### **Supplemental Information**

# Inhibition of Estrogen Signaling Reduces the Incidence of *BRCA1*-associated Mammary Tumor Formation

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#### **Development of branch software**

To calculate the ductal length and branching number of mammary glands from images, we first preprocessed the images with skeletonization, which transforms the RGB input image to a gray-scale image, as follows:

$$Gray \ color \ image = (Red + Green + Blue)/3$$
 [1]

Second, we eliminated the background noise by adopting a mean filter, as follows:

*Improved image=(Original image) –(Mean filtered image)* [2]

Third, we converted the gray-scale image to a binary image using the OTSU threshold (1). We then applied binary-image thinning using the Hessian matrix and templatematching methods (2). The Hessian algorithm reduces noise while retaining shape information and detecting line patterns, and template matching eliminates noise lines and end points. After this processing, we counted the lines that divided at each of the remaining points. After this processing, we clustered to represent a single true branch point. As an input, this algorithm needs a morphological image. In the absence of the usual binary imaging (I), it supposes that the background is valued as 0 and the image is valued as 1 The

Hessian matrix of an N-dimensional continuous function f contains the second-order derivatives. As we are working on a 2-dimensional image, our Hessian matrix is given as [3]:

$$H(f) = \begin{pmatrix} \frac{\partial^2 f}{\partial x^2} & \frac{\partial^2 f}{\partial x \partial y} \\ \frac{\partial^2 f}{\partial y \partial x} & \frac{\partial^2 f}{\partial y^2} \end{pmatrix} \quad [3].$$

The Hessian matrix  $H_{0,s}$  was calculated at each pixel position  $x_0$  and scale s. Kim (3) used s as the standard deviation  $\sigma$  of Gaussians to approximate the second-order derivatives. A celline vessel feature  $V_0(s)$  was calculated at pixel position  $x_0$  from the eigenvalues  $\lambda_1 < \lambda_2$  of the Hessian matrix  $H_{0,s}$  using equations of "dissimilarity measure"  $R_E$  and "second order structuredness" S, as follows:

$$R_B = \frac{\lambda_1}{\lambda_2} \quad [4],$$

$$S = \sqrt{\lambda_1^2 + \lambda_2^2}$$
 [5], and

$$v_0(s) = \begin{cases} 0, & \text{if } \lambda_2 > 0\\ \exp\left(-\frac{R_B^2}{2\beta^2}\right) \left(1 - \exp\left(-\frac{s^2}{2c^2}\right)\right) & [6], \end{cases}$$

where  $\beta$  and c are constants that control the sensitivity of the filter.  $\mathbf{R}_{\mathbf{F}}$  accounts for the deviation from blob-like structures, but cannot differentiate background noise from the

real cellline. Since the background pixels have a small magnitude, and thus small eigenvalues, S helps to distinguish between noise and background. If  $V_0$  in equation [6] represents the duct thickness at a specific scale  $\sigma$ , it can be expressed as equation [7] if it  $V_0(s)$  is expanded to multiple scales, as follows:

$$V(s) = \max_{\sigma_{\min} \le \sigma \le \sigma_{\max}} v(s, \sigma) \qquad [7].$$

We can then detect ducts of various thicknesses. The larger the scale  $\sigma$ , the size variable the duct can be detected. After the Hessian matrix algorithm was applied, the noise decreased and the duct could be observed. To enable template matching during image processing, different line templates were used in the proposed scheme to search for directional components along all possible orientations. The number of dividing lines was counted at each branch point. Adjacent points were clustered to represent one point. For the evaluation of computation times, we used a single personal computer equipped with a 2.3-GHz processor, 4-GB RAM, and a single core implementation of the algorithms. The template matching and Hessian matrix algorithm were measured using a homemade software branching point detector. Each branching point was classified based on how many lines were detected. As node point detection is an important means of characterizing some

features in an image, it is notable that we herein introduce a simple algorithm to detect node points in a skeletonized image via template matching and the Hessian matrix algorithm. This program should prove very useful for calculating branching points in cell images.

