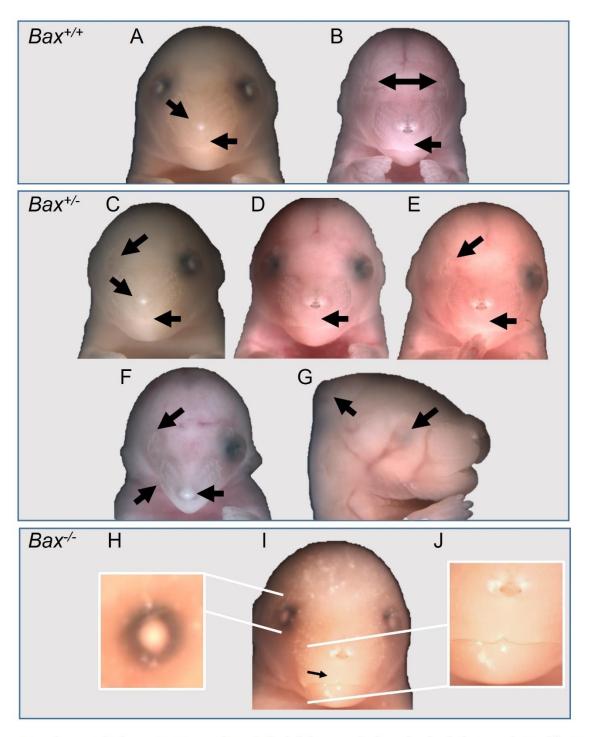
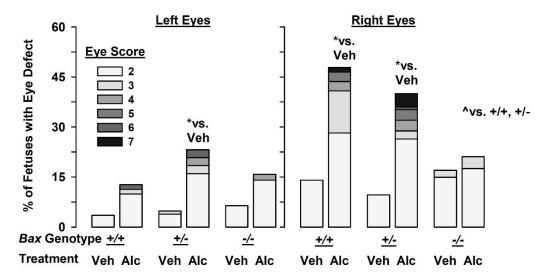
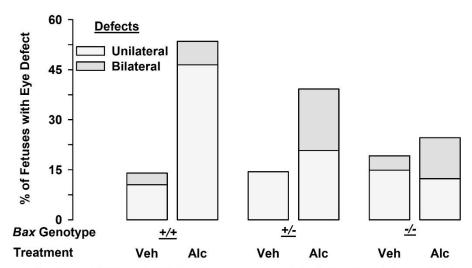


Supplemental Figure 1. Comparison of spontaneously occurring and alcohol-induced minor right eye defects. The *left and center sets of bars* portray the mean size ( $\pm$ SEM) of the lens and globe, respectively for vehicle (*open bars*) and alcohol (*filled bars*) treated  $Bax^{+/+}$  and  $Bax^{-/-}$  fetuses. The *right set of bars* portrays the mean ( $\pm$ SEM) lens area expressed as a percent of the entire globe. \* denotes significance (p<0.05) vs. unaffected control eyes (eye score 1).

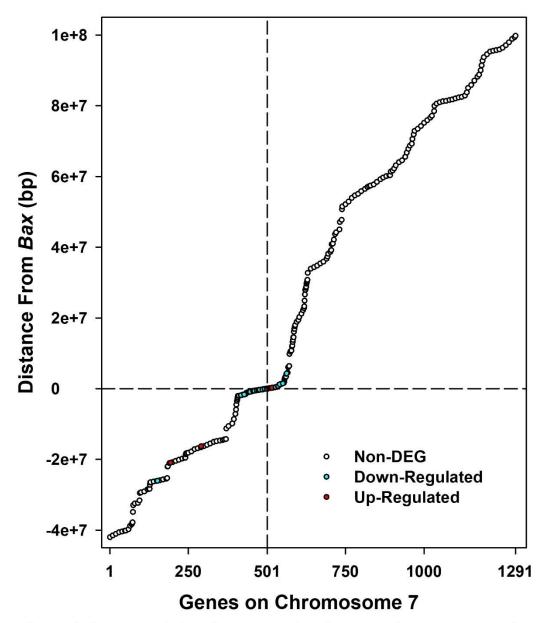


Supplemental Figure 2. Cases of craniofacial dysmorphology in alcohol-treated,  $Bax^{+/+}$ ,  $Bax^{+/-}$ , and  $Bax^{-/-}$  fetuses. Shown here are photographs of either live (B, D, E, F, & G), or formalinfixed (A, C, & H) fetuses. The  $Bax^{-/-}$  fetus had evidence for a smaller lip notch that was not noticed upon the initial evaluation. The upper lip has been outlined in J to highlight the lip notch. In contrast to the other cases of craniofacial dysmorphology, this fetus had only a minor shape alteration in the right pupil (H). The speckled appearance of this fetus is caused by prolonged fixation.

