3.50E–03
G6PD			0.111	0.143	0.767	0.319	0.564	0.942
GAPDH	11.36 (11.22, 11.51)	11.59 (11.47, 11.72)	7.00E–03	0.015	7.90E–04	6.30E–07	3.40E–03	2.60E–08
GPI			0.406	0.441	0.15	0.02	0.049	0.06
HK1	5.99 (5.86, 6.12)	5.78 (5.67, 5.90)	0.015	0.026	0.03	4.00E–03	4.00E–03	4.40E–04
HK2			0.077	0.108	2.30E–03	5.40E–03	6.40E–03	1.30E–03
IDH1	9.06 (8.76, 9.37)	8.64 (8.37, 8.91)	0.02	0.033	0.011	0.011	0.012	6.90E–03
IDH2	9.03 (8.87, 9.18)	9.23 (9.09, 9.36)	0.038	0.058	0.081	0.144	0.104	0.108
IDH3A			0.184	0.223	3.50E–03	6.10E–06	1.50E–03	3.40E–05
IDH3B	8.91 (8.82, 9.01)	8.75 (8.67, 8.84)	9.80E–03	0.019	0.017	0.011	0.091	2.10E–03
IDH3G	8.43 (8.31, 8.54)	8.74 (8.63, 8.84)	2.60E–08	4.10E–07	0.032	7.20E–03	0.019	0.017
LDHA			0.072	0.105	3.60E–04	0.073	0.027	0.045
LDHB	9.44 (9.05, 9.83)	8.83 (8.49, 9.17)	0.012	0.023	0.039	0.14	0.227	0.028
MDH1	10.34 (10.18, 10.50)	10.15 (10.01, 10.29)	0.038	0.058	0.227	0.023	0.077	0.068
MDH2	11.89 (11.80, 11.99)	12.14 (12.06, 12.22)	4.10E–05	2.58E–04	3.60E–05	2.30E–04	4.50E–05	6.00E–05
NPY	10.41 (9.34, 11.48)	13.24 (12.33, 14.15)	6.40E–05	3.36E–04	4.70E–04	8.20E–07	3.00E–03	3.70E–06
OAZ	6.57 (6.33, 6.81)	6.38 (6.15, 6.62)	3.10E–03	0.008	0.123	0.029	0.026	0.08
ODC	10.68 (10.28, 11.09)	11.22 (10.86, 11.58)	0.028	0.045	9.10E–23	5.50E–23	2.50E–21	1.80E–24
OGDH	8.35 (8.24, 8.47)	8.54 (8.44, 8.64)	8.60E–03	0.017	0.062	0.055	0.044	0.07
OGDHL	5.95 (5.70, 6.21)	7.62 (7.41, 7.84)	3.40E–24	2.14E–22	4.80E–04	9.40E–04	2.40E–03	6.30E–05
PDHA			0.096	0.129	4.60E–07	2.50E–12	4.60E–07	4.70E–13
PDHB			0.107	0.140	2.20E–04	1.30E–03	4.40E–04	4.40E–04
PGD	8.38 (8.23, 8.52)	8.70 (8.59, 8.82)	3.30E–04	0.001	3.60E–04	3.40E–04	2.40E–04	3.00E–04

PGK1	10.36 (10.15, 10.57)	9.97 (9.79, 10.16)	4.40E–03	0.010	0.133	0.164	0.107	0.186
PGLS	8.69 (8.54, 8.84)	8.97 (8.84, 9.10)	2.10E–03	0.006	0.017	0.019	0.045	0.015
PGLS	8.69 (8.54, 8.84)	8.97 (8.84, 9.10)	2.10E–03	0.006	0.37	0.974	0.732	0.407
PGM1	9.64 (9.41, 9.88)	9.15 (8.95, 9.35)	1.80E–03	0.005	0.123	0.211	0.12	0.1
PKM2	9.06 (8.95, 9.18)	9.43 (9.32, 9.54)	2.90E–13	9.14E–12	4.10E–03	0.01	7.30E–03	3.80E–03
RBKS	6.73 (6.60, 6.86)	7.05 (6.94, 7.16)	3.80E–04	0.001	0.062	0.087	0.079	0.063
RPE			0.755	0.793	5.90E–04	1.90E–04	3.10E–03	3.90E–05
RPIA			0.241	0.281	9.50E–04	1.90E–03	3.60E–03	2.00E–03
SAT1	12.05 (11.82, 12.27)	12.64 (12.45, 12.83)	9.10E–05	4.10E–04	0.123	0.22	0.16	0.116
SDHA	8.70 (8.63, 8.78)	8.53 (8.46, 8.60)	3.30E–05	2.31E–04	0.966	0.901	0.92	0.955
SDHB			0.206	0.245	9.80E–03	0.148	0.25	0.012
SDHC	7.75 (7.53, 7.96)	7.30 (7.11, 7.49)	9.00E–04	0.003	0.951	0.703	0.716	0.957
SDHD	7.72 (7.52, 7.92)	7.19 (7.01, 7.37)	8.90E–06	7.01E–05	0.814	0.931	0.873	0.915
SHMT1			0.077	0.108	2.30E–03	5.40E–03	6.40E–03	1.30E–03
SMOX	7.21 (6.92, 7.51)	8.08 (7.80, 8.36)	1.40E–11	2.94E–10	3.10E–03	6.50E–04	1.80E–03	2.90E–03
SMS			0.094	0.129	1.10E–03	5.00E–03	1.70E–03	2.10E–03
SRM	8.06 (7.90, 8.21)	8.35 (8.22, 8.47)	5.00E–03	0.011	9.50E–03	0.017	0.011	0.01
SUCLG	9.62 (9.49, 9.75)	9.32 (9.20, 9.44)	7.40E–05	3.59E–04	0.012	0.014	0.011	0.017
TALDO1			0.122	0.154	0.221	0.383	0.4	0.228
TKT	9.30 (9.07, 9.52)	10.00 (9.80, 10.19)	8.10E–07	1.02E–05	0.1	0.36	0.177	0.447
TPI1	9.73 (9.50, 9.95)	9.29 (9.10, 9.48)	3.30E–03	0.008	0.088	0.019	0.092	0.01

ACACA: Acetyl-CoA carboxylase alpha, ACO1: Aconitase 1, ACO2: Aconitase 2, ACSL1: Acyl-CoA synthetase 1, ACSL3: Acyl-CoA synthetase 3, ACSL4: Acyl-CoA synthetase 4,ACSL5: Acyl-CoA synthetase 5, ACSL6: Acyl-CoA synthetase 6, AGXT1: Alanine-glyoxylate aminotransferase 1, ALDOA: Aldolase A, ALDOB: Aldolase B, ALDOC: Aldolase C,AMD1: Adenosylmethionine decarboxylase, CHKA: Choline kinase alpha, CS: Citrate synthase, DLD: Dihydrolipoamide dehydrogenase, DLST: Dihydrolipoamides-succinyltransferase, ENO1: Enolase 1, FASN: Fatty acid synthase, FH: Fumarate hydratase, G6PD: Glucose-6-phosphate dehydrogenase, GAPDH: Glyceraldehyde-3-phosphatedehydrogenase, GPI: Glucose-6-phosphate isomerase, HK1: Hexokinase 1, HK2: Hexokinase 2, IDH1: Isocitrate dehydrogenase 1, IDH2: Isocitrate dehydrogenase 2, IDH3A:Isocitrate dehydrogenase 3A, IDH3B: Isocitrate dehydrogenase 3B, IDH3G: Isocitrate dehydrogenase 3G, MDH1: Malate dehydrogenase 1, MDH2: Malate dehydrogenase 2, NPY:Neuropeptide Y, OAZ: Ornithine decarboxylase antizyme, ODC: Ornithine decarboxylase, OGDH: Oxoglutarate (alpha-ketoglutarate) dehydrogenase, OGDHL: Oxoglutarate dehydrogenase-like, PDHA: Pyruvate dehydrogenase alpha, PDHB: Pyruvate dehydrogenase beta, PGK1: Phosphoglycerate kinase, PGD: Phosphogluconate dehydrogenase, PGLS: 6-phosphogluconolactonase, PGM1: Phosphoglucomutase, PKM2: Pyruvate kinase, RBKS: Ribokinase, RPE: Ribulose-5-phosphate-3-epimerase, RPIA: Ribose 5-phosphate isomerase, SAT1: Spermidine/spermine-N1-acetyltransferase 1, SDHA: Succinate dehydrogenase complex, subunit A, SDHB: Succinate dehydrogenase complex, subunit B, SDHD: Succinate dehydrogenase complex, subunit D, SHMT1: Serine hydroxymethyltransferase 1, SMOX: Spermine oxidase, SMS: Spermine synthase, SRM: Spermidine synthase, SUCLG: Succinyl-CoA ligase, TALDO1: Transaldolase 1, TKT: Transketolase, TPI1: Triosephosphate isomerase 1. Since the gene expression values were log2 transformed, a difference inexpression by one unit corresponds to a twofold mean change in probe intensities. *Benjamini-Hochberg corrected.

Supplementary Table S7: Differences in expression levels of key metabolic genes comparing ERG$_{high}$ and ERGl$_{ow}$ in high Gleason (Gleason ≥ 4 + 3) samples in the main cohort, including estimated means and adjusted for benign epithelia, stroma, cancer and luminal space

Gene	Estimated/predicted means med 95 % CI		*p*-value	*p*-value*	Adjusted for benign epithelial content	Adjusted for stromal content	Adjusted for cancer content	Adjusted for luminal space content
	ERG$_{low}$	ERG$_{high}$						
ACACA			0.054	0.144	0.741	0.55	0.794	0.431
ACO1	9.68 (9.52, 9.84)	9.37 (9.21, 9.52)	1.10E–03	0.023	0.402	0.699	0.395	0.708
ACO2			0.253	0.349	0.247	0.01	0.047	5.00E–03
ACSL1			0.444	0.519	0.665	0.418	0.488	0.386
ACSL3	10.55 (10.32, 10.78)	10.89 (10.66, 11.11)	0.017	0.082	0.048	0.094	0.107	0.036
ACSL4			0.201	0.288	0.247	0.01	0.047	5.00E–03
ACSL5			0.055	0.144	0.277	0.395	0.365	0.363
ACSL6			0.099	0.164	0.94	0.837	0.769	0.964
AGXT1			0.062	0.147	0.143	0.06	0.16	0.998
ALDOA	9.27(9.03, 9.51)	8.88 (8.63, 9.12	0.022	0.089	0.273	0.25	0.238	0.175
ALDOB			0.079	0.158	0.133	0.633	0.204	0.829
ALDOC			0.382	0.491	0.167	0.191	0.17	0.158
AMD1			0.085	0.158	0.932	0.738	0.632	0.95
CHKA	8.96 (8.83, 9.09)	9.44 (9.30, 9.57)	6.60E–07	2.08E–05	0.015	1.20E–03	2.90E–03	2.10E–03
CS			0.255	0.349	0.444	0.063	0.432	0.055
DLD			0.088	0.158	7.00E–03	1.20E–03	6.60E–04	0.025
DLST	6.89 (6.70, 7.07)	7.28 (7.09, 7.46)	1.50E–03	0.024	0.539	0.433	0.57	0.44
ENO1	11.47 (11.35, 11.59)	11.66 (11.53, 11.78)	0.024	0.089	5.80E–04	7.20E–04	1.70E–04	1.30E–04
FASN			0.115	0.186	1.30E–10	1.20E–10	4.60E–11	1.10E–10
FH			0.596	0.636	0.891	0.174	0.383	0.123
G6PD			0.194	0.284	0.468	0.123	0.309	0.228
GAPDH			0.531	0.589	0.035	0.018	0.013	0.01
GPI			0.533	0.589	9.40E–03	6.80E–03	0.011	1.60E–03
HK1			0.394	0.496	0.18	0.081	0.143	7.60E–03
HK2			0.453	0.519	0.774	0.896	0.771	0.931
IDH1			0.43	0.519	0.062	0.188	0.155	0.239
IDH2			0.063	0.147	0.167	0.448	0.27	0.483
IDH3A			0.093	0.160	8.40E–03	3.30E–03	2.90E–03	3.30E–03
IDH3B	8.92 (8.81, 9.03)	8.70 (8.59, 8.81)	4.30E–03	0.039	1.10E–03	0.057	0.011	0.042
IDH3G			0.592	0.636	0.012	0.064	0.014	0.102
LDHA			0.307	0.403	0.733	0.03	0.118	0.041
LDHB	9.39 (9.02, 9.75)	8.77 (8.40, 9.13)	0.011	0.063	0.034	0.092	0.205	6.20E–03
MDH1			0.903	0.918	0.308	0.083	0.179	0.029
MDH2			0.077	0.158	0.023	0.081	0.04	0.13
NPY	11.48 (10.49, 12.48)	13.35 (12.36, 14.34)	3.80E–03	0.039	0.888	0.156	0.544	0.285
OAZ	5.30 (5.12, 5.48)	4.92 (4.75, 5.10)	3.20E–03	0.039	0.012	0.018	0.014	0.016
ODC			0.084	0.158	0.106	0.011	0.03	1.10E–03

