

Appendix 6. IPA: Upstream Regulators Activated in Term Amniotic Fluid

Upstream Regulator	Name	Function	Fold Change	Bias-corrected z score	No. of target genes
<i>IL8</i>	interleukin 8	This chemokine is one of the major mediators of the inflammatory response. IL-8 is a chemotactic factor that attracts neutrophils, basophils, and T-cells, but not monocytes. It is also involved in neutrophil activation.	47.5	2.2	9
<i>IL1B</i>	interleukin 1, beta	This cytokine is an important mediator of the inflammatory response. Produced by activated macrophages, IL-1 stimulates thymocyte proliferation by inducing IL-2 release, B-cell maturation and proliferation, and fibroblast growth factor activity.	27.6	3.9	150
<i>AGER</i>	advanced glycosylation end product-specific receptor	The receptor encoded by this gene is a member of the immunoglobulin superfamily of cell surface receptors; implicated in homeostasis, development, and inflammation, and certain diseases	26.3	3.0	13
<i>NKX2-1</i>	NK2 homeobox 1	Transcription factor that binds and activates the promoter of thyroid specific genes such as thyroglobulin, thyroperoxidase, and thyrotropin receptor. Crucial in the maintenance of the thyroid differentiation phenotype. May play a role in lung development and surfactant homeostasis	7.7	2.1	41

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<i>VEGFA</i>	vascular endothelial growth factor A	Growth factor active in angiogenesis, vasculogenesis and endothelial cell growth. Induces endothelial cell proliferation, promotes cell migration, inhibits apoptosis and induces permeabilization of blood vessels.	7.2	2.3	42
<i>C3</i>	complement component 3	Complement component C3 plays a central role in the activation of complement system. Its activation is required for both classical and alternative complement activation pathways.	6.8	2.5	6
<i>IL6R</i>	interleukin 6 receptor	This gene encodes a subunit of the interleukin 6 (IL6) receptor complex. Interleukin 6 is a potent pleiotropic cytokine that regulates cell growth and differentiation and plays an important role in the immune response.	6.5	2.1	14
<i>RUNX2</i>	runt-related transcription factor 2	Transcription factor involved in osteoblastic differentiation and skeletal morphogenesis. Essential for the maturation of osteoblasts and both intramembranous and endochondral ossification.	4.1	2.1	20
<i>CD24</i>	CD24 molecule	This gene encodes a sialoglycoprotein that is expressed on mature granulocytes and in many B cells. Modulates B-cell activation responses.	3.7	2.7	35
<i>PRKCD</i>	protein kinase C, delta	this kinase is involved in B cell signaling and in the regulation of growth, apoptosis, and differentiation of a variety of cell types	2.9	2.6	18

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<i>RAD21</i>	RAD21 homolog (S. pombe)	Cleavable component of the cohesin complex, involved in chromosome cohesion during cell cycle, in DNA repair, and in apoptosis. The cohesin complex is required for the cohesion of sister chromatids after DNA replication.	2.6	2.1	4
<i>NAMPT</i>	nicotinamide phosphoribosyltransferase	Catalyzes the condensation of nicotinamide with 5-phosphoribosyl-1-pyrophosphate to yield nicotinamide mononucleotide, an intermediate in the biosynthesis of NAD. It is the rate limiting component in the mammalian NAD biosynthesis pathway. It is thought to be involved in many important biological processes, including metabolism, stress response and aging.	2.4	2.5	6
<i>BNIP3L</i>	BCL2/adenovirus E1B 19kDa interacting protein 3-like	The protein encoded by this gene is a functional homolog of BNIP3, a proapoptotic protein. Interacts with viral and cellular anti-apoptosis proteins. May function as a tumor suppressor.	2.4	2.3	12
<i>NFKB1</i>	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1	NF-kappa-B is a transcription factor which is present in almost all cell types and is involved in many biological processes such as inflammation, immunity, differentiation, cell growth, tumorigenesis and apoptosis.	2.4	2.1	40

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<i>S100A9</i>	S100 calcium binding protein A9	Calcium-binding protein. Has antimicrobial activity towards bacteria and fungi. Important for resistance to invasion by pathogenic bacteria. Up-regulates transcription of genes that are under the control of NF-kappa-B. Plays a role as a pro-inflammatory mediator in acute and chronic inflammation and up-regulates the release of IL8 and cell-surface expression of ICAM1	1.8	2.1	5
<i>SMC3</i>	structural maintenance of chromosomes 3	Central component of cohesin, a complex required for chromosome cohesion during the cell cycle.	1.7	2.2	4
<i>MAP2K3</i>	mitogen-activated protein kinase kinase 3	Activated by mitogenic and environmental stress, and participates in the MAP kinase-mediated signaling cascade. This kinase can be activated by insulin, and is necessary for the expression of glucose transporter.	1.7	2.2	10

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