#### REFERENCES

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- Kim SH, Lee JM, Lee JG, Kim JH, Lefere PA, Han JK, et al. Computer-Aided Detection of Colonic Polyps at CT Colonography Using a Hessian Matrix–Based Algorithm: Preliminary Study, *Am J Roentgenol.* 2007; 189(1): 41-51.



**Supplementary Fig. 1. Measurement of mammary gland density and networks using the Branch software.** (A) Images of mammary glands were analyzed by a simple algorithm that we designed to detect node points in a skeletonized image. The sequential image-processing scheme is shown. (B) Representative results from Branch software analysis of a mammary gland from a 2-month-old mouse.

Gene	EntrezID	Rank correlation	Gene	EntrezID	Rank correlation	Gene	EntrezID	Rank correlation
Scarf2	224024	0.9833	Uroc1	243537	0.7950	Prdx6	11758	0.7333
Sprr2k	20765	0.9400	Slurp1	57277	0.7921	Scai	320271	0.7333
Bend6	320705	0.9333	Crispld1	83691	0.7866	Sepw1	20364	0.7333
Syna	214292	0.9333	D16Ertd472e	67102	0.7833	Sned1	208777	0.7333
Actr6	67019	0.9167	Epb4.111	13821	0.7833	Sys1	66460	0.7333
Dst cl- 2	13518	0.9167	Gaint15	44500	0.7833	Tctex1d2	66061	0.7333
Siaz Sprr1b	20754	0.9167	Gfra4 Gm20257	14588	0.7833	Tmom227	201250	0.7333
Sprrib Code148	20754	0.9154	Hist1b1c	50708	0.7833	Trdmt1	13/13/	0.7333
Dhv35	71715	0.9000	Pfdn4	109054	0.7833	Tro53rka	13434	0.7333
Sprr1a	20753	0.9000	Plk2	20620	0.7833	Zfp457	431706	0.7311
Ywhab	54401	0.9000	Rpl31-ps12	665562	0.7833	Gpr17	574402	0.7289
Zfp622	52521	0.9000	Sipa1l2	244668	0.7833	Ptgs2os2		0.7289
Gm527	217648	0.8833	Trim23	81003	0.7833	Cyp2t4	384724	0.7280
Naa20	67877	0.8833	Xrn2	24128	0.7833	Tmprss11d	231382	0.7257
Pou2af1	18985	0.8833	4930556M19Rik	75259	0.7782	4930405A21Rik	74846	0.7197
Steap4	117167	0.8833	Trim69	70928	0.7782	1700067K01Rik	73453	0.7167
Tmem45a2		0.8833	Anxa8	11752	0.7667	1810013L24Rik	69053	0.7167
Ccr9	12769	0.8815	Cdk20	105278	0.7667	4930447M23Rik		0.7167
4921504A21Rik		0.8667	Cryzl1	66609	0.7667	Arhgap35		0.7167
Angpt1	11600	0.8667	Dynirb1	67068	0.7667	B3gnt2	53625	0.7167
Dobs1	10/581	0.8667	Ei01 Fam13a	58521	0.7667	Briv1	12161	0.7167
Gli2	233051	0.8667	Empl2	58909	0.7667	Cycl5	20211	0.7167
Gss	14033	0.8667	Gm13547	/1409 433416	0.7667	Ebxo8	50753	0.7167
Mapre1	13589	0.8667	Gm16675	100503498	0 7667	Fem1c	240263	0.7167
Ppbp	57349	0.8667	Gzf1	74533	0.7667	Fkbp1a	14225	0,7167
Ttpal	76080	0.8667	Hist1h4h	69386	0.7667	Gls	14660	0.7167
Ccdc14	239839	0.8500	Мурор	232934	0.7667	Gm16861	100503704	0.7167
Enah	13800	0.8500	Pde6a	225600	0.7667	Gm17762	100034739	0.7167
Frg1	14300	0.8500	Rbpms	19663	0.7667	Gtf2e1	74197	0.7167
Fst	14313	0.8500	Trpc4ap	56407	0.7667	ler5	15939	0.7167