OGDH			0.805	0.831	0.964	0.798	0.755	0.626
OGDHL	6.33 (6.06, 6.60)	7.32 (7.06, 7.59)	1.70E–10	1.07E–08	0.747	0.053	0.135	0.038
PDHA	5.84 (5.74, 5.95)	5.66 (5.55, 5.77)	0.019	0.086	3.20E–03	6.80E–05	1.90E–04	1.60E–04
PDHB			0.951	0.951	0.09	0.033	0.062	0.024
PGD			0.142	0.224	0.069	0.02	0.016	0.012
PGK1	8.21 (8.05, 8.37)	8.01 (7.85, 8.17)	0.032	0.099	0.489	0.595	0.444	0.91
PGLS	8.68 (8.54, 8.81)	8.90 (8.77, 9.03)	1.00E–02	0.063	0.14	0.056	0.079	0.119
PGLS	8.68 (8.54, 8.81)	8.90 (8.77, 9.03)	1.00E–02	0.063	0.195	0.013	0.079	0.034
PGM1			0.094	0.160	0.085	0.097	0.162	0.039
PKM2			0.445	0.519	0.088	0.026	0.042	0.042
RBKS	6.89 (6.78, 7.00)	7.06 (6.94, 7.17)	0.037	0.106	0.717	0.625	0.752	0.347
RPE			0.194	0.284	0.013	0.037	0.023	4.20E–03
RPIA			0.08	0.158	0.678	0.518	0.692	0.314
SAT1	12.38 (12.18, 12.58)	12.66 (12.46, 12.85)	0.033	0.099	0.761	0.133	0.418	0.252
SDHA			0.061	0.147	0.496	0.48	0.921	0.452
SDHB			0.414	0.511	0.036	0.026	0.018	0.082
SDHC	6.29 (6.15, 6.44)	6.06 (5.91, 6.21)	0.028	0.098	0.21	0.025	0.055	0.021
SDHD			0.295	0.395	0.756	0.426	0.468	0.372
SHMT1	6.98 (6.76, 7.21)	7.32 (7.10, 7.55)	0.023	0.089	0.142	0.083	0.106	0.164
SMOX	6.87 (6.47, 7.27)	7.45 (7.06, 7.84)	9.50E–03	0.063	0.167	0.095	0.104	0.079
SMS			0.078	0.158	3.00E–03	8.40E–03	9.00E–03	2.40E–03
SRM			0.166	0.255	0.918	0.946	0.996	0.718
SUCLG	8.90 (8.77, 9.03)	9.11 (8.98, 9.24)	0.016	0.082	0.785	0.324	0.309	0.519
TALDO1			0.801	0.831	6.80E–03	0.017	8.80E–03	5.90E–03
TKT			0.086	0.158	0.149	0.083	0.117	0.059
TPI1	9.68 (9.43, 9.92)	9.33 (9.08, 9.57)	0.03	0.099	0.094	0.114	0.118	0.064

ACACA: Acetyl-CoA carboxylase alpha, ACO1: Aconitase 1, ACO2: Aconitase 2, ACSL1: Acyl-CoA synthetase 1, ACSL3: Acyl-CoA synthetase 3, ACSL4: Acyl-CoA synthetase 4,ACSL5: Acyl-CoA synthetase 5, ACSL6: Acyl-CoA synthetase 6, AGXT1: Alanine-glyoxylate aminotransferase 1, ALDOA: Aldolase A, ALDOB: Aldolase B, ALDOC: Aldolase C,AMD1: Adenosylmethionine decarboxylase, CHKA: Choline kinase alpha, CS: Citrate synthase, DLD: Dihydrolipoamide dehydrogenase, DLST: Dihydrolipoamides-succinyltransferase, ENO1: Enolase 1, FASN: Fatty acid synthase, FH: Fumarate hydratase, G6PD: Glucose-6-phosphate dehydrogenase, GAPDH: Glyceraldehyde-3-phosphatedehydrogenase, GPI: Glucose-6-phosphate isomerase, HK1: Hexokinase 1, HK2: Hexokinase 2, IDH1: Isocitrate dehydrogenase 1, IDH2: Isocitrate dehydrogenase 2, IDH3A:Isocitrate dehydrogenase 3A, IDH3B: Isocitrate dehydrogenase 3B, IDH3G: Isocitrate dehydrogenase 3G, MDH1: Malate dehydrogenase 1, MDH2: Malate dehydrogenase 2, NPY:Neuropeptide Y, OAZ: Ornithine decarboxylase antizyme, ODC: Ornithine decarboxylase, OGDH: Oxoglutarate (alpha-ketoglutarate) dehydrogenase, OGDHL: Oxoglutarate dehydrogenase-like, PDHA: Pyruvate dehydrogenase alpha, PDHB: Pyruvate dehydrogenase beta, PGK1: Phosphoglycerate kinase, PGD: Phosphogluconate dehydrogenase, PGLS: 6-phosphogluconolactonase, PGM1: Phosphoglucomutase, PKM2: Pyruvate kinase, RBKS: Ribokinase, RPE: Ribulose-5-phosphate-3-epimerase, RPIA: Ribose 5-phosphate isomerase, SAT1: Spermidine/spermine-N1-acetyltransferase 1, SDHA: Succinate dehydrogenase complex, subunit A, SDHB: Succinate dehydrogenase complex, subunit B, SDHD: Succinate dehydrogenase complex, subunit D, SHMT1: Serine hydroxymethyltransferase 1, SMOX: Spermine oxidase, SMS: Spermine synthase, SRM: Spermidine synthase, SUCLG: Succinyl-CoA ligase, TALDO1: Transaldolase 1, TKT: Transketolase, TPI1: Triosephosphate isomerase 1. Since the gene expression values were log2 transformed, a difference in expression by one unit corresponds to a twofold mean change in probe intensities. *Benjamini-Hochberg corrected.

Supplementary Table S8: Differences in levels of quantified metabolites in the main cohort comparing ERG$_{\text{high}}$ samples to ERG$_{\text{low}}$ samples in low Gleason samples (Gleason ≤ 3 + 4), corrected for multiple testing with Benjamini-Hochberg correction and adjusted for stroma, cancer, benign epithelia and luminal space

Metabolites	**ERG$_{\text{low}}$**	**ERG$_{\text{high}}$**						
	(*n* = 12)	**(*n* = 17)**						
	Concentrations mmoles/kg wet weight, median (IQR)	**Concentrations mmoles/kg wet weight, median (IQR)**	***p*-value**	***p*-value***	**Adjusted for stromal content**	**Adjusted for cancer content**	**Adjusted for benign epithelial content**	**Adjusted for luminal space content**
Alanine	1.99 (1.64 to 2.43)	2.60 (1.78 to 2.85)	0.651	0.83	0.766	0.702	0.622	0.667
Choline	0.78 (0.49 to 1.43)	1.23 (0.84 to 1.48)	0.087	0.16	0.364	0.143	0.075	0.082
Citrate	13.95 (8.62 to 17.06)	7.07 (3.43 to 7.82)	0.001	0.004	7.70E–05	1.10E–03	9.90E–04	8.00E–04
Creatine	2.23 (1.63 to 2.58)	2.23 (1.68 to 2.67)	0.679	0.83	0.708	0.634	0.663	0.742
Ethm	0.00 (0.00 to 0.00)	0.02 (0.00 to 0.41)	0.06	0.132	0.176	0.117	0.058	0.052
Glucose	0.23 (0.00 to 0.43)	0.00 (0.00 to 0.07)	0.12	0.203	0.222	0.203	0.126	0.095
Glutamate	4.58 (3.77 to 5.48)	4.55 (4.20 to 7.79)	0.068	0.136	0.161	0.259	0.087	0.065
Glutamine	2.35 (2.05 to 2.68)	3.18 (2.27 to 3.66)	0.005	0.018	0.012	8.40E–03	5.20E–03	5.80E–03
Glycine	1.71 (1.43 to 2.22)	2.68 (1.93 to 3.51)	< 0.001	0.002	8.00E–04	4.60E–04	1.70E–04	2.90E–04
GPC	0.67 (0.48 to 1.18)	0.98 (0.68 to 1.24)	0.908	0.951	0.762	0.855	0.755	0.783
GPE	0.33 (0 to 0.53)	0.00 (0.00 to 0.73)	< 0.001	< 0.001	1.30E–40	4.10E–10	1.30E–03	6.00E–32
Isoleucine	0.16 (0.00 to 0.18)	0.16 (0.11 to 0.28)	0.027	0.085	5.50E–04	0.015	0.029	0.016
Lactate	19.77 (16.68 to 22.66)	17.81 (15.69 to 22.01)	0.997	0.997	0.845	0.833	0.984	0.984
Leucine	0.33 (0.26 to 0.45)	0.44 (0.28 to 0.63)	0.364	0.501	0.447	0.329	0.353	0.37
Myo–inositol	9.94 (7.71 to 10.25)	8.79 (7.23 to 10.09)	0.795	0.875	0.702	0.744	0.796	0.78
PCh	0.43 (0.26 to 0.81)	0.90 (0.54 to 1.17)	0.039	0.107	0.014	0.033	0.032	0.043
PE	2.18 (1.49 to 2.54)	2.63 (2.26 to 3.71)	0.055	0.132	0.016	0.053	0.039	0.034
Putrescine	0.20 (0.00 to 0.83)	0.05 (0.00 to 0.16)	0.001	0.004	4.60E–03	0.075	0.029	1.00E–03
Scyllo–inositol	0.40 (0.27 to 0.87)	0.41 (0.32 to 0.61)	0.742	0.859	0.286	0.257	0.783	0.738
Spermine	3.56 (1.64 to 6.07)	1.18 (0.69 to 1.54)	< 0.001	< 0.001	9.10E–08	2.00E–05	4.50E–05	5.60E–06
Succinate	0.51 (0.39 to 0.73)	0.62 (0.52 to 0.94)	0.151	0.237	0.325	0.191	0.142	0.133
Taurine	4.83 (3.20 to 6.05)	4.23 (3.03 to 4.73)	0.344	0.501	0.488	0.46	0.333	0.519
Valine	1.99 (1.64 to 2.43)	2.60 (1.78 to 2.85)	0.651	0.83	0.026	0.021	0.013	8.40E–03

Ethm: Ethanolamine, GPC: Glycerophosphocholine, GPE: Glycerophosphoethanolamine, PCh: Phosphocholine, PE: Phosphoethanolamine *Benjamini-Hochberg corrected.

