

Correction: Pregnancy-Induced Protection against Mammary Tumorigenesis

In the article on pregnancy-induced protection against mammary tumorigenesis in the June 15, 2006 issue of *Cancer Research* (1), the parity status of six of the 43 arrays used to derive the 70-gene expression signature was misclassified through an error in data entry. These arrays represented six of the 14 arrays run for Fischer 344 rats. The remaining 37 arrays for the Lewis, Wistar-Furth, Copenhagen, and Fischer 344 mammary samples were properly classified, as were the independent Lewis rat and FVB mouse samples used to validate the findings. This misclassification both obscured genuine parity-induced changes in the Fischer 344 strain and added biological noise due to genes that were covarying but unrelated to parity. As a consequence, after correcting the parity status for the six Fischer 344 arrays and applying the same analytical criteria described in the article, the authors found that the core parity-induced gene expression signature was reduced from 70 to 47 genes. Similar to the original 70-gene signature, this 47-gene signature is sufficient to distinguish between independent nulliparous and parous samples from all rat and mouse strains

analyzed in the article. Corrected versions of Tables 1 and 2 appear below.

Each of the five originally identified functional gene categories (Tgf- β 3, differentiation, immune markers, growth hormone/Igf-1 axis, and extracellular matrix components) are retained within this signature. Genes lost from the original 70-gene signature remain significantly altered in two of the four rat strains and are still plausible candidates for contributing to parity-induced protection against mammary tumorigenesis. Notably, a role for downregulation of *Ghr*, which is not included in the corrected signature, in parity-induced protection is still supported by the FVB mouse data and the QRT-PCR analysis of independent Lewis rat samples presented in the article. Also consistent with a role for the GH/Igf-1 pathway in parity-induced protection, *Igf-1* remains downregulated — and *Igfbp5* remains upregulated — on the corrected list of genes.

Overall, despite the reassignment of six samples, the conclusions of the article remain unaltered. Moreover, as a primary goal of the original article was to narrow down the list of genes to those most robustly associated with parity-induced protection, the corrected signature accomplishes this and provides an even

Table 1. Genes up-regulated in parous rats

Gene name	Symbol	Gene ID	Function	Category	Fold-change G1P1 versus G0P0				
					Lewis	WF	F344	Cop	Median
Immunoglobulin heavy chain	<i>Igha</i>	314487	Immunoglobulin	Immune	39.4	25.4	12.4	6.9	18.9
Casein beta	<i>Csn2</i>	29173	Milk protein	Differentiation	8.0	5.2	1.6	1.5	3.4
IgM light chain		287965	Immunoglobulin	Immune	2.5	3.8	2.0	1.6	2.2
Insulin-like growth factor binding protein 5	<i>Igfbp5</i>	25285	Igf1-binding	Growth factor/ECM	2.4	1.4	1.1	2.7	1.9
Casein gamma	<i>Csng</i>	114595	Milk protein	Differentiation	3.1	1.9	1.8	0.9	1.9
Lipopolysaccharide binding protein	<i>Lbp</i>	29469	Antibacterial	Immune	2.1	1.3	1.0	2.0	1.7
Matrix metalloproteinase 12	<i>Mmp12</i>	117033	Proteolysis	ECM/Immune	2.6	1.4	1.6	1.3	1.5
Carbonic anhydrase 2	<i>Ca2</i>	54231	Carbon metabolism	Metabolism	1.5	1.5	1.5	1.1	1.5
Fatty acid synthase	<i>Fasn</i>	50671	Fatty acid biosynthesis	Metabolism/Differentiation	2.0	1.6	1.3	0.9	1.5
Cytochrome P450, family 4, subfamily b,1	<i>Cyp4b1</i>	24307	Monoxygenase activity	Metabolism	1.6	1.5	1.4	1.2	1.4
Transforming growth factor, beta 3	<i>Tgfb3</i>	25717	Cell growth/proliferation	Tgf- β	1.5	1.3	0.9	1.4	1.4
Thioesterase domain containing 1	<i>Thedc1</i>	64669	Fatty acid biosynthesis	Metabolism/Differentiation	1.9	1.2	0.8	1.5	1.3
Malic enzyme 1	<i>Me1</i>	24552	Pyruvate synthesis	Metabolism	1.3	1.4	1.4	1.1	1.3
Phosphodiesterase 4B	<i>Pde4b</i>	24626	cAMP phosphodiesterase	Signal transduction	1.3	1.4	0.8	1.4	1.3
Polymeric immunoglobulin receptor	<i>Pigr</i>	25046	Trancytosis	Immune	1.7	1.4	1.2	1.1	1.3
Kruppel-like factor 9	<i>Klf9</i>	117560	Transcription Factor	Signal transduction	1.3	1.4	1.2	1.1	1.3
Matrix metalloproteinase 11	<i>Mmp11</i>	25481	Proteolysis	ECM	1.2	1.2	1.2	1.2	1.2

NOTE: Genes identified as up-regulated by at least 1.2-fold in three out of four rat strains as a result of parity are reported from highest to lowest median fold-change. Gene names and symbols are reported based on the Rat Genome Database, and Gene ID according to Entrez Gene. Gene functions and categories are based upon GeneOntology.