Nsfl1c	386649	0.8500	Tslp	53603	0.7667	Pcdhb15	93886	0.7167
Peg3os		0.8500	Ttc8	76260	0.7667	Pnpt1	71701	0.7167
Pter	19212	0.8500	Adgrb1		0.7615	Rbl1	19650	0.7167
Zfp382	233060	0.8500	Pou2f3	18988	0.7615	Rcor3	214742	0.7167
Spats1	71020	0.8476	115	16191	0.7572	Rpl13	270106	0.7167
Etaalos	44703	0.8443	Ccdc176	72873	0.7531	Slc25a29	214663	0.7167
Amd1,Amd2	220212	0.8416	Crnkii	14300	0.7500	Vasn	246154	0.7167
A430035B10RIK	320312	0.8356	Gabpa Gabol	14390	0.7500	UDK3DI Gm16998	100502020	0.7143
Cann6	17338	0.8333	lmng2	224224	0.7500	Gm5483	433016	0.7120
Cfap45	12550	0.8333	Kifan3	16579	0.7500	Mrgpra2a	668727	0.7120
Fam169a	320557	0.8333	Mgat3	17309	0.7500	1600023N17Rik	69788	0.7113
Fitm2	228859	0.8333	Mterf4		0.7500	1110008F13Rik	67388	0.7000
H2afy3	67552	0.8333	Nr3c1	14815	0.7500	1500012F01Rik	68949	0.7000
Man2a1	17158	0.8333	Nxt1	56488	0.7500	A430093F15Rik	403202	0.7000
Rwdd4a	192174	0.8333	Rplp2-ps1	665931	0.7500	Ago2		0.7000
Serpinc1	11905	0.8333	Rpn2	20014	0.7500	Atxn3	110616	0.7000
Slpi	20568	0.8333	S100a3	20197	0.7500	Cab39	12283	0.7000
Uap111	227620	0.8333	Serf1	20365	0.7500	Ccdc127	67433	0.7000
Uchl5	56207	0.8333	Serpini1	20713	0.7500	Cep250	16328	0.7000
Sic10a1	20493	U.8182	Synj2bp	24071	0.7500	Cpe	12876	0.7000
Arme2	212402	0.8167	W/dr8	/5425	0.7500	Cula	12995	0.7000
Cdo1	12592	0.0107	Gm13986	39002	0.7500	Ehbn1	20054	0.7000
Ctnnd2	18163	0.8167	Gm3230	100041244	0.7398	Fam71f1	330277	0.7000
Kik10	69540	0.8167	Tas1r2	83770	0.7398	Foxf1	15227	0.7000
Lalba	16770	0.8167	Gm5468	432939	0.7364	Gpatch1	67471	0.7000
Mettl21a	67099	0.8167	2500002B13Rik		0.7333	lft57	73916	0.7000
Ndrg3	29812	0.8167	Abhd8	64296	0.7333	Itprip	414801	0.7000
Pcdhb8	93879	0.8167	Abl1	11350	0.7333	Lefty1	13590	0.7000
Peg3	18616	0.8167	Blcap	53619	0.7333	Pcgf5	76073	0.7000
Sema3e	20349	0.8167	Cmc2		0.7333	Polr3f	70408	0.7000
Gm6194	620966	0.8117	Cyp4b1	13120	0.7333	Ppil2	66053	0.7000
Spo11	26972	0.8095	Dixdc1	330938	0.7333	Rae1	66679	0.7000
Agap3	213990	0.8000	Dnase1	13419	0.7333	Rgag1	209540	0.7000
Arsk	77041	0.8000	Ephx3	71932	0.7333	Kpl35	66489	0.7000
Cbr2	12409	0.8000	⊦gf10	14165	0.7333	SIc25a37	67712	0.7000
Ell Wetth 2	13716	0.8000	+pgs	14287	0.7333	SIX4	52864	0.7000
HIST1h2ac	319164	0.8000	Gas1	14451	0.7333	The22	15278	0.7000
NIrc5	0/042	0.8000	Horpor	74226	0.7333	Vanh	6/515	0.7000
Nnat	454541	0.8000	Kitl	17211	0.7333	8930018H10Pil	50491	0.7000
Phf20	228820	0.8000	March10	1/311	0.7333	Clca1	12722	0.6950
Ptx3	19788	0.8000	Mrgpra2h	235712	0 7333	Unc13c	208898	0.6950
Rdh13	108841	0.8000	Mtmr10	233315	0.7333	Rptoros	200030	0,6946
Tigit	100043314	0.8000	Pcm1	18536	0.7333	Krt222	268481	0.6876
Aox4	71872	0.7950	Ppp2r1b	73699	0.7333	Lhfpl4	269788	0.6862
-			-			-		