Supplementary Table S9: Differences in levels of quantified metabolites in the main cohort comparing $\mathrm{ERG}_{\mathrm{high}}$ samples to $\mathrm{ERG}_{\mathrm{low}}$ samples in high Gleason samples (Gleason $\geq 4 + 3$), corrected for multiple testing with Benjamini-Hochberg correction and adjusted for stroma, cancer, benign epithelia and luminal space

Metabolites	**$\mathrm{ERG}_{\mathrm{low}}$**	**$\mathrm{ERG}_{\mathrm{high}}$**						
	(*n* = 18)	**(*n* = 17)**						
	Concentrations mmoles/kg wet weight, median (IQR)	**Concentrations mmoles/kg wet weight, median (IQR)**	***p*–value**	***p* value***	**Adjusted for stromal content**	**Adjusted for cancer content**	**Adjusted for benign epithelial content**	**Adjusted for luminal space content**
Alanine	2.34 (1.83 to 3.34)	2.36 (1.97 to 2.78)	0.762	0.922	0.723	0.51	0.453	0.785
Choline	1.01 (0.66 to 1.43)	1.23 (0.90 to 1.66)	0.372	0.611	0.381	0.508	0.454	0.322
Citrate	7.58 (5.51 to 10.69)	2.95 (2.34 to 4.04)	< 0.001	0.003	1.60E–04	1.00E–04	1.30E–04	3.20E–04
Creatine	2.27 (1.71 to 2.75)	1.97 (1.60 to 2.22)	0.825	0.928	0.841	0.761	0.865	0.848
Ethm	0.00 (0.00 to 0.08)	0.00 (0.00 to 0.19)	0.6	0.812	0.619	0.79	0.969	0.676
Glucose	0.15 (0.00 to 1.00)	0.00 (0.00 to 0.04)	0.016	0.087	6.10E–03	0.068	0.313	0.017
Glutamate	4.67 (4.11 to 7.28)	6.31 (5.75 to 7.74)	0.241	0.504	0.294	0.54	0.517	0.215
Glutamine	2.80 (2.45 to 3.89)	2.93 (2.69 to 3.70)	0.907	0.948	0.812	0.461	0.361	0.946
Glycine	2.57 (1.85 to 3.08)	3.17 (2.11 to 3.65)	0.366	0.611	0.389	0.58	0.833	0.417
GPC	0.81 (0.54 to 1.43)	0.84 (0.44 to 1.08)	0.714	0.912	0.798	0.886	0.908	0.38
GPE	0.00 (0.00 to 0.55)	0.00 (0.00 to 0.36)	0.541	0.778	0.538	0.518	0.507	0.413
Isoleucine	0.18 (0.07 to 0.27)	0.24 (0.12 to 0.32)	0.188	0.48	0.183	0.133	5.50E–03	0.208
Lactate	22.02 (15.64 to 27.75)	16.45 (15.70 to 20.85)	0.065	0.249	0.064	0.046	0.056	0.04
Leucine	0.52 (0.34 to 0.65)	0.59 (0.45 to 0.83)	0.974	0.974	0.978	0.86	0.828	0.966
Myo–inositol	10.82 (6.72 to 12.76)	9.39 (7.43 to 11.35)	0.226	0.504	0.236	0.226	0.401	0.377
PCh	0.72 (0.45 to 1.03)	1.12 (0.74 to 1.36)	0.019	0.087	0.021	0.079	0.232	0.011
PE	2.62 (1.35 to 3.69)	2.95 (2.78 to 3.80)	0.087	0.286	0.088	0.087	0.081	0.03
Putrescine	0.11 (0.00 to 0.56)	0.00 (0.00 to 0.00)	0.008	0.058	7.70E–03	6.80E–03	0.096	0.01
Scyllo–inositol	0.38 (0.34 to 0.59)	0.50 (0.41 to 0.60)	0.366	0.611	0.487	0.295	0.191	0.604
Spermine	1.65 (1.15 to 2.27)	0.58 (0.39 to 1.02)	< 0.001	0.004	3.10E–04	4.30E–04	3.10E–03	4.90E–04
Succinate	0.60 (0.54 to 0.74)	0.63 (0.46 to 0.76)	0.847	0.928	0.824	0.516	0.637	0.963
Taurine	6.21 (4.05 to 7.15)	4.30 (3.70 to 6.49)	0.172	0.48	0.176	0.314	0.581	0.222
Valine	0.46 (0.28 to 0.58)	0.40 (0.28 to 0.52)	0.441	0.676	0.38	0.272	0.463	0.363

Ethm: Ethanolamine, GPC: Glycerophosphocholine, GPE: Glycerophosphoethanolamine, PCh: Phosphocholine, PE: Phosphoethanolamine *Benjamini-Hochberg corrected.

Supplementary Table S10: INMEX-analysis of KEGG-pathways in the main cohort

Pathway	Total	Expected	Hits	*P*-Value	Topology
Glutathione metabolism	75	6.5205	17	0.000155	0.79245
Purine metabolism	234	20.344	33	0.00267	0.66667
Glycerolipid metabolism	72	6.2597	14	0.002904	0.78378
Arginine and proline metabolism	102	8.8679	17	0.005846	0.63441
Cyanoamino acid metabolism	12	1.0433	4	0.015752	1.25
Pyruvate metabolism	64	5.5642	11	0.019979	0.78261
Glycolysis / Gluconeogenesis	91	7.9116	14	0.023299	0.57627
Glycosaminoglycan degradation	20	1.7388	5	0.024915	0.42105
Glycine, serine and threonine metabolism	68	5.9119	11	0.030255	0.66667
Pentose and glucuronate interconversions	52	4.5209	9	0.032529	0.89655
Lysine degradation	73	6.3466	11	0.04783	0.46512
beta–Alanine metabolism	50	4.347	8	0.063613	0.38095
Propanoate metabolism	52	4.5209	8	0.076871	0.63415
Glyoxylate and dicarboxylate metabolism	53	4.6078	8	0.084079	0.52
Valine, leucine and isoleucine degradation	82	7.1291	11	0.094732	0.43333
Pentose phosphate pathway	48	4.1731	7	0.11797	0.97561
Vitamin B6 metabolism	15	1.3041	3	0.13563	0.4
Ether lipid metabolism	51	4.4339	7	0.14941	0.34483
Fatty acid metabolism	83	7.216	10	0.17989	1.2621
Ascorbate and aldarate metabolism	35	3.0429	5	0.18309	0.83333
Alanine, aspartate and glutamate metabolism	56	4.8686	7	0.20941	0.40816
Aminoacyl–tRNA biosynthesis	87	7.5638	10	0.2201	0.27536
One carbon pool by folate	28	2.4343	4	0.22201	0.26667
Sphingolipid metabolism	67	5.825	8	0.22271	0.35849
Nicotinate and nicotinamide metabolism	39	3.3907	5	0.24769	0.43243
Pyrimidine metabolism	142	12.346	15	0.24795	0.49558
Arachidonic acid metabolism	100	8.694	11	0.24825	0.41026
Riboflavin metabolism	20	1.7388	3	0.24925	0.46154
Mucin type O–Glycan biosynthesis	32	2.7821	4	0.30123	0.15
Histidine metabolism	44	3.8254	5	0.33492	0.1875
Glycerophospholipid metabolism	119	10.346	12	0.33741	0.37333
Glycosphingolipid biosynthesis – ganglio series	14	1.2172	2	0.34713	0.26087
Glycosaminoglycan biosynthesis – chondroitin sulfate	14	1.2172	2	0.34713	0.42857
Pantothenate and CoA biosynthesis	35	3.0429	4	0.3626	0.58065
Glycosaminoglycan biosynthesis – heparan sulfate	5	0.4347	1	0.36563	0.33333
Butanoate metabolism	47	4.0862	5	0.38864	0.5625
Tryptophan metabolism	80	6.9552	8	0.39387	0.325
Glycosphingolipid biosynthesis – lacto and neolacto series	26	2.2604	3	0.39675	0.067797
Porphyrin and chlorophyll metabolism	70	6.0858	7	0.408	0.29787
Metabolism of xenobiotics by cytochrome P450	139	12.085	13	0.43406	0.4
Retinol metabolism	83	7.216	8	0.43514	0.51163
N–Glycan biosynthesis	50	4.347	5	0.44211	0.17143
Citrate cycle (TCA cycle)	50	4.347	5	0.44211	0.75
Butirosin and neomycin biosynthesis	7	0.60858	1	0.47135	0.66667
Taurine and hypotaurine metabolism	18	1.5649	2	0.47262	0.4

Sulfur metabolism	19	1.6519	2	0.50172	0.5
Drug metabolism – other enzymes	77	6.6944	7	0.51018	0.31579
Starch and sucrose metabolism	78	6.7813	7	0.52435	0.35185
Galactose metabolism	55	4.7817	5	0.52831	0.36735
Fructose and mannose metabolism	55	4.7817	5	0.52831	0.43243
Inositol phosphate metabolism	90	7.8246	8	0.52956	0.375
Drug metabolism – cytochrome P450	127	11.041	11	0.55364	0.14815
Fatty acid elongation	57	4.9556	5	0.56115	0.35616
Amino sugar and nucleotide sugar metabolism	84	7.303	7	0.60576	0.2716
Thiamine metabolism	11	0.95634	1	0.63303	0.36364
Valine, leucine and isoleucine biosynthesis	13	1.1302	1	0.69432	0.72727
Synthesis and degradation of ketone bodies	14	1.2172	1	0.72102	0.44444
Phenylalanine metabolism	29	2.5213	2	0.7326	0.36364
Caffeine metabolism	17	1.478	1	0.78799	0.11765
Selenocompound metabolism	33	2.869	2	0.79592	0.21429
Primary bile acid biosynthesis	63	5.4772	4	0.8118	0.34043
Glycosylphosphatidylinositol(GPI)–anchor biosynthesis	20	1.7388	1	0.83893	0.096774
Tyrosine metabolism	80	6.9552	5	0.83931	0.27586
Biosynthesis of unsaturated fatty acids	27	2.3474	1	0.91528	0.6875
Folate biosynthesis	32	2.7821	1	0.94652	0.11429
alpha–Linolenic acid metabolism	34	2.956	1	0.95552	0.1
Linoleic acid metabolism	34	2.956	1	0.95552	0.25
Terpenoid backbone biosynthesis	39	3.3907	1	0.97196	0.057143
Cysteine and methionine metabolism	63	5.4772	2	0.97836	0.072727
Fatty acid biosynthesis	49	4.2601	1	0.98888	0.11111
Steroid biosynthesis	54	4.6948	1	0.99301	0.029412
Steroid hormone biosynthesis	137	11.911	4	0.99854	0.17978

Supplementary Table S11: INMEX-analysis of KEGG-pathways in the main cohort in low Gleason (Gleason ≤ 3 + 4) samples

Pathway	Total	Expected	Hits	P.Value	Topology
Purine metabolism	234	15.941	34	8.98E–06	0.57471
Glutathione metabolism	75	5.1091	14	0.000393	0.75472
Pyrimidine metabolism	142	9.6733	18	0.006584	0.58407
Glycolysis / Gluconeogenesis	91	6.1991	13	0.007606	0.57627
Glycosaminoglycan degradation	20	1.3624	5	0.009281	0.42105
Valine, leucine and isoleucine degradation	82	5.586	11	0.021342	0.45556
Lysine degradation	73	4.9729	10	0.024199	0.46512
Arginine and proline metabolism	102	6.9484	12	0.041654	0.31183
Tryptophan metabolism	80	5.4498	10	0.042465	0.375
Cyanoamino acid metabolism	12	0.81746	3	0.043309	1.25
Nicotinate and nicotinamide metabolism	39	2.6568	6	0.045681	0.48649
beta–Alanine metabolism	50	3.4061	7	0.050052	0.33333
Glycerolipid metabolism	72	4.9048	9	0.052883	0.2973
Pentose and glucuronate interconversions	52	3.5423	7	0.05985	0.48276
Vitamin B6 metabolism	15	1.0218	3	0.077143	0.4
Sphingolipid metabolism	67	4.5642	8	0.081965	0.32075
Ascorbate and aldarate metabolism	35	2.3843	5	0.08539	0.83333
Pentose phosphate pathway	48	3.2699	6	0.10428	0.87805
Fatty acid metabolism	83	5.6541	9	0.10817	1.1456
Citrate cycle (TCA cycle)	50	3.4061	6	0.12099	0.75
Ether lipid metabolism	51	3.4742	6	0.12981	0.2069
Propanoate metabolism	52	3.5423	6	0.13894	0.58537
Glyoxylate and dicarboxylate metabolism	53	3.6105	6	0.14836	0.48
Drug metabolism – cytochrome P450	127	8.6515	12	0.15174	0.16667
Glycine, serine and threonine metabolism	68	4.6323	7	0.17714	0.53968
Amino sugar and nucleotide sugar metabolism	84	5.7222	8	0.20982	0.39506
Pantothenate and CoA biosynthesis	35	2.3843	4	0.21232	0.58065
Aminoacyl–tRNA biosynthesis	87	5.9266	8	0.23802	0.21739
Pyruvate metabolism	64	4.3598	6	0.26789	0.34783
Retinol metabolism	83	5.6541	7	0.33519	0.37209
Metabolism of xenobiotics by cytochrome P450	139	9.4689	11	0.34633	0.36364
Fatty acid elongation	57	3.883	5	0.34699	0.35616
Histidine metabolism	44	2.9974	4	0.35192	0.125
Riboflavin metabolism	20	1.3624	2	0.39995	0.30769
Starch and sucrose metabolism	78	5.3135	6	0.44142	0.33333
Arachidonic acid metabolism	100	6.8122	7	0.5286	0.4359
Glycosphingolipid biosynthesis – lacto and neolacto series	26	1.7712	2	0.53782	0.050847
Thiamine metabolism	11	0.74934	1	0.54049	0.36364
Biosynthesis of unsaturated fatty acids	27	1.8393	2	0.55861	0.6875
One carbon pool by folate	28	1.9074	2	0.57873	0.2
Inositol phosphate metabolism	90	6.131	6	0.5844	0.25
Glycosphingolipid biosynthesis – globo series	13	0.88559	1	0.60122	0.22222
Valine, leucine and isoleucine biosynthesis	13	0.88559	1	0.60122	0.72727
Drug metabolism – other enzymes	77	5.2454	5	0.61177	0.17544

