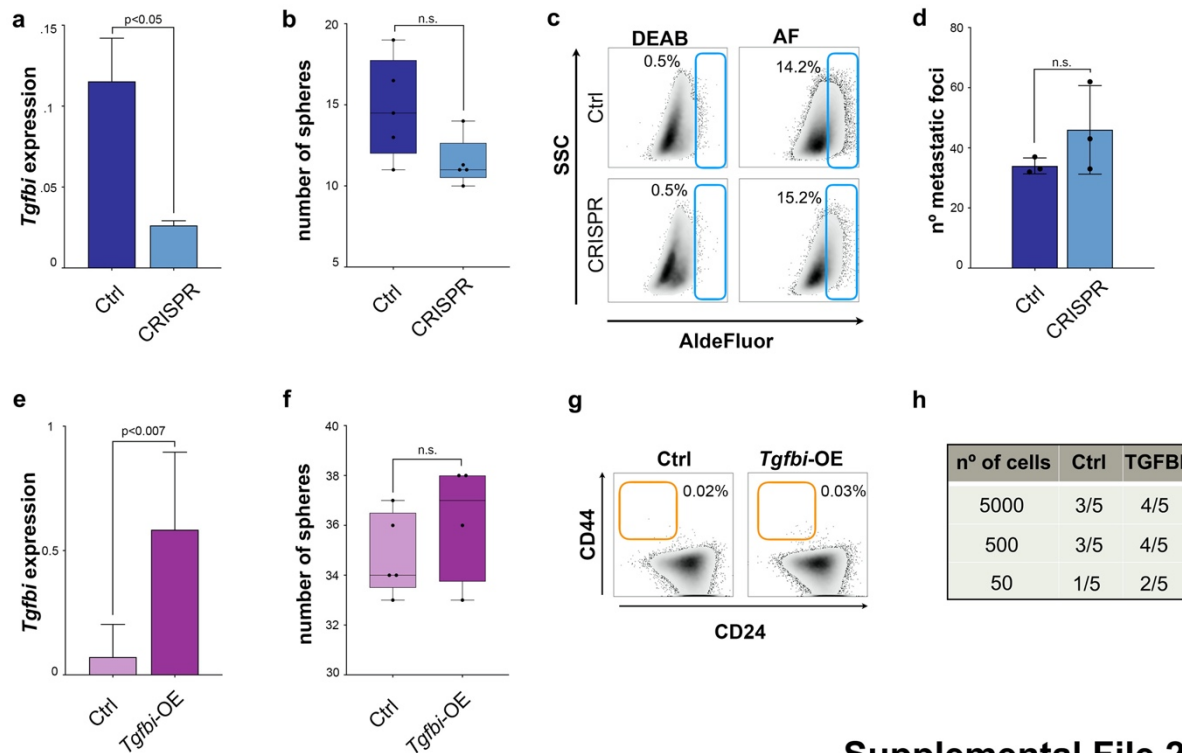


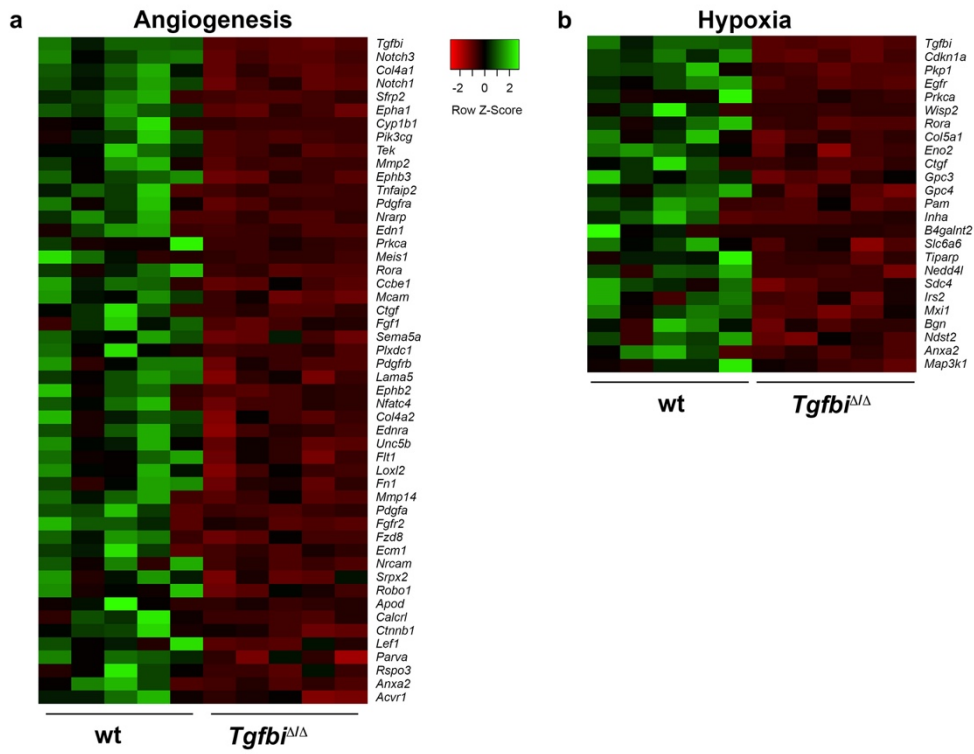
Supplemental File 1

Supplemental File 1: (a) CD11b⁺ cells from fresh MMTV-PyMT tumours were sorted by MACS and reanalysed by FACS for their expression of F4/80. (b) TGFBI immunohistochemistry of MMTV-PyMT, MMTV-ErbB2, C(3)Tag, and 4T1 tumours. (c) Genotyping PCR of *Tgfbi*^{+/+}, *Tgfbi*^{Δ/Δ} and *Tgfbi*^{Δ/+} mice. (d) Western blot for TGFBI and vinculin (loading control) for 3 MMTV-PyMT;*Tgfbi*^{+/+} and 3 MMTV-PyMT;*Tgfbi*^{Δ/Δ} tumours. (e) Representative TGFBI IHC of a MMTV-PyMT;*Tgfbi*^{+/+} and a MMTV-PyMT;*Tgfbi*^{Δ/Δ} tumour. (f) Representative AldeFluor analysis FACS analysis of MMTV-PyMT;*Tgfbi*^{+/+} and MMTV-PyMT;*Tgfbi*^{Δ/Δ} tumours. (g) MMTV-PyMT;*Tgfbi*^{+/+} and MMTV-PyMT;*Tgfbi*^{Δ/Δ} tumours were pulverised, their RNA was extracted, subjected to reverse transcription and analysed by qPCR for the expression of *Aldh1a3*. Data were analysed by unpaired t test (n=4 wt, n=5 ko). *Rplp0* was used as a housekeeping gene.



Supplemental File 2

Supplemental File 2: (a) C(3)TAG cells were infected with lentiviruses containing a CRISPR-*Tgfb1*, cells were selected and tested for expression of *Tgfb1* by qPCR. Data were analysed by unpaired t test ($n=2$). *Rplp0* was