Abbreviations: WF, Wistar-Furth; F344, Fischer 344; Cop, Copenhagen.

smaller overlap of evolutionarily conserved gene expression changes associated with parity-induced protection against mammary tumorigenesis.

1. Blakely CM, Stoddard AJ, Belka GK, Dugan KD, Notarfrancesco KL, Moody SE, D'Cruz CM, Chodosh LA. Hormone-induced protection against mammary tumorigenesis is conserved in multiple rat strains and identifies a core gene expression signature induced by pregnancy. *Cancer Res* 2006;66:6421-31.

Table 2. Genes down-regulated in parous rats

Gene name	Symbol	Gene ID	Function	Category	Fold-change G0P0 versus G1P1				
					Lewis	WF	F344	Cop	Median
Periostin	<i>Postn</i>	361945	Cell adhesion	ECM	1.9	2.1	1.6	2.2	2.0
Amphiregulin	<i>Areg</i>	29183	Epidermal growth factor receptor ligand	Growth factor	3.5	2.1	1.9	1.9	2.0
Cellular retinoic acid binding protein I	<i>Crabp1</i>	25061	Retinoic acid receptor signaling	Signal transduction	1.8	2.1	1.3	1.5	1.7
Glycosylation dependent cell adhesion molecule 1	<i>Glycam1</i>	25258	Selectin ligand	Differentiation	0.5	2.2	1.3	1.7	1.5
Secreted acidic cysteine rich glycoprotein	<i>Sparc</i>	24791	ECM Formation	ECM	1.9	1.3	1.1	1.7	1.5
Lumican	<i>Lum</i>	81682	Proteoglycan	ECM	1.3	1.5	1.5	1.4	1.5
3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2	<i>Hmgcs2</i>	24450	Cholesterol/ketone body biosynthesis	Metabolism	2.9	1.3	1.6	1.0	1.5
Fibronectin 1	<i fn1<="" i=""></i>	25661	Integrin signaling	ECM	1.4	1.3	1.3	1.6	1.4
Cbp/p300-interacting transactivator with Glu/Asp-rich carboxy-terminal domain 1	<i>Cited1</i>	64466	Transcription factor	Signal transduction	1.4	1.9	1.3	1.3	1.4
Ectonucleotide pyrophosphatase/phosphodiesterase 2	<i>Enpp2</i>	84050	Lysophospholipase	Cell motility	1.7	1.4	0.8	1.3	1.4
Insulin-like growth factor 1	<i>Igf1</i>	24482	Cell proliferation/survival	Growth factor	1.7	1.2	1.1	1.5	1.3
Sushi-repeat-containing protein	<i>Sprx</i>	64316			1.3	1.3	1.1	1.5	1.3
Lectin, galactose binding, soluble 1	<i>Lgals1</i>	56646	Integrin signaling	ECM	1.5	1.2	0.8	1.4	1.3
A kinase (PRKA) anchor protein (gravin) 12	<i>Akap12</i>	83425	Scaffolding protein	Signal transduction	1.2	1.6	1.2	1.3	1.3
Lectin, galactose binding, soluble 7	<i>Lgals7</i>	29518	Galactose binding		1.1	1.8	1.4	1.2	1.3
Tropomyosin 1, alpha	<i>Tpm1</i>	24851	Actin binding		1.1	1.3	1.3	1.3	1.3
Activity and neurotransmitter induced early gene protein 4	<i>Ania4</i>	360341	CAM kinase	Kinase	1.5	1.2	1.0	1.3	1.3
Cytosolic cysteine dioxygenase 1	<i>Cdo1</i>	81718	Cysteine metabolism	Metabolism	1.5	1.2	0.8	1.3	1.3
Carbonic anhydrase 3	<i>Ca3</i>	54232	Carbon metabolism	Metabolism	1.8	1.2	0.8	1.3	1.2
CD74 antigen	<i>Cd74</i>	25599		Immune	1.2	1.2	1.3	1.3	1.2
Tubulin, alpha 1	<i>Tuba1</i>	64158	Microtubule component	Cell structure	1.5	1.2	0.9	1.2	1.2
Similar to RIKEN cDNA 6330406I15	<i>RGD1307396</i>	360757			1.6	1.2	1.0	1.3	1.2
Collagen, type 1, alpha 1	<i>Colla1</i>	29393	ECM structural protein	ECM	0.9	1.2	1.2	1.6	1.2
Phosphoglycerate kinase 1	<i>Pgk1</i>	24644	Phosphoprotein glycolysis	Metabolism	1.6	1.2	0.9	1.2	1.2
Annexin A5	<i>Anxa5</i>	25673	Calcium ion binding		1.6	1.2	0.8	1.2	1.2
Prohibitin	<i>Phb</i>	25344	Regulation of cell cycle	Signal transduction	1.3	1.2	1.2	1.1	1.2
Valosin-containing protein	<i>Vcp</i>	116643	Endoplasmic reticulum protein catabolism		1.2	1.2	1.2	1.2	1.2
Tropomyosin 4	<i>Tpm4</i>	24852	Actin binding		1.1	1.3	1.2	1.2	1.2
Tubulin, beta 5	<i>Tubb5</i>	29214	Microtubule component	Cell structure	1.1	1.3	1.2	1.2	1.2
MORF-related gene X	<i>Morf412</i>	317413			1.4	1.2	1.0	1.2	1.2

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