Glycosaminoglycan biosynthesis – chondroitin sulfate	14	0.95371	1	0.62852	0.28571
Synthesis and degradation of ketone bodies	14	0.95371	1	0.62852	0.44444
Tyrosine metabolism	80	5.4498	5	0.64615	0.22989
N–Glycan biosynthesis	50	3.4061	3	0.6735	0.11429
Caffeine metabolism	17	1.1581	1	0.69976	0.11765
Glycerophospholipid metabolism	119	8.1065	7	0.71401	0.17333
Taurine and hypotaurine metabolism	18	1.2262	1	0.72034	0.13333
Galactose metabolism	55	3.7467	3	0.73553	0.22449
Fructose and mannose metabolism	55	3.7467	3	0.73553	0.27027
Glycosylphosphatidylinositol(GPI)–anchor biosynthesis	20	1.3624	1	0.75739	0.096774
Primary bile acid biosynthesis	63	4.2917	3	0.81507	0.25532
Butanoate metabolism	47	3.2017	2	0.84148	0.375
Porphyrin and chlorophyll metabolism	70	4.7685	3	0.86718	0.10638
Phenylalanine metabolism	29	1.9755	1	0.8722	0.18182
Mucin type O–Glycan biosynthesis	32	2.1799	1	0.89684	0.15
Alanine, aspartate and glutamate metabolism	56	3.8148	2	0.90443	0.12245
Linoleic acid metabolism	34	2.3161	1	0.91058	0.5
Cysteine and methionine metabolism	63	4.2917	2	0.93638	0.10909
Steroid hormone biosynthesis	137	9.3327	2	0.99944	0.10112

Supplementary Table S12: INMEX-analysis of KEGG-pathways in the main cohort in high Gleason (Gleason ≥ 4 + 3) samples

Pathway	Total	Expected	Hits	*P*-Value	Topology
Purine metabolism	234	5.4603	13	0.002268	0.41954
Pyrimidine metabolism	142	3.3135	9	0.004933	0.49558
Glutathione metabolism	75	1.7501	6	0.007251	0.49057
Glycosphingolipid biosynthesis – lacto and neolacto series	26	0.6067	3	0.02147	0.067797
Nicotinate and nicotinamide metabolism	39	0.91005	3	0.061006	0.37838
Glycine, serine and threonine metabolism	68	1.5868	4	0.072199	0.2381
Arginine and proline metabolism	102	2.3801	5	0.087048	0.16129
Retinol metabolism	83	1.9368	4	0.1264	0.37209
Arachidonic acid metabolism	100	2.3335	4	0.20307	0.12821
Cyanoamino acid metabolism	12	0.28002	1	0.24718	0.5
Drug metabolism – other enzymes	77	1.7968	3	0.26692	0.10526
Glycosaminoglycan biosynthesis – chondroitin sulfate	14	0.32668	1	0.28207	0.14286
Glycosphingolipid biosynthesis – ganglio series	14	0.32668	1	0.28207	0.17391
Vitamin B6 metabolism	15	0.35002	1	0.29891	0.1
Fatty acid metabolism	83	1.9368	3	0.3056	0.19417
N–Glycan biosynthesis	50	1.1667	2	0.32651	0.057143
Citrate cycle (TCA cycle)	50	1.1667	2	0.32651	0.29545
Caffeine metabolism	17	0.39669	1	0.33143	0.11765
Drug metabolism – cytochrome P450	127	2.9635	4	0.3441	0.50926
Taurine and hypotaurine metabolism	18	0.42002	1	0.34713	0.13333
Inositol phosphate metabolism	90	2.1001	3	0.35105	0.125
Glyoxylate and dicarboxylate metabolism	53	1.2367	2	0.35238	0.12
Fructose and mannose metabolism	55	1.2834	2	0.36944	0.16216
Riboflavin metabolism	20	0.46669	1	0.37746	0.15385
Metabolism of xenobiotics by cytochrome P450	139	3.2435	4	0.40908	0.36364
One carbon pool by folate	28	0.65337	1	0.48549	0.2
Glycerolipid metabolism	72	1.6801	2	0.50592	0.18919
Lysine degradation	73	1.7034	2	0.51337	0.13953
Folate biosynthesis	32	0.74671	1	0.53236	0.11429
Mucin type O–Glycan biosynthesis	32	0.74671	1	0.53236	0.15
Linoleic acid metabolism	34	0.79338	1	0.55419	0.5
Tryptophan metabolism	80	1.8668	2	0.56346	0.05
Tyrosine metabolism	80	1.8668	2	0.56346	0.068966
Pantothenate and CoA biosynthesis	35	0.81671	1	0.56473	0.12903
Valine, leucine and isoleucine degradation	82	1.9134	2	0.57709	0.044444
beta–Alanine metabolism	50	1.1667	1	0.6963	0.047619
Ether lipid metabolism	51	1.1901	1	0.70352	0.068966
Pentose and glucuronate interconversions	52	1.2134	1	0.71058	0.13793
Alanine, aspartate and glutamate metabolism	56	1.3067	1	0.73718	0.081633
Fatty acid elongation	57	1.3301	1	0.74344	0.041096
Primary bile acid biosynthesis	63	1.4701	1	0.77806	0.19149
Sphingolipid metabolism	67	1.5634	1	0.79854	0.037736
Porphyrin and chlorophyll metabolism	70	1.6334	1	0.81267	0.042553
Steroid hormone biosynthesis	137	3.1968	2	0.83921	0.05618

Starch and sucrose metabolism	78	1.8201	1	0.84576	0.037037
Amino sugar and nucleotide sugar metabolism	84	1.9601	1	0.86673	0.049383
Glycolysis / Gluconeogenesis	91	2.1234	1	0.88767	0.067797
Glycerophospholipid metabolism	119	2.7768	1	0.94357	0.053333

Supplementary Table S13: GSEA of KEGG-pathways in the main cohort, enrichment in $\mathrm{ERG}_{\mathrm{low}}$

PATHWAY	SIZE	ES	NES	NOM p-val	FDR *q*-val
DRUG METABOLISM CYTOCHROME P450	55	–0.6651254	–1.7795105	0.002132196	0.38855085
GLYCOLYSIS GLUCONEOGENESIS	56	–0.4682116	–1.6126508	0.013100437	0.8536236
HEMATOPOIETIC CELL LINEAGE	68	–0.6377796	–1.5941937	0.01632653	0.66214764
BETA ALANINE METABOLISM	19	–0.6408701	–1.563926	0.020242915	0.62843364
GLUTATHIONE METABOLISM	45	–0.5840763	–1.5582185	0.052738335	0.528509
PRION DISEASES	30	–0.5652002	–1.5239826	0.03285421	0.57103133
HYPERTROPHIC CARDIOMYOPATHY HCM	66	–0.5525483	–1.521536	0.04592902	0.49907997
CARDIAC MUSCLE CONTRACTION	58	–0.5234164	–1.5056521	0.033126295	0.4885571
METABOLISM OF XENOBIOTICS BY CYTOCHROME P450	50	–0.5358754	–1.4941844	0.017094018	0.47057903
VALINE LEUCINE AND ISOLEUCINE DEGRADATION	44	–0.556476	–1.491827	0.0741483	0.43163717
PPAR SIGNALING PATHWAY	51	–0.52109236	–1.4773304	0.027139874	0.43209052
FATTY ACID METABOLISM	35	–0.4665317	–1.4668512	0.07385229	0.42450482
DILATED CARDIOMYOPATHY	73	–0.51889294	–1.4528376	0.07660455	0.4315167
HISTIDINE METABOLISM	24	–0.5824359	–1.4319005	0.043912176	0.4642199
APOPTOSIS	75	–0.35446638	–1.4161711	0.0503876	0.48000923
TYROSINE METABOLISM	31	–0.51137507	–1.3706481	0.07236842	0.5867568
RETINOL METABOLISM	40	–0.4578147	–1.3549248	0.06313646	0.6055808
ARGININE AND PROLINE METABOLISM	46	–0.47907144	–1.3485328	0.09325397	0.5914392
PROXIMAL TUBULE BICARBONATE RECLAMATION	18	–0.5100017	–1.3183355	0.11677282	0.6578999
ALDOSTERONE REGULATED SODIUM REABSORPTION	33	–0.5453702	–1.3126537	0.1122449	0.64245903
GLYCOSPHINGOLIPID BIOSYNTHESIS LACTO AND NEOLACTO SERIES	17	–0.47345862	–1.2855277	0.15303983	0.6999029
PROPANOATE METABOLISM	31	–0.42541942	–1.2627256	0.2413793	0.74142903
MELANOGENESIS	82	–0.38168576	–1.2602468	0.12931034	0.71696585
COLORECTAL CANCER	54	–0.3426833	–1.2553287	0.16260162	0.7035733
NICOTINATE AND NICOTINAMIDE METABOLISM	19	–0.5683716	–1.249494	0.15118791	0.69425493
REGULATION OF ACTIN CYTOSKELETON	176	–0.32957068	–1.2489338	0.18371607	0.6691262
MTOR SIGNALING PATHWAY	43	–0.32117867	–1.2314632	0.15748031	0.7004713
FOCAL ADHESION	168	–0.38118944	–1.2233069	0.20910972	0.70139503
STEROID HORMONE BIOSYNTHESIS	36	–0.44694844	–1.2228109	0.16115703	0.6786272
B CELL RECEPTOR SIGNALING PATHWAY	70	–0.39102882	–1.2056568	0.24158415	0.7087562
GLIOMA	57	–0.33602458	–1.2041162	0.16297787	0.6909752
PANCREATIC CANCER	63	–0.33796537	–1.2031119	0.21850394	0.67281705
PHENYLALANINE METABOLISM	17	–0.50094825	–1.1898077	0.21638656	0.6888747
CELL ADHESION MOLECULES CAMS	112	–0.4456652	–1.1702002	0.26814517	0.7239068

VASCULAR SMOOTH MUSCLE CONTRACTION	89	–0.3525924	–1.1684161	0.2516269	0.70892125
PHOSPHATIDYLINOSITOL SIGNALING SYSTEM	65	–0.32815862	–1.1536041	0.26326963	0.73398
NATURAL KILLER CELL MEDIATED CYTOTOXICITY	101	–0.3900806	–1.1503791	0.3156823	0.72411835
MAPK SIGNALING PATHWAY	218	–0.2851731	–1.1377566	0.22937626	0.74028134
ADHERENS JUNCTION	62	–0.31532508	–1.1332755	0.2838983	0.7337195
WNT SIGNALING PATHWAY	129	–0.31501043	–1.1323106	0.24347825	0.7179757
ANTIGEN PROCESSING AND PRESENTATION	65	–0.43509716	–1.1301155	0.33467743	0.7065309
TRYPTOPHAN METABOLISM	33	–0.43367508	–1.1286054	0.27272728	0.6938948
PYRUVATE METABOLISM	38	–0.31179887	–1.1273845	0.3224401	0.68096334
CHEMOKINE SIGNALING PATHWAY	152	–0.3680516	–1.1199098	0.31451613	0.683802
ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY ARVC	59	–0.38263643	–1.1110188	0.32415253	0.6903247
PROSTATE CANCER	83	–0.2898831	–1.1048385	0.30181086	0.69068277
P53 SIGNALING PATHWAY	61	–0.36322063	–1.1022831	0.31013918	0.6820439
VIRAL MYOCARDITIS	62	–0.4290487	–1.102143	0.35918367	0.66820705
CALCIUM SIGNALING PATHWAY	124	–0.32479998	–1.0972714	0.29817444	0.666126
LEISHMANIA INFECTION	58	–0.41226605	–1.094746	0.3478261	0.6588297
PYRIMIDINE METABOLISM	90	–0.27208874	–1.0883919	0.33539096	0.66017336
ENDOCYTOSIS	156	–0.25955555	–1.080931	0.3253012	0.6651845
FC EPSILON RI SIGNALING PATHWAY	62	–0.33219257	–1.0740509	0.35458168	0.66915274
INOSITOL PHOSPHATE METABOLISM	49	–0.29495132	–1.0660963	0.36134455	0.6755806
SNARE INTERACTIONS IN VESICULAR TRANSPORT	34	–0.33910057	–1.059901	0.40361446	0.6771761
LEUKOCYTE TRANSENDOTHELIAL MIGRATION	94	–0.3551334	–1.0428008	0.3970894	0.70556414
PARKINSONS DISEASE	103	–0.23767659	–1.0376086	0.39478958	0.70493156
ASCORBATE AND ALDARATE METABOLISM	18	–0.4042498	–1.0335944	0.41910332	0.7018473
FC GAMMA R MEDIATED PHAGOCYTOSIS	83	–0.29817593	–1.0322497	0.39959016	0.69348305
TIGHT JUNCTION	106	–0.27402833	–1.0200877	0.41908714	0.7086325
PATHWAYS IN CANCER	279	–0.26002625	–1.0173993	0.40248963	0.7030485
HEDGEHOG SIGNALING PATHWAY	39	–0.38406587	–1.0157797	0.40900195	0.69598156
OXIDATIVE PHOSPHORYLATION	107	–0.22497028	–1.0146433	0.42720306	0.68765503
PORPHYRIN AND CHLOROPHYLL METABOLISM	33	–0.33246934	–1.0108454	0.4486166	0.6846646
NEUROTROPHIN SIGNALING PATHWAY	114	–0.224331	–1.007843	0.4305835	0.6805984
EPITHELIAL CELL SIGNALING IN HELICOBACTER PYLORI INFECTION	65	–0.25337642	–0.9983357	0.4385246	0.69139266
COMPLEMENT AND COAGULATION CASCADES	52	–0.4048311	–0.9914725	0.46666667	0.69601685
RENAL CELL CARCINOMA	61	–0.27857324	–0.98580015	0.47572815	0.69756716
LINOLEIC ACID METABOLISM	16	–0.4168835	–0.97966015	0.47358122	0.7009005
GRAFT VERSUS HOST DISEASE	31	–0.47203773	–0.97773933	0.47912526	0.6949405
LONG TERM POTENTIATION	60	–0.29623806	–0.97161144	0.49275362	0.69866616
MELANOMA	58	–0.26884857	–0.9689658	0.52165353	0.6946373
PRIMARY IMMUNODEFICIENCY	29	–0.46399686	–0.9642447	0.5423387	0.6954509
ARACHIDONIC ACID METABOLISM	40	–0.3602123	–0.94764656	0.5665962	0.72030175
AXON GUIDANCE	119	–0.26357418	–0.9413953	0.55737704	0.723444
HUNTINGTONS DISEASE	157	–0.20142505	–0.9413445	0.53816044	0.7140554
CYTOKINE CYTOKINE RECEPTOR INTERACTION	183	–0.31934986	–0.93090165	0.5535714	0.7261811