used as a housekeeping gene. (b) C(3)TAG cells wt or ko for TGFB1 were seeded as spheres (10^3 cells/ well). Spheres were counted 10 days later. Data were analysed by unpaired t test ($n = 5$ wt, $n=5$ ko). (c) C(3)TAG cells wt or ko for TGFB1 were analysed by FACS using the AldeFluor assay. (d) 5×10^5 C(3)TAG cells wt or ko for TGFB1 were injected into NSG mice via tail vein. Metastatic foci were counted 4 weeks later. Data were analysed by unpaired t test ($n=3$). (e) *Tgfb1* qPCR in MDA-MB-453 cells infected with control or *Tgfb1* lentiviruses. *SNRPD3* was used as a housekeeping gene. (f) MDA-MB-453 cells overexpressing *Tgfb1* and their respective controls were seeded as spheres (10^3 cells/ well). Spheres were counted 10 days later. Data were analysed by unpaired t test ($n = 5$ wt, $n=4$ *Tgfb1*-OE). (g) MDA-MB-453 cells overexpressing *Tgfb1* and their respective controls were analysed by FACS for the presence of $CD24^{low}CD44^{high}$ cells. (h) MDA-MB-453 cells overexpressing *Tgfb1* and their respective controls were trypsinised, counted, and injected orthotopically in limiting dilution assays in NSG mice. The presence or absence of tumours was evaluated for a maximum of 3 months after injection. Data were analysed using ELDA ($P=0.14$).