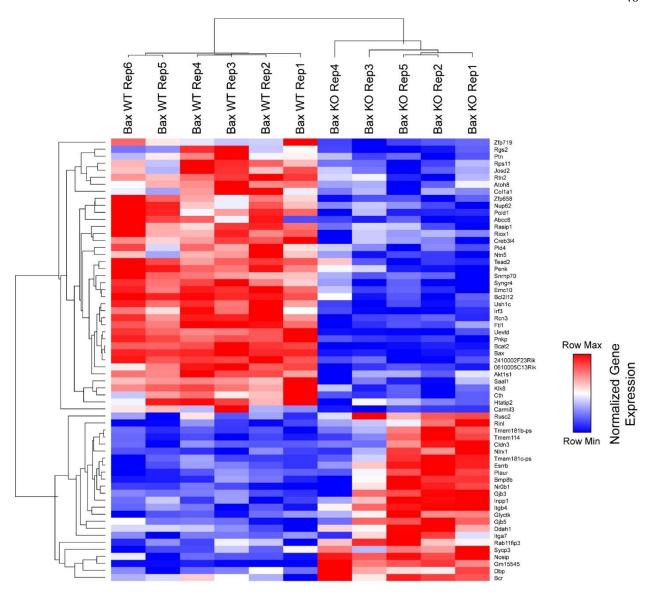




Supplemental Figure 3. Effects of Bax genotype and alcohol on the sidedness of fetal eye defects. Panel A portrays the percent of fetuses with defects in the left or the right eye, plotted separately in the left and right figures.  $Stacked\ bars$  indicate the percent of fetuses with an eye categorized as a 2 (smaller globe or minor change in pupil shape) to 7 (complete anophthalmia) for  $Bax^{+/+}$ ,  $Bax^{+/-}$ , and  $Bax^{-/-}$  fetuses (left, center,  $and\ right$  sets of bars, respectively). Panel B portrays the incidence of unilateral ( $light\ gray\ bars$ ) and bilateral ( $gray\ bars$ ) for  $Bax^{+/+}$ ,  $Bax^{+/-}$ , and  $Bax^{-/-}$  fetuses (left, center,  $and\ right$  sets of bars, respectively). \* denotes significance vs. vehicle treated fetuses of the same genotype, while the ^ denotes significance (p<0.05) vs. alcohol-treated the  $Bax^{+/+}$  and  $Bax^{+/-}$  fetuses.

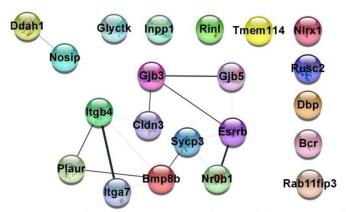


Supplemental Figure 4. Depiction of gene expression changes on chromosome 7. *Circles* represent all genes across chromosome 7, with the *y-axis* indicating distance (in base pairs) between the gene and *Bax* (gene 501, intersection between the *vertical* and *horizontal* hatched lines). *Open circles* represent genes that are not differentially expressed, whereas genes with significantly lower- and higher-expression in the *Bax*-- embryos are shown in *cyan* and *red circles*, respectively. For genes earlier on the chromosome compared to *Bax* (genes 1-500), distance between *Bax* and a given gene is designated as the number of base pairs between the 3' end of *Bax* and the nearest end (5' or 3') for that particular gene. For genes later on the chromosome relative to *Bax* (genes 502-1291), distance is designated as the number of base pairs from the 5' end of *Bax* and the nearest end (5' or 3') for that particular gene. Gene location was determined by using the Mouse Genome Informatics database. N.B., for clarity, and to avoid extensively overlapping symbols, circles for non-differentially expressed genes can represent between one and ten genes.

