

Supplemental File

Table S1 Mouse *ODC1* knockout phenotypes from the IMPC
(<https://www.mousephenotype.org/data/genes/MGI:97402>).

Phenotype	Zygosity	Sex	Procedure	Parameter	Phenotyping Center	Source	P Value
preweaning lethality, complete penetrance	homozygote	female	Viability Primary Screen	Viability Outcome	JAX	IMPC	0.0
preweaning lethality, complete penetrance	homozygote	male	Viability Primary Screen	Viability Outcome	JAX	IMPC	0.0
decreased lean body mass	heterozygote	female	Body Composition (DEXA lean/fat)	Lean mass	JAX	IMPC	4.21E-6
decreased lean body mass	heterozygote	male	Body Composition (DEXA lean/fat)	Lean mass	JAX	IMPC	4.21E-6
decreased total body fat amount	heterozygote	male	Body Composition (DEXA lean/fat)	Fat mass	JAX	IMPC	3.08E-5

Table S2 Geno2MP Missense SNPs for *ODC1*.

Variant	AA	Var	#	HPO profiles	heterozygous	homozygous	Phenotypes	polyphen2	Provean	SIFT	Impact Total
G84R	G	R	84	72	121	1	Nervous System	probably-damaging	Deleterious	Damaging	125.8
C202R	C	R	202	1	1	0	Abnormality of hindbrain morphology	possibly-damaging	Deleterious	Damaging	103.5
S195G	S	G	195	5	6	0	head and neck	possibly-damaging	Deleterious	Damaging	100.5
T285M	T	M	285	1	1	0	cardiovascular	possibly-damaging	Deleterious	Damaging	85.4
F383L	F	L	383	1	1	0	Abnormality of brain morphology	benign	Deleterious	Damaging	72.9
A258V	A	V	258	4	4	0	head and neck	possibly-damaging	Deleterious	Damaging	72.6
N398S	N	S	398	1	1	0	Abnormality of adipose tissue	probably-damaging	Deleterious	Tolerated	70.35
S410L	S	L	410	1	1	0	Abnormal cellular physiology	benign	Deleterious	Damaging	61.25
D204N	D	N	204	2	2	0	nervous system; metabolism/homeostasis	benign	Deleterious	Tolerated	60.5
D243H	D	H	243	1	1	0	Nephrotic syndrome	benign	Deleterious	Damaging	60.075
V322I	V	I	322	1	1	0	skeletal system	possibly-damaging	Neutral	Tolerated	54.2
R183W	R	W	183	15	17	0	nervous system	benign	Deleterious	Damaging	52.65
G268R	G	R	268	19	24	0	nervous system	benign	Deleterious	Damaging	50
Y122N	Y	N	122	1	1	0	Aplasia/Hypoplasia affecting the eye	benign	Deleterious	Damaging	46.575
R365L	R	L	365	1	1	0	Omphalocele	benign	Deleterious	Tolerated	44.91
A287G	A	G	287	1	1	0	Abnormality of brain morphology	benign	Deleterious	Damaging	44.685
L363F	L	F	363	1	1	0	Arnold-Chiari malformation	benign	Deleterious	Tolerated	39.625
R178K	R	K	178	7	6	1	nervous system	benign	Neutral	Tolerated	31.25
D15N	D	N	15	1	1	0	Retinitis pigmentosa	benign	Neutral	Damaging	26.75
V62I	V	I	62	1	1	0	Abnormality of the musculature	benign	Neutral	Damaging	23.6875
T157A	T	A	157	1	1	0	Dystonia	benign	Deleterious	Tolerated	22.225
A452V	A	V	452	1	1	0	Abnormality of the urinary system	benign	Neutral	Damaging	22.15
S456L	S	L	456	2	3	0	Intellectual disability	benign	Neutral	Tolerated	11.65
V254I	V	I	254	2	2	0	cardiovascular and nervous	benign	Neutral	Tolerated	10.95
H335Y	H	Y	335	1	1	0	Seizures	benign	Neutral	Tolerated	5.346
A452T	A	T	452	4	4	0	Renal agenesis	benign	Neutral	Tolerated	4.87
H376Y	H	Y	376	1	2	0	Abnormality of brain morphology	benign	Neutral	Tolerated	4.7625
T301R	T	R	301	1	1	0	Seizures	benign	Neutral	Tolerated	2.00025
T301M	T	M	301	1	1	0	Agenesis of corpus callosum	benign	Neutral	Tolerated	1.871
F4S	F	S	4	1	1	0	Bicuspid aortic valve	benign	Neutral	Tolerated	0
I23L	I	L	23	3	3	0	Abnormality of the lung	benign	Neutral	Tolerated	0
S32F	S	F	32	1	1	0	Abnormality of blood and blood-forming tissues	benign	Neutral	Tolerated	0
S100R	S	R	100	1	1	0	Abnormality of the abdominal wall	benign	Neutral	Tolerated	0
Q129R	Q	R	129	2	2	0	Intellectual disability	benign	Neutral	Tolerated	0
A143V	A	V	143	4	4	0	lissencephaly	benign	Neutral	Tolerated	0
V163I	V	I	163	1	2	0	Seizures	benign	Neutral	Tolerated	0
N188S	N	S	188	1	1	0	Abnormal hemoglobin	benign	Neutral	Tolerated	0
V225A	V	A	225	1	1	0	Absence of the sacrum	benign	Neutral	Tolerated	0
G253R	G	R	253	11	14	0	musculature	benign	Neutral	Tolerated	0
G253S	G	S	253	6	6	0	cardiovascular	benign	Neutral	Tolerated	0
D307G	D	G	307	1	1	0	Abnormality of the lung	benign	Neutral	Tolerated	0
S309L	S	L	309	1	1	0	Global developmental delay	benign	Neutral	Tolerated	0
S310N	S	N	310	1	1	0	Intellectual disability	benign	Neutral	Tolerated	0
K349Q	K	Q	349	3	3	0	Abnormal eye morphology	benign	Neutral	Tolerated	0
R369C	R	C	369	2	2	0	Nephronophthisis	benign	Neutral	Tolerated	0
R449C	R	C	449	1	1	0	cardiovascular system	benign	Neutral	Tolerated	0
S458G	S	G	458	2	2	0	nervous system	benign	Neutral	Tolerated	0

Table S3 Allele frequency for ODC G84R (rs138359527) from population genomic projects.

Study	Sub Study	Population	Sub Population	Sub Population	C Freq	C Count	T Freq	T Count
1000GENOME S	phase_3	SAS	GIH	Gujarati Indians in Houston, TX	0.985	203	0.015	3
1000GENOME S	phase_3	SAS	PJL	Punjabi in Lahore, Pakistan	0.99	190	0.01	2
gnomADe	exome	sas			0.992	30257	0.008	233
1000GENOME S	phase_3	AMR	PUR	Puerto Ricans from Puerto Rico	0.995	207	0.005	1
1000GENOME S	phase_3	EUR	FIN	Finnish in Finland	0.995	197	0.005	1
gnomADg	genome	sas			0.995	3020	0.005	16
UK10K		TWINSUK			0.996	3560	0.004	14
gnomADe	exome	nfe			0.997	112938	0.003	314
gnomADg	genome	nfe			0.997	64359	0.003	211
UK10K		ALSPAC			0.997	3841	0.003	13
gnomADe	exome	oth			0.998	6104	0.002	14
gnomADe	exome	amr			0.999	34444	0.001	20
gnomADg	genome	ami			0.999	899	0.001	1
gnomADg	genome	amr			0.999	13641	0.001	13
gnomADg	genome	asj			0.999	3320	0.001	2
gnomADg	genome	oth			0.999	2149	0.001	3
gnomADe	exome	asj			0.9995003	10001	0.0004997	5
					0.99957179		0.00042820	
gnomADg	genome	afr			6	42018	4	18
					0.99961788		0.00038211	
gnomADg	genome	fin			3	10464	7	4
					0.99972217		0.00027782	
gnomADe	exome	fin			1	21590	9	6
					0.99975375		0.00024624	
gnomADe	exome	afr			5	16240	5	4
					0.99983681		0.00016318	
gnomADe	exome	eas			5	18381	5	3
gnomADg	genome	eas			1	3134	0	0
1000GENOME S	phase_3	AFR	ACB	African Caribbeans in Barbados	1	192	0	0
1000GENOME S	phase_3	AFR	ASW	Americans of African Ancestry in SW USA	1	122	0	0
1000GENOME S	phase_3	AFR	ESN	Esan in Nigeria	1	198	0	0
1000GENOME S	phase_3	AFR	GWD	Gambian in Western Divisions in the Gambia	1	226	0	0
1000GENOME S	phase_3	AFR	LWK	Luhya in Webuye, Kenya	1	198	0	0
1000GENOME S	phase_3	AFR	MSL	Mende in Sierra Leone	1	170	0	0
1000GENOME S	phase_3	AFR	YRI	Yoruba in Ibadan, Nigeria	1	216	0	0
1000GENOME S	phase_3	AMR	CLM	Colombians from Medellin, Colombia	1	188	0	0
1000GENOME S	phase_3	AMR	MXL	Mexican Ancestry from Los Angeles USA	1	128	0	0
1000GENOME S	phase_3	AMR	PEL	Peruvians from Lima, Peru	1	170	0	0
1000GENOME S	phase_3	EAS	CDX	Chinese Dai in Xishuangbanna, China	1	186	0	0
1000GENOME S	phase_3	EAS	CHB	Han Chinese in Beijing, China	1	206	0	0
1000GENOME S	phase_3	EAS	CHS	Southern Han Chinese	1	210	0	0
1000GENOME S	phase_3	EAS	JPT	Japanese in Tokyo, Japan	1	208	0	0
1000GENOME S	phase_3	EAS	KHV	Kinh in Ho Chi Minh City, Vietnam	1	198	0	0
1000GENOME S	phase_3	EUR	CEU	Utah Residents (CEPH) with Northern and Western European Ancestry	1	198	0	0
1000GENOME S	phase_3	EUR	GBR	British in England and Scotland	1	182	0	0
1000GENOME S	phase_3	EUR	IBS	Iberian Population in Spain	1	214	0	0
1000GENOME S	phase_3	EUR	TSI	Toscans in Italia	1	214	0	0
1000GENOME S	phase_3	SAS	BEB	Bengali from Bangladesh	1	172	0	0
1000GENOME S	phase_3	SAS	ITU	Indian Telugu from the UK	1	204	0	0
1000GENOME S	phase_3	SAS	STU	Sri Lankan Tamil from the UK	1	204	0	0

Table S4 PheWAS for ODC G84R (rs138359527) extracted from Open Targets Genetics.

