

Appendix 7. IPA: Upstream Regulators Activated in Second Trimester Amniotic Fluid

Upstream Regulator	Name	Function	Fold Change	Bias-corrected z score	No. of target genes
<i>HNF4A</i>	hepatocyte nuclear factor 4, alpha	Transcriptionally controlled transcription factor. Binds to DNA sites required for the transcription of alpha 1-antitrypsin, apolipoprotein CIII, transthyretin genes and HNF1-alpha. May be essential for development of the liver, kidney and intestine.	388.7	4.8	316
<i>NR1H4</i>	nuclear receptor subfamily 1, group H, member 4	This gene encodes a ligand-activated transcription factor. This protein functions as a receptor for bile acids, and when bound to bile acids, regulates the expression of genes involved in bile acid synthesis and transport.	51.8	2.4	24
<i>MYBL2</i>	v-myb myeloblastosis viral oncogene homolog (avian)-like 2	Member of the MYB family of transcription factor genes, involved in cell cycle progression, regulation of cell survival, proliferation, and differentiation.	15.6	2.3	17
<i>DIO3</i>	deiodinase, iodothyronine, type III	Catalyzes the inactivation of thyroid hormone to inactive metabolites. Regulates circulating fetal thyroid hormone concentrations throughout gestation to prevent premature exposure of developing fetal tissues to adult levels of thyroid hormones.	2.5	2.4	9
<i>GPX1</i>	glutathione peroxidase 1	Glutathione peroxidase functions in the detoxification of hydrogen peroxide, and is one of the most important antioxidant enzymes in humans. Protects the hemoglobin in erythrocytes from oxidative breakdown.	1.8	2.4	7

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<i>CCND1</i>	cyclin D1	Cyclins function as regulators of CDK kinases. This cyclin forms a complex with and functions as a regulatory subunit of CDK4 or CDK6, whose activity is required for cell cycle G1/S transition. This protein has been shown to interact with tumor suppressor protein Rb.	1.7	2.5	47
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