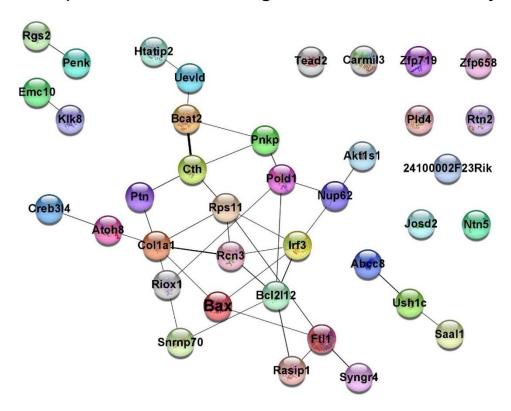


Supplemental Figure 5. Heat map showing differentially expressed genes in individual  $Bax^{+/+}$  and  $Bax^{-/-}$  embryos. Red-shaded boxes indicate greater expression, while blue-shaded boxes indicate lower expression. Note that Bax\_KO\_rep4 (*left-most KO column*) had an expression pattern of certain genes that were expressed more like the  $Bax^{+/+}$  embryos (Bax\_WT) than the other  $Bax^{-/-}$  embryos

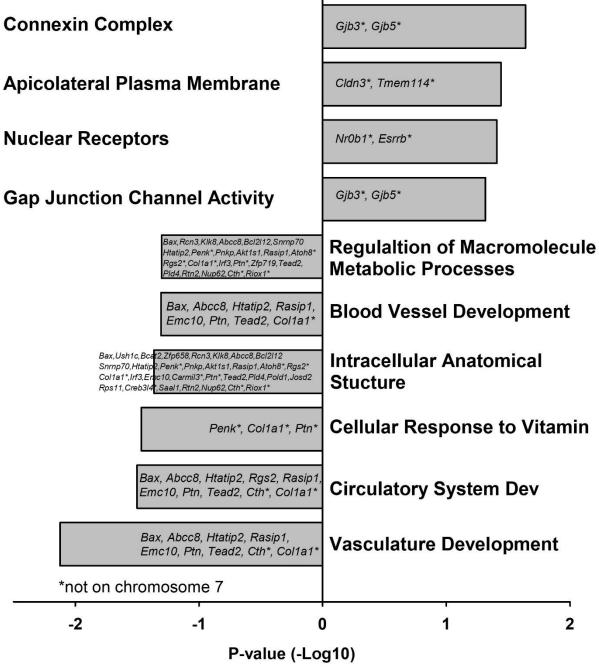
## A Gene Expression Up-Regulated in Bax-/- Embryos



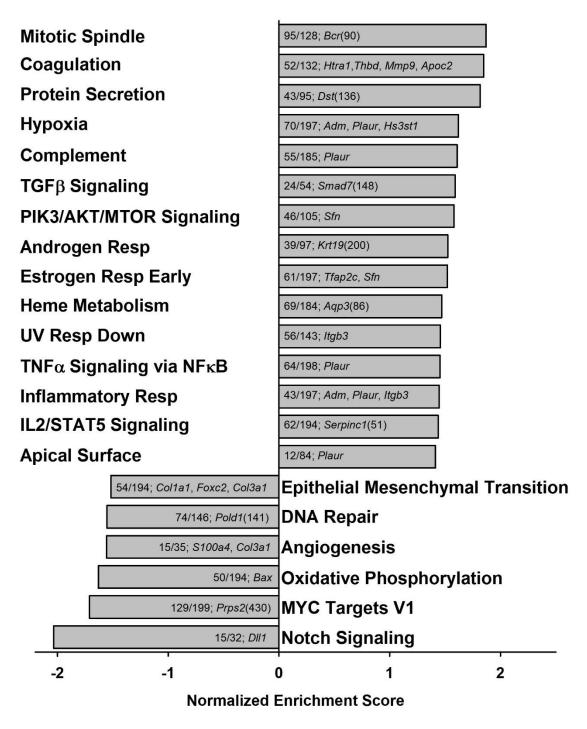
## B Gene Expression Down-Regulated in Bax-/- Embryos



Supplemental Figure 6. Cytoscape-generated gene network map between differentially expressed genes that are up-regulated and down-regulated in untreated  $Bax^{-/-}$  vs.  $Bax^{+/+}$  embryos. Line thickness denotes relative strength of associations between genes.



Supplemental Figure 7. g:profiler analysis of significantly dysregulated pathways in  $Bax^{-/-}$  vs  $Bax^{+/+}$  embryos. Differentially expressed genes within each pathway are inset in each bar. \* indicates genes that are not located on chromosome 7.