## Supplementary Table 1. List of fulvestrant positive response-associated genes

Gene	EntrezID	Rank correlation	Gene	EntrezID	Rank correlation	Gene	EntrezID	Rank correlation
Rgl3	71746	-0.9667	Aff1	17355	-0.7667	Plxna3	18846	-0.7333
Otud5	54644	-0.9333	Amd2	1E+08	-0.7667	Rpap1	68925	-0.7333
Prickle3	54630	-0.9333	Anxa9 71790 -0.7667 S		Shisa4	77552	-0.7333	
Tyms-ps	22172	-0.9167	Btbd10 68815 -0.7667 S		Smpd5		-0.7333	
Gzmm	16904	-0.9000	Dip2c 208440 -0.7667 St		Stbd1	52331	-0.7333	
Ebp	13595	-0.8833	Eif2ak4 27103 -0.7667 Sy		Synj2bp-cox16		-0.7333	
Kdm4c	76804	-0.8833	Fam214a		-0.7667	Ttn	22138	-0.7333
Prr5l	72446	-0.8833	Frs3	107971	-0.7667	Zc3h6	78751	-0.7333
Srprb	20818	-0.8833	Hcn2	15166	-0.7667	Dusp15	252864	-0.7224
Fam53b	77938	-0.8667	Myh7b	668940	-0.7667	Lemd1	213409	-0.7224
Gcn1l1	231659	-0.8667	Plekha2	83436	-0.7667	Cabp4	73660	-0.7197
Ppm1h	319468	-0.8667	Plp2	18824	-0.7667	5730508B09Rik	70617	-0.7167
Trp53i11	277414	-0.8667	Ppp1r3b	244416	-0.7667	Aco1	11428	-0.7167
Foxd3	15221	-0.8645	Prrg3	208748	-0.7667	Асрб	66659	-0.7167
1810030007Rik	69155	-0.8500	Tbc1d25	209815	-0.7667	Actn3	11474	-0.7167
Fads3	60527	-0.8500	Tnni1	21952	-0.7667	Adcy6	11512	-0.7167
ler2	15936	-0.8500	Tspan31	67125	-0.7667	Atp6v1g2	66237	-0.7167
Pdgfb	18591	-0.8500	Gm13275,Gm13285	545652	-0.7659	Atrnl1	226255	-0.7167
Ankrd40	71452	-0.8333	Tmem202	73893	-0.7628	Eml4	78798	-0.7167
As3mt	57344	-0.8333	Tshr	22095	-0.7628	Hdac6	15185	-0.7167
Csrnp2	207785	-0.8333	1810062O18Rik	75602	-0.7615	Kcnj10	16513	-0.7167
Fads1	76267	-0.8333	2610507B11Rik	72503	-0.7500	Kcnmb1	16533	-0.7167
Fnbp4	55935	-0.8333	Actr8	56249	-0.7500	Lrif1	321000	-0.7167
Med14	26896	-0.8333	Alox15	11687	-0.7500	Me1	17436	-0.7167
Slc46a1	52466	-0.8333	Arhgap26	71302	-0.7500	Nlk	18099	-0.7167
Socs7	192157	-0.8333	Hiat1	15247	-0.7500	Olfr1372-ps1	257871	-0.7167
Tbxa2r	21390	-0.8333	ltga1	109700	-0.7500	Paqr4	76498	-0.7167
Tm7sf2	73166	-0.8333	Lxn	17035	-0.7500	Pnpla3	116939	-0.7167
Utp6	216987	-0.8333	Mid1ip1	68041	-0.7500	Pyroxd2	74580	-0.7167
Bhlhe40	20893	-0.8167	Mycl		-0.7500	Rad54l2	81000	-0.7167
Dhrs13	70451	-0.8167	Nphp3	74025	-0.7500	Rnf123	84585	-0.7167
Gal3st4	330217	-0.8167	Ppcdc	66812	-0.7500	Smarcc2	68094	-0.7167
