

**Supplemental Table S5.** Variant Analysis Results of Retinoic Acid and Alcohol Metabolism Candidate Genes.

rsID	Gene	Type of Mutation	Ref Allele	Presumptive Risk Allele	Biological Impact of Variant	Ref.	FASD Cohort Risk Allele Count Frequency	Thousand Genomes Risk Allele Count (Frequency)	PolyPhen / Sift Prediction	CADD PHRED Score	Statistic	<i>p</i> -Value	Passed Benjamini-Hochberg Threshold	Risk or Resilience
rs1229984	<i>ADH1B</i>	Missense	T	C	C allele associated with higher levels of alcohol consumption and FASD	[32,36, 83]	45/46 (0.96)	8428/10016 (0.82)	Probably Damaging / Tolerated	14.83	8.2	1.70×10 <sup>-2</sup>	No	Risk *
rs113075608	<i>ADH1B</i>	Missense	A	G	Variant has damaging PolyPhen score and Sift Score	-	1/46 (0.02)	50/10016 (5×10 <sup>-3</sup> )	Damaging / Damaging	23.8	97.8	5.83×10 <sup>-22</sup>	Yes	Risk *
rs2066702	<i>ADH1B</i>	Missense	G	G	A allele is noted to be protective against PAE outcomes	[32,85]	46/46 (1)	9484/10016 (0.95)	NA / NA	26.3	10.55	5.00×10 <sup>-3</sup>	Yes	Risk *
rs1612735	<i>ADH1C</i>	Intron	T	C	C allele is associated with alcohol dependence	[72]	24/56 (0.52)	2148/10016 (0.21)	NA / NA	7.85	26.5	1.77×10 <sup>-6</sup>	Yes	Risk
rs698	<i>ADH1C</i>	Missense	T	C	C variant 2-fold less kinetically active and associated with alcohol dependence and use	[38,86]	25/46 (0.54)	2146/10016 (0.21)	NA / NA	14.59	30.28	2.66×10 <sup>-6</sup>	Yes	Risk *
rs2241894	<i>ADH1C</i>	Silent	T	C	C allele is associated with alcohol dependence	[73]	4/46 (0.087)	4724/10016 (0.47)	Probably Damaging / Tolerated	0.088	27.21	1.23×10 <sup>-6</sup>	Yes	Resilience
rs2298753	<i>ADH1C</i>	3' UTR	T	C	VUS	-	13/46 (0.28)	644/10016 (0.06)	NA/NA	6.19	41.89	7.28×10 <sup>-10</sup>	Yes	— *
rs1614972	<i>ADH1C</i>	Intron	C	C	T variant is associated with reduced risk of alcohol dependence	[37]	43/46 (0.93)	4804/10016 (0.48)	NA / NA	4.8	37.99	5.61×10 <sup>-9</sup>	Yes	Risk *
rs1042364	<i>ADH4</i>	3' UTR	T	T	T allele is associated with alcohol dependence	[39]	8/46 (0.17)	1174/10016 (0.11)	NA / NA	6.24	4.24	1.20×10 <sup>-1</sup>	No	—
rs1126671	<i>ADH4</i>	Missense	T	T	T variant affects alcohol binding and protein stability. T allele is assoc. with alcohol dependence	[87]	11/46 (0.24)	1532/10016 (0.15)	Probably Damaging / Tolerated	0.005	4.47	1.07×10 <sup>-1</sup>	No	Resilience
rs3762894	<i>ADH4</i>	Upstream	T	T	A allele – less alcohol consumption; T variant with alcohol dependence	[39]	42/46 (0.91)	6824/10016 (0.68)	NA / NA	0.39	11.65	4.00×10 <sup>-3</sup>	Yes	Risk *
rs971074	<i>ADH7</i>	Silent	C	T	T allele is associated with heroin addition	[74]	10/46 (0.22)	1200/10016 (0.12)	NA / NA	7.79	6.84	3.20×10 <sup>-2</sup>	No	Risk
rs1154470	<i>ADH7</i>	Upstream	G	A	A variant associated with alcohol use disorders	[88]	15/46 (0.33)	2424/10016 (0.24)	NA / NA	0.72	2.48	2.90×10 <sup>-1</sup>	No	—