Supplemental Figure 8. Dysregulated pathways in  $Bax^{-/-}$  vs.  $Bax^{+/+}$  embryos following GSEA Hallmarks analysis. *Inset text* indicates number of genes with core-enrichment/total genes in gene set, and the top ranked enriched genes. Genes are ranked in the top 50, unless otherwise noted in parentheses.

Table S1. Differentially Expressed Genes that are Up-regulated in Bax-/- vs Bax+/+ Embryos

Gene	Protein Protein	Chrom.	Up-regulated in Bax vs Bax  Function	Log2 Fold Change	Adj p- value
Gm15545	Predicted gene 15545	7	– Unknown	2.3	5.2x10 <sup>-57</sup>
Itgb4	Integrin beta 4	11	<ul> <li>Forms heterodimer with Itga6.</li> <li>Laminin receptor, binds NRG1, IGF1, IGF2.</li> <li>Important for cell adhesion and migration.</li> <li>Role in cancer, epidermolysis bullosa, trophoblast invasion, anti-inflammatory effects in lung</li> </ul>	1.1	9.3x10 <sup>-9</sup>
Nr0b1 (Dax1)	Nuclear receptor subfamily 0, group B, member 1	X	<ul> <li>Interacts with Esrrb.</li> <li>Limits embryonic stem cell pluripotency.</li> <li>Suppresses testes development, promotes ovary development</li> </ul>	0.79	1.2x10 <sup>-4</sup>
Gjb3	Gap junction beta 3 (Connexin 31)	4	<ul><li>Formation of gap junctions.</li><li>Critical embryonic role.</li><li>Expressed in trophoblasts.</li></ul>	0.75	0.001
Plaur	Urokinase plasminogen activator surface receptor	7	<ul> <li>Role in vascular development, cancer, inflammation, extracellular matrix degradation.</li> <li>Stimulates proliferation and inhibits apoptosis.</li> </ul>	0.75	2.8x10 <sup>-4</sup>
Rinl	Ras and Rab interactor-like protein	7	– Endocytosis	0.73	0.001
Sycp3	Synaptonemal complex protein 3	10	Formation of synaptonemal complex during meiosis.      Expressed in cancer cells and may induce homologous recombination defect.	0.69	0.006
Gjb5	Gap junction beta 5 (Connexin 31.1)	4	<ul> <li>Formation of gap junctions.</li> <li>Critical embryonic role.</li> <li>Expressed in trophoblasts.</li> <li>Affects pluripotency</li> </ul>	0.66	0.005
Nlrx1	NOD-like receptor family X1	9	<ul><li>Role in inflammation.</li><li>Down-regulated in cancer.</li><li>Found in placenta</li></ul>	0.66	0.007
Cldn3	Claudin-3	5	<ul><li>Formation of tight junctions.</li><li>Critical for neural tube closure.</li><li>Role in cancer.</li></ul>	0.65	0.014
Bmp8b	Bone morphogenic protein 8b	4	- Important for osteogenesis, primordial germ cells, and	0.64	0.004

			metabolism through brown adipose tissue.  – Role in liver disease		
Tmem114	Transmembrane protein 114	16	<ul> <li>Role in liver disease</li> <li>Important for eye development.</li> <li>Down-regulation can cause microphthalmia.</li> <li>Upregulated in cataracts</li> </ul>	0.64	0.004
Inpp1	Inositol polyphosphate 1- phosphotase	1	<ul> <li>Hyperactive in certain cancers.</li> <li>Gene variants associated with psychiatric disease and lithium responses.</li> </ul>		0.006
Esrrb	Estrogen-related receptor 2	12	<ul> <li>Transcription factor affecting embryonic and trophoblast cells through FGF and Wnt signaling.</li> <li>Involved in pluripotency and expressed in primordial germ cells.</li> <li>Promotes oxidative phosphorylation.</li> <li>Interacts with Nr0b1.</li> </ul>	0.59	8.6x10 <sup>-4</sup>
Tmem181b-ps	Predicted gene	?	- Unknown	0.58	0.003
Ddah1	N(g),N(g)- dimethylarginine dimethylaminohydrol ase 1	3	<ul> <li>Hydrolyzes ADMA and MMA which are inhibitors of NOS.</li> <li>Critical for embryonic development.</li> <li>May protect against apoptosis, can upregulate Bcl-2</li> </ul>	0.57	0.014
Dbp	D site-binding protein- transcriptional activator	7	Modulator of clock output genes.      Under circadian control in placenta, but unknown embryonic role	0.57	0.014
Rusc2	Iporin	4	<ul><li>Interacts with Rab1, Rab 35,</li><li>GM130, EGFR.</li><li>May inhibit Shh signaling</li></ul>	0.56	0.035
Itga7	Integrin alpha-7	10	<ul><li>Laminin receptor.</li><li>Important for cell adhesion, vascular development</li></ul>	0.52	0.032
Nosip	Nitric oxide synthase- interacting protein	7	<ul> <li>Negative regulator of nitric oxide.</li> <li>Modulates PP2a and may protect against eye defects, holoprosencephaly, midline facial defects.</li> </ul>	0.52	3.4x10 <sup>-8</sup>
Glyctk	Glycerate kinase	9	Deficiency in humans     causes d-glyceric aciduria,     which has range of effects.	0.51	0.006
Bcr	Breakpoint cluster region protein	10	– Oncoprotein.	0.51	0.032

