

Table e-1: WGS association results in HPV 12q24 region & in WMH 17q25 region

Chr:Pos	SNV	Alleles	AC	GENOCNT	MAF	Pvalue	Beta	SE
HPV								
12:117.32	rs7132910	T/C	631	1587/535/48	0.145	3.40E-05	0.101	0.024
12:117.32	rs7315280	A/G	561	1646/487/37	0.129	2.29E-04	0.095	0.026
12:117.32	rs7137149	T/C	506	1700/434/36	0.117	1.72E-04	0.101	0.027
12:117.32	rs77956314	T/C	391	1805/339/26	0.090	9.47E-03	0.077	0.030
12:117.32	rs11068224	G/A	361	1832/315/23	0.083	1.06E-02	0.079	0.031
12:117.33	rs12311895	T/C	464	1740/396/34	0.107	4.38E-04	0.097	0.028
12:117.33	rs113205216	C/A	385	1811/333/26	0.089	3.95E-03	0.086	0.030
12:117.33	rs113179672	G/A	385	1811/333/26	0.089	2.86E-03	0.089	0.030
12:117.33	rs7294919	T/C	464	1740/396/34	0.107	4.38E-04	0.097	0.028
12:117.33	rs7305705	G/T	438	1762/378/30	0.101	1.83E-03	0.088	0.028
12:117.33	rs10850728	T/C	465	1739/397/34	0.107	5.23E-04	0.096	0.028
12:117.33	rs11836634	A/G	464	1740/396/34	0.107	4.80E-04	0.097	0.028
12:117.33	rs111865233	T/C	360	1832/316/22	0.083	1.56E-02	0.075	0.031
12:117.33	rs7312900	A/T	485	1720/415/35	0.112	3.52E-04	0.097	0.027
12:117.33	rs112608342	G/A	484	1721/414/35	0.112	2.74E-04	0.099	0.027
12:117.33	rs12313220	T/C	484	1721/414/35	0.112	2.74E-04	0.099	0.027
12:117.33	rs7309079	G/C	436	1764/376/30	0.100	3.07E-03	0.084	0.028
12:117.33	rs76845667	C/T	438	1762/378/30	0.101	2.13E-03	0.087	0.028
12:117.34	rs12310299	C/G	484	1721/414/35	0.112	2.74E-04	0.099	0.027
12:117.34	rs7131959	G/A	438	1762/378/30	0.101	2.13E-03	0.087	0.028
12:117.34	rs80001826	G/C	484	1721/414/35	0.112	2.74E-04	0.099	0.027
12:117.34	rs7132339	G/A	483	1722/413/35	0.111	2.73E-04	0.099	0.027

12:117.34	rs7133290	C/T	437	1763/377/30	0.101	2.13E-03	0.087	0.028
12:117.34	rs113844630	T/C	485	1720/415/35	0.112	3.12E-04	0.098	0.027
12:117.34	rs78666825	C/T	485	1720/415/35	0.112	3.12E-04	0.098	0.027
12:117.34	rs113315762	T/C	437	1763/377/30	0.101	2.13E-03	0.087	0.028
12:117.34	rs75337356	T/C	483	1722/413/35	0.111	2.73E-04	0.099	0.027
12:117.34	rs12302173	G/A	314	1870/286/14	0.072	2.12E-03	0.102	0.033

WMH

17:73.87	rs9908862	A/G	500	1210/414/43	0.150	1.60E-06	0.256	0.053
17:73.87	rs1105917	C/T	512	1203/416/48	0.154	6.76E-06	0.237	0.052
17:73.87	rs3903010	T/G	500	1210/414/43	0.150	1.60E-06	0.256	0.053
17:73.87	17:73874071	G/A	498	1212/412/43	0.149	1.89E-06	0.255	0.053
17:73.87	rs4072479	G/C	499	1211/413/43	0.150	1.36E-06	0.258	0.053
17:73.87	rs116044941	G/C	492	1212/412/40	0.148	1.82E-06	0.258	0.054
17:73.87	rs9889965	A/G	499	1210/413/43	0.150	1.22E-06	0.259	0.053
17:73.89	rs55823223	G/A	473	1232/397/38	0.142	4.04E-06	0.252	0.055
17:73.88	rs7214628	A/G	648	1089/508/70	0.194	1.96E-03	0.149	0.048