Trait	P-value	Beta	Odds Ratio	Author (Year)
Hiatus hernia non-cancer illness code, self-reported	0.000611209	0.552269905	1.737191806	UKB Neale v2
Cetirizine treatment/medication code	0.00104885	0.753210099	2.123806716	UKB Neale v2
Spine arthritis/spondylitis non-cancer illness code, self-reported	0.00210866	0.801101223	2.227993096	UKB Neale v2
Fracture of ankle and foot	0.00623	0.821	2.272771473	UKB SAIGE
Mean signal-to-noise ratio (snr), (left)	0.0081056	-718.818		UKB Neale v2
Felt very upset when reminded of stressful experience in past month	0.00857595	0.0916764		UKB Neale v2
Urethral stricture (not specified as infectious)	0.009	-0.651	0.521523992	UKB SAIGE
Reaction time	0.00909346	0.120451		Davies G
Nervous feelings	0.00915901	-0.149873195	0.860817126	UKB Neale v2
Inguinal hernia	0.00927	-0.324	0.723250242	UKB SAIGE

Table S5 HPO variants for *ODC1* from Geno2MP.

rsid	Allele Change	gnomAD Allele	gnomAD rank	HPO Count	heterozygous Count	homozygous Count	Annotation
rs138359527	C>T	0.0023907	16	72	121	1	missense
rs28362399	A>G	0.00763489	9	32	61	0	intron
rs28362396	T>C	0.0158858	6	24	38	4	intron
rs28362409	C>T	0.0016156	24	23	32	0	intron
rs115655138	C>T	0.00142553	26	22	28	0	intron
rs201790435	G>A	9.04E-04	35	21	28	0	intron
rs192090667	C>T	0.0216535	1	20	27	4	intron
rs61733046	C>T	0.00104276	31	19	24	0	missense
rs13396481	C>T	0.00185292	22	18	26	0	intron
NA	G>A	0.00106587	30	18	19	4	synonymous
rs115102834	G>A	1.07E-04	72	15	17	0	missense
rs143840340	G>A	0.0163755	4	13	20	0	intron
rs150152038	C>G	2.86E-04	52	11	14	0	missense
rs28362381	T>C	0.0193076	2	10	15	1	intron
NA	A>C	1.19E-05	150	9	14	0	synonymous
rs189662188	A>G	0.00142477	27	8	9	0	3-prime-UTR
NA	A>T	0.00116175	29	8	9	0	intron
rs180900746	A>C	0.00237835	17	7	7	0	intron
rs61733045	C>T	5.17E-05	94	7	6	1	missense
NA	G>A	0	195	7	7	0	intron
rs7558222	T>A	0.0162433	5	7	7	0	intron
rs28362411	T>C	2.66E-04	53	7	7	0	synonymous
NA	A>AC	0.00309096	15	6	12	0	intron
rs183432213	A>G	3.30E-04	47	6	7	0	synonymous
NA	A>G	2.93E-04	50	6	7	0	3-prime-UTR
rs150152038	C>T	4.21E-05	105	6	6	0	missense
rs188227508	C>T	3.60E-05	110	6	6	0	synonymous
rs28362398	G>C	7.08E-04	39	6	6	0	intron
NA	C>A	0	202	5	5	0	intron
NA	C>A	0	219	5	5	0	intron
rs192347282	C>T	0.0044144	13	5	6	0	intron-near-splice
NA	C>T	1.95E-04	56	5	7	0	synonymous
rs144846017	C>T	1.39E-04	65	5	6	0	synonymous
NA	C>T	7.47E-05	84	5	8	0	intron
rs145483973	G>A	0.0020752	19	5	5	0	intron
NA	G>A	9.54E-05	73	5	5	0	intron
rs28362372	GGGC>G	2.87E-04	51	5	1	4	5-prime-UTR
rs189035164	T>A	0	223	5	8	0	intron
NA	T>C	1.19E-05	148	5	6	0	missense-near-splice

Table S6 Phenotypes in HPO for Abnormality of the nervous system for ODC G84R (rs138359527).

#C/T	T/T	Status	HPOcode:broad	HPOterm:medium	HPOcode:medium	HPOterm:narrow	HPOcode:narrow
6	0	affected	HP:0000707;	Neurodevelopmental abnormality;	HP:0012759;	Intellectual disability;	HP:0001249;
4	0	affected	HP:0000707;	Abnormality of nervous system physiology;	HP:0012638;	Seizures;	HP:0001250;
3	1	affected	HP:0000707;	Abnormality of nervous system physiology;	HP:0012638;	Epileptic encephalopathy;	HP:0200134;
3	0	affected	HP:0000707;	Abnormality of brain morphology;	HP:0012443;	Agenesis of corpus callosum;	HP:0001274;
3	0	affected	HP:0000707;	Abnormality of nervous system morphology;	HP:0012639;		
2	0	affected	HP:0000707;	Morphological abnormality of the central nervous system;	HP:0002011;	Neurodegeneration;	HP:0002180;
2	0	affected	HP:0000707;	Morphological abnormality of the central nervous system;	HP:0002011;		
2	0	affected	HP:0000707;	Abnormality of brain morphology;	HP:0012443;	Abnormality of hindbrain morphology;	HP:0002438;
2	0	affected	HP:0000707;	Abnormality of brain morphology;	HP:0012443;		
1	0	affected	HP:0000707;HP:0000707;	Behavioral abnormality;Neurodevelopmental abnormality;	HP:0000708;HP:0012759;	Intellectual disability;	HP:0001249;
1	0	affected	HP:0000707;	Seizures;	HP:0001250;		
1	0	affected	HP:0000707;HP:0000707;	Abnormality of brain morphology;Abnormality of nervous system physiology;	HP:0012443;HP:0012638;	microcephaly;Seizures;	HP:0000252;HP:0001250;
1	0	affected	HP:0000707;HP:0000152;	Abnormality of brain morphology;Abnormality of skull size;	HP:0012443;HP:0000240;		
1	0	affected	HP:0000707;HP:0003011;HP:0003011	Abnormality of nervous system physiology;Abnormal muscle physiology;Abnormal muscle physiology	HP:0012638;HP:0011804;HP:0011804	Fatigable weakness;Progressive muscle weakness	HP:0003473;HP:0003323
1	0	affected	HP:0000707;	Abnormality of nervous system morphology;	HP:0012639;	Leukodystrophy;	HP:0002415;
1	0	affected	HP:0000707;HP:0002086;HP:0000707	Neurodevelopmental abnormality;Functional respiratory abnormality;Abnormality of nervous system physiology	HP:0012759;HP:0002795;HP:0012638	Global developmental delay;Breathing dysregulation;Babinski sign	HP:0001263;HP:0005957;HP:0003487
1	0	affected	HP:0000707;	Neurodevelopmental abnormality;	HP:0012759;	Global developmental delay;	HP:0001263;
2	0	relative	HP:0000707;HP:0000707;	Behavioral abnormality;Neurodevelopmental abnormality;	HP:0000708;HP:0012759;	Intellectual disability;	HP:0001249;
2	0	relative	HP:0000707;	Abnormality of brain morphology;	HP:0012443;	Abnormality of hindbrain morphology;	HP:0002438;
2	0	relative	HP:0000707;	Abnormality of nervous system physiology;	HP:0012638;	Seizures;	HP:0001250;
2	0	relative	HP:0000707;	Abnormality of nervous system physiology;	HP:0012638;	Epileptic encephalopathy;	HP:0200134;
2	0	relative	HP:0000707;HP:0003011;HP:0003011	Abnormality of nervous system physiology;Abnormal muscle physiology;Abnormal muscle physiology	HP:0012638;HP:0011804;HP:0011804	Fatigable weakness;Progressive muscle weakness	HP:0003473;HP:0003323
1	0	relative	HP:0000707;	Morphological abnormality of the central nervous system;	HP:0002011;		
1	0	relative	HP:0000707;HP:0000152;	Abnormality of brain morphology;Abnormality of skull size;	HP:0012443;HP:0000240;		
1	0	relative	HP:0000707;	Neurodevelopmental abnormality;	HP:0012759;	Intellectual disability;	HP:0001249;
1	0	relative	HP:0000707;	Neurodevelopmental abnormality;	HP:0012759;	Global developmental delay;	HP:0001263;

