

Supplemental Material to:

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Autophagy and senescence in cancer-associated fibroblasts metabolically supports tumor growth and metastasis, via glycolysis and ketone production

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Supplemental Table 1.

Transcriptional Over-Expression of Senescence-Associated Genes in Tumor Stroma Isolated from Breast Cancer Patients.

Symbol	Gene Description	Tumor-Stroma	Recurrence-Stroma	Metastasis-Stroma
<u>Senescence Pathway</u>				
Atm	ataxia telangiectasia mutated homolog (human)	3.79E-04	3.18E-02	2.84E-02
Bmi1	Bmi1 polycomb ring finger oncogene	1.49E-24		
Ccnd1	cyclin D1	1.42E-14	3.67E-02	4.21E-02
Cdkn2a	cyclin-dependent kinase inhibitor 2A (p16 INK4A)	5.71E-29		
Cdkn1a	cyclin-dependent kinase inhibitor 1A (p21 WAF1/CIP1)	3.73E-19		
Ciz1	Cdkn1a interacting zinc finger protein 1	2.13E-02	4.59E-03	
Chek1	checkpoint kinase 1 homolog (S. pombe)		3.71E-03	
Col3a1	collagen, type III, alpha 1	3.32E-27	8.00E-05	
Col1a1	collagen, type I, alpha 1	3.20E-17	2.46E-03	
E2f1	E2F transcription factor 1		5.87E-04	
Ets1	E26 avian leukemia oncogene 1, 5' domain	2.17E-15	7.54E-05	
Ets2	E26 avian leukemia oncogene 2, 3' domain	3.22E-09	4.05E-02	
Mdm2	transformed mouse 3T3 cell double minute 2	2.27E-14	8.68E-03	
Rb1	retinoblastoma 1	1.46E-16	2.30E-03	
Twist1	twist homolog 1 (Drosophila)	8.64E-08	2.82E-02	
<u>Senescence Initiators & Responders</u>				
Abi1	c-abl oncogene 1, receptor tyrosine kinase	1.70E-30	3.86E-02	1.96E-02
Aldh1a3	aldehyde dehydrogenase family 1, subfamily A3	2.03E-09		
Akt3	thymoma viral proto-oncogene 3	2.18E-13		
Calr3	calreticulin 3	6.13E-12		
Calr	calreticulin		3.60E-02	

Ccnb1	cyclin B1	1.53E-04	8.59E-03	
Cdkn2b	cyclin-dependent kinase inhibitor 2B (p15, inhibits CDK4)	4.47E-07		9.38E-03
Cdkn2c	cyclin-dependent kinase inhibitor 2C (p18, inhibits CDK4)	1.04E-05		
Cdkn1b	cyclin-dependent kinase inhibitor 1B (p27 KIP1)			4.82E-02
Cdkn3	cyclin-dependent kinase inhibitor 3			4.12E-02
Pak2	p21 (Cdkn1a)-activated kinase 2	2.46E-28		
Pak3	p21 (Cdkn1a)-activated kinase 3	3.04E-04	4.21E-02	
Pak4	p21 (Cdkn1a)-activated kinase 4	2.50E-21	5.49E-03	
Pak7	p21 (Cdkn1a)-activated kinase 7	3.12E-03		
Cdc25c	cell division cycle 25 homolog C (S. pombe)			2.64E-02
Creg2	cellular repressor of E1A-stimulated genes 2	9.29E-18		
Egr1	early growth response 1	2.01E-06		
Fn1	fibronectin 1	8.19E-13	6.23E-04	
Glb1	galactosidase, beta 1	1.91E-23		
Ifng	interferon gamma	5.76E-04		
Irf5	interferon regulatory factor 5	1.93E-17		
Irf7	interferon regulatory factor 7	6.99E-17	4.58E-02	2.85E-02
Igf1r	insulin-like growth factor I receptor	2.20E-17	4.95E-04	
Igfbp1	insulin-like growth factor binding protein 1			2.84E-02
Igfbp2	insulin-like growth factor binding protein 2		1.86E-03	1.12E-03
Igfbp5	insulin-like growth factor binding protein 5	6.27E-15	5.54E-03	4.99E-02
Igfbp7	insulin-like growth factor binding protein 7	5.46E-13		
Igfbpl1	insulin-like growth factor binding protein-like 1	1.54E-17	9.78E-04	
Igf2bp1	insulin-like growth factor 2 mRNA binding protein 1			4.70E-03
Map2k3	mitogen-activated protein kinase kinase 3	1.24E-17		
Map2k6	mitogen-activated protein kinase kinase 6	9.14E-10		
Mapk14	mitogen-activated protein kinase 14	2.32E-02		
Myc	myelocytomatosis oncogene	3.16E-13	1.32E-04	
Mycn	myelocytomatosis oncogene, neuroblastoma derived	1.55E-02	1.35E-02	4.01E-03
Mycbp	c-myc binding protein	3.67E-02		3.67E-02
Mycbp2	c-myc binding protein 2		4.16E-02	
Ndr3	N-myc downstream regulated gene 3	4.53E-02		4.53E-02