rs4646626	<i>ALDH1A2</i>	Missense	C	T	T variant found in Tetralogy of Fallot patients	[89]	23/46 (0.50)	3734/10016 (0.37)	Begin / Tolerated	17.53	2.31	3.10×10 <sup>-1</sup>	No	— *
rs16939660	<i>ALDH1A2</i>	Silent	T	C	C variant found in patients with congenital heart defects, spina bifida and neural tube defects	[89,90]	1/46 (0.02)	110/10016 (0.01)	NA / NA	10.19	43.92	2.90×10 <sup>-10</sup>	Yes	Risk
rs2073478	<i>ALDH1B1</i>	Missense	G	G	TT genotype has been shown to be protective against drinking	[75]	19/46 (0.41)	6060/10016 (0.60)	Probably Damaging / Damaging	20.8	7.15	3.00×10 <sup>-2</sup>	No	Resilience
rs671	<i>ALDH2</i>	Missense	G	G	A allele – reduced alcohol consumption and flushing; enzyme nearly inactive	[40]	46/46 (1)	9658/10016 (0.96)	NA / NA	33	14.24	8.10×10 <sup>-4</sup>	Yes	Risk *
rs10891338	<i>BCO2</i>	Missense	T	C	C allele has a probably Damaging PolyPhen and damaging CADD score	-	46/46 (1)	9720/10016 (0.97)	Probably Damaging / Tolerated	16.04	16.86	2.20×10 <sup>-4</sup>	Yes	Risk
rs35361223	<i>BCO2</i>	Missense	C	G	G allele has a damaging SIFT prediction	-	2/46 (0.04)	184/10016 (0.02)	Benign / Damaging	7.127	68.53	1.37×10 <sup>-6</sup>	Yes	Risk *
rs61743167	<i>CES3</i>	Missense	C	T	T allele has a damaging SIFT and CADD prediction	-	1/46 (0.02)	114/10016 (0.011)	Benign / Damaging	16.67	42.32	6.45×10 <sup>-10</sup>	Yes	Risk
rs12263200	<i>CYP26C1</i>	Intron	G	G	T allele has a damaging SIFT prediction	-	27/46 (0.59)	1224/10016 (0.12)	NA / Damaging	2.71	93.39	1.00×10 <sup>-3</sup>	Yes	Risk *
rs58993699	<i>CYP26C1</i>	Intron	C	C	T allele has a damaging SIFT and CADD prediction	-	45/46 (0.96)	9686/10016 (0.97)	NA / Damaging	14.23	11.86	1.00×10 <sup>-3</sup>	Yes	Risk
rs55962377	<i>DGAT1</i>	Missense	G	T	T allele has damaging PolyPhen and CADD Score	-	1/46 (0.02)	360/10016 (0.036)	Probably Damaging / Tolerated	18.73	12.69	2.00×10 <sup>-3</sup>	Yes	Resilience
rs148632765	<i>FABP4</i>	Missense	C	G	G allele has damaging PolyPhen and CADD Score	-	1/46 (0.02)	4/10016 (4×10 <sup>-4</sup> )	Probably Damaging / Tolerated	22	872.33	3.77×10 <sup>-190</sup>	Yes	Risk
rs3829462	<i>LIPC</i>	Missense	C	A	A allele has damaging PolyPhen and CADD Score	-	30/46 (0.65)	9376/10016 (0.94)	Probably Damaging / Tolerated	20.6	68.69	3.30×10 <sup>-15</sup>	Yes	Resilience
rs61753150	<i>NCOR1</i>	Missense	T	T	G allele has probably damaging PolyPhen score and damaging SIFT and CADD Score	-	1/46 (0.02)	40/10016 (4×10 <sup>-3</sup> )	Probably Damaging / Damaging	22.3	121.8	3.55×10 <sup>-27</sup>	Yes	Risk
rs2227277	<i>NCOR2</i>	Missense	C	C	T allele has probably damaging PolyPhen score and damaging SIFT and CADD Score	-	3/46 (0.065)	574/10016 (0.06)	Probably Damaging / Damaging	17.1	7.29	3.00×10 <sup>-2</sup>	No	Resilience

rs2134095	<i>RXRG</i>	Silent	G	A	A allele is associated with lower cholesterol levels and gestational diabetes mellitus	[41]	33/46 (0.72)	4796/10316 (0.48)	NA / NA	5.66	12.43	2.80×10 <sup>-3</sup>	Yes	Risk *
rs971756	<i>STRA6</i>	Missense	A	T	T variant found in a patient with Matthew-Woods Syndrome	[42]	6/46 (0.13)	546/10016 (0.05)	NA / Damaging	3.86	12.71	2.00×10 <sup>-3</sup>	Yes	Risk *
rs11857410	<i>STRA6</i>	Silent	G	A	A allele found with ano- and microphthalmia; and with Matthew-Wood Syndrome	[43]	6/46 (0.13)	618/10016 (0.06)	NA / NA	8.72	10.3	5.00×10 <sup>-3</sup>	Yes	Risk *

\* Genotype validated by TaqMan