rs6761678	60.0	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.95	7	18	40	eQTLs,C-HiC
rs10929682	59.4	2.80E-07	-0.13	0.56	0.63	0.40	0.77	0.52	0.65	7	23	64	eQTLs,C-HiC
rs7563816	58.7	2.80E-07	-0.13	0.56	0.63	0.40	0.77	0.52	1.73	7	9	19	eQTLs,C-HiC
rs4668691	58.2	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	1.35	5	12	22	eQTLs,C-HiC
rs728282	53.7	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	3.58	5	4	6	eQTLs,C-HiC
rs3814388	50.3	2.30E-07	-0.13	1.20	2b	9	25	
rs4997810	49.7	2.80E-07	-0.13	0.56	0.62	0.41	0.78	0.52	0.90	4	20	25	eQTLs,C-HiC
rs6432125	49.0	2.80E-07	-0.13	0.56	0.62	0.41	0.77	0.52	1.26	7	12	22	eQTLs,C-HiC
rs6432120	47.4	2.80E-07	-0.13	2.26	3a	5	5	eQTLs,C-HiC
rs6432119	47.2	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	1.89	4	7	7	eQTLs,C-HiC
rs4331474	46.4	1.60E-07	-0.13	0.56	0.61	0.41	0.78	0.52	0.83	4	21	26	eQTLs,C-HiC
rs13034061	44.7	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	1.15	7	12	22	eQTLs,C-HiC
rs4669596	43.0	2.80E-07	-0.13	0.56	0.63	0.40	0.78	0.52	0.93	4	15	28	eQTLs,C-HiC
rs7608498	41.3	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.42	2b	34	54	eQTLs,C-HiC
rs10929687	38.8	2.80E-07	-0.13	0.56	0.63	0.40	0.78	0.52	0.97	5	4	31	eQTLs,C-HiC
rs12464817	34.7	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	2.48	6	5	8	
rs6432117	33.3	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	1.07	5	6	20	eQTLs,C-HiC
rs6721514	32.3	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	1.90	4	4	7	eQTLs,C-HiC
rs6432121	31.7	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	1.76	4	5	5	eQTLs,C-HiC
rs4371336	31.6	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.59	7	20	25	eQTLs,C-HiC
rs6759740	31.1	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	1.24	6	6	14	eQTLs,C-HiC
rs11683335	29.3	2.80E-07	-0.13	0.56	0.63	0.40	0.78	0.52	0.68	5	6	32	eQTLs,C-HiC
rs9679581	29.1	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.88	4	3	25	eQTLs,C-HiC
rs12632417	28.1	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.94	#N/A	9	16	eQTLs,C-HiC
rs6432109	27.9	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.37	7	16	53	eQTLs,C-HiC
rs6714413	27.9	1.60E-06	-0.12	0.56	0.62	0.39	0.77	0.49	0.93	6	7	17	eQTLs,C-HiC
rs6748036	26.1	2.80E-07	-0.13	0.56	0.62	0.40	0.78	0.52	0.24	5	39	65	eQTLs,C-HiC
rs7570118	24.9	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.61	7	17	22	eQTLs,C-HiC
rs6719701	23.1	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	1.77	6	5	2	eQTLs,C-HiC
rs2287062	23.0	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.38	1f	18	35	eQTLs,C-HiC
rs12995159	20.6	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	1.14	4	3	7	eQTLs,C-HiC
rs7355649	20.5	5.20E-07	-0.13	0.56	0.56	0.40	0.77	0.52	1.86	6	3	3	eQTLs,C-HiC
rs2018512	20.2	1.60E-06	-0.12	0.56	0.62	0.39	0.77	0.49	0.52	#N/A	11	23	eQTLs,C-HiC
rs728283	19.9	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	1.42	5	4	5	eQTLs,C-HiC
rs4622695	18.3	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.23	5	21	55	eQTLs,C-HiC
rs6742448	17.9	1.60E-06	-0.12	0.56	0.63	0.40	0.77	0.49	0.53	6	12	16	eQTLs,C-HiC
rs6721510	17.5	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	1.09	4	4	7	eQTLs,C-HiC
rs6709466	17.4	3.20E-07	-0.13	0.56	0.62	0.40	0.77	0.52	1.45	#N/A	5	2	eQTLs,C-HiC
rs61447318	16.5	#N/A	#N/A	0.36	#N/A	8	27	eQTLs,C-HiC
rs4284804	15.9	2.80E-07	-0.13	0.56	0.63	0.40	0.77	0.52	0.30	5	11	39	eQTLs,C-HiC
rs6706763	15.0	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.75	7	6	9	eQTLs,C-HiC
rs6744599	14.9	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.39	6	13	19	eQTLs,C-HiC
rs2110778	13.6	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.91	#N/A	5	1	eQTLs,C-HiC
rs12472807	13.0	3.90E-06	-0.12	0.56	0.63	0.39	0.77	0.49	0.50	5	7	10	eQTLs,C-HiC
rs712304	12.5	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.15	5	16	28	eQTLs,C-HiC
rs11683148	12.0	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.18	7	6	38	eQTLs,C-HiC
rs61424402	8.9	#N/A	#N/A	0.56	0.63	0.39	0.74	0.52	0.23	#N/A	11	23	eQTLs,C-HiC
rs12995602	8.9	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.33	4	7	9	eQTLs,C-HiC
rs6750891	8.9	2.80E-07	-0.13	0.12	4	27	44	eQTLs,C-HiC
rs6432118	8.2	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.30	7	3	19	eQTLs,C-HiC
rs9287720	7.5	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.34	7	3	14	eQTLs,C-HiC
rs6432115	6.8	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.57	5	3	2	eQTLs,C-HiC
rs10203664	6.0	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.43	7	2	7	eQTLs,C-HiC
rs6751075	5.9	2.80E-07	-0.13	0.56	0.63	0.40	0.77	0.52	0.11	5	14	37	eQTLs,C-HiC
rs10167676	5.9	#N/A	#N/A	0.56	0.62	0.40	0.77	0.52	0.35	#N/A	2	9	eQTLs,C-HiC
rs6432116	5.4	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.23	4	8	8	eQTLs,C-HiC
rs2110776	4.5	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.30	5	6	1	eQTLs,C-HiC
rs13003763	3.4	2.30E-07	-0.13	0.56	0.61	0.40	0.78	0.51	0.26	5	2	11	
rs175246	0.5	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.01	5	7	27	eQTLs,C-HiC
rs2287061	0.2	2.80E-07	-0.13	0.56	0.62	0.40	0.77	0.52	0.00	5	18	34	eQTLs,C-HiC

Table S8 Scoring of eQTL SNPs for rs77575195 LD block

RSID	Score	GWAS	Nerve - Tibial p-value	Nerve - Tibial NES	AMR	EAS	SAS	AFR	EUR	CADD	RegulomeDB	ENCODE Hits	ROADMAP Hits	GeneHancer
rs77575195	104.368		8.30E-09	0.16	0.1873	0.128	0.1207	0.0113	0.2773	2.372	4	7	35	#N/A
rs77767350	797.552		1.50E-08	0.16	0.1859	0.127	0.1227	0.0113	0.2744	7.121	4	29	78	eQTLs,C-HIC
rs76761022	369.936		1.20E-08	0.16	0.1859	0.128	0.1227	0.0333	0.2763	3.303	3a	54	53	eQTLs,C-HIC
rs113441467	332.674		1.00E-08	0.16	0.1859	0.128	0.1227	0.0121	0.2744	4.057	3a	18	57	eQTLs,C-HIC
rs1012580	265.85		3.60E-08	0.16	0.1873	0.124	0.1227	0.0113	0.2833	4.09	4	29	31	eQTLs,C-HIC
rs11903800	247.028		1.70E-06	0.13	0.2205	0.1429	0.136	0.3472	0.3002	2.988	5	26	50	eQTLs,C-HIC
rs75295272	232.416		1.00E-08	0.16	0.1859	0.128	0.1227	0.0113	0.2744	6.456	6	11	19	eQTLs,C-HIC
rs74979008	228.285		1.00E-08	0.16	0.1844	0.128	0.1227	0.0113	0.2744	3.265	5	12	53	eQTLs,C-HIC
rs17455388	218.018		9.60E-08	0.16	0.183	0.124	0.1237	0.0098	0.2694	3.254	5	32	29	eQTLs,C-HIC
rs111861993	166.14		4.50E-08	0.15	0.1873	0.124	0.1237	0.0113	0.2833	2.556	5	17	43	eQTLs,C-HIC
rs35516187	161.211		1.50E-08	0.16	0.183	0.128	0.1227	0.0113	0.2744	1.479	7	32	73	eQTLs,C-HIC
rs7603803	117.208		3.60E-08	0.16	2.392	5	9	35	eQTLs,C-HIC
rs114684284	85.6		#N/A	#N/A	0.1873	0.124	0.1237	0.0212	0.2833	2.675	6	3	24	eQTLs,C-HIC
rs78463923	66.56		1.00E-08	0.16	0.1844	0.128	0.1227	0.0113	0.2753	1.04	6	23	41	#N/A
rs7603290	64.752		#N/A	#N/A	0.8112	0.876	0.8763	0.9493	0.7167	1.349	#N/A	10	31	eQTLs,C-HIC
rs74799085	53.872		1.20E-08	0.16	0.1859	0.128	0.1227	0.0333	0.2773	0.518	5	50	52	eQTLs,C-HIC
rs149307648	45.856		7.10E-08	0.15	0.1873	0.123	0.1247	0.0113	0.2833	5.732	5	1	6	#N/A
rs77047837	35.786		1.70E-08	0.16	0.617	5	9	45	eQTLs,C-HIC
rs77909024	35.232		1.00E-08	0.16	0.1859	0.127	0.1227	0.0113	0.2744	2.202	7	3	8	eQTLs,C-HIC
rs78979433	28.458		1.00E-08	0.16	0.1844	0.128	0.1227	0.0113	0.2744	0.459	#N/A	23	32	eQTLs,C-HIC
rs764526	26.892		4.50E-08	0.15	0.1873	0.124	0.1237	0.0113	0.2833	0.249	4	40	62	eQTLs,C-HIC
rs115591000	22.219		5.90E-08	0.15	0.1873	0.124	0.1237	0.0113	0.2833	1.307	7	1	11	eQTLs,C-HIC
rs77793365	10.735		5.70E-08	0.15	0.1873	0.124	0.1237	0.0129	0.2833	2.147	5	3	2	#N/A
rs1546026	7.774		3.60E-08	0.16	0.1873	0.124	0.1237	0.0129	0.2833	3.887	5	1	1	#N/A
rs75419580	7.192		1.20E-07	0.15	0.1873	0.126	0.1227	0.0121	0.2833	0.058	3a	41	76	eQTLs,C-HIC
rs76923771	5.324		1.00E-08	0.16	0.1844	0.128	0.1227	0.0113	0.2744	0.004	4	24	52	eQTLs,C-HIC
rs78712844	2.496		1.00E-08	0.16	0.1844	0.128	0.1227	0.0113	0.2753	0.064	5	15	21	eQTLs,C-HIC
rs113291671	2.484		4.50E-08	0.15	0.036	5	17	45	eQTLs,C-HIC
rs2287059	0		1.00E-08	0.16	0.1844	0.128	0.1227	0.0113	0.2744	0	7	1	1	eQTLs,C-HIC

Table S9 IEU open GWAS project PheWAS returns for top SNPs of Geno2MP. Traits for rs138359527 (ODC G84R) are colored red.