			<ul> <li>Activated by tyrosine kinase.</li> <li>Can activate NFkB. Modulates GTP-binding proteins, RAC1, RAC2, CDC42.</li> <li>Fusion with ABL causes forms of leukemia.</li> <li>Inhibition of apoptosis?</li> </ul>		
Rab11fip3	Rab11 family- interacting protein 3	17	- Involved in endocytic traffic	0.45	0.027
Tmem181c-ps	Transmembrane protein 181c-pseudogene	17	– Unknown	0.40	0.047

Table S2. Differentially Expressed Genes that are Down-Regulated in Bax<sup>-/-</sup> vs Bax<sup>+/+</sup> Embryos

Gene	Protein	Chrom.	e Down-Regulated in <i>Bax</i> **  Function	Log2 Fold Change	Adj <i>p</i> - value
Riox1	Ribosomal oxygenase 1. Nucleolar protein 66.	12	<ul> <li>Histone lysine demethylase and ribosomal histidine hydroxylase.</li> <li>Osteoblast differentiation, ribosome biogenesis.</li> <li>Role in cancer via antiapoptotic, proliferative effect.</li> <li>Important for sensitivity to alcohol (<i>Drosophila</i>).</li> </ul>		0.022
Cth	Cystathione gamma- lyase	3	<ul> <li>Catalyzing methionine to cysteine.</li> <li>Crucial for protection from reactive oxygen species.</li> <li>Regulated by PI3K/AKT pathway</li> </ul>	-0.32	0.022
Nup62	Nucleoporin 62	7	<ul><li>Protein recruitment to centrosome after nuclear breakdown.</li><li>Role in autophagy</li></ul>	-0.33	0.034
Rtn2	Reticulon-2	7	<ul> <li>Inhibits amyloid precursor protein processing.</li> <li>Traffics intracellular membranes to cell membrane.</li> <li>Lipid metabolism.</li> <li>Formation of ER</li> </ul>	-0.37	0.027
Saal1	Serum amyloid A- like 1	7	<ul><li>Enhances proliferation.</li><li>Possible role in arthritis and cancer</li></ul>	-0.42	4.4x10 <sup>-4</sup>
Creb3l4	Cyclic AMP- response element binding protein 3- like protein 4	3	<ul> <li>Upregulated in cancers.</li> <li>Associated with reduced apoptosis.</li> <li>May affect male germ cell development.</li> </ul>	-0.47	0.035
Rps11	40s ribosomal protein s11	7	<ul> <li>Protects against apoptosis in certain cancers.</li> <li>Higher expression predicts worse outcomes in glioblastoma.</li> </ul>	-0.47	0.003
Josd2	Josephin-2	7	Deubiquitinating enzyme.     Positive regulator of cancer cell proliferation	-0.48	0.003
Pold1	DNA polymerase delta catalytic subunit	7	<ul><li>High fidelity genome replication.</li><li>Mutated in cancers.</li></ul>	-0.49	3.2x10 <sup>-5</sup>