ALLOGRAFT REJECTION	26	–0.48169452	–0.92606074	0.56363636	0.7267475
BASAL CELL CARCINOMA	40	–0.32223517	–0.9183921	0.59163344	0.733288
NOD LIKE RECEPTOR SIGNALING PATHWAY	48	–0.3053208	–0.9062703	0.5923077	0.7488158
DRUG METABOLISM OTHER ENZYMES	39	–0.30631727	–0.898475	0.6105675	0.755737
T CELL RECEPTOR SIGNALING PATHWAY	92	–0.26117206	–0.88521665	0.58171207	0.77357084
BUTANOATE METABOLISM	30	–0.35817483	–0.882406	0.62896824	0.76976794
TERPENOID BACKBONE BIOSYNTHESIS	15	–0.365085	–0.8818788	0.6188605	0.76160514
SYSTEMIC LUPUS ERYTHEMATOSUS	88	–0.31776744	–0.88100976	0.6051081	0.7542704
LYSOSOME	117	–0.23417728	–0.87776816	0.6113281	0.7519492
ECM RECEPTOR INTERACTION	70	–0.33946648	–0.86563253	0.64656967	0.7670777
RNA POLYMERASE	27	–0.26543185	–0.86558276	0.63723606	0.75846314
TYPE I DIABETES MELLITUS	32	–0.40558252	–0.8645699	0.6372549	0.75184464
TOLL LIKE RECEPTOR SIGNALING PATHWAY	76	–0.2723002	–0.86427546	0.63527054	0.74425393
AUTOIMMUNE THYROID DISEASE	34	–0.40742585	–0.8585488	0.6356275	0.7463378
JAK STAT SIGNALING PATHWAY	114	–0.24149683	–0.84474975	0.6859504	0.7643172
GALACTOSE METABOLISM	20	–0.24985434	–0.8222984	0.67701864	0.79740804
DORSO VENTRAL AXIS FORMATION	23	–0.27150398	–0.81813145	0.68136275	0.7966562
ASTHMA	21	–0.38351947	–0.7867748	0.7321063	0.8421756
PEROXISOME	67	–0.2196404	–0.7829821	0.7924528	0.8402849
INTESTINAL IMMUNE NETWORK FOR IGA PRODUCTION	34	–0.34740373	–0.7700342	0.7526427	0.85196656
PATHOGENIC ESCHERICHIA COLI INFECTION	50	–0.2641702	–0.7688507	0.7628866	0.8450977
O GLYCAN BIOSYNTHESIS	19	–0.28100225	–0.75185394	0.8367347	0.8638152
VIBRIO CHOLERAE INFECTION	51	–0.19520424	–0.7430977	0.8526971	0.868085
TASTE TRANSDUCTION	25	–0.2806909	–0.72318774	0.8623482	0.88615614
STEROID BIOSYNTHESIS	16	–0.2878557	–0.7064701	0.83657587	0.8987915
CYTOSOLIC DNA SENSING PATHWAY	42	–0.2202738	–0.6797214	0.86875	0.92031956
CELL CYCLE	108	–0.17019337	–0.63154733	0.9644269	0.9548837
GLYCOSYLPHOSPHATIDYLINOSITOL GPI ANCHOR BIOSYNTHESIS	24	–0.20134689	–0.5982353	0.868	0.9676463
PROTEASOME	41	–0.16021891	–0.54751354	0.8828125	0.97920084

Supplementary Table S14: GSEA of KEGG-pathways in the main cohort, enrichment in ERG_{high}

PATHWAY	SIZE	ES	NES	NOM *p*-val	FDR *q*-val
NOTCH SIGNALING PATHWAY	44	0.570646	1.8939956	0	0.055041593
PENTOSE AND GLUCURONATE INTERCONVERSIONS	22	0.539804	1.477712	0.07157895	1
CITRATE CYCLE TCA CYCLE	31	0.379956	1.4168941	0.097087376	1
SPLICEOSOME	106	0.315289	1.4022022	0.15665236	1
ENDOMETRIAL CANCER	45	0.37221	1.3950136	0.084337346	0.9674002
GLYCOSAMINOGLYCAN DEGRADATION	19	0.442775	1.3926028	0.120527305	0.8168873
RNA DEGRADATION	52	0.31642	1.3648297	0.15400411	0.82250255
TYPE II DIABETES MELLITUS	32	0.417495	1.3610706	0.057692308	0.7334166
ETHER LIPID METABOLISM	23	0.463213	1.2851268	0.14164905	0.97442824
SPHINGOLIPID METABOLISM	33	0.407494	1.283116	0.092929296	0.88598776
N GLYCAN BIOSYNTHESIS	43	0.387991	1.2674928	0.21501014	0.86686134
ADIPOCYTOKINE SIGNALING PATHWAY	56	0.352025	1.2573285	0.11890838	0.83355254
ABC TRANSPORTERS	35	0.405498	1.2435976	0.17958412	0.81864834
SELENOAMINO ACID METABOLISM	21	0.420925	1.2259183	0.25940594	0.82157844
VEGF SIGNALING PATHWAY	61	0.344259	1.2232822	0.16765286	0.77542835
GLYCOSAMINOGLYCAN BIOSYNTHESIS HEPARAN SULFATE	20	0.382288	1.219865	0.19569471	0.73947895
NITROGEN METABOLISM	16	0.533677	1.219607	0.1902834	0.6969087
PURINE METABOLISM	137	0.295115	1.2109817	0.15090543	0.68312067
GLYCEROLIPID METABOLISM	38	0.354304	1.1863607	0.17751479	0.720392
BASE EXCISION REPAIR	32	0.315088	1.1661458	0.24395162	0.7446007
PROGESTERONE MEDIATED OOCYTE MATURATION	74	0.331903	1.1658318	0.248	0.7097456
AMINOACYL TRNA BIOSYNTHESIS	40	0.340565	1.1531861	0.3215859	0.7137402
LYSINE DEGRADATION	41	0.305711	1.136898	0.27131784	0.72547805
ERBB SIGNALING PATHWAY	74	0.268035	1.1329427	0.23326571	0.7061263
LONG TERM DEPRESSION	53	0.325049	1.1232173	0.26185566	0.70176786
CHRONIC MYELOID LEUKEMIA	65	0.289681	1.1228493	0.29545453	0.6758072
GAP JUNCTION	73	0.349332	1.1220355	0.29400387	0.6528848
GLYCOSAMINOGLYCAN BIOSYNTHESIS CHONDROITIN SULFATE	19	0.43838	1.1136811	0.30812854	0.6488753
UBIQUITIN MEDIATED PROTEOLYSIS	127	0.247331	1.1013335	0.3417191	0.6578307
INSULIN SIGNALING PATHWAY	114	0.258285	1.1009762	0.3029703	0.63664
RIBOSOME	82	0.305605	1.0945854	0.37787056	0.63081235
PROTEIN EXPORT	22	0.379509	1.0859424	0.39918533	0.6306105
VASOPRESSIN REGULATED WATER REABSORPTION	38	0.288508	1.0723445	0.3472222	0.64245826
GLYOXYLATE AND DICARBOXYLATE METABOLISM	15	0.368145	1.0647148	0.4090909	0.63977957
BLADDER CANCER	41	0.338338	1.0609249	0.3580786	0.62997067
GLYCEROPHOSPHOLIPID METABOLISM	59	0.260367	1.0561461	0.36507937	0.622571
PENTOSE PHOSPHATE PATHWAY	24	0.308604	1.024085	0.44421053	0.6753275
ACUTE MYELOID LEUKEMIA	53	0.268619	1.0056236	0.43217054	0.6977903
RIG I LIKE RECEPTOR SIGNALING PATHWAY	54	0.284634	1.003308	0.44399184	0.6847781

GLYCINE SERINE AND THREONINE METABOLISM	29	0.363609	0.99739045	0.4529058	0.67987096
NEUROACTIVE LIGAND RECEPTOR INTERACTION	144	0.290831	0.9860564	0.4940476	0.6868037
MISMATCH REPAIR	22	0.296132	0.97391146	0.47268906	0.69548035
STARCH AND SUCROSE METABOLISM	38	0.297813	0.96517473	0.53195876	0.6982206
GNRH SIGNALING PATHWAY	84	0.261413	0.95846295	0.53154874	0.69538563
THYROID CANCER	29	0.288496	0.9438243	0.5331992	0.7112361
OOCYTE MEIOSIS	98	0.252336	0.94085276	0.5365854	0.7022131
BASAL TRANSCRIPTION FACTORS	28	0.243772	0.91830355	0.5484536	0.7325656
ONE CARBON POOL BY FOLATE	16	0.356132	0.9163467	0.552521	0.7210434
NON SMALL CELL LUNG CANCER	50	0.249019	0.9008779	0.5807087	0.7362479
TGF BETA SIGNALING PATHWAY	71	0.297991	0.88788795	0.6529081	0.74723715
SMALL CELL LUNG CANCER	77	0.248611	0.87011284	0.6429942	0.7668747
REGULATION OF AUTOPHAGY	24	0.226453	0.8181001	0.70623744	0.85259765
AMINO SUGAR AND NUCLEOTIDE SUGAR METABOLISM	41	0.236854	0.80509555	0.7211155	0.8610756
ALZHEIMERS DISEASE	141	0.201338	0.8043591	0.69246435	0.8465044
AMYOTROPHIC LATERAL SCLEROSIS ALS	44	0.249455	0.75974053	0.82077396	0.9104104
ALANINE ASPARTATE AND GLUTAMATE METABOLISM	28	0.253045	0.73419213	0.8477801	0.93348867
CYSTEINE AND METHIONINE METABOLISM	29	0.212136	0.72075784	0.8646465	0.9367848
HOMOLOGOUS RECOMBINATION	24	0.218325	0.7071195	0.8479657	0.9396755
FRUCTOSE AND MANNOSE METABOLISM	30	0.222205	0.70003974	0.88957053	0.93191516
BIOSYNTHESIS OF UNSATURATED FATTY ACIDS	20	0.278155	0.6484301	0.8965517	0.97063565
NUCLEOTIDE EXCISION REPAIR	42	0.1579	0.6299698	0.9227557	0.97013724
DNA REPLICATION	36	0.18302	0.5928331	0.9354839	0.9776261
OLFACTORY TRANSDUCTION	131	0.168927	0.4935225	0.989899	0.99249303

Supplementary Table S15: GSEA of KEGG-pathways in the main cohort, low Gleason (Gleason $\leq 3 + 4$) samples, enrichment in $\mathrm{ERG_{low}}$