SNP	ID	Sub category	Trait	Position	P	Beta	SE	N	CHR	EA	NEA	EAF
rs138359527	ubm-a-2869	Psychiatric / neurological	a2009s rh G Ins Ig&S cent ins area	10584626	0.000562	0.451	0.1307	7916	2	T	C	0.002551
rs138359527	ukb-a-109	NA	Non-cancer illness code self-reported: hiatus hernia	10584626	0.000626	0.012867	0.003762	337159	2	T	C	0.00239
rs138359527	ukb-a-544	NA	Diagnoses - main ICD10: K20 Oesophagitis	10584626	0.000675	0.008427	0.002479	337199	2	T	C	0.00239
rs138359527	ubm-a-2583	Psychiatric / neurological	NET100 1427	10584626	0.000813	0.5165	0.1542	7916	2	T	C	0.002551
rs138359527	ubm-a-1136	Psychiatric / neurological	NET25 0190	10584626	0.000955	-0.5066	0.1532	7916	2	T	C	0.002551
rs61754475	eqtl-a-ENSG00000172059	NA	ENSG00000172059	10268999	1.34E-12	-0.33828	0.047714	7967	2	T	C	0.015753
rs61754475	eqtl-a-ENSG00000115756	NA	ENSG00000115756	10268999	1.11E-06	0.232671	0.047759	7967	2	T	C	0.015753
rs61754475	eqtl-a-ENSG00000115750	NA	ENSG00000115750	10268999	0.000123	0.183471	0.047774	7218	2	T	C	0.015753
rs61754475	ubm-a-1286	Psychiatric / neurological	NET100 0130	10268999	0.000186	-0.337	0.0901	7916	2	T	C	0.00819
rs61754475	ubm-a-2101	Psychiatric / neurological	NET100 0945	10268999	0.000324	0.3252	0.0904	7916	2	T	C	0.00819
rs61754475	prot-a-1438	Immune system	Interferon omega-1	10268999	0.000372	-0.4582	0.1287	3301	2	T	C	0.01108
rs61754475	prot-a-2836	Immune system	Serine palmitoyltransferase 1	10268999	0.000589	-0.4425	0.1288	3301	2	T	C	0.01108
rs61754475	ubm-a-594	Psychiatric / neurological	IDP dMRI TBSS ISOVF Cerebral peduncle R	10268999	0.000617	-0.2696	0.0788	7916	2	T	C	0.00819
rs61754475	prot-a-170	Immune system	Arrestin domain-containing protein 3	10268999	0.000646	0.4392	0.1288	3301	2	T	C	0.01108
rs61754475	ukb-a-237	NA	Pack years of smoking PREVIEW ONLY	10268999	0.000805	-0.08429	0.025151	101726	2	T	C	0.007998
rs61754475	prot-a-2407	Immune system	Pregnancy-specific beta-1-glycoprotein 2	10268999	0.000832	-0.43	0.1288	3301	2	T	C	0.01108
rs61754475	ukb-a-238	NA	Pack years adult smoking as proportion of life span exposed to smoking PREVIEW ONLY	10268999	0.000839	-0.08428	0.025237	101726	2	T	C	0.007998
rs138712410	ukb-a-125	NA	Treatment/medication code: kapake tablet	10929938	5.16E-06	0.001417	0.000311	337159	2	A	G	0.004518
rs138712410	ubm-a-2724	Psychiatric / neurological	DKTAtlas lh laterorbitofrontal area	10929938	3.31E-05	-0.3377	0.0813	7916	2	A	G	0.004401
rs138712410	ubm-a-144	Psychiatric / neurological	IDP T1 FAST ROIs L cerebellum crus I	10929938	8.51E-05	-0.408	0.1037	7916	2	A	G	0.004401
rs138712410	ukb-d-1468_5	NA	Cereal type: Other (e.g. Cornflakes, Frosties)	10929938	0.000209	-0.02882	0.007774	299898	2	A	G	0.004586
rs138712410	ukb-d-1428_1	NA	Spread type: Butters/spreadable butter	10929938	0.000623	-0.02961	0.008654	360291	2	A	G	0.004595
rs138712410	ubm-a-2466	Psychiatric / neurological	NET100 1310	10929938	0.000851	0.4014	0.1202	7916	2	A	G	0.004401
rs138712410	ukb-a-165	NA	Treatment/medication code: nicorandil	10929938	0.000851	0.003519	0.001055	337159	2	A	G	0.004518
rs190385156	prot-a-2805	Immune system	Protein SPACA7	11273459	0.000155	0.3614	0.0956	3301	2	T	C	0.01831
rs190385156	ubm-a-3043	Psychiatric / neurological	DKTAtlas rh lingual thickness	11273459	0.000347	-0.2059	0.0576	7916	2	T	C	0.019227
rs190385156	ubm-a-605	Psychiatric / neurological	IDP dMRI TBSS ISOVF Superior corona radiata L	11273459	0.000501	-0.1753	0.0504	7916	2	T	C	0.019227
rs190385156	ukb-a-446	NA	Blood clot: DVT bronchitis emphysema asthma rhinitis eczema allergy diagnosed by doctor: Asthma	11273459	0.000589	0.01055	0.00307	336782	2	T	C	0.017863
rs190385156	ubm-a-3086	Psychiatric / neurological	a2009s rh G oc-temp med-Lingual thickness	11273459	0.000661	-0.1959	0.0575	7916	2	T	C	0.019227
rs190385156	ubm-a-1854	Psychiatric / neurological	NET100 0698	11273459	0.000676	0.2042	0.06	7916	2	T	C	0.019227
rs190385156	prot-a-1778	Immune system	Low-density lipoprotein receptor-related protein 1B	11273459	0.000813	0.3202	0.0956	3301	2	T	C	0.01831
rs190385156	finn-a-L12_INFECT_SKIN_NAS	NA	Other and unspecified local infections of skin and subcutaneous tissue	11133333	0.000906	-1.264	0.3809		2	C	T	0.98903
rs143556651	ubm-a-3005	Psychiatric / neurological	a2009s lh S circular insula ant thickness	10904524	7.76E-05	0.6	0.1518	7916	2	T	C	0.002499
rs143556651	ukb-b-13231	NA	Place of birth in UK - east coordinate	10904524	0.0001	0.075512	0.019412	434576	2	T	C	0.002399
rs143556651	ukb-a-157	NA	Treatment/medication code: liothyronine	10904524	0.000111	0.001581	0.000409	337159	2	T	C	0.002347
rs143556651	ukb-a-469	NA	Pain type(s) experienced in last month: Headache	10904524	0.000205	0.037803	0.010181	336650	2	T	C	0.002347
rs143556651	ubm-a-2942	Psychiatric / neurological	DKTAtlas lh parsopercularis thickness	10904524	0.000219	0.5334	0.1443	7916	2	T	C	0.002499
rs143556651	ubm-a-2970	Psychiatric / neurological	a2009s lh G front inf-Opercular thickness	10904524	0.000234	0.5387	0.1465	7916	2	T	C	0.002499
rs143556651	ubm-a-2308	Psychiatric / neurological	NET100 1152	10904524	0.000245	-0.586	0.1599	7916	2	T	C	0.002499
rs143556651	ubm-a-1257	Psychiatric / neurological	NET100 0101	10904524	0.000363	-0.5822	0.1632	7916	2	T	C	0.002499
rs143556651	ukb-a-391	NA	Average weekly intake of other alcoholic drinks	10904524	0.000543	0.033674	0.009736	79291	2	T	C	0.002347
rs143556651	ubm-a-3129	Psychiatric / neurological	a2009s rh S parieto occipital thickness	10904524	0.000724	0.4971	0.1469	7916	2	T	C	0.002499
rs143556651	ubm-a-2001	Psychiatric / neurological	NET100 0845	10904524	0.000891	-0.5454	0.164	7916	2	T	C	0.002499
rs143556651	ubm-a-3055	Psychiatric / neurological	DKTAtlas rh precuneus thickness	10904524	0.000891	0.4838	0.1457	7916	2	T	C	0.002499