Supplemental File 3

Supplemental File 3: Heatmaps of statistically significant changed genes from the enrichment score analyses showed in Figure 2a.

a

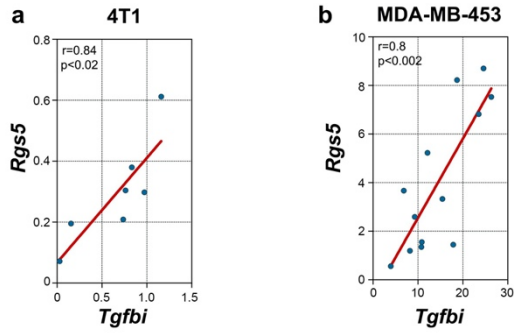
Hypoxia

ID	Gene	ENSMUSE	transcript	log2FCChange	FCSE	pvalue	adj. p
7142	Tgfb1	ENSMUSE0000000189	548.56456	-0.207141	1.165663	6.38E-07	1.18E-02
3808	Ccl6l1	ENSMUSE00000002367	4066.48474	-1.2474683	6.1645155	4.67E-14	5.54E-12
5143	Pgcl1	ENSMUSE000000026413	964.102497	-0.2204213	0.3700506	9.34E-12	8.40E-10
2408	Egr1	ENSMUSE00000002122	1574.00481	-0.9319081	1.1702882	4.39E-08	1.87E-06
489	Erm1	ENSMUSE00000002141	103.711948	-0.440081	0.1832677	0.0027148	0.0002768
1209	Cp3	ENSMUSE0000000563	136.14584	-0.2430658	0.3458884	0.0028982	0.0005861
8040	Rora	ENSMUSE00000002238	596.122596	-0.796702	1.1690147	4.79E-05	0.0008106
5498	Ccl3a1	ENSMUSE00000002867	2689.26322	-1.4387068	3.3546619	5.08E-05	0.0008213
7138	Id4	ENSMUSE00000002098	2766.88209	-0.8562999	2.4271206	0.0007412	0.0007629
6127	Pgcn	ENSMUSE00000001035	2929.76268	-0.845212	2.2463561	0.0001614	0.0007624
8884	Itih4	ENSMUSE00000002968	32.783768	-2.5130366	7.2881808	0.0005406	0.0008112
7827	Cpca1	ENSMUSE00000001119	1340.30031	-0.583711	0.6199515	0.0002577	0.0008588
2136	Cg1	ENSMUSE00000001997	4602.86334	-1.1732089	3.3119021	0.0014624	0.0003276
10223	It2	ENSMUSE00000001894	547.17702	-1.2213883	1.3881706	0.0146098	0.0147239
17432	Spx	ENSMUSE00000000884	82.5006644	-0.647111	0.2570284	0.0119029	0.0464110
7757	Bgn	ENSMUSE00000001375	2607.89812	-0.684399	2.8281715	0.0024196	0.0167419
10681	Nes2	ENSMUSE00000001038	619.484446	-0.821981	1.1833398	0.0026965	0.0110912
4285	Hes6l1	ENSMUSE00000001689	3654.40045	-0.4400344	0.1412088	0.0111267	0.0001775
12358	Phox2a	ENSMUSE00000000965	5394.53623	-1.884082	4.4371244	1.12E-05	0.0004078
8307	Anxa2	ENSMUSE00000002021	16566.8611	-0.1024655	0.2041007	0.0087756	0.0468941
1681	Scl4	ENSMUSE00000001709	13748.7755	-0.4454027	0.1407289	0.0115049	0.0141143