PATHWAY	SIZE	ES	NES	NOM *p*-val	FDR *q*-val
FATTY ACID METABOLISM	35	–0.5748	–1.75733	0.003976	0.428658
VALINE LEUCINE AND ISOLEUCINE DEGRADATION	44	–0.67001	–1.73347	0.006342	0.270427
GLYCOLYSIS GLUCONEOGENESIS	56	–0.53319	–1.7318	0.00396	0.183222
DRUG METABOLISM CYTOCHROME P450	55	–0.64306	–1.6711	0.002024	0.243507
PROPANOATE METABOLISM	31	–0.53258	–1.66536	0.037815	0.209191
HEMATOPOIETIC CELL LINEAGE	68	–0.65124	–1.63053	0	0.240902
PPAR SIGNALING PATHWAY	51	–0.56741	–1.58869	0.002151	0.294395
TYROSINE METABOLISM	31	–0.55823	–1.51035	0.022587	0.467732
HISTIDINE METABOLISM	24	–0.62194	–1.50656	0.026639	0.430377
GLUTATHIONE METABOLISM	45	–0.55473	–1.49415	0.056863	0.42461
BETA ALANINE METABOLISM	19	–0.62699	–1.49271	0.056604	0.389144
METABOLISM OF XENOBIOTICS BY CYTOCHROME P450	50	–0.53636	–1.48458	0.02988	0.377124
RETINOL METABOLISM	40	–0.52352	–1.47665	0.02268	0.369106
CARDIAC MUSCLE CONTRACTION	58	–0.54267	–1.4481	0.076152	0.417485
HYPERTROPHIC CARDIOMYOPATHY HCM	66	–0.54303	–1.43106	0.057613	0.436884
PYRUVATE METABOLISM	38	–0.3643	–1.41729	0.085774	0.44844
DILATED CARDIOMYOPATHY	73	–0.52784	–1.39136	0.08125	0.498288
NICOTINATE AND NICOTINAMIDE METABOLISM	19	–0.63499	–1.37941	0.079399	0.50922
ARACHIDONIC ACID METABOLISM	40	–0.49731	–1.36389	0.025105	0.526413
VIRAL MYOCARDITIS	62	–0.52378	–1.36242	0.130952	0.50457
CELL ADHESION MOLECULES CAMS	112	–0.51387	–1.34666	0.116564	0.523981
B CELL RECEPTOR SIGNALING PATHWAY	70	–0.41894	–1.3323	0.165975	0.54144
BUTANOATE METABOLISM	30	–0.50098	–1.32435	0.136821	0.540635
PRIMARY IMMUNODEFICIENCY	29	–0.59903	–1.31789	0.184874	0.535373
PROXIMAL TUBULE BICARBONATE RECLAMATION	18	–0.4973	–1.30566	0.121339	0.549594
FC EPSILON RI SIGNALING PATHWAY	62	–0.39485	–1.29086	0.122699	0.572681
VASCULAR SMOOTH MUSCLE CONTRACTION	89	–0.39253	–1.2908	0.164905	0.551471
REGULATION OF ACTIN CYTOSKELETON	176	–0.34923	–1.28702	0.145791	0.541866
GLYCOSPHINGOLIPID BIOSYNTHESIS LACTO AND NEOLACTO SERIES	17	–0.49558	–1.28193	0.158635	0.535908
LEISHMANIA INFECTION	58	–0.48024	–1.26	0.188017	0.579365
OXIDATIVE PHOSPHORYLATION	107	–0.25188	–1.25928	0.223158	0.563622
LINOLEIC ACID METABOLISM	16	–0.52279	–1.25469	0.152361	0.556829
PHENYLALANINE METABOLISM	17	–0.5513	–1.25461	0.163223	0.540131
LEUKOCYTE TRANSENDOTHELIAL MIGRATION	94	–0.42807	–1.25319	0.160825	0.527582
ADHERENS JUNCTION	62	–0.35074	–1.24188	0.177291	0.539059
NATURAL KILLER CELL MEDIATED CYTOTOXICITY	101	–0.40518	–1.24066	0.214592	0.527223
EPITHELIAL CELL SIGNALING IN HELICOBACTER PYLORI INFECTION	65	–0.28888	–1.24058	0.131466	0.5131
PARKINSONS DISEASE	103	–0.26831	–1.24027	0.235294	0.500656
FC GAMMA R MEDIATED PHAGOCYTOSIS	83	–0.34748	–1.22995	0.207039	0.512762
CHEMOKINE SIGNALING PATHWAY	152	–0.39003	–1.22606	0.202479	0.509208
FOCAL ADHESION	168	–0.37517	–1.22213	0.194861	0.505357
PHOSPHATIDYLINOSITOL SIGNALING SYSTEM	65	–0.34458	–1.2177	0.169661	0.50295

PANCREATIC CANCER	63	–0.34855	–1.21172	0.208511	0.505366
ENDOCYTOSIS	156	–0.28012	–1.20086	0.170782	0.517217
ANTIGEN PROCESSING AND PRESENTATION	65	–0.46206	–1.19376	0.287234	0.522465
PYRIMIDINE METABOLISM	90	–0.2891	–1.18693	0.221766	0.525949
ARGININE AND PROLINE METABOLISM	46	–0.40073	–1.18367	0.189655	0.522112
PRION DISEASES	30	–0.43579	–1.18351	0.240816	0.511485
ASCORBATE AND ALDARATE METABOLISM	18	–0.47857	–1.18189	0.273092	0.504342
SYSTEMIC LUPUS ERYTHEMATOSUS	88	–0.41173	–1.17882	0.237323	0.500253
STEROID HORMONE BIOSYNTHESIS	36	–0.43597	–1.17244	0.224	0.503355
WNT SIGNALING PATHWAY	129	–0.31684	–1.1669	0.225873	0.505087
TIGHT JUNCTION	106	–0.32125	–1.14441	0.243083	0.543737
MTOR SIGNALING PATHWAY	43	–0.29399	–1.14222	0.273101	0.537842
MELANOGENESIS	82	–0.34923	–1.13872	0.264151	0.535669
GLYCEROLIPID METABOLISM	38	–0.33329	–1.12194	0.278481	0.561586
LYSOSOME	117	–0.28709	–1.1122	0.317328	0.571848
MAPK SIGNALING PATHWAY	218	–0.28331	–1.10765	0.269737	0.571201
ALDOSTERONE REGULATED SODIUM REABSORPTION	33	–0.45758	–1.10048	0.335541	0.576414
INOSITOL PHOSPHATE METABOLISM	49	–0.31283	–1.09895	0.331959	0.569941
TOLL LIKE RECEPTOR SIGNALING PATHWAY	76	–0.32024	–1.09699	0.316222	0.565621
COLORECTAL CANCER	54	–0.29807	–1.08723	0.327766	0.575742
SNARE INTERACTIONS IN VESICULAR TRANSPORT	34	–0.3634	–1.07756	0.382892	0.586732
TYPE I DIABETES MELLITUS	32	–0.52346	–1.07534	0.40257	0.582921
APOPTOSIS	75	–0.26781	–1.06279	0.335484	0.600432
VIBRIO CHOLERAE INFECTION	51	–0.26823	–1.06249	0.331276	0.591874
CYTOKINE CYTOKINE RECEPTOR INTERACTION	183	–0.35607	–1.05478	0.377682	0.598656
TRYPTOPHAN METABOLISM	33	–0.40505	–1.05363	0.368973	0.592153
CALCIUM SIGNALING PATHWAY	124	–0.31068	–1.05021	0.368644	0.590896
HEDGEHOG SIGNALING PATHWAY	39	–0.38985	–1.04884	0.378099	0.584801
T CELL RECEPTOR SIGNALING PATHWAY	92	–0.28932	–1.04161	0.397872	0.591842
AUTOIMMUNE THYROID DISEASE	34	–0.49558	–1.04001	0.440426	0.586462
ASTHMA	21	–0.50737	–1.03382	0.428571	0.59034
ALLOGRAFT REJECTION	26	–0.54805	–1.0317	0.471215	0.586535
AXON GUIDANCE	119	–0.27966	–1.03134	0.36646	0.579415
JAK STAT SIGNALING PATHWAY	114	–0.28618	–1.02503	0.417671	0.584776
ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY ARVC	59	–0.34725	–1.02209	0.430353	0.582792
GLIOMA	57	–0.28234	–1.02111	0.436059	0.57718
COMPLEMENT AND COAGULATION CASCADES	52	–0.42698	–1.02096	0.448637	0.570092
STARCH AND SUCROSE METABOLISM	38	–0.316	–1.02012	0.415612	0.564567
GRAFT VERSUS HOST DISEASE	31	–0.50635	–1.01979	0.487288	0.558214
GAP JUNCTION	73	–0.30982	–1.01693	0.409871	0.556332
ADIPOCYTOKINE SIGNALING PATHWAY	56	–0.27146	–1.01226	0.435374	0.558633
PATHWAYS IN CANCER	279	–0.25379	–1.00408	0.418605	0.567434
LONG TERM DEPRESSION	53	–0.29765	–0.99491	0.431535	0.577069
NON SMALL CELL LUNG CANCER	50	–0.27431	–0.99275	0.494759	0.574468
PATHOGENIC ESCHERICHIA COLI INFECTION	50	–0.32015	–0.9716	0.483607	0.606761
GNRH SIGNALING PATHWAY	84	–0.26309	–0.96915	0.493802	0.605055

MELANOMA	58	–0.27091	–0.95161	0.561181	0.630692
LONG TERM POTENTIATION	60	–0.27998	–0.9468	0.544699	0.632693
FRUCTOSE AND MANNOSE METABOLISM	30	–0.29582	–0.94543	0.543651	0.628576
GLYCEROPHOSPHOLIPID METABOLISM	59	–0.23849	–0.93851	0.57551	0.635078
HUNTINGTONS DISEASE	157	–0.19111	–0.93586	0.507592	0.633028
RENAL CELL CARCINOMA	61	–0.25307	–0.93248	0.541667	0.632276
BASAL CELL CARCINOMA	40	–0.31747	–0.92139	0.60334	0.64651
ALZHEIMERS DISEASE	141	–0.22165	–0.9201	0.53139	0.642262
VEGF SIGNALING PATHWAY	61	–0.25292	–0.91574	0.622129	0.643416
TERPENOID BACKBONE BIOSYNTHESIS	15	–0.36513	–0.90732	0.578189	0.650887
PROSTATE CANCER	83	–0.24162	–0.90552	0.597895	0.647442
PORPHYRIN AND CHLOROPHYLL METABOLISM	33	–0.30215	–0.89355	0.612774	0.662094
PEROXISOME	67	–0.24244	–0.88397	0.659919	0.67278
AMINO SUGAR AND NUCLEOTIDE SUGAR METABOLISM	41	–0.24287	–0.88212	0.675676	0.669515
GALACTOSE METABOLISM	20	–0.2704	–0.87744	0.612971	0.671198
DRUG METABOLISM OTHER ENZYMES	39	–0.30971	–0.87682	0.638211	0.665909
INTESTINAL IMMUNE NETWORK FOR IGA PRODUCTION	34	–0.3731	–0.84708	0.645435	0.711469
STEROID BIOSYNTHESIS	16	–0.34029	–0.81211	0.696121	0.764039
RNA POLYMERASE	27	–0.23329	–0.79392	0.72211	0.787158
P53 SIGNALING PATHWAY	61	–0.25305	–0.78393	0.795031	0.796277
ALANINE ASPARTATE AND GLUTAMATE METABOLISM	28	–0.26272	–0.78148	0.796334	0.792567
BIOSYNTHESIS OF UNSATURATED FATTY ACIDS	20	–0.30046	–0.72265	0.814196	0.869183
GLYCOSYLPHOSPHATIDYLINOSITOL GPI ANCHOR BIOSYNTHESIS	24	–0.20336	–0.65816	0.869121	0.929164
PROTEASOME	41	–0.12487	–0.47125	0.949686	0.995191

Supplementary Table S16: GSEA of KEGG-pathways in the main cohort, low Gleason (Gleason ≤ 3 + 4) samples, enrichment in ERG$_{high}$