Map4k1	26411	-0.8167	Rpusd2	271842	-0.7500	Zfp655	72611	-0.7167
Pdlim5	56376	-0.8167	Rsrc1	66880	-0.7500	Zfp770	228491	-0.7167
Pqbp1	54633	-0.8167	Rtcb		-0.7500	5031434O11Rik	1E+08	-0.7113
Rad51d		-0.8167	Slc16a2	20502	-0.7500	1700001L05Rik	69291	-0.7000
Rnf103	22644	-0.8167	Slc29a3	71279	-0.7500	Adora2a	11540	-0.7000
Tmem229b	268567	-0.8167	Srgap1	117600	-0.7500	Atr	245000	-0.7000
Trim15	69097	-0.8008	Sspo	243369	-0.7500	Clpx	270166	-0.7000
1700052K11Rik	73431	-0.8000	Tbx5	21388	-0.7500	Cyp51	13121	-0.7000
Acta1	11459	-0.8000	Tmbim4	68212	-0.7500	Des	13346	-0.7000
Cyb561d1	72023	-0.8000	Tmem98	103743	-0.7500	Dis3l2	208718	-0.7000
Fbxo34	78938	-0.8000	Zfp651	270210	-0.7500	Filip1	70598	-0.7000
Herc1	235439	-0.8000	Gpr88	64378	-0.7491	Irgq	210146	-0.7000
Insl3	16336	-0.8000	Lrtm2	211187	-0.7448	Kctd12	239217	-0.7000
Naga	17939	-0.8000	Lgi1	56839	-0.7395	Klhdc2	69554	-0.7000
Nkrf	77286	-0.8000	5031439G07Rik	223739	-0.7333	Krt8	16691	-0.7000
Rnf135	71956	-0.8000	AI464131	329828	-0.7333	Map3k15	270672	-0.7000
Sh3bp2	24055	-0.8000	Amz1	231842	-0.7333	Megf9	230316	-0.7000
Tmx2	66958	-0.8000	Camk1	52163	-0.7333	Pdcd7	50996	-0.7000
Zfp607	545938	-0.7950	Caprin2	232560	-0.7333	Pisd-ps1	236604	-0.7000
Hfe2	69585	-0.7921	Ccrl2	54199	-0.7333	Pmm1	29858	-0.7000
Gak	231580	-0.7833	Cers4		-0.7333	Pygl	110095	-0.7000
Gpkow	209416	-0.7833	Ckm	12715	-0.7333	Rara	19401	-0.7000
Madd	228355	-0.7833	Dcp1b	319618	-0.7333	Rnf13	24017	-0.7000
Magi3	99470	-0.7833	Ddhd1	114874	-0.7333	Slc35a2	22232	-0.7000
Msrb1		-0.7833	Dhx34	71723	-0.7333	Stac3	237611	-0.7000
Paqr8	74229	-0.7833	Dusp13	27389	-0.7333	Tha1	71776	-0.7000
Poldip2	67811	-0.7833	Fbxl14	101358	-0.7333	Timeless	21853	-0.7000
Pole	18973	-0.7833	Gm10364		-0.7333	Tmem68	72098	-0.7000
Prox1	19130	-0.7833	Hoxc5	15424	-0.7333	Tox4	268741	-0.7000
Ptcd1	71799	-0.7833	Lrp10	65107	-0.7333	Tssk6	83984	-0.7000
Slc39a2	214922	-0.7833	Lrrc39	109245	-0.7333	TxInb	378431	-0.7000
Rep15	66532	-0.7782	Lrrc8e	72267	-0.7333	Zdhhc13	243983	-0.7000
Rgs9bp	243923	-0.7746	Mtfmt	69606	-0.7333	Klhl31	244923	-0.6995
Ap3b2	11775	-0.7699	Nckipsd	80987	-0.7333	Dpyd	99586	-0.6950
Robo3	19649	-0.7699	Nf1	18015	-0.7333	Lin28b	380669	-0.6950
Acy1	109652	-0.7667	Pip5k1b	18719	-0.7333	Foxp3	20371	-0.6862