1742	Bcl6l1	ENSMUSE00000001493	3886.56161	-0.5166981	0.2981848	0.0107271	0.0141229
2637	Hes9	ENSMUSE00000001709	1029.32869	-1.0486852	3.5149723	0.0043348	0.0001930
1407	Slc11	ENSMUSE000000014813	302.74281	-0.0826654	0.2396127	0.0104843	0.0008363
3047	Mmp14	ENSMUSE00000002174	2735.46268	-0.8713233	2.2332003	0.0079239	0.0048774
13379	Hes14	ENSMUSE00000001919	2357.81948	-0.440081	0.1832677	0.0027148	0.0002768
9039	Tgfb1	ENSMUSE00000002374	805.58474	-0.4743691	1.165663	0.0027489	0.0127224
8144	Ets1	ENSMUSE00000002035	1002.64603	-0.738877	1.2813358	0.0006055	0.0104108
14523	Chem3	ENSMUSE00000007337	23.8901137	-1.0488151	4.8817839	0.0038229	0.118496
4929	Erm3	ENSMUSE00000002929	23.1918305	-0.7192926	0.4503736	0.0791924	0.2001976
14251	Bcl2	ENSMUSE00000001729	1029.32869	-0.738877	1.2813358	0.0006055	0.0104108
4145	Dna	ENSMUSE00000002452	282.40746	-0.4285446	0.2181868	0.0111502	0.1772614
722	Pgf	ENSMUSE000000004791	2386.89202	-0.709986	1.3995449	0.0043487	0.1909022
4783	Gat1	ENSMUSE00000002579	6442.16577	-0.889884	2.9295114	0.0147893	0.0758874
4621	Bcl1	ENSMUSE00000001763	829.87622	-0.4743691	1.165663	0.0027489	0.0127224
3101	Bqsmc2	ENSMUSE00000001318	164.202488	-0.5488881	0.2298799	0.0007827	0.0054802
2105	Don	ENSMUSE00000001989	1739.41028	-0.6234195	0.8827698	0.0052028	0.1703263
6081	F3	ENSMUSE00000002128	3386.47358	-0.845212	2.2463561	0.0001614	0.0007624
4112	Maf1	ENSMUSE00000002025	1703.18827	-0.4002939	0.1761763	0.0028431	0.0170025
9468	Irf3	ENSMUSE00000003847	1043.14086	-0.5488881	0.2298799	0.0007827	0.1703263
808	Hmcr1	ENSMUSE00000005413	1105.82214	-0.4002939	0.1761763	0.0028431	0.0170025
9645	Phc2b1	ENSMUSE00000001780	995.490423	-0.6938833	0.2346373	0.0749521	0.2031994
495	Hes1	ENSMUSE00000002241	2.9219166	-0.845212	2.2463561	0.0001614	0.0007624
5005	Ahr1	ENSMUSE00000002819	597.542123	-0.9308813	1.2243001	0.0019431	0.0240819
8933	Cp1	ENSMUSE00000003429	812.18274	-0.5132855	0.2607761	0.0009994	0.0205051
2805	Tgfb1	ENSMUSE00000002123	691.1757	-0.387857	0.1517949	0.0419453	0.1932426

