Supporting Information

Tell and Horvath 10.1073/pnas.1404881111



Fig. S1. Principal components analysis of differentially expressed genes detected in basal-like breast cancer. Genes differentially expressed when comparing STAT3 high (red) with STAT3 low (blue) patients were analyzed via principal components analysis to determine the overall difference in groups when comparing principal variance characteristics. Each patient is graphed along the component of highest variance on the *x* axis and the second highest variance on the *y* axis. Despite the smaller sample size of the basal-like group, the 438 differentially expressed genes clearly divide patients into separate sections of the graph as determined by the first principal component (PC).



Fig. S2. Predicted protein interaction network for differentially expressed genes. Differentially expressed genes were analyzed for potential interactions via g:GOSt in g:Profiler. Black lines indicate connections between genes not detected in the analysis, whereas red lines indicate known interactions between differentially expressed genes.

Table S1. Enriched GO annotations and their associated P v	values and FDR-adjusted P values
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GO term	GO annotation GO category		OT P value	Corrected P value	
Basal genes					
GO:0019882	Antigen processing and presentation	Р	2.67E-12	4.99E-09	
GO:0045087	Innate immune response	Р	3.79E-12	7.07E-09	
GO:0006954	Inflammatory response	Р	1.67E-11	3.12E-08	
GO:0007166	Cell-surface receptor-linked signaling pathway	Р	4.40E-11	8.22E-08	
GO:0019221	Cytokine-mediated signaling pathway	Р	6.02E-11	1.12E-07	
GO:0071260	Cellular response to mechanical stimulus	Р	3.80E-10	7.10E-07	
GO:0031295	T-cell costimulation	Р	1.01E-09	1.89E-06	
GO:0007155	Cell adhesion	Р	8.49E-09	1.58E-05	
GO:0009615	Response to virus	Р	3.29E-08	6.14E-05	
GO:0002474	Antigen processing and presentation of peptide antigen via MHC class I	Р	9.22E-09	1.72E-05	
Global differential	genes				
GO:0006955 Immune response		Р	1.04E-10	7.63E-08	
GO:0045087	0045087 Innate immune response		2.62E-07	0.000192251	
GO:0006954	Inflammatory response	Р	8.42E-06	0.006171593	
GO:0005125	Cytokine activity	F	1.81E-05	0.013265602	
GO:0043123	Positive regulation of I-κB kinase/NF-κB cascade	Р	0.000213657	0.156610707	
GO:0007166	Cell-surface receptor-linked signaling pathway	Р	0.000220761	0.161817555	
GO:0009615	Response to virus	Р	0.000251176	0.18411191	
GO:0007155	Cell adhesion	Р	0.000251863	0.184615309	

Genes with significant enrichments (adjusted P value of 0.1 or less) are indicated in bold. FDR, false discovery rate; GO, Gene Ontology. F, molecular function; OT, ontology term; P, process.

microRNA	Log_2 fold change	Cancer association	Ref.
Luminal A			
hsa-mir-128-2	0.88	Mammary cell transformation	(1)
hsa-mir-128-1	0.74	p70S6K1 degradation	(2)
hsa-mir-483	-1.23	Overexpressed in epithelial malignancies	(3)
hsa-mir-224	-1.4	Associated with colorectal cancer proliferation	(4)
hsa-mir-1180	0.89	No direct evidence	
hsa-mir-145	-0.88	Inhibition of lung cancer	(5)
hsa-mir-107	0.47	Cell-cycle arrest in lung cancer	(6)
hsa-mir-214	-0.73	PTEN degradation in ovarian cancer	(7)
hsa-mir-299	-0.85	Degrades osteopontin in breast cancer	(8)
hsa-mir-423	0.5	Promotes proliferation in hepatocellular carcinoma	(9)
Luminal B			
hsa-mir-326	2.393873	MDR1 regulation in breast cancer	(10)
hsa-mir-3677	1.899579	No direct evidence	
hsa-mir-92a-2	0.979293	Hepatocellular carcinoma development	(11)
hsa-mir-215	1.677733	Positive regulator of p53	(12)
hsa-mir-760	1.946421	Plasma-level potential colorectal cancer biomarker	(13)
Basal-like			
hsa-mir-375	-3.05893	Associated with cervical cancer carcinogenesis	(14)
hsa-mir-183	-1.9353	Alteration of cellular migration in breast cancer	(15)
hsa-mir-3161	2.798385	No direct evidence	
hsa-mir-142	1.98575	Negative regulator of proliferation in pancreatic cancer	(16)
hsa-mir-196a-2	-2.17022	Polymorphism associated with cancer susceptibility	(17)
hsa-mir-3690	-1.48909	No direct evidence	
hsa-mir-150	1.398504	Promotes malignant behavior in breast cancer cells	(18)
hsa-mir-20b	-2.02197	Affects VEGF expression	(19)
hsa-mir-182	1.758854	Potential breast cancer biomarker	(20)
hsa-mir-342	1.98575	Associated with HER2 expression	(21)
hsa-mir-222	1.398886	Important for epithelial-mesenchymal transition in breast cancer	(22)
hsa-mir-3614	1.758854	No direct evidence	
hsa-mir-363	-1.75518	Regulation of metastasis and tumorigenesis	(23)

Table S2. Differentially regulated microRNAs by breast cancer subtype with FDR-adjusted P value <0.1

1. Qian P, et al. (2012) Loss of SNAIL regulated miR-128-2 on chromosome 3p22.3 targets multiple stem cell factors to promote transformation of mammary epithelial cells. Cancer Res 72(22):6036–6050.