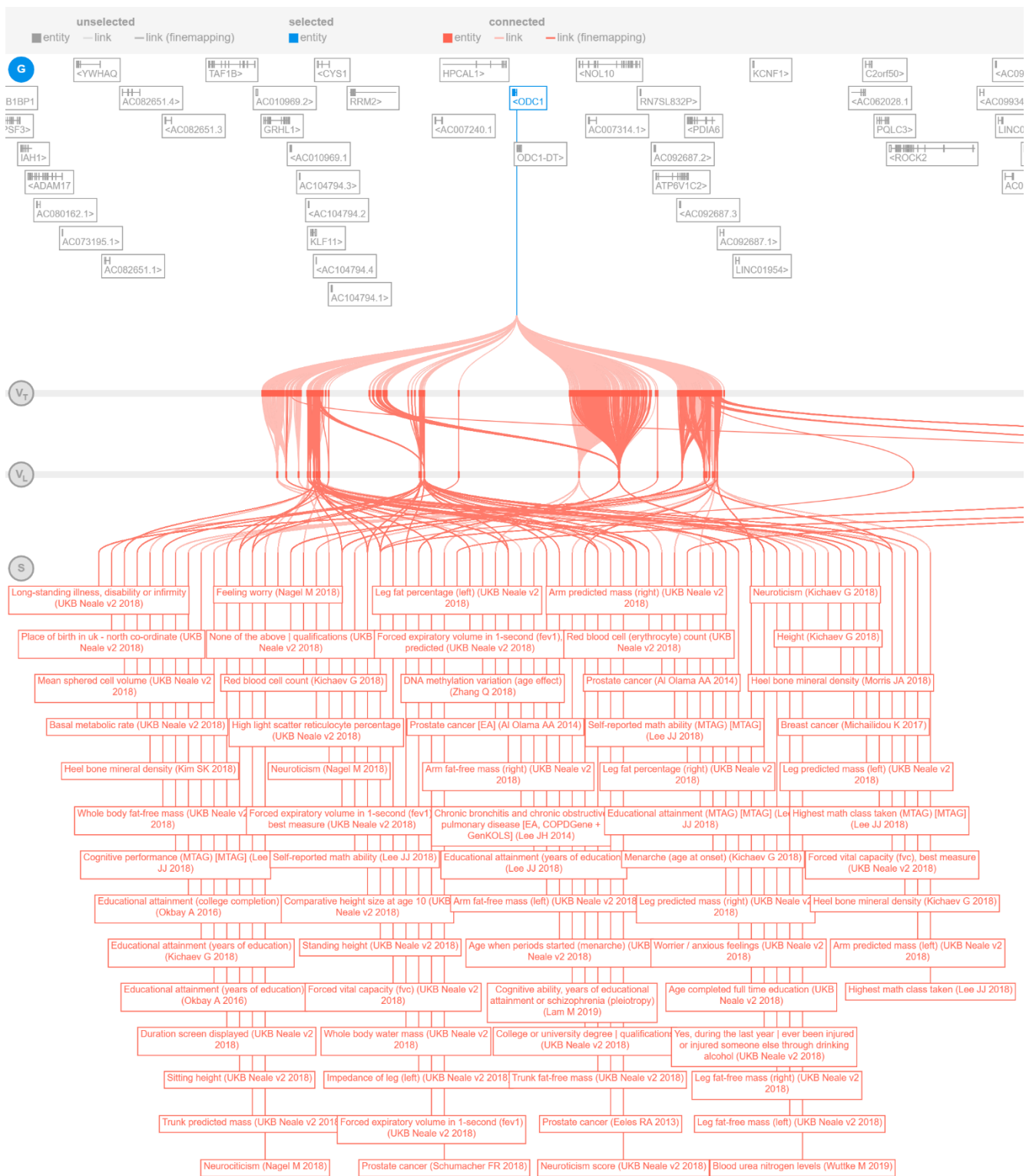


Figure S1 Phenotypes associated with *ODC1* genomic region from Open Targets Genetics.

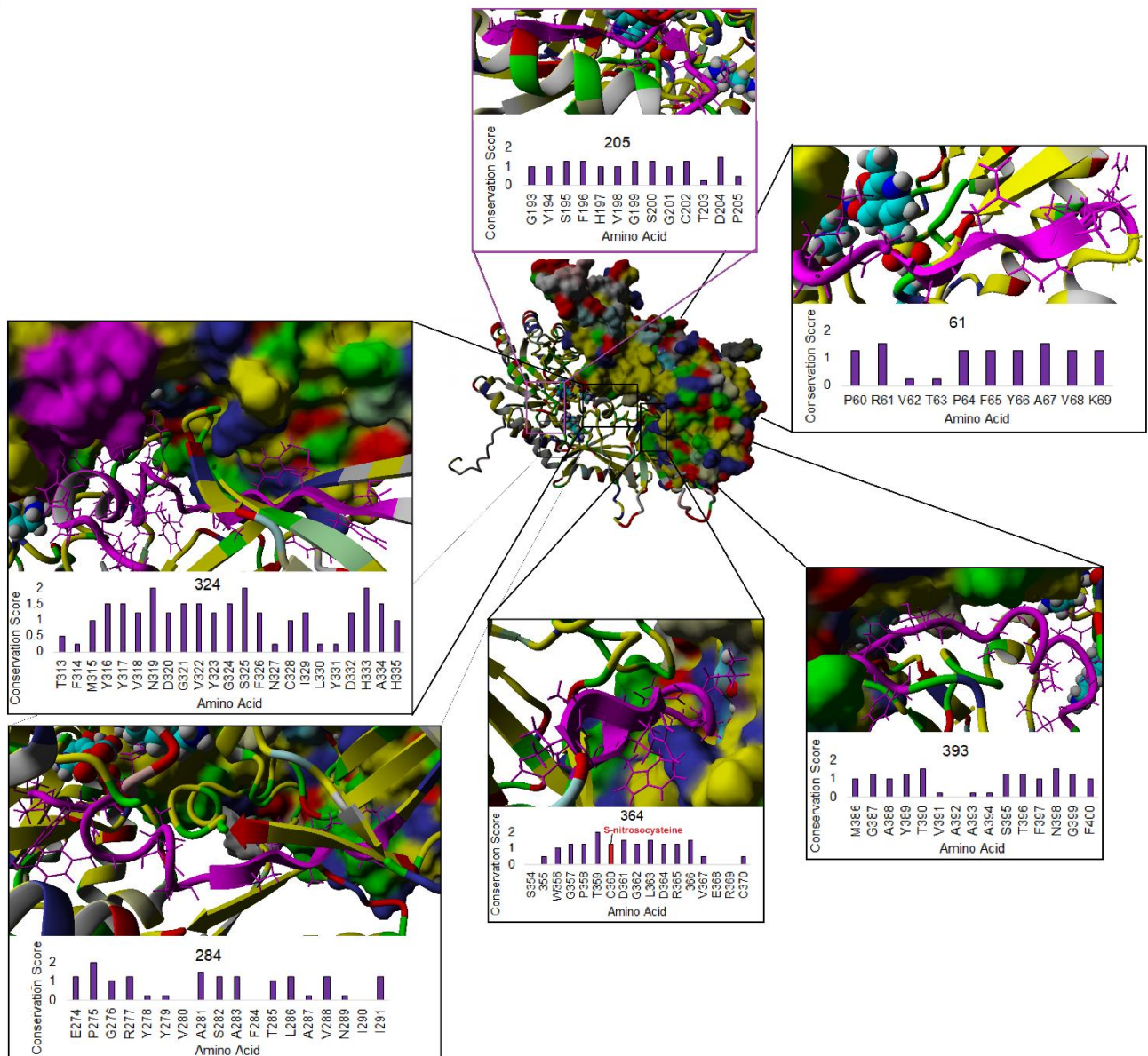


Figure S2 Sequence and structural evolution of ODC. Structure of ODC as a dimer (one unit shown with surface plot and other as secondary structure with amino acids colored based on ConSurf mapping (yellow- conserved hydrophobic, green- conserved hydrophilic, red- conserved acidic, blue- conserved basic, gray- not conserved). The six top motifs are shown with zoomed in view, colored magenta, and conservation shown below.