b

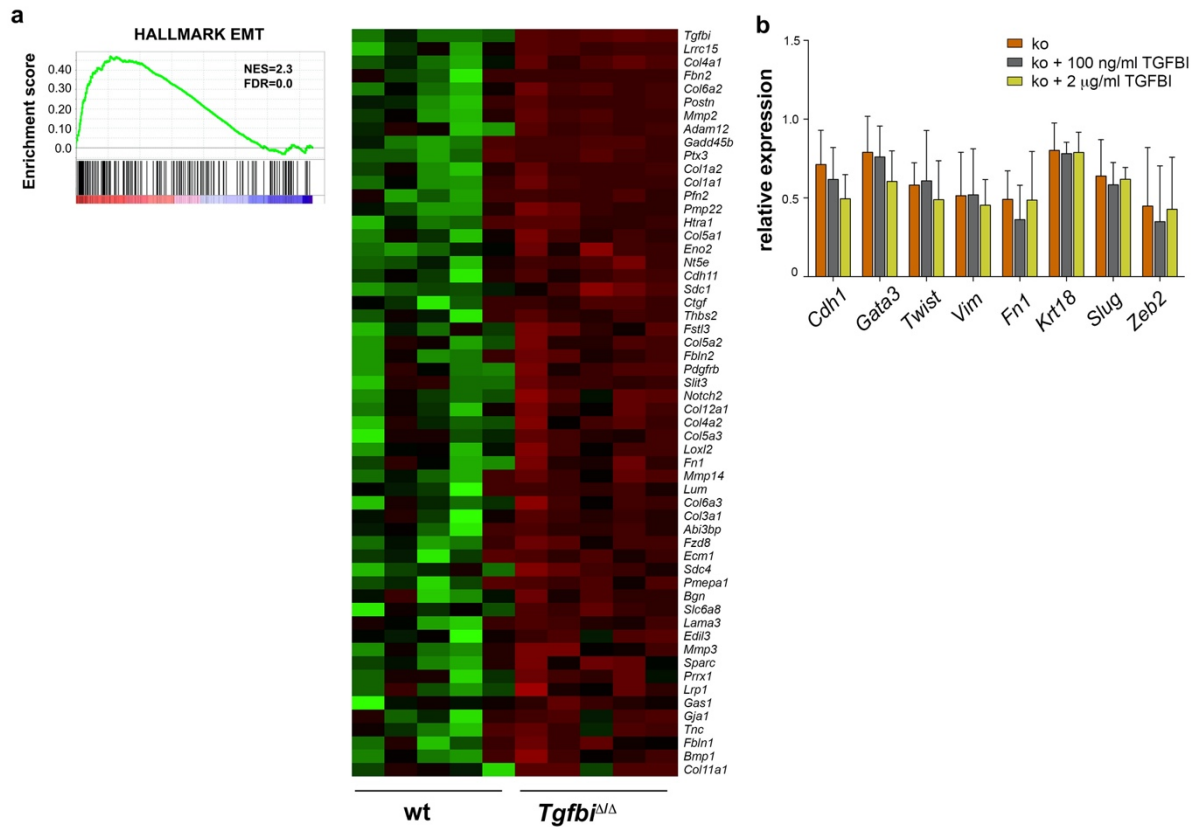
Angiogenesis

ID	Gene	ENSMUSE	transcript	log2FCChange	FCSE	pvalue	adj. p
8713	Tgfb1	ENSMUSE0000000189	548.56456	-0.207141	1.165663	6.38E-07	1.18E-02
10218	Nes2	ENSMUSE00000001038	2003.2157	-1.787255	3.0504572	8.17E-18	1.92E-15
5451	Nes1	ENSMUSE00000002803	3725.2157	-1.21517	0.1870006	5.67E-10	3.46E-08
7825	Ccl4a1	ENSMUSE00000003102	11789.209	-1.22019	0.2180779	3.08E-10	2.42E-08
7013	Pgcl1	ENSMUSE000000026413	964.102497	-0.2204213	0.3700506	9.34E-12	8.40E-10
890	Erm3	ENSMUSE00000002929	1764.01919	-0.85047	1.1725043	8.29E-07	2.44E-05
961	It2	ENSMUSE00000000838	106.36987	-1.89802	0.3131849	3.81E-07	1.26E-05
5999	Spc2	ENSMUSE00000002799	893.19875	-2.84981	0.4862287	1.39E-09	8.35E-08
2455	Pdgfra	ENSMUSE00000001979	185.02079	-1.24827	0.2412717	2.71E-07	9.37E-06
7892	Erm6	ENSMUSE00000001916	582.54241	-0.76271	0.2246828	0.0007264	0.0004508
7960	Mmp2	ENSMUSE000000031740	1987.2498	-1.48137	0.2981919	7.80E-07	2.37E-05
6716	Pdgfra	ENSMUSE00000002821	336.87634	-1.58387	0.3001401	6.13E-06	0.00139
8204	Miam	ENSMUSE00000003136	1873.6319	-0.70703	0.1702923	7.02E-05	0.001203
3363	Smedd1	ENSMUSE00000002231	207.8881	-1.11093	0.250426	0.0010265	0.0024884
12462	Ccl6l1	ENSMUSE00000004618	173.90699	-1.87076	0.408917	4.80E-05	0.0008294
6949	F11	ENSMUSE00000002968	368.88412	-0.78885	0.2283581	0.0005983	0.0002356
8240	Nes1	ENSMUSE00000003208	1968.12259	-0.796702	1.1690151	4.79E-05	0.0008106
8783	Foxl1	ENSMUSE00000000894	180.89369	-0.28877	0.2612021	0.0012969	0.0117171
7828	Ccl4a2	ENSMUSE00000001503	3365.3862	-0.83544	0.2351008	0.000861	0.0040401
16610	Nwap	ENSMUSE00000002022	800.87448	-2.16658	0.5021007	1.98E-05	0.000136
3875	Mafk4	ENSMUSE00000002411	145.1885	-1.16546	0.3326998	0.000173	0.0003884