Ndrp4	N-myc downstream regulated gene 4		4.89E-02	
Nfkb1	NF kappa light polypeptide gene enhancer in B-cells 1, p105	1.40E-05		
Nox4	NADPH oxidase 4	2.75E-31		
Prkcd	protein kinase C, delta	5.67E-12	6.24E-04	
Pten	phosphatase and tensin homolog	2.87E-06		
Pink1	PTEN induced putative kinase 1	5.28E-09		4.60E-02
Plau	plasminogen activator, urokinase	3.64E-38	2.42E-03	
Serpib2	serine (or cysteine) peptidase inhibitor cladeB member2 (PAI-2)			4.27E-02
Sirt7	sirtuin 7 (silent mating type information regulation 2 homolog) 7			2.42E-02
Sirt5	sirtuin 5 (silent mating type information regulation 2 homolog) 5	4.19E-23		
Sirt6	sirtuin 6 (silent mating type information regulation 2 homolog) 6	2.31E-15		
Sirt3	sirtuin 3 (silent mating type information regulation 2 homolog) 3	1.25E-14		
Sirt2	sirtuin 2 (silent mating type information regulation 2 homolog) 2	4.12E-08	4.51E-04	
Sod2	superoxide dismutase 2, mitochondrial	1.45E-11		
Sod3	superoxide dismutase 3, extracellular	1.33E-04		
Sparc	secreted acidic cysteine rich glycoprotein	1.49E-35		
Tbx3	T-box 3	1.03E-02		
Tert	telomerase reverse transcriptase	1.34E-11	1.23E-02	2.17E-02
Terf1	telomeric repeat binding factor 1			4.49E-02
Terf2	telomeric repeat binding factor 2	3.56E-08	1.63E-02	
Tep1	telomerase associated protein 1	2.21E-07	5.05E-05	
Tinf2	Terf1 (TRF1)-interacting nuclear factor 2	8.40E-06		
Rtel1	regulator of telomere elongation helicase 1	6.03E-06		
Tgfb3	transforming growth factor, beta 3	2.16E-23		
Tgfr1	transforming growth factor, beta receptor I	1.56E-20		
Tgfr2	transforming growth factor, beta receptor II	3.22E-08		
Tgfi	transforming growth factor, beta induced	4.22E-12	1.14E-02	
Smad1	MAD homolog 1 (Drosophila)	2.47E-12		
Smad2	MAD homolog 2 (Drosophila)	4.94E-18		3.01E-03

Smad4	MAD homolog 4 (Drosophila)	1.16E-12	
Smad5	MAD homolog 5 (Drosophila)	4.17E-10	
Smad9	MAD homolog 9 (Drosophila)	4.49E-10	7.64E-03
Smurf1	SMAD specific E3 ubiquitin protein ligase 1	1.16E-16	4.24E-02
Thbs1	thrombospondin 1	6.83E-06	6.87E-03

Data Mining from the Morag Park Data Set: Finak et al., 2008, Nature Medicine, 14 (5): 518-27.

Note that six Cyclin-dependent kinase (CDK) Inhibitors, SA-beta-galactosidase (Glb1), cyclin D1, and telomerase (Tert) are all highlighted in BOLD. P-values are as shown.