			- Role in embryonic development.		
			- May inhibit apoptosis		
Pld4	5'-3' exonuclease PLD4.	12	- Regulates inflammatory cytokine responses	-0.51	0.041
Tead2	Transcriptional enhancer factor TEF-4	7	<ul> <li>Hippo pathway.</li> <li>Restricts proliferation and promotes apoptosis.</li> <li>Embryonic role in neural tube closure</li> </ul>	-0.52	1.2x10 <sup>-4</sup>
Zfp719	Zinc finger protein 719	7	- Unknown	-0.55	0.010
Ptn	Pleiotrophin	6	<ul> <li>Growth factor involved in cell proliferation, survival, growth, and differentiation in neurons and bone.</li> <li>Upregulated in cancer and by alcohol exposure</li> </ul>	-0.58	0.038
Carmil3	Capping protein, Arp2/3 and myosin-I linker protein 3.	14	<ul> <li>Role in tumor migration, cell adhesions, epitheliamesenchymal transition.</li> <li>Regulates proinflammatory cytokines associated with apoptosis</li> </ul>	-0.59	0.028
Emc10	ER membrane protein complex subunit 10.	7	<ul><li>Incorporation of proteins into ER membrane.</li><li>Angiogenesis.</li></ul>	-0.60	7.7x10 <sup>-11</sup>
Irf3	Interferon regulatory factor 3	7	<ul> <li>Innate immune responses.</li> <li>Regulates transcription of IFN-α and IFN-β.</li> <li>Important for alcoholic liver disease.</li> <li>Associates with BAX to affect apoptosis.</li> </ul>	-0.60	6.1x10 <sup>-7</sup>
Col1a1	Collagen alpha-1(1) chain	11	<ul> <li>Role in osteogenesis, fibrogenesis, cancer, extracellular matrix accumulation in glaucoma, extraembryonic membrane rupture.</li> <li>Linked to mandibular prognathism</li> </ul>	-0.62	0.032
Rgs2	Regulator of G-protein signaling 2	1	<ul> <li>Inhibits signal transduction.</li> <li>Loss of Rgs2 impairs neural crest development.</li> <li>Increased by ischemic stress to enhance apoptosis</li> </ul>	-0.62	0.025
Ntn5	Netrin-5	7	- Neurogenesis	-0.66	0.006

Syngr4	Synaptogyrin-4	7	<ul><li>Increased levels associated with ALS.</li></ul>	-0.66	4.2x10 <sup>-4</sup>
Atoh8 (Math6)	Atonal homolog 8	6	6 - Key embryonic role in somitogenesis, neural crest, bone development, placentation, mesenchymal-epithelial transition.  - Tumor suppressor in cancer		0.006
Rasip1	Ras-interacting protein 1	7	<ul> <li>Angiogenesis, cell</li> <li>adhesion, endothelial cell</li> <li>morphogenesis</li> </ul>		1.2x10 <sup>-4</sup>
Akt1s1	Proline-rich AKT1 substrate 1 (Pras)	7	<ul><li>Subunit of mTORC1.</li><li>Augments activation of PI3K/AKT.</li><li>Inhibits apoptosis</li></ul>	-0.71	9.5x10 <sup>-7</sup>
Pnkp	Bifunctional polynucleotide phosphatase/kinase	7	Repair of DNA damage.      Appears to inhibit apoptosis.      Inhibitors sensitize cells to chemotherapies.      Knockdown causes microcephaly	-0.72	3.2x10 <sup>-21</sup>
Penk	Preproenkephalin. Proenkephalin-A	4	<ul> <li>Precursor to Met- and Leu-enkephalin.</li> <li>Involved in apoptosis, associated with Huntington's disease.</li> <li>Hypermethylated in pancreatic cancer.</li> <li>Tumor suppressor gene.</li> </ul>	-0.72	3.1x10 <sup>-5</sup>
Htatip2	Oxioreductase HTATIP2. Also, Tip30/CC3	7	<ul> <li>Redox sensor required for tumor suppression.</li> <li>Role in cancer and HIV.</li> <li>Overexpression also upregulates p27, Bax, p53, caspase 3/9, downregulates cyclin D1, Bcl-2, Bcl-xL.</li> </ul>	-0.73	0.002
Snrnp70	U1 small nuclear ribonucleoprotein 70kDa.	7	- Spliceosome, removes introns from pre-mRNA	-0.75	4.0x10 <sup>-8</sup>
Bcl2l12	BCL2-like 12	7	- Inhibits apoptosis by dimerizing with Bax, inhibiting Tp53	-0.84	2.2x10 <sup>-10</sup>
Abcc8 (Sur1)	ATP-binding cassette, sub-family C (CFTR/MRP), member 8	7	<ul> <li>Important for K+ channels.</li> <li>Mutated in diabetes, monogenic cause of neonatal diabetes</li> </ul>	-0.85	2.8x10 <sup>-5</sup>
Klk8	Kallikrein-8, Neuropsin	7	- Serine protease cleaves casein, fibrinogen, kininogen, fibronectic,	-0.93	2.7x10 <sup>-9</sup>