4029	Foxl1	ENSMUSE00000001417	189.71709	-0.28877	0.2612021	0.0012969	0.0117171
6374	Erm3	ENSMUSE00000002929	1764.01919	-1.24827	0.2412717	2.71E-07	9.37E-06
2183	Unc5b1	ENSMUSE00000002009	773.74185	-0.72018	0.200808	0.0008101	0.00119
8945	Lmo2	ENSMUSE00000003205	589.43788	-0.88289	0.2864726	0.000561	0.0047985
11719	Hes1	ENSMUSE00000002025	1703.18827	-0.4002939	0.1761763	0.0028431	0.0170025
9652	Fgl1	ENSMUSE00000002585	86.47403	-1.08325	0.822379	0.0001811	0.002448
5051	F11	ENSMUSE00000002819	4798.7017	-1.18176	0.2445403	0.0006083	0.0005683
1160	Mmp14	ENSMUSE00000002174	4793.2027	-1.02748	0.301246	0.000647	0.008741
4072	Hgfa	ENSMUSE00000002958	235.03519	-0.84487	0.2401795	0.010967	0.0030909
2138	Ccl4a1	ENSMUSE00000002982	2142.6208	-1.17522	0.2180779	0.001267	0.0004988
7528	Fgfr2	ENSMUSE00000003049	148.85927	-1.38023	0.4821975	0.0011785	0.0110086
4028	Cyp11a1	ENSMUSE000000024087	704.83821	-0.68926	0.820291	1.11E-07	4.29E-06
7996	Spry2	ENSMUSE00000001253	190.46627	-0.87422	0.29703	0.003394	0.026295
2289	Mmp1	ENSMUSE00000001985	102.86989	-0.36087	0.182691	0.001268	0.0117171
5407	Acor1	ENSMUSE00000002838	505.98813	-0.31179	0.1817286	0.0007608	0.0008767
4673	Mmp19	ENSMUSE00000002173	170.02817	-0.60225	0.287698	0.010171	0.007223
6071	Emr1	ENSMUSE00000002108	869.17402	-1.29413	0.461499	0.001267	0.0120127
9139	Mmp1	ENSMUSE00000001985	102.86989	-0.36087	0.182691	0.001268	0.0117171
7484	Par1	ENSMUSE00000003070	4293.7347	-0.75019	0.1714348	0.0008215	0.0082582
16628	Canal	ENSMUSE00000002958	146.39819	-0.70918	0.252427	0.0004845	0.0037818
13366	Phox2a	ENSMUSE00000000965	5394.53623	-1.884082	4.4371244	1.12E-05	0.0004078
989	Hes1	ENSMUSE00000002241	2.9219166	-0.845212	2.2463561	0.0001614	0.0007624