2. Shi ZM, et al. (2012) MiR-128 inhibits tumor growth and angiogenesis by targeting p7056K1. PLoS ONE 7(3):e32709.

3. Veronese A, et al. (2010) Oncogenic role of miR-483-3p at the IGF2/483 locus. Cancer Res 70(8):3140-3149.

Liao WT, et al. (2013) microRNA-224 promotes cell proliferation and tumor growth in human colorectal cancer by repressing PHLPP1 and PHLPP2. *Clin Cancer Res* 19(17):4662–4672.
Cho WC, Chow AS, Au JS (2009) Restoration of tumour suppressor hsa-miR-145 inhibits cancer cell growth in lung adenocarcinoma patients with epidermal growth factor receptor mutation. *Eur J Cancer* 45(12):2197–2206.

6. Takahashi Y, et al. (2009) MiR-107 and MiR-185 can induce cell cycle arrest in human non small cell lung cancer cell lines. PLoS ONE 4(8):e6677.

7. Yang H, et al. (2008) MicroRNA expression profiling in human ovarian cancer: miR-214 induces cell survival and cisplatin resistance by targeting PTEN. Cancer Res 68(2):425-433.

8. Shevde LA, et al. (2010) Spheroid-forming subpopulation of breast cancer cells demonstrates vasculogenic mimicry via hsa-miR-299-5p regulated de novo expression of osteopontin. J Cell Mol Med 14(6B):1693–1706.

9. Lin J, et al. (2011) MicroRNA-423 promotes cell growth and regulates G(1)/S transition by targeting p21Cip1/Waf1 in hepatocellular carcinoma. Carcinogenesis 32(11):1641–1647.

10. Liang Z, et al. (2010) Involvement of miR-326 in chemotherapy resistance of breast cancer through modulating expression of multidrug resistance-associated protein 1. Biochem Pharmacol 79(6):817-824.

11. Shigoka M, et al. (2010) Deregulation of miR-92a expression is implicated in hepatocellular carcinoma development. Pathol Int 60(5):351–357.

12. Song B, et al. (2010) Molecular mechanism of chemoresistance by miR-215 in osteosarcoma and colon cancer cells. *Mol Cancer* 9:96.

13. Wang Q, et al. (2012) Plasma miR-601 and miR-760 are novel biomarkers for the early detection of colorectal cancer. PLoS ONE 7(9):e44398.

14. Bierkens M, et al. (2013) Focal aberrations indicate EYA2 and hsa-miR-375 as oncogene and tumor suppressor in cervical carcinogenesis. Genes Chromosomes Cancer 52(1):56–68. 15. Lowery AJ, Miller N, Dwyer RM, Kerin MJ (2010) Dysregulated miR-183 inhibits migration in breast cancer cells. BMC Cancer 10:502.

16. MacKenzie TN, et al. (2013) Triptolide induces the expression of miR-142-3p: A negative regulator of heat shock protein 70 and pancreatic cancer cell proliferation. *Mol Cancer Ther* 12(7):1266–1275.

17. Jedlinski DJ, Gabrovska PN, Weinstein SR, Smith RA, Griffiths LR (2011) Single nucleotide polymorphism in hsa-mir-196a-2 and breast cancer risk: A case control study. Twin Res Human Genet 14(5):417–421.

18. Huang S, et al. (2013) miR-150 promotes human breast cancer growth and malignant behavior by targeting the pro-apoptotic purinergic P2X7 receptor. PLoS ONE 8(12):e80707.

19. Cascio S, et al. (2010) miR-20b modulates VEGF expression by targeting HIF-1 alpha and STAT3 in MCF-7 breast cancer cells. J Cell Physiol 224(1):242-249.

20. Wang PY, et al. (2013) Higher expression of circulating miR-182 as a novel biomarker for breast cancer. Oncol Lett 6(6):1681-1686.

21. Leivonen SK, et al. (2014) High-throughput screens identify microRNAs essential for HER2 positive breast cancer cell growth. Mol Oncol 8(1):93-104.

22. Chen WX, et al. (2013) miR-221/222: promising biomarkers for breast cancer. Tumour Biol 34(3):1361-1370.

23. Qiao J, et al. (2013) miR-335 and miR-363 regulation of neuroblastoma tumorigenesis and metastasis. Surgery 154(2):226-233.

Dataset S1. Patient reverse-phase protein array data expressed as a z score for all patients analyzed for each cancer subtype

Dataset S1

Dataset S2. List of differentially expressed genes used in this study

Dataset S2

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