			collagen type 4, L1CAM (linked to fetal alcohol syndrome).  – May be oncogenic		
2410002F23Rik	?	7	– Unknown	-0.98	3.0x10 <sup>-25</sup>
Rcn3	Reticulocalbin-3	7	<ul> <li>Molecular chaperone,</li> <li>biosynthesis and transport</li> <li>in ER.</li> <li>Regulates collagen</li> <li>fibrillogenesis</li> </ul>		1.8x10 <sup>-20</sup>
Zfp658	Zinc finger protein 658	7	7 – Unknown		4.0x10 <sup>-9</sup>
Bcat2	Branched chain aminotransferase, mitochondrial	7	- Associated with diabetes and nutrient signaling.	-1.8	2.0x10 <sup>-59</sup>
Ftl1	Ferritin light chain 1	7	7 – Iron storage and delivery. – Role in ferroptosis.		4.9x10 <sup>-23</sup>
Ush1c	Harmonin	7	<ul> <li>Anchoring/scaffolding protein.</li> <li>Important in cochlear hair cells and brush border differentiation.</li> <li>Mutated in Usher syndrome</li> </ul>	-1.6	3.3x10 <sup>-20</sup>
0610005C13Rik	?	7	– Unknown	-1.7	2.5x10 <sup>-22</sup>
Uevld	Ubiquitin- conjugating enzyme E2 variant 3	7	Negative regulator of polyubiquitination	-2.2	2.0x10 <sup>-38</sup>
Bax (Bcl-2l4)	Bcl-2-associated X protein	7	- Activates apoptosis	-4.3	4.7x10 <sup>-183</sup>

Supplemental Table S3. Gene Ontology (GSEA) Sets Positively Enriched in Bax-/-

Embryos vs Bax <sup>+/+</sup> Embryos				
Gene Set	Enriched/ Total Genes	Normalized Enrichment Score	Adj <i>p</i> -value	High-Ranked Genes (rank- metric ≥0.1)
Gene Sets Related to Placental Development				
Placenta development*	35/133	2.0	0.017	Wnt7a, Adm,
Cell differentiation in embryonic placental	9/23	1.9	0.036	Htra1, Gjb3,
development*				Gjb5, Plac1, Etv2, Igf2, Tfeb,
Embryonic placenta development*	24/78	2.1	0.009	Gata2, Fosl1,
				Ascl2, Hand1
Gene Sets Related to Apoptosis				
Negative regulation of endothelial cell apoptotic	11/32	2.0	0.012	Gata2, Cdh5,
process*				Fga
Negative regulation of epithelial cell apoptotic	17/48	1.9	0.032	
process*	17/50	1.0	0.027	C . 2 E .
Endothelial cell apoptotic process	17/59	1.9	0.037	Gata2, Faslg, Cdh5, Fga
				Cuns, 1 ga
Gene Sets Related to Coagulation				
Regulation of coagulation*	23/70	2.0	0.013	Plaur, Thbd,
Negative regulation of coagulation*	16/53	2.0	0.014	Procr, Serpinc1,
Fibrinolysis*	9/25	1.9	0.028	Ubash3b, Fga
Gene Sets Related to Membranes and Permeability				
Establishment of endothelial barrier	21/48	1.9	0.035	Wnt7a, Cldn3,
Establishment of endotherial barrier	21/40	1.7	0.033	Cdh5, Pecam1
Regulation of vascular permeability	25/41	1.8	0.044	Adm, Nppb,
				Ddah1, Cdh5
Vacuolar membrane	126/390	1.9	0.034	Thbd, Tfeb,
				Mreg, Myo6, C3ar1, Dram1
Brush border membrane	23/59	1.9	0.031	Pdzk1
Microvillus membrane	13/24	1.8	0.043	Itgb3, Slc7a8,
G 10	22/40	4.0	0.040	Pdzk1
Sulfur compound transport	23/49	1.8	0.049	Slc13a3, Slc44a4
Sulfur compound transmembrane transporter activity	24/47	1.9	0.031	Slc13a3, Slc44a4, Abcc6
activity				510 1 10 1 10 10 10
Genes Sets Related to Gene Expression or Replicati				
DNA methylation involved in gamete generation*	11/19	1.9	0.020	Dnmt3l, Piwil2,
DNA methylation or demethylation*	34/88	1.9	0.045	Mov10l1
Regulation of gene expression by genetic	5/15	1.9	0.034	Igf2, Dnmt3l
imprinting  Regulation of translation NCRNA mediated	12/67	2.2	0.002	
Regulation of translation, NCRNA-mediated Mitotic spindle pole	12/67 14/33	2.3 1.8	0.002 0.044	
whous spinus pois	14/33	1.0	0.044	