3708	Nes1	ENSMUSE00000002819	302.14933	-1.89801	0.3792989	0.0006867	0.003781
8217	Ahr1	ENSMUSE00000003231	1668.865	-0.62446	0.2041021	0.0007786	0.048984
18133	Vsmg1	ENSMUSE00000002848	1738.5872	-0.86276	0.1871298	0.001338	0.0076582
7123	Bcl2	ENSMUSE00000001729	1029.32869	-0.738877	1.2813358	0.0006055	0.0104108
5543	Bcl1a2	ENSMUSE00000001130	513.40783	-0.59702	0.243801	0.0217482	0.09225
10689	Tgfb1	ENSMUSE00000002374	1420.3917	-0.4743691	1.165663	0.0027489	0.0127224
11372	Mmp2	ENSMUSE00000001445	238.19501	-0.45811	0.2112416	0.000808	0.103327
8144	Ets1	ENSMUSE00000002035	1002.64603	-0.738877	1.2813358	0.0006055	0.0104108
14627	Bcl3a3	ENSMUSE00000001439	385.45446	-0.40781	0.1633201	0.0137779	0.07205
83	Acor1	ENSMUSE00000000030	908.89099	-0.46572	0.2304265	0.045121	0.161203
2087	Hmcr1	ENSMUSE00000001989	186.195027	-1.19905	0.4398449	0.0008226	0.011713
8029	Ccl13	ENSMUSE00000001841	162.4403	-0.72988	0.2400075	0.192141	0.0078278
12113	Scl2	ENSMUSE00000004791	1871.9007	-0.54782	0.2217287	0.0016287	0.0021885
13695	Lmo15	ENSMUSE00000002873	1733.7802	-0.89245	0.300827	0.064438	0.000182
7928	Pgf	ENSMUSE000000004791	2386.89202	-0.709986	1.3995449	0.0043487	0.1909022
7389	Mmp2	ENSMUSE00000002605	6487.209	-1.28843	0.5432607	0.001848	0.0018144
989	Spc2	ENSMUSE00000002799	893.19875	-2.84981	0.4862287	0.0012969	0.0004508
7981	Ccl3l1	ENSMUSE00000001778	3891.3841	-0.80255	0.228275	0.0004675	0.1989035
3123	F11	ENSMUSE00000002819	173.13655	-0.55159	0.2534584	0.0008084	0.1215044
9917	Cv2d	ENSMUSE00000003729	144.48927	-0.72096	0.3344861	0.0042255	0.190903
8144	Ets1	ENSMUSE00000002035	1002.64603	-0.738877	1.2813358	0.0006055	0.0104108
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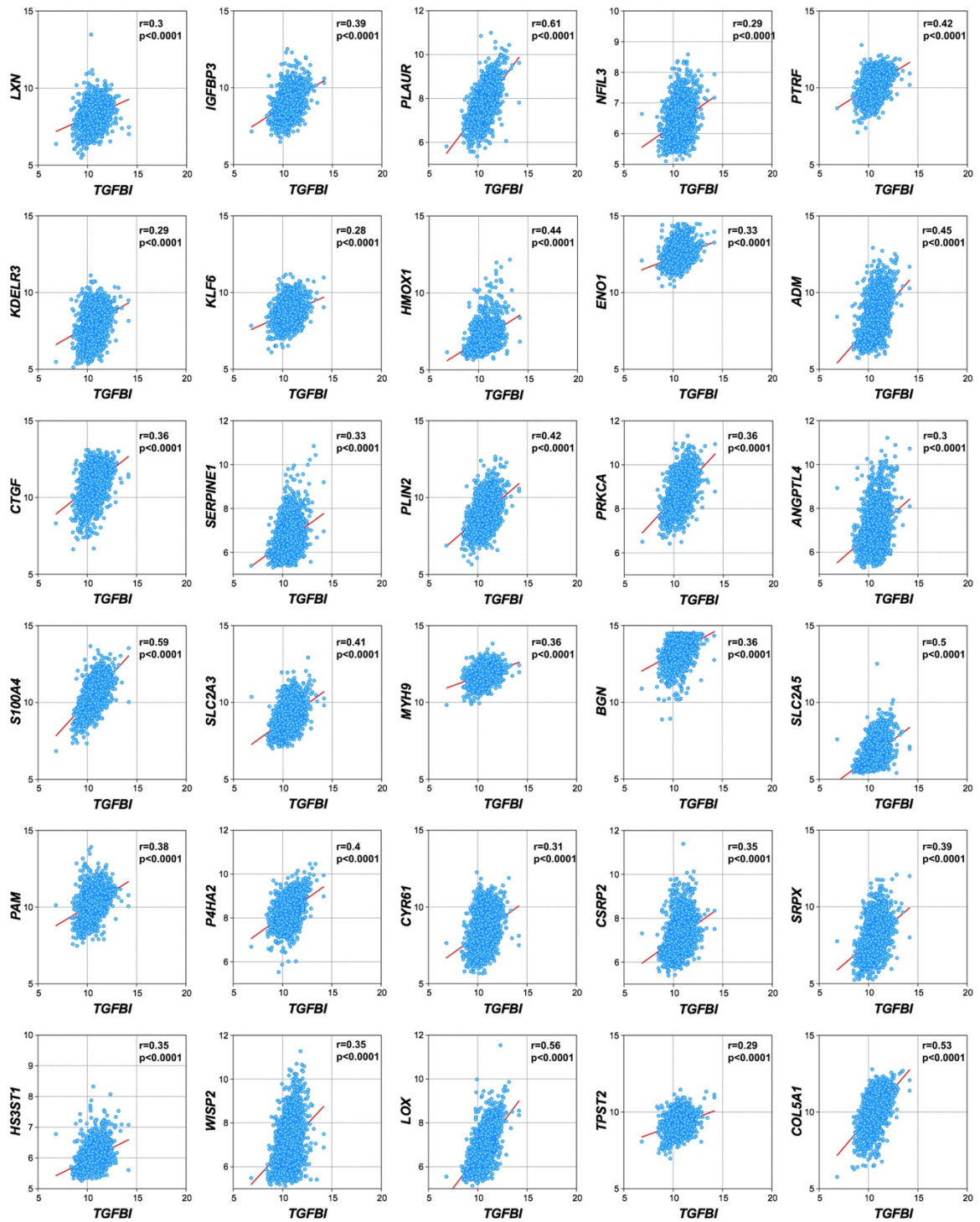
Supplemental File 5