Chr:Pos: Chromosome:Position in Mb on Build 37

Alleles: Coded/Non-coded

AC: Allele count

GENOCNT: Count of individuals per genotypes

MAF: Minor Allele Frequency

Table e-2: Top Pathways in MAGENTA analysis using a FDR 95th percentile

enrichment < 0.2 or a FDR 75th percentile enrichment < 0.2

Gene set		95th percentile			75th percentile		
		enrichment cut-off			enrichment cut-off		
		P	FDR	EE (obs)	P	FDR	EE (obs)
Genes (mapped)							
WMH							
Protein_ADP-ribosylation	10 (9)	0.37	0.83	0 (1)	0.001	0.06	2 (7)
Mitosis	156 (134)	0.04	0.68	7 (12)	0.001	0.17	34 (49)
Ubiquitin_proteasome_pathway	52 (51)	0.25	0.89	3 (4)	0.0004	0.04	13 (24)
cAMP-mediated.Signaling	11 (11)	0.02	0.19	1 (3)	0.12	0.84	3 (5)
BLYMPHOCYTE_PATHWAY	11 (9)	0.01	0.09	0 (3)	0.04	0.74	2 (5)
CTL_PATHWAY	15 (12)	0.47	0.79	1 (1)	0.0004	0.02	3 (9)
EIF_PATHWAY	16 (16)	0.01	0.14	1 (4)	0.08	0.83	4 (7)
EDG1_PATHWAY	27 (27)	4.50E-05	0.005	1 (8)	0.02	0.96	7 (12)
BARRESTIN_SRC_PATHWAY	15 (15)	0.004	0.11	1 (4)	0.14	0.77	4 (6)
BARRESTIN_PATHWAY	10 (10)	0.001	0.03	1 (4)	0.08	0.94	3 (5)
TCBV							
nucleotide binding	1934 (1684)	0.04	0.87	84 (96)	0.0001	0.17	421 (472)
ATP binding	1469 (1306)	0.31	0.98	65 (68)	0.0001	0.16	327 (374)
myosin filament	15 (11)	1.00	1.00	1 (0)	0.001	0.18	3 (8)
Regulation_of_nucleoside, nucleotide_metabolism	15 (15)	0.17	0.99	1 (2)	0.005	0.20	4 (9)
Adrenaline and noradrenaline biosynthesis	15 (14)	0.03	0.78	1 (3)	0.0001	0.01	4 (10)
Fructose_galactose_metabolism	7 (7)	0.003	0.06	0 (3)	0.001	0.02	2 (6)
TR.RXR.Activation	62 (59)	0.81	1.00	3 (2)	0.02	0.13	15 (22)
Antigen.Presentation.Pathway	11 (7)	0.04	0.25	0 (2)	0.01	0.07	2 (5)

Gene set	Genes (mapped)	95th percentile			75th percentile		
		enrichment cut-off			enrichment cut-off		
		P	FDR	EE (obs)	P	FDR	EE (obs)
IL-6.Signaling	29 (28)	0.76	1.00	1 (1)	0.004	0.04	7 (14)
GM-CSF.Signaling	23 (22)	0.67	1.00	1 (1)	0.03	0.14	6 (10)
Mitochondrial.Dysfunction	76 (75)	0.03	0.56	4 (8)	0.04	0.17	19 (26)
JAK.Stat.Signaling	10 (10)	0.09	0.53	1 (2)	0.003	0.04	3 (7)
Insulin.Receptor.Signaling	35 (35)	0.53	1.00	2 (2)	0.03	0.15	9 (14)
p38.MAPK.Signaling	27 (27)	0.74	1.00	1 (1)	0.02	0.14	7 (12)
Glucocorticoid.Receptor.Signaling	102 (96)	0.35	1.00	5 (6)	0.001	0.03	24 (39)
PTEN.Signaling	24 (23)	0.33	1.00	1 (2)	0.04	0.15	6 (10)
Integrin.Signaling	38 (37)	0.29	1.00	2 (3)	0.02	0.15	9 (15)
Erythropoietin.Signaling	15 (15)	0.54	1.00	1 (1)	0.02	0.09	4 (8)
Phototransduction.Pathway	12 (12)	0.002	0.04	1 (4)	0.01	0.07	3 (7)
Hepatic.Fibrosis.Hepatic.Stellate Cell Activation	83 (80)	0.21	1.00	4 (6)	0.03	0.15	20 (28)
IL-4.Signaling	18 (18)	0.01	0.18	1 (4)	0.001	0.02	5 (11)
KEGG_HISTIDINE_METABOLISM	29 (28)	0.003	0.07	1 (6)	0.03	0.39	7 (12)
KEGG_TYROSINE_METABOLISM	42 (38)	0.0001	0.01	2 (9)	0.03	0.35	10 (15)
KEGG_PHENYLALANINE METABOLISM	18 (17)	0.01	0.12	1 (4)	0.24	0.54	4 (6)
KEGG_MAPK_SIGNALING PATHWAY	267 (249)	0.97	1.00	12 (7)	0.001	0.14	62 (85)
KEGG_PRIMARY IMMUNODEFICIENCY	35 (32)	0.004	0.13	2 (6)	0.04	0.34	8 (13)
IL4_PATHWAY	11 (11)	0.10	0.87	1 (2)	0.002	0.12	3 (8)
HPV							

Gene set	Genes (mapped)	95th percentile			75th percentile		
		enrichment cut-off			enrichment cut-off		
		P	FDR	EE (obs)	P	FDR	EE (obs)
mRNA_transcription	296 (228)	0.06	1.00	11 (17)	0.0001	0.07	57 (80)
Pyruvate_metabolism	11 (11)	0.42	1.00	1 (1)	0.01	0.12	3 (7)
Alzheimer_disease-presenilin pathway	69 (68)	0.44	0.96	3 (4)	0.002	0.10	17 (29)
Serotonin.Receptor.Signaling	14 (14)	0.004	0.08	1 (4)	0.11	1.00	4 (6)
DEATH_PATHWAY	33 (32)	0.001	0.16	2 (7)	0.15	0.91	8 (11)
DEATH_RECEPTOR_SIGNALLING	13 (12)	0.0001	0.01	1 (5)	0.0003	0.06	3 (9)

EE (obs): Enrichment Exp (obs), expected number of genes at enrichment threshold (observed number of genes)