PATHWAY	SIZE	ES	NES	NOM *p*-val	FDR *q*-val
NOTCH SIGNALING PATHWAY	44	0.516836	1.717935	0.001942	0.301009
AMINOACYL TRNA BIOSYNTHESIS	40	0.462563	1.56396	0.059917	0.617156
RNA DEGRADATION	52	0.354821	1.419818	0.118609	1
NITROGEN METABOLISM	16	0.588849	1.329333	0.118367	1
CITRATE CYCLE TCA CYCLE	31	0.329703	1.304396	0.142342	1
SPHINGOLIPID METABOLISM	33	0.417907	1.277418	0.118952	1
ABC TRANSPORTERS	35	0.413801	1.277238	0.148148	1
ONE CARBON POOL BY FOLATE	16	0.446341	1.241598	0.219959	1
TYPE II DIABETES MELLITUS	32	0.409184	1.20927	0.201195	1
PENTOSE PHOSPHATE PATHWAY	24	0.331508	1.207402	0.213018	1
GLYOXYLATE AND DICARBOXYLATE METABOLISM	15	0.400063	1.203525	0.245902	1
ETHER LIPID METABOLISM	23	0.443994	1.194557	0.198853	1
GLYCOSAMINOGLYCAN BIOSYNTHESIS HEPARAN SULFATE	20	0.343143	1.071101	0.349693	1
SPLICEOSOME	106	0.22487	1.047405	0.391837	1
GLYCOSAMINOGLYCAN DEGRADATION	19	0.358777	1.041911	0.423554	1
N GLYCAN BIOSYNTHESIS	43	0.283753	1.040282	0.413927	1
SMALL CELL LUNG CANCER	77	0.299533	1.031481	0.406977	1
BLADDER CANCER	41	0.317529	1.031392	0.412121	1
OLFACTORY TRANSDUCTION	131	0.321648	1.020145	0.440162	1
BASE EXCISION REPAIR	32	0.27957	1.018931	0.430672	1
PURINE METABOLISM	137	0.229031	1.012979	0.449807	1
PENTOSE AND GLUCURONATE INTERCONVERSIONS	22	0.375712	0.980591	0.516832	1
NEUROACTIVE LIGAND RECEPTOR INTERACTION	144	0.287321	0.970639	0.497154	1
DNA REPLICATION	36	0.306206	0.965192	0.480808	1
GLYCOSAMINOGLYCAN BIOSYNTHESIS CHONDROITIN SULFATE	19	0.374668	0.959322	0.517578	1
LYSINE DEGRADATION	41	0.276211	0.950357	0.538023	1
TGF BETA SIGNALING PATHWAY	71	0.323419	0.932605	0.573674	1
DORSO VENTRAL AXIS FORMATION	23	0.318803	0.913324	0.569573	1
UBIQUITIN MEDIATED PROTEOLYSIS	127	0.19352	0.909368	0.55814	1
ECM RECEPTOR INTERACTION	70	0.341929	0.900604	0.611632	1
GLYCINE SERINE AND THREONINE METABOLISM	29	0.31782	0.899822	0.619718	1
PROGESTERONE MEDIATED OOCYTE MATURATION	74	0.24859	0.88205	0.654297	1
MISMATCH REPAIR	22	0.267798	0.872425	0.608696	1
CELL CYCLE	108	0.229027	0.872099	0.646943	1
ERBB SIGNALING PATHWAY	74	0.192177	0.860207	0.731313	1
RIG I LIKE RECEPTOR SIGNALING PATHWAY	54	0.230037	0.852649	0.697495	1
OOCYTE MEIOSIS	98	0.220263	0.847816	0.732284	1
VASOPRESSIN REGULATED WATER REABSORPTION	38	0.240948	0.844498	0.646341	1
AMYOTROPHIC LATERAL SCLEROSIS ALS	44	0.281079	0.83691	0.672414	1

INSULIN SIGNALING PATHWAY	114	0.187648	0.79114	0.801181	1
O GLYCAN BIOSYNTHESIS	19	0.275072	0.784538	0.810176	1
HOMOLOGOUS RECOMBINATION	24	0.236923	0.777339	0.755144	1
NEUROTROPHIN SIGNALING PATHWAY	114	0.179373	0.77006	0.825203	1
PROTEIN EXPORT	22	0.236003	0.764155	0.708098	1
CYSTEINE AND METHIONINE METABOLISM	29	0.220384	0.753994	0.841176	1
BASAL TRANSCRIPTION FACTORS	28	0.19441	0.750105	0.825203	1
SELENOAMINO ACID METABOLISM	21	0.244671	0.747654	0.793587	0.996678
RIBOSOME	82	0.195386	0.737388	0.690909	0.991515
ENDOMETRIAL CANCER	45	0.199174	0.732926	0.799599	0.978085
CHRONIC MYELOID LEUKEMIA	65	0.193513	0.729681	0.813627	0.963081
ACUTE MYELOID LEUKEMIA	53	0.198753	0.728204	0.884086	0.946406
TASTE TRANSDUCTION	25	0.243484	0.68766	0.948077	0.979054
NOD LIKE RECEPTOR SIGNALING PATHWAY	48	0.215297	0.672106	0.900778	0.978148
NUCLEOTIDE EXCISION REPAIR	42	0.155527	0.611816	0.902153	1
THYROID CANCER	29	0.193289	0.605692	0.926878	0.993572
REGULATION OF AUTOPHAGY	24	0.177812	0.605173	0.937736	0.97612
CYTOSOLIC DNA SENSING PATHWAY	42	0.143015	0.491659	0.992481	0.99366

Supplementary Table S17: GSEA of KEGG-pathways in the main cohort, high Gleason (Gleason ≥ 4 + 3) samples, enrichment in ERG$_{low}$

PATHWAY	SIZE	ES	NES	NOM *p*-val	FDR *q*-val
GLUTATHIONE METABOLISM	45	–0.58109	–1.49226	0.062753	1
DRUG METABOLISM CYTOCHROME P450	55	–0.52313	–1.45852	0.018256	1
GLYCOLYSIS GLUCONEOGENESIS	56	–0.40615	–1.44262	0.053254	1
P53 SIGNALING PATHWAY	61	–0.45124	–1.38952	0.070342	1
APOPTOSIS	75	–0.33517	–1.38622	0.045455	1
BETA ALANINE METABOLISM	19	–0.53945	–1.33119	0.124	1
ARGININE AND PROLINE METABOLISM	46	–0.48317	–1.31523	0.110442	1
GLYCOSPHINGOLIPID BIOSYNTHESIS LACTO AND NEOLACTO SERIES	17	–0.46753	–1.30379	0.120623	1
HISTIDINE METABOLISM	24	–0.54079	–1.3033	0.09	1
MELANOGENESIS	82	–0.38026	–1.29089	0.093361	1
ALDOSTERONE REGULATED SODIUM REABSORPTION	33	–0.53263	–1.27956	0.136095	1
HYPERTROPHIC CARDIOMYOPATHY HCM	66	–0.43965	–1.27941	0.187373	0.9968
METABOLISM OF XENOBIOTICS BY CYTOCHROME P450	50	–0.43719	–1.25665	0.117647	1
PYRUVATE METABOLISM	38	–0.36316	–1.23956	0.208413	1
PROSTATE CANCER	83	–0.30743	–1.21731	0.155419	1
MTOR SIGNALING PATHWAY	43	–0.30711	–1.18744	0.1917	1
O GLYCAN BIOSYNTHESIS	19	–0.45238	–1.18317	0.239837	1
DILATED CARDIOMYOPATHY	73	–0.40563	–1.18086	0.264463	1
TYROSINE METABOLISM	31	–0.43806	–1.17859	0.211765	0.984351
PRION DISEASES	30	–0.44281	–1.17312	0.29505	0.957145
CARDIAC MUSCLE CONTRACTION	58	–0.34436	–1.14871	0.26938	1
PPAR SIGNALING PATHWAY	51	–0.39044	–1.12762	0.262425	1
GLIOMA	57	–0.31679	–1.12513	0.25102	1
TASTE TRANSDUCTION	25	–0.42644	–1.07992	0.373016	1
STEROID HORMONE BIOSYNTHESIS	36	–0.37043	–1.07989	0.325671	1
FATTY ACID METABOLISM	35	–0.3198	–1.07466	0.351515	1
PYRIMIDINE METABOLISM	90	–0.26562	–1.07115	0.339286	1
CYSTEINE AND METHIONINE METABOLISM	29	–0.31216	–1.0571	0.397895	1
HEMATOPOIETIC CELL LINEAGE	68	–0.42636	–1.046	0.397638	1
TRYPTOPHAN METABOLISM	33	–0.39935	–1.03939	0.393375	1
NICOTINATE AND NICOTINAMIDE METABOLISM	19	–0.4544	–1.03812	0.371717	1
VALINE LEUCINE AND ISOLEUCINE DEGRADATION	44	–0.38296	–1.03049	0.423387	1
PROXIMAL TUBULE BICARBONATE RECLAMATION	18	–0.39738	–1.0253	0.41966	0.996142
GLYCINE SERINE AND THREONINE METABOLISM	29	–0.38587	–1.01423	0.426195	1
ARACHIDONIC ACID METABOLISM	40	–0.38977	–0.99708	0.441955	1
ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY ARVC	59	–0.34466	–0.98655	0.48394	1
AMYOTROPHIC LATERAL SCLEROSIS ALS	44	–0.30689	–0.96829	0.48855	1
PHENYLALANINE METABOLISM	17	–0.41873	–0.96135	0.516	1
LINOLEIC ACID METABOLISM	16	–0.39795	–0.94534	0.564777	1

NOD LIKE RECEPTOR SIGNALING PATHWAY	48	–0.31988	–0.93946	0.53229	1
OLFACTORY TRANSDUCTION	131	–0.33618	–0.93875	0.53816	1
ADHERENS JUNCTION	62	–0.25968	–0.93686	0.537473	1
FOCAL ADHESION	168	–0.29155	–0.93682	0.521739	1
TERPENOID BACKBONE BIOSYNTHESIS	15	–0.39638	–0.93531	0.560078	0.984399
PROPANOATE METABOLISM	31	–0.31655	–0.92299	0.546667	0.99571
WNT SIGNALING PATHWAY	129	–0.25453	–0.92235	0.572614	0.975564
PHOSPHATIDYLINOSITOL SIGNALING SYSTEM	65	–0.26402	–0.91989	0.566596	0.961487
RETINOL METABOLISM	40	–0.29044	–0.91814	0.634	0.945594
ALANINE ASPARTATE AND GLUTAMATE METABOLISM	28	–0.32715	–0.9138	0.59802	0.936682
CALCIUM SIGNALING PATHWAY	124	–0.2778	–0.91263	0.577963	0.9206
PATHWAYS IN CANCER	279	–0.23088	–0.9015	0.640657	0.931577
PORPHYRIN AND CHLOROPHYLL METABOLISM	33	–0.29245	–0.89562	0.598441	0.928584
AXON GUIDANCE	119	–0.25724	–0.89225	0.664	0.918983
LONG TERM POTENTIATION	60	–0.27098	–0.88623	0.655319	0.916726
CYTOSOLIC DNA SENSING PATHWAY	42	–0.28958	–0.88511	0.591356	0.902483
DRUG METABOLISM OTHER ENZYMES	39	–0.29008	–0.88207	0.672549	0.893022
PANCREATIC CANCER	63	–0.24008	–0.87586	0.667355	0.891418
DORSO VENTRAL AXIS FORMATION	23	–0.26575	–0.87206	0.633401	0.884406
VASCULAR SMOOTH MUSCLE CONTRACTION	89	–0.25807	–0.84826	0.658174	0.921096
HEDGEHOG SIGNALING PATHWAY	39	–0.30239	–0.81983	0.735537	0.968674
COLORECTAL CANCER	54	–0.22429	–0.81853	0.772257	0.955406
COMPLEMENT AND COAGULATION CASCADES	52	–0.33958	–0.8171	0.68	0.942883
BLADDER CANCER	41	–0.26128	–0.81446	0.761044	0.933214
HUNTINGTONS DISEASE	157	–0.17929	–0.81213	0.683168	0.923699
NUCLEOTIDE EXCISION REPAIR	42	–0.20196	–0.80325	0.714004	0.927309
DNA REPLICATION	36	–0.24967	–0.79526	0.678208	0.929258
CYTOKINE CYTOKINE RECEPTOR INTERACTION	183	–0.27434	–0.7898	0.749515	0.925759
CHEMOKINE SIGNALING PATHWAY	152	–0.26392	–0.77536	0.762295	0.938934
EPITHELIAL CELL SIGNALING IN HELICOBACTER PYLORI INFECTION	65	–0.1986	–0.76677	0.833652	0.941243
RENAL CELL CARCINOMA	61	–0.20876	–0.75937	0.79065	0.940721
CELL CYCLE	108	–0.19763	–0.7411	0.85567	0.957485
GALACTOSE METABOLISM	20	–0.22163	–0.73411	0.790476	0.955116
SMALL CELL LUNG CANCER	77	–0.20928	–0.72354	0.89834	0.957566
B CELL RECEPTOR SIGNALING PATHWAY	70	–0.23307	–0.72088	0.819106	0.948205
RNA POLYMERASE	27	–0.2329	–0.69867	0.792887	0.965847
CELL ADHESION MOLECULES CAMS	112	–0.25326	–0.66414	0.89	0.991479
HOMOLOGOUS RECOMBINATION	24	–0.19277	–0.6397	0.932939	1
PROTEASOME	41	–0.18083	–0.62023	0.806911	1
ANTIGEN PROCESSING AND PRESENTATION	65	–0.22812	–0.59258	0.919075	1
PARKINSONS DISEASE	103	–0.13483	–0.57441	0.925996	1
OXIDATIVE PHOSPHORYLATION	107	–0.13049	–0.55556	0.900952	0.99953
GLYCOSYLPHOSPHATIDYLINOSITOL GPI ANCHOR BIOSYNTHESIS	24	–0.17695	–0.51881	0.924419	0.998504
AMINOACYL TRNA BIOSYNTHESIS	40	–0.12514	–0.40487	0.993776	0.998799