Accession	Species	Sequence	Position
ODCI_NM_001287189.1	Homo sapiens	QNFDFPFVEEEDASTLFSVCAMESGMRHFAA	450
ODCI_NM_013614.2	Mus musculus	QSHGFPFVEEEDDG-LMSSCAQESGMDRHPAA	459
ODCI_NM_001302083.1	Rattus norvegicus	QSHGFPFVEEEDVVG-LMSSCAQESGMDRHPAA	459
220 Species conserved in >70%			
ODCI_NM_131801.2	Danio rerio	RAQGIPLALPEKFSAMVFSHCGRESSLDMVPAK	459
ODCI_XM_023834734.1	Paramormyrops kingsleyae	CAQGLPDALEEQ--CSNATSCGRESSLDMVPAK	455
ODCI_XM_001005441.1	Xenopus tropicalis	REHGILFVPEL--SAHRVSCAQESGIELAFTI	458
ODCI_XM_014152087.1	Salmo salar	CAQGMPTTVEE--ACVFSACGRESSLDMVPAK	454
ODCI_XM_018695117.1	Latex calcarifer	CSQGMF-APVEESCLVEFACGRESSLDMPTFK	458
ODCI_XM_015969159.1	Nothobranchius furzeri	CSQGLP-APAEESFEVACGRESSLDMPTFK	457
ODCI_XM_007257318.3	Astyanax mexicanus	HAQGMFALT-EQCENMESNCGRESSLDMPTFK	458
ODCI_XM_01480632.2	Dryzius latipes	FAQVLPFLFEGSQEIPACCGRSTFDMPAK	455
ODCI_XM_023394794.1	Seriola lalandi dorsalis	RSQGMF-APAVESGFEVACGRESSLDMPTFK	455
ODCI_XM_023274288.1	Amphiprion ocellaris	CSQGMF-APAEESCLVEFACGROSSMMDATKS	458
ODCI_XM_022750707.1	Seriola dumerili	RSQGMF-APAEESGFEVACCGRESSLDMPTFK	455
ODCI_XM_021574142.1	Oncorhynchus mykiss	CAQGMPTTVEE--ACVFSACGRESSLDMVPAK	454
ODCI_XM_020919597.1	Boleophthalmus pectinirostris	CSQGLP--TDELVEFACGRESSLDMPTFK	455
ODCI_XM_020641608.1	Labrus bergylla	CSQGLP-APAEESLVEFACGRESSLDMPTFK	458
ODCI_XM_020608704.1	Monopterus albus	CSQGMF-TKEDCFDMFVSCGESSLDMPTKS	458
ODCI_XM_020487858.1	Oncorhynchus kisutch	CAQGMPTTVEE--ACVFSACGRESSLDMVPAK	454
ODCI_XM_019894148.1	Hippocampus comes	CAQGLP-VPA-ESCMVFACGERRLEIFSSQARV	454
ODCI_XM_018734541.1	Scleropages formosus	RTQGFPLL-EESCPMFACGRESSLDMPTFK	457
ODCI_XM_017698008.1	Pygocentrus nattereri	HAQGMFALA-EQCENMESHCGRESSLDMPTFK	458
ODCI_XM_017476167.1	Ictalurus punctatus	HAQGMFALV-EQSPNMFHCGCGSTLDMPTFK	455
ODCI_XM_017411702.1	Kryptolebias marmoratus	CSQGLP-APAEESLVEFACGROSSMMDPTFK	457
ODCI_XM_016242144.1	Sinocyclocheilus grahami	HAQGVPLA-AEQCALDFEACGRESSLDMPTFK	457
ODCI_XM_015384865.1	Cyprinodon variegatus	CSEGLP-APAEESALDFEACGRESSLDMPTFK	457
ODCI_XM_015043133.1	Poecilia latipinna	CSQGLP-APVEESLDFACGRESSLDMPTFK	457
ODCI_XM_014982742.1	Poecilia mexicana	CSQGLP-APVEESLDFACGRESSLDMPTFK	457
ODCI_XM_012881856.2	Fundulus heteroclitus	CSQGLP-TFA-ESSLDFACGRESSLDMPTFK	456
ODCI_XM_012823489.1	Clupea harengus	HAQGMFAPA-EELSQMFSGRESSLDMPTFK	457
ODCI_XM_010892375.3	Esox lucius	RAQGMPTVEE--TSVFSACGESSLDMVPAK	456
ODCI_XM_010794674.1	Motoclenia coriiceps	CSQGMF-APAEESLVEFACGRESSLDMPTFK	456
ODCI_XM_010736389.2	Larimichthys crocea	CSQGMF-APAEESLVEFACGRESSLDMPTFK	456
ODCI_XM_008399661.2	Poecilia reticulata	CSQGLP-APAEESLDFEACGRESSLDMPTFK	457
ODCI_XM_008317949.2	Cynoglossus semilaevis	RLQGLP-APLDDRLDVSQCGEGLEMTFK	458
ODCI_XM_008304940.1	Stegastes partitus	CSQGMF-APAEESLVEFACGRESSLDMPTFK	458
ODCI_XM_007575237.2	Poecilia formosa	CSQGLP-APVEESLDFEACGRESSLDMPTFK	457
ODCI_XM_006626044.2	Lepisosteus oculatus	QEQGLIQVVEELCPSTMEICCAEESGIELFESS	459
ODCI_XM_00593952.2	Haplochromis burtoni	CSQGLP-APAEESLVEFACGRESSLDMPTFK	458
ODCI_XM_005799115.3	Xiphophorus maculatus	CSQGLP-APVEESLDFEACGRESSLDMPTFK	457
ODCI_XM_005746470.1	Fundamillia nyererei	CSQGLP-APAEESLVEFACGRESSLDMPTFK	458
ODCI_XM_004539891.2	Maylandia zebra	CSQGLP-APAEESLVEFACGRESSLDMPTFK	458
ODCI_XM_003962281.2	Takifugu rubripes	SQGMPLFAE--ESSLEAVCGRESSLDMPTKS	450
ODCI_XM_003445449.4	Oreochromis niloticus	CSQGLP-APAEESLVEFACGRESSLDMPTFK	458

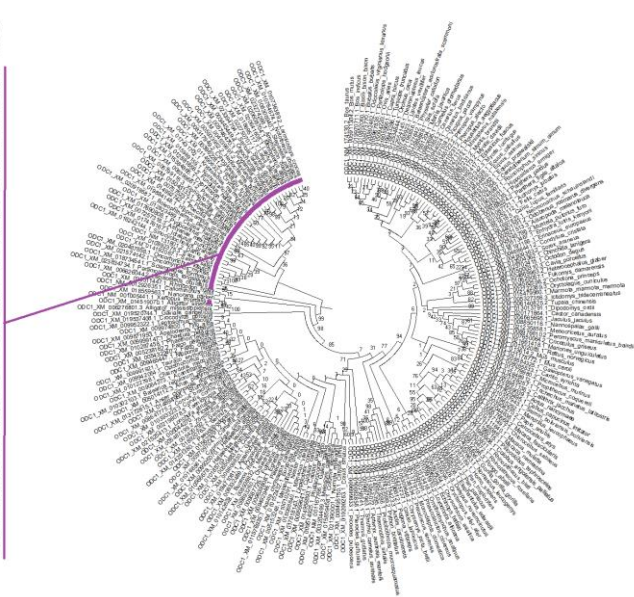


Figure S3 ODC lipidation site. The predicted farnesylation site falls at Cys 354, which is conserved (red) in all but a handful of fish and invertebrate genomes (magenta). The phylogenetic tree shows the bootstrap consensus of 1000 runs, listing the clustering of trees at each node. The high conservation of flanking amino acids (yellow) contribute to the 12.669 score by GPS-Lipid 1.0 for non-consensus S-Farnesylation and a 3.64 score for non-consensus S-Geranylgeranylation.

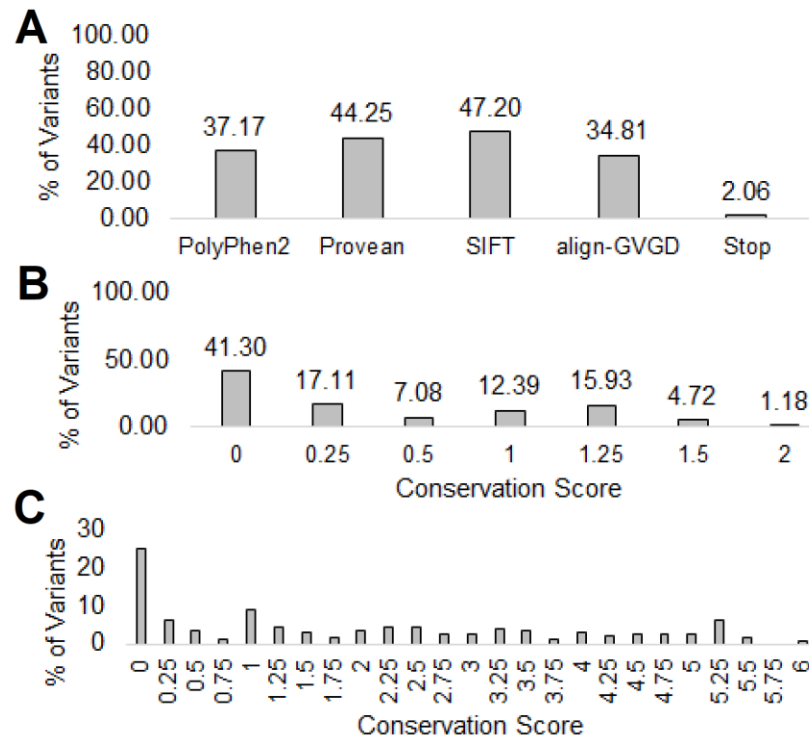


Figure S4 Human variation in *ODC1*. **A-C)** A total of 338 variants seen for *ODC1* in gnomAD, TOPMed (BRAVO), COSMIC, and ClinVar shown for those predicted damaging in several publicly available tools (**A**), our conservation scores (**B**), or the combined metrics of all tools (**C**).