Gene Sets Related to Receptor Binding and Channel	Activity			
Quaternary ammonium group binding	15/29	1.9	0.036	Apoa2, 4, 5, Pltp
Phosphatidylinositol phosphate phosphatase	16/31	1.8	0.043	
activity*				
Phosphatidylinositol dephosphorylation*	14/29	1.9	0.025	
Negative regulation of receptor-mediated	12/33	1.9	0.023	Itgb3, Apoc2
endocytosis				
Receptor serine threonine kinase binding	5/25	1.8	0.042	Bmp4, Bmp8b, Cdh5
Calcium release channel activity	10/17	1.8	0.042	Mcoln2
Gene Sets Related to Cellular Organelles				
Microtubule end	13/32	1.9	0.033	
Actin filament depolymerization	23/55	1.8	0.043	
Negative regulation of actin filament bundle	18/33	2.0	0.017	Tacstd2
assembly				
Comp Cata Deleted to Other December				
Gene Sets Related to Other Processes	C/17	1.0	0.044	BMP4, MMP9,
Negative regulation of kidney development	6/17	1.9	0.044	Tacstd2, Hnf1b
Positive regulation of vascular-associated smooth	10/21	1.9	0.035	1ucsiu2, 11nj10
muscle cell migration	10/21	1.7	0.033	
Keratinocyte migration	6/18	1.9	0.036	Mmp9
Hydrogen peroxide biosynthetic process	4/15	1.8	0.042	Duoxa2, Duox2
Positive regulation of ROS biosynthetic process	11/50	1.9	0.035	Duoxa2, H19,
				Ddah1
Regulation of hormone metabolic process	6/32	1.9	0.038	Duox2, Adm,
Regulation of urine volume	5/20	1.8	0.042	Adm, Nppb
Response to thyroid hormone*	14/22	2.0	0.017	
Response to acidic pH	11/23	1.8	0.044	
Lipase inhibitor activity	7/17	1.9	0.040	Apoc2, Apoa2

<sup>\*</sup>Indicates significant clustering of adjacent gene sets

Supplemental Table S4. Gene Ontology (GSEA) Sets Negatively Enriched in  $\it Bax-/-$  Embryos vs Bax+/+ Embryos

Gene Set	Enriched/ Total Genes	Normalized Enrichment Score	Adj p-value	High-Ranked Genes (rank- metric ≥0.1)
Gene Sets Related Apoptosis				
Apoptotic process involved in development*	12/35	-2.3	0.008	Bax, Cryab, Foxc2,
Apoptotic process involved in morphogenesis*	9/23	-2.3	0.013	Hand2, Fgf4
HSP70 protein binding	5/39	-2.2	0.017	Bax
Response to salt stress	3/23	-2.2	0.033	Bax
Gene Sets Related to Cellular Organelles				
Regulation of ER unfolded protein response	3/28	-2.1	0.033	Bax
ER calcium ion homeostasis	2/25	-2.1	0.046	Bax
Mitochondrial fusion	2/28	-2.2	0.025	Bax
Gene Sets Related to Development				
Somite development*	31/83	-2.2	0.020	Foxc2, Pcdh8,
Somitogenesis*	21/64	-2.3	0.009	Dll1, Wnt3a, Aldh1a2, Mesp2,
				<i>Tbx</i> 6, <i>Hes</i> 7
Ovarian follicle development	17/52	-2.2	0.021	Bax
Gene Sets Related to Remodeling				
Blood vessel remodeling	12/43	-2.1	0.049	Bax, Foxc2, Bgn

<sup>\*</sup>Indicates significant clustering of adjacent gene sets