Supplementary Table S18: GSEA of KEGG-pathways in the main cohort, high Gleason (Gleason ≥ 4 + 3) samples, enrichment in ERG_{high}

PATHWAY	SIZE	ES	NES	NOM *p*-val	FDR *q*-val
NOTCH SIGNALING PATHWAY	44	0.5045062	1.6738925	0	0.62938935
PENTOSE AND GLUCURONATE INTERCONVERSIONS	22	0.5123342	1.4166561	0.08817204	1
GLYCOSAMINOGLYCAN BIOSYNTHESIS CHONDROITIN SULFATE	19	0.542504	1.3943979	0.07114624	1
SELENOAMINO ACID METABOLISM	21	0.47533673	1.3648516	0.10714286	1
ENDOMETRIAL CANCER	45	0.36318752	1.3550841	0.086519115	1
PROTEIN EXPORT	22	0.48945096	1.3471158	0.19421488	1
SPLICEOSOME	106	0.31644973	1.3434168	0.17	1
ETHER LIPID METABOLISM	23	0.44876847	1.3325243	0.06832298	1
GAP JUNCTION	73	0.40344366	1.2925855	0.13872832	1
LONG TERM DEPRESSION	53	0.35514474	1.2659172	0.1002004	1
TYPE II DIABETES MELLITUS	32	0.36255944	1.2274318	0.15039062	1
UBIQUITIN MEDIATED PROTEOLYSIS	127	0.27910286	1.227381	0.24418604	1
TIGHT JUNCTION	106	0.2995418	1.1919937	0.18426104	1
GLYOXYLATE AND DICARBOXYLATE METABOLISM	15	0.41961658	1.1883075	0.28985506	1
PROGESTERONE MEDIATED OOCYTE MATURATION	74	0.329471	1.171812	0.25494072	1
LYSINE DEGRADATION	41	0.2979997	1.171253	0.19444445	1
ABC TRANSPORTERS	35	0.3798634	1.1644273	0.2576336	1
RNA DEGRADATION	52	0.2598646	1.1500181	0.30754352	1
RIBOSOME	82	0.3375702	1.129038	0.3858586	1
GLYCEROLIPID METABOLISM	38	0.3245482	1.1109859	0.3046092	1
STARCH AND SUCROSE METABOLISM	38	0.34416395	1.1031003	0.32040817	1
GLYCEROPHOSPHOLIPID METABOLISM	59	0.2613262	1.091921	0.28870293	1
RIG I LIKE RECEPTOR SIGNALING PATHWAY	54	0.3146344	1.0732448	0.35976788	1
CITRATE CYCLE TCA CYCLE	31	0.29832336	1.0654979	0.39300412	1
VEGF SIGNALING PATHWAY	61	0.3033966	1.0607156	0.37058824	1
SPHINGOLIPID METABOLISM	33	0.3293276	1.0508296	0.35849056	1
PURINE METABOLISM	137	0.26441482	1.0403163	0.39648438	1
N GLYCAN BIOSYNTHESIS	43	0.32496336	1.0089209	0.45759368	1
VIBRIO CHOLERAE INFECTION	51	0.2632098	0.99514633	0.43838385	1
GLYCOSAMINOGLYCAN BIOSYNTHESIS HEPARAN SULFATE	20	0.3191126	0.9949526	0.49115914	1
GLYCOSAMINOGLYCAN DEGRADATION	19	0.3005399	0.965958	0.5010309	1
THYROID CANCER	29	0.29003474	0.9657133	0.5121951	1
BASE EXCISION REPAIR	32	0.26781192	0.963137	0.49707603	1
MISMATCH REPAIR	22	0.303365	0.95994514	0.5051546	1
ALZHEIMERS DISEASE	141	0.23473425	0.94902	0.5030303	1
MAPK SIGNALING PATHWAY	218	0.2395718	0.94869226	0.560241	1
BASAL TRANSCRIPTION FACTORS	28	0.25926867	0.9475964	0.5235294	1
NON SMALL CELL LUNG CANCER	50	0.27112022	0.9459981	0.52566737	1
VASOPRESSIN REGULATED WATER REABSORPTION	38	0.23592153	0.93527263	0.5808967	1
GNRH SIGNALING PATHWAY	84	0.25247583	0.92241526	0.5753425	1
OOCYTE MEIOSIS	98	0.24481033	0.9178716	0.5795678	1

ERBB SIGNALING PATHWAY	74	0.22490917	0.9112399	0.6229508	1
NEUROACTIVE LIGAND RECEPTOR INTERACTION	144	0.2674146	0.90514165	0.68801653	1
AMINO SUGAR AND NUCLEOTIDE SUGAR METABOLISM	41	0.28475586	0.89959615	0.57758623	1
ASCORBATE AND ALDARATE METABOLISM	18	0.3372187	0.887614	0.6293996	1
TGF BETA SIGNALING PATHWAY	71	0.28805873	0.8791876	0.64176244	1
T CELL RECEPTOR SIGNALING PATHWAY	92	0.27073228	0.8785631	0.61044174	1
PENTOSE PHOSPHATE PATHWAY	24	0.27586928	0.87095606	0.6260504	1
ENDOCYTOSIS	156	0.20839994	0.86836064	0.6947162	1
FC EPSILON RI SIGNALING PATHWAY	62	0.272123	0.8679006	0.612326	1
ADIPOCYTOKINE SIGNALING PATHWAY	56	0.254351	0.8639951	0.70726913	1
ECM RECEPTOR INTERACTION	70	0.33320397	0.8552361	0.6287425	1
TYPE I DIABETES MELLITUS	32	0.4039086	0.84916973	0.64123714	1
JAK STAT SIGNALING PATHWAY	114	0.24348678	0.8405615	0.6825397	1
SYSTEMIC LUPUS ERYTHEMATOSUS	88	0.31594077	0.8378146	0.69896907	1
MELANOMA	58	0.23131153	0.8347135	0.80846775	1
INSULIN SIGNALING PATHWAY	114	0.19043854	0.83018816	0.74810606	1
SNARE INTERACTIONS IN VESICULAR TRANSPORT	34	0.24903408	0.82990885	0.7033399	1
NITROGEN METABOLISM	16	0.36240193	0.82630676	0.7225807	1
PEROXISOME	67	0.23194745	0.82561415	0.7344961	0.99797565
REGULATION OF AUTOPHAGY	24	0.22092693	0.82355046	0.7057654	0.9860101
BASAL CELL CARCINOMA	40	0.28743526	0.82145005	0.78149605	0.97474784
CHRONIC MYELOID LEUKEMIA	65	0.20110641	0.8113076	0.7887324	0.981718
NEUROTROPHIN SIGNALING PATHWAY	114	0.17418417	0.81061876	0.8224852	0.9678766
ASTHMA	21	0.3933154	0.79921764	0.7057654	0.9763035
ONE CARBON POOL BY FOLATE	16	0.32356194	0.798125	0.68604654	0.9636205
INOSITOL PHOSPHATE METABOLISM	49	0.2127568	0.7812778	0.8507752	0.9808415
LYSOSOME	117	0.21278796	0.7681107	0.8032787	0.99078923
BIOSYNTHESIS OF UNSATURATED FATTY ACIDS	20	0.31573716	0.72537094	0.8079332	1
LEISHMANIA INFECTION	58	0.28457937	0.7233578	0.8353909	1
BUTANOATE METABOLISM	30	0.28861216	0.7105619	0.85626286	1
PATHOGENIC ESCHERICHIA COLI INFECTION	50	0.24425834	0.70852464	0.8627859	1
LEUKOCYTE TRANSENDOTHELIAL MIGRATION	94	0.24133033	0.7067604	0.8313953	1
REGULATION OF ACTIN CYTOSKELETON	176	0.17993955	0.6648534	0.9596154	1
TOLL LIKE RECEPTOR SIGNALING PATHWAY	76	0.21081783	0.65017754	0.9047619	1
FC GAMMA R MEDIATED PHAGOCYTOSIS	83	0.19004686	0.6495817	0.90335304	1
ACUTE MYELOID LEUKEMIA	53	0.16568136	0.6410138	0.9823875	1
FRUCTOSE AND MANNOSE METABOLISM	30	0.19758251	0.6064993	0.95669293	1
NATURAL KILLER CELL MEDIATED CYTOTOXICITY	101	0.2088917	0.6036799	0.92622954	1
PRIMARY IMMUNODEFICIENCY	29	0.29064822	0.58000416	0.88188976	1
ALLOGRAFT REJECTION	26	0.3025116	0.57801336	0.93890023	1
INTESTINAL IMMUNE NETWORK FOR IGA PRODUCTION	34	0.261487	0.5624501	0.94949496	1
GRAFT VERSUS HOST DISEASE	31	0.26586834	0.5504549	0.9738956	1
STEROID BIOSYNTHESIS	16	0.22409485	0.55034274	0.96825397	1
AUTOIMMUNE THYROID DISEASE	34	0.26633847	0.5500026	0.9534413	0.98951966
VIRAL MYOCARDITIS	62	0.21385355	0.5458711	0.9785575	0.9793871

Supplementary Table S19: Pearson correlations between individual metabolites and selected tissue composition parameters among cancer samples in the main cohort

Metabolites	**Cancer content**		**Stroma content**		**Benign epithelium content**		**Relative luminal space**	
	Correlations	***p*-value**	**Correlations**	***p*-value**	**Correlations**	***p*-value**	**Correlations**	***p*-value**
Alanine	0.2295	0.0253	–0.2269	0.027	–0.0803	0.439	–0.0087	0.9337
Choline	0.5395	< 0.001	–0.5233	< 0.001	–0.3218	0.0002	–0.2185	0.0132
Citrate	–0.0618	0.5518	–0.1113	0.2828	0.2662	0.0091	0.436	< 0.001
Creatine	–0.0642	0.4699	0.0024	0.9783	0.1075	0.2254	0.0397	0.6564
Ethm	–0.0341	0.701	0.0277	0.7557	0.0267	0.7643	–0.0687	0.4412
Glucose	–0.6205	< 0.001	0.514	< 0.001	0.4716	< 0.001	0.1263	0.1554
Glutamate	0.5898	< 0.001	–0.4871	< 0.001	–0.45	< 0.001	–0.1672	0.0592
Glutamine	0.4315	< 0.001	–0.3368	0.0001	–0.3519	< 0.001	–0.2222	0.0117
Glycine	–0.4881	< 0.001	0.3687	< 0.001	0.4122	< 0.001	0.2114	0.0166
GPC	0.491	< 0.001	–0.4792	< 0.001	–0.2894	0.0009	–0.0006	0.9946
GPE	–0.0362	0.6839	0.0357	0.6876	0.0208	0.8146	–0.0531	0.5518
Isoleucine	0.2005	0.0227	–0.1439	0.1036	–0.178	0.0436	–0.1519	0.087
Lactate	0.4693	< 0.001	–0.4064	< 0.001	–0.338	0.0001	–0.1843	0.038
Leucine	0.368	< 0.001	–0.2978	0.0006	–0.2878	0.0009	–0.2375	0.007
Myo–inositol	0.0784	0.3771	–0.1006	0.2568	–0.0184	0.8359	–0.0644	0.4704
PCh	0.4436	< 0.001	–0.2875	0.001	–0.4296	< 0.001	–0.1757	0.0472
PE	0.3601	< 0.001	–0.2105	0.0167	–0.3752	< 0.001	–0.2391	0.0066
Putrescine	–0.3059	0.0004	0.0277	0.7555	0.4935	< 0.001	0.1555	0.0796
Scyllo–inositol	0.1097	0.216	–0.0281	0.752	–0.1559	0.0776	0.0436	0.6254
Spermine	–0.0485	0.6405	–0.1098	0.2897	0.2407	0.0188	0.4536	< 0.001
Succinate	0.374	< 0.001	–0.3517	< 0.001	–0.2358	0.0071	–0.0454	0.6106
Taurine	–0.0895	0.3131	0.0881	0.3211	0.052	0.5586	–0.1108	0.2129
Valine	0.2057	0.0193	–0.1288	0.1457	–0.2045	0.0201	–0.182	0.0398

Ethm: Ethanolamine, GPC: Glycerophosphocholine, GPE: Glycerophosphoethanolamine, PCh: Phosphocholine, PE: Phosphoethanolamine.