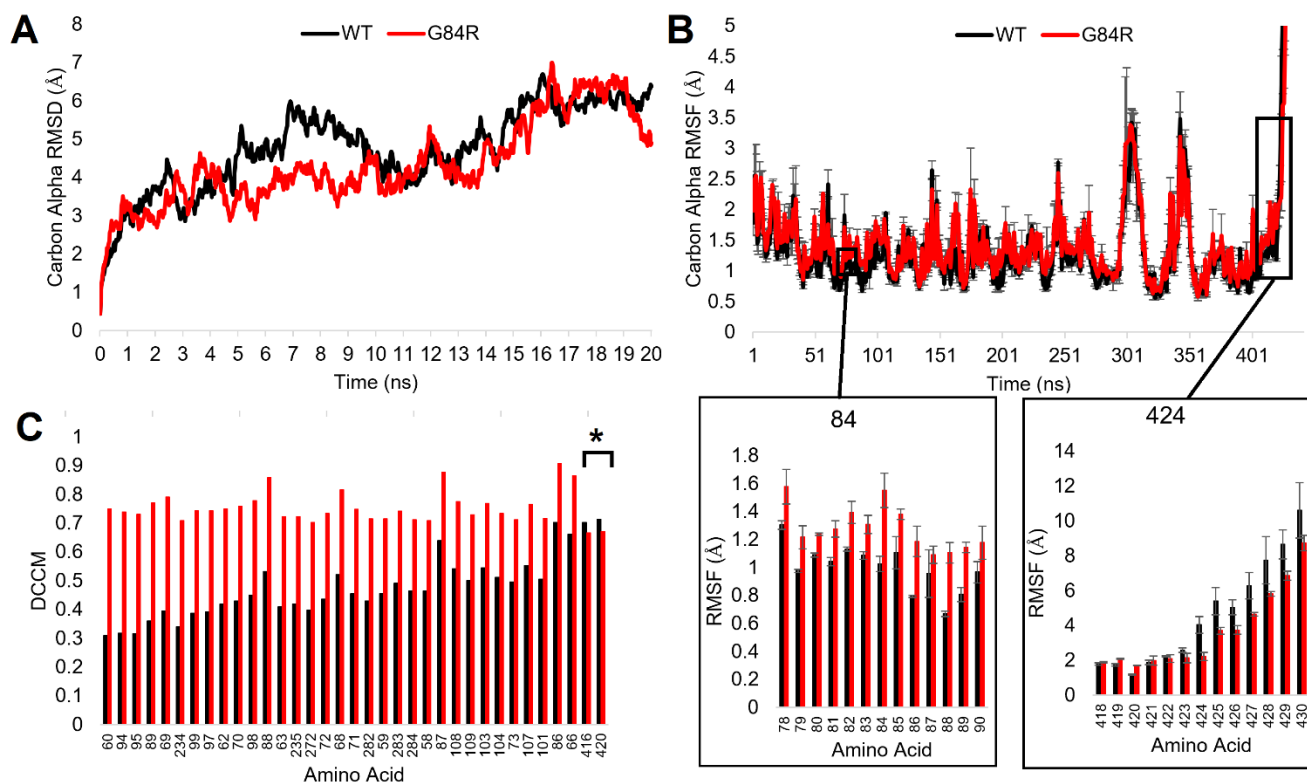


Figure S5 Molecular dynamic simulations (mds) for ODC and ODC G84R. **A)** Overall protein movement (root mean square deviation, RMSD) over 20 nanoseconds showing that both wild type (WT, black) and G84R (red) proteins reach relative equilibrium over the simulation. **B)** Amino acid movement shown as root mean squared fluctuation (RMSF) for WT (black) or G84R (red). Shown below is a zoom in of amino acid 84 and 424 regions. Error bars represent the standard error of the mean of the two ODC units of the dimer structure. **C)** Amino acid correlations throughout the 20 nanoseconds of simulation (dynamics cross-correlation matrix information, DCCM) for amino acids with WT amino acid 84 (black) or G84R (red). Shown are those sites with at least one of the two >0.7 correlation and are in order of largest differences. Only two amino acids show increased stability in wild type (*), while G84R is higher for 33 amino acids by 0.2 or more.

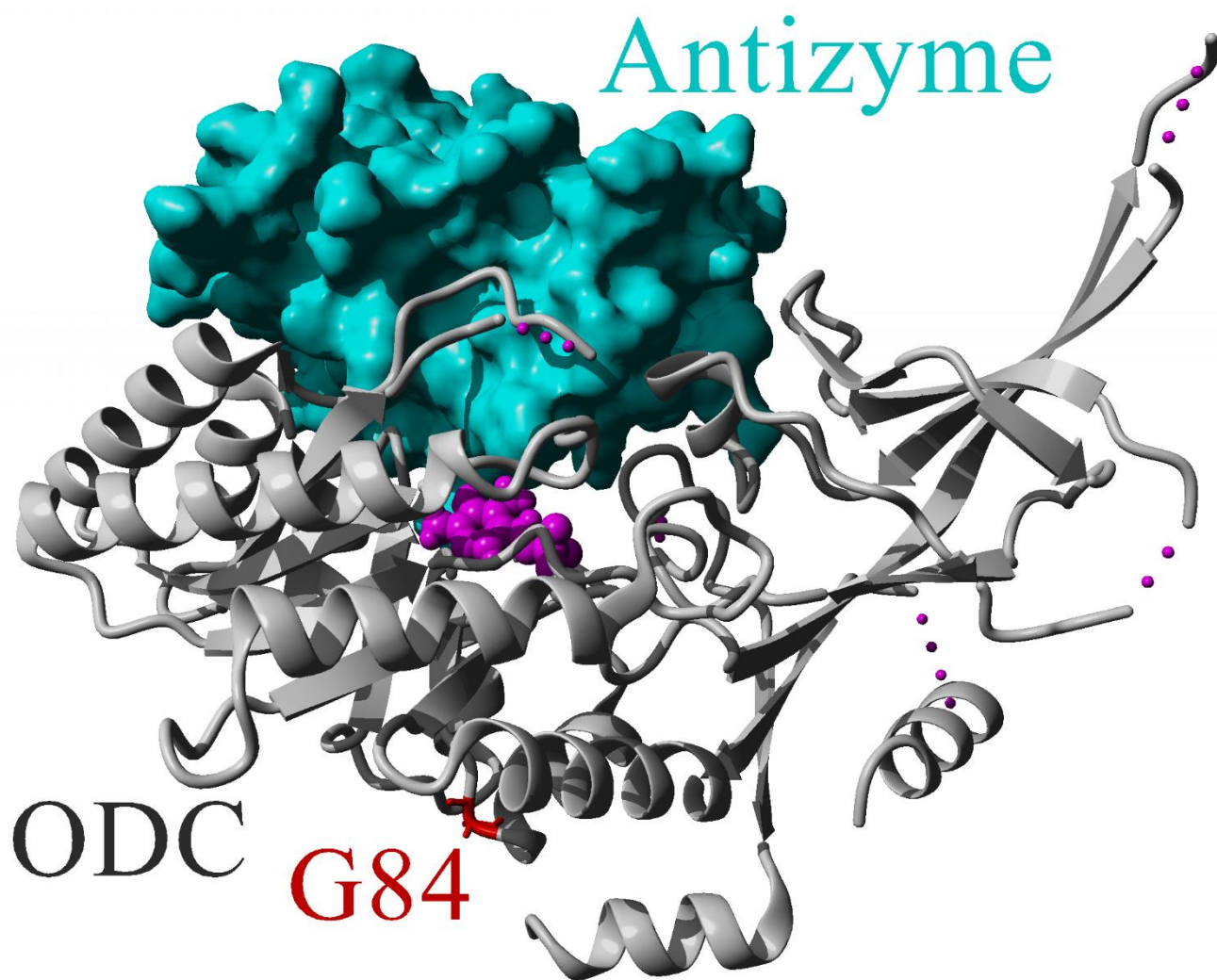


Figure S6 ODC G84 location relative to antizyme binding. The PDB file 4ZGY of ODC (gray) interacting with antizyme (cyan) with the G84 marked in red.

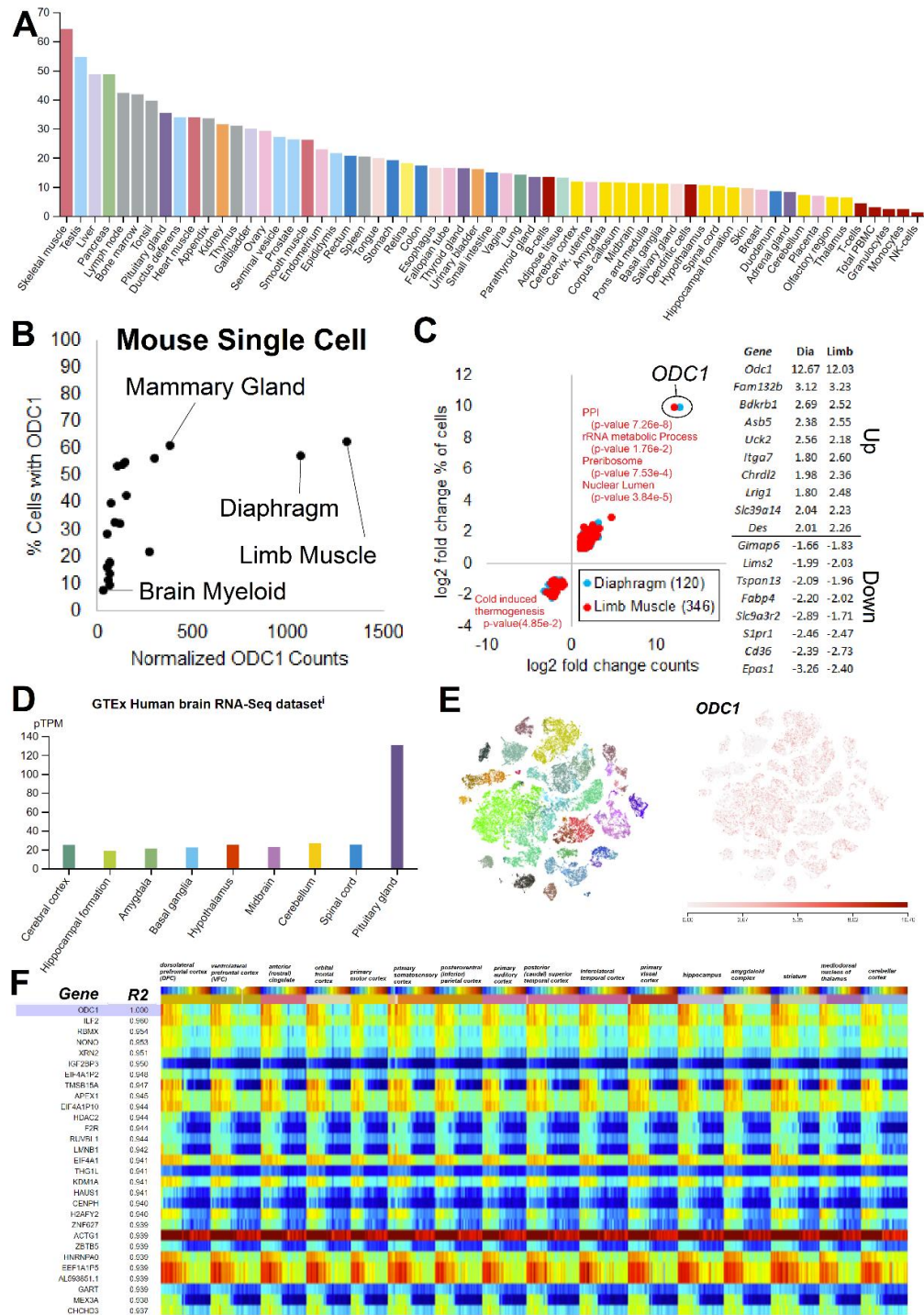


Figure S7 Expression analysis of *ODC1*. **A)** Expression of *ODC1* from Human Protein Atlas. **B)** Dissection of mouse single cell datasets for *ODC1* showing the average normalized counts per cell (x-axis) and the percent of cells *ODC1* is expressed in (y-axis). **C)** Clustering of genes following single cell levels of *ODC1* in diaphragm (blue) and limb muscle (red), identifying overlapping genes (right) and GO enrichment for positive or negative *ODC1* expressing cells (red text). **D)** Expression of *ODC1* in human brain regions from GTEx. **E)** *ODC1* single cell expression from Allen Brain Atlas Human multiple cortical areas- SMART-seq. On the left is coloring based on cell grouping of the 49,495 nuclei and on the right is expression of *ODC1* (red) based on the scale below. **F)** *ODC1* expression from human samples of Allen Brain Atlas Developmental Transcriptome over various ages and brain regions with highly correlated genes to *ODC1* over all brain regions shown below.