## Supplementary Table 2. List of fulvestrant negative response-associated genes

ID	GO term	No. genes	P-value	P-value corrected with Bonferroni step down	Associated genes
GO:0008593	regulation of Notch signaling pathway		0.032722025520891505	0.032722025520891505	[Bend6, Fgf10, Synj2bp]
GO:0030879	mammary gland development	7	0.0010530295197157165	0.049492387426638675	[Arhgap35, Cdo1, Fgf10, Foxf1, Gli2, Nr3c1, Serpinc1]
GO:0032924	activin receptor signaling pathway	5	4.5138662294543454E-5	0.0025277650884944335	[Fgf10, Fkbp1a, Fst, Lefty1, Synj2bp]
GO:0032925	regulation of activin receptor signaling pathway	5	3.944648710434323E-6	2.2484497649475642E-4	[Fgf10, Fkbp1a, Fst, Lefty1, Synj2bp]
GO:0032926	negative regulation of activin receptor signaling pathway	3	1.699061341328352E-4	0.009344837377305936	[Fst, Lefty1, Synj2bp]
GO:0035024	negative regulation of Rho protein signal transduction	3	9.649347883772568E-4	0.046316869842108324	[Arhgap35, Cul3, Scai]
GO:0035735	intraciliary transport involved in cilium assembly	3	5.072289788484075E-4	0.026375906900117187	[lft27, lft57, Pcm1]
GO:0044380	protein localization to cytoskeleton	4	7.711984909731779E-4	0.03778872605768572	[Ccdc14, Cep250, Mapre1, Pcm1]
GO:0051702	interaction with symbiont	5	5.540353849051075E-4	0.027701769245255376	[Cxcl5, Pou2f3, Ptx3, Tfap4, Vapb]
GO:0051851	modification by host of symbiont morphology or physiology	5	3.9500669210341174E-4	0.020935354681480823	[Cxcl5, Pou2f3, Ptx3, Tfap4, Vapb]
GO:0072698	protein localization to microtubule cytoskeleton	4	5.346441290799397E-4	0.027266850583076926	[Ccdc14, Cep250, Mapre1, Pcm1]
GO:0090092	regulation of transmembrane receptor protein serine/threonine kinase signaling pathway	9	2.0270815202244738E-4	0.010946240209212157	[Abl1, Bmp6, Fgf10, Fkbp1a, Fst, Lefty1, Rbpms, Synj2bp, Vasn]
GO:1903901	negative regulation of viral life cycle	5	0.0010681929126127756	0.04913687398018768	[Pou2f3, Ptx3, Slpi, Tfap4, Vapb]