Supplemental File 5: Correlation analyses of *Rgs5* and *Tgfb1* transcripts in 4T1 (n=7) and MDA-MB-453 (n=13) tumours. Tumours were pulverised, their RNA was extracted, subjected to reverse transcription, and analysed by qPCR for the expression of *Rgs5* and *Tgfb1*. *Rplp0* was used as a housekeeping gene for mouse and *SNRPD3* for human.



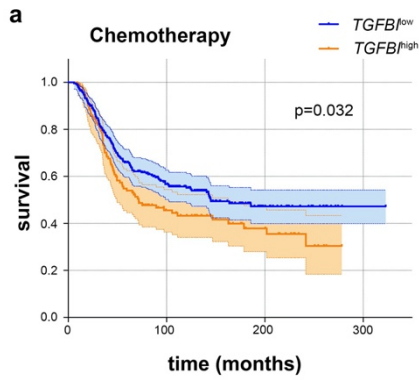
Supplemental File 6

Supplemental File 6: (a) Enrichment score analysis of MMTV-PyMT;*Tgfb1*^{+/+} and MMTV-PyMT;*Tgfb1*^{ΔΔ} tumours for Hallmark EMT (n=5) and heatmap of statistically significant changed genes. (b) qPCR of MMTV-PyMT;*Tgfb1*^{ΔΔ} tumour cells grown with either 100 ng/ml or 2 μg/ml exogenous TGFBI. Data were analysed using one-way ANOVA, and are presented as mean and SD (n=5). *Rplp0* was used as a housekeeping gene.



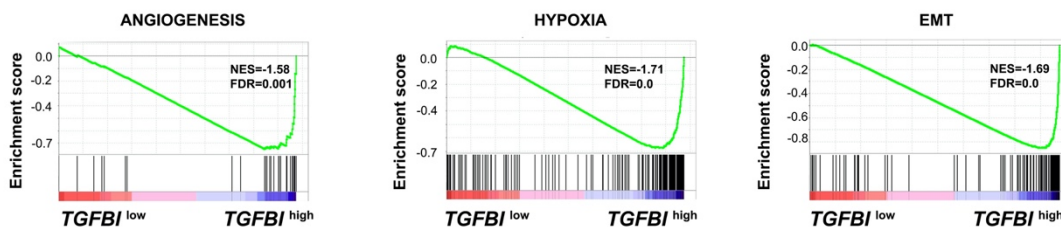
Supplemental File 7

Supplemental File 7: Spearman's correlation of hypoxia-related genes with *TGFBI* in the METABRIC cohort.



Supplemental File 8

Supplemental File 8: Survival curves of breast cancer patients in the METABRIC cohort who received chemotherapy classified according to the expression of *TGFBI*. Patients were stratified using the application *Evaluate cutpoints*, and the survival curves were compared using the Log-rank (Mantel-Cox) test ($n_{high}=123$, $n_{low}=250$).



Supplemental File 9

Supplemental File 9: Enrichment score analyses of $TGFBI^{low}$ (<75th percentile) and $TGFBI^{high}$ (≥ 75 th percentile) tumours in the METABRIC

Supplemental File 10. Table 1: Primer Sets Used in This Study.

ID	Forward 5'-3'	Reverse 5'-3'
<i>Rplp0</i>	GATTCGGGATATGCTGTTGG	GTTCTGAGCTGGCACAGTGA
<i>Krt18</i>	CGAGGCACTCAAGGAAGAAC	AATCTGGGCTTCCAGACCTT
<i>Aldh1a3</i>	GAGCGATCCTGGCTACTCTG	GACGAAAAAGGCATGAAGGA
<i>Tgfb1</i>	ATCACCAACAACATCCAGCA	CCAGCACGGTATTGAGTCCT
<i>TGFBI</i>	AAGTCTCTCCAAGGTGACAAGC	CCTTGTTGACACTCACCACATT
<i>SNRPD3</i>	GCCCAGATTGTGAAGGACAT	TCAGCTCAGCACGGTAGTTG
<i>Gata3</i>	GCTACGGTGCAGAGGTATCC	AGAGATCCGTGCAGCAGAG
<i>Mmp2</i>	ACACTGGGACCTGTCACTCC	TGTCACTGTCCGCCAAATAA
<i>Mmp9</i>	CCAGATGATGGGAGAGAAGC	TTGAGGCCTTTGAAGGTTTG
<i>Snai2</i>	GAACCCACACATTGCCTTGT	GCAGAAGCGACATTCTGGAG
<i>Zeb2</i>	CTATTCCCCTGCATCAGCAT	GGCTTGTCAGTCCTTTCTCG
<i>Vim</i>	GCGAGGAGAGCAGGATTTCTC	GGGTGTCAACCAGAGGAAGT
<i>Fn1</i>	TGCACGTGTGTGGGGAACGG	CCCGGCCCTGACCAAAGCAG
<i>Rgs5</i>	AGACGGTTCCACCAGGTTC	CAGACAGAGGCCCTAAAGA
<i>Hif1a</i>	CAGTCGACACAGCCTCGATA	CGGCTCATAACCCATCAACT