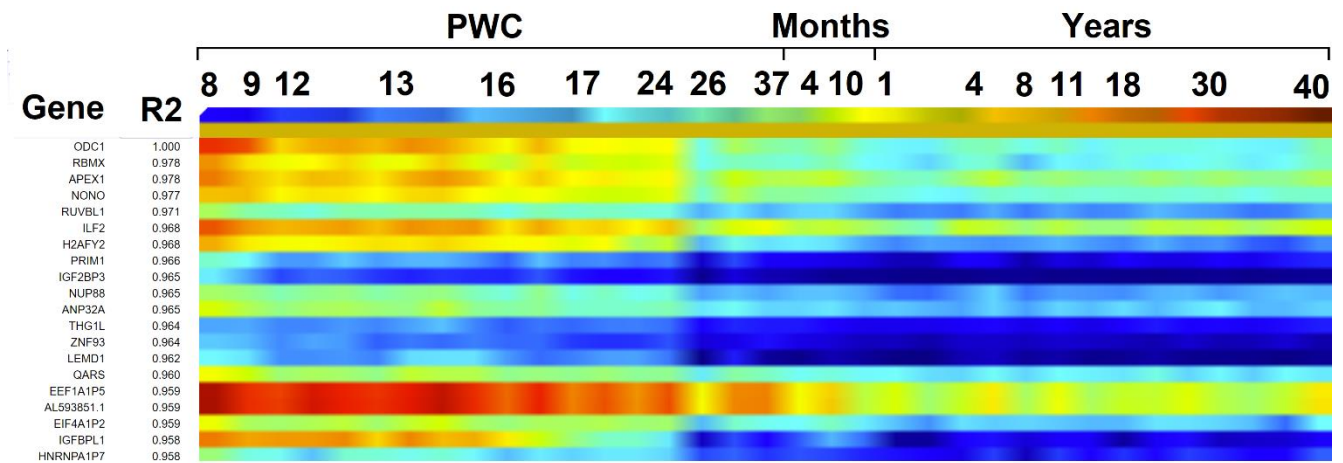


Figure S8 Brain developmental time analysis of *ODC1* for dorsolateral prefrontal cortex (DFC). *ODC1* expression from human samples of Allen Brain Atlas Developmental Transcriptome over various ages (left to right increase) for dorsolateral prefrontal cortex, with highly correlated genes to *ODC1* within this tissue shown below.

Cellular Nitrogen compound metabolic (96, FDR 2.7e-16)
nucleic acid metabolic process (83, FDR 3.8 e-16)
Gene expression (79, FDR 1.8 e-15)

nucleic acid binding (74, FDR 2.9e-15)

Nucleus (111, FDR 2.0e-16)

Metabolism of RNA (28, FDR 4.3e-10)

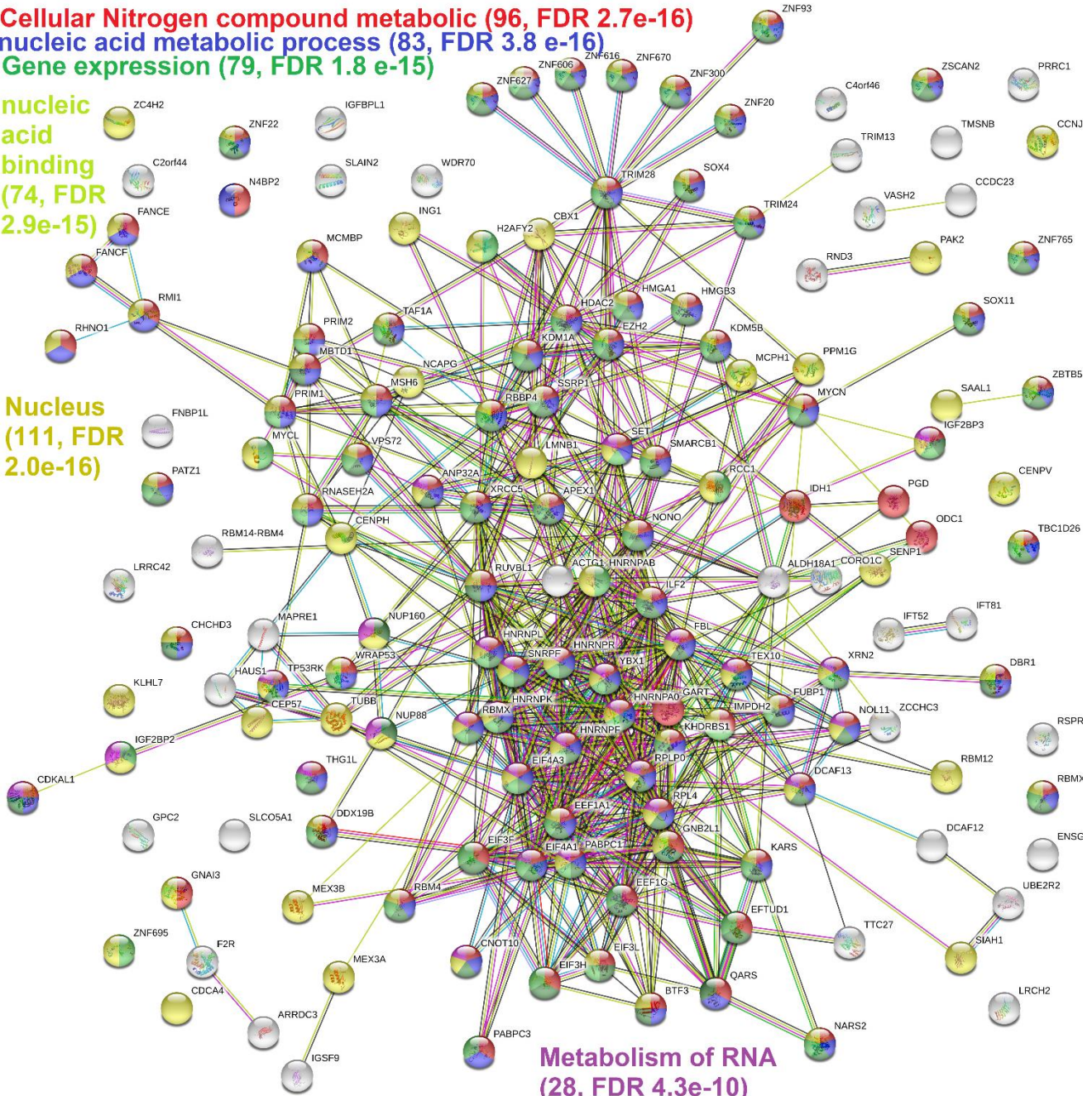
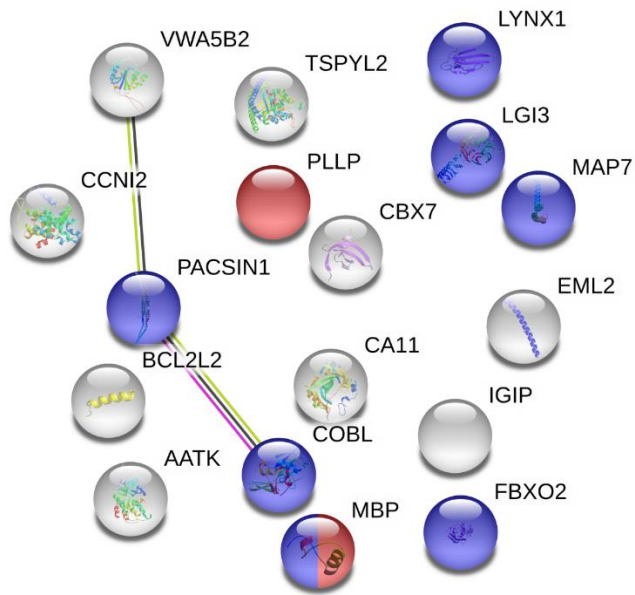


Figure S9 *ODC1* brain positive correlated gene network. 213 genes with greater than 0.9 R² correlation in expression over all brain regions of the Allen Brain Atlas Developmental Transcriptome shown as a STRING protein network with significantly elevated gene ontology terms labeled in various colors.



structural constituent of myelin sheath
 (2; FDR 0.0034)
 neuron projection (7; FDR 0.0036)

Figure S10 *ODC1* brain negative correlated gene network. 17 genes with less than $-0.9 R^2$ correlation in expression over all brain regions of the Allen Brain Atlas Developmental Transcriptome shown as a STRING protein network with significantly elevated gene ontology terms labeled in various colors.

ClinVar Phenotypes for 0.9 R² *ODC1* correlated brain genes