## Supplementary Table 3. Enriched pathways for genes with positive correlation (r>0.6)

ID	GO term	No. genes	P-value	P-value corrected with Bonferroni step down	Associated genes
KEGG:00100	Steroid biosynthesis	3	5.55653095247979E-4	0.0316722264291348	[Cyp51, Ebp, Tm7sf2]
WP:216	Striated Muscle Contraction	5	4.217267286186855E-5	0.002699051063159587	[Acta1, Actn3, Des, Tnni1, Ttn]
GO:0000272	polysaccharide catabolic process	3	6.495659485404102E-4	0.03637569311826297	[Ppp1r3b, Pygl, Stbd1]
http- // <u>reactome.org/PathwayBro</u> wser/#/R-MMU- <u>390522:0759</u>	Striated Muscle Contraction	4	1.6070433520821604E-4	0.009963668782909394	[Acta1, Actn3, Des, Tnni1]
GO:0003009	skeletal muscle contraction	4	2.562422423229233E-4	0.015374534539375397	[Actn3, Myh7b, Stac3, Tnni1]
GO:0005980	glycogen catabolic process	3	3.9492566455868696E-4	0.022905688544403845	[Ppp1r3b, Pygl, Stbd1]
GO:0007026	negative regulation of microtubule depolymerization	3	8.664018398395041E-4	0.04678569935133322	[Eml4, Hdac6, Mid1ip1]
GO:0007519	skeletal muscle tissue development	8	2.053106868734865E-4	0.012523951899282676	[Al464131, Acta1, Actn3, Hdac6, Klhl31, Myh7b, Nf1, Stac3]
GO:0009251	glucan catabolic process	3	3.9492566455868696E-4	0.022905688544403845	[Ppp1r3b, Pygl, Stbd1]
GO:0014866	skeletal myofibril assembly	3	5.133767428876803E-5	0.003234273480192386	[Acta1, Prox1, Ttn]
GO:0014904	myotube cell development	5	2.9985790540490588E-5	0.0019490763851318883	[Al464131, Acta1, Actn3, Hdac6, Stac3]
GO:0030240	skeletal muscle thin filament assembly	3	1.2459813774808226E-5	8.597271504617676E-4	[Acta1, Prox1, Ttn]
GO:0035296	regulation of tube diameter	6	8.370916868275812E-4	0.046040042775516966	[Adcy6, Adora2a, Itga1, Kcnmb1, Pdgfb, Tbxa2r]
GO:0044247	cellular polysaccharide catabolic process	3	3.9492566455868696E-4	0.022905688544403845	[Ppp1r3b, Pygl, Stbd1]
GO:0048741	skeletal muscle fiber development	5	1.8195453224746833E-5	0.0012372908192827847	[Al464131, Acta1, Actn3, Hdac6, Stac3]
GO:0048747	muscle fiber development	6	1.9015420245044652E-5	0.0012740331564179918	[Al464131, Acta1, Actn3, Hdac6, Stac3, Ttn]
GO:0055001	muscle cell development	9	2.3330331211372258E-5	0.001539801859950569	[Al464131, Acta1, Actn3, Hdac6, Krt8, Pdlim5, Prox1, Stac3, Ttn]
GO:0055002	striated muscle cell development	9	1.0365747538139738E-5	7.256023276697817E-4	[Al464131, Acta1, Actn3, Hdac6, Krt8, Pdlim5, Prox1, Stac3, Ttn]
GO:0055008	cardiac muscle tissue morphogenesis	3	0.027231975222209718	0.027231975222209718	[Prox1, Tnni1, Ttn]
GO:0060538	skeletal muscle organ development	8	2.938149363103292E-4	0.017335081242309425	[Al464131, Acta1, Actn3, Hdac6, Klhl31, Myh7b, Nf1, Stac3]
GO:0097746	regulation of blood vessel diameter	6	8.370916868275812E-4	0.046040042775516966	[Adcy6, Adora2a, Itga1, Kcnmb1, Pdgfb, Tbxa2r]

## Supplementary Table 4. Enriched pathways for genes with positive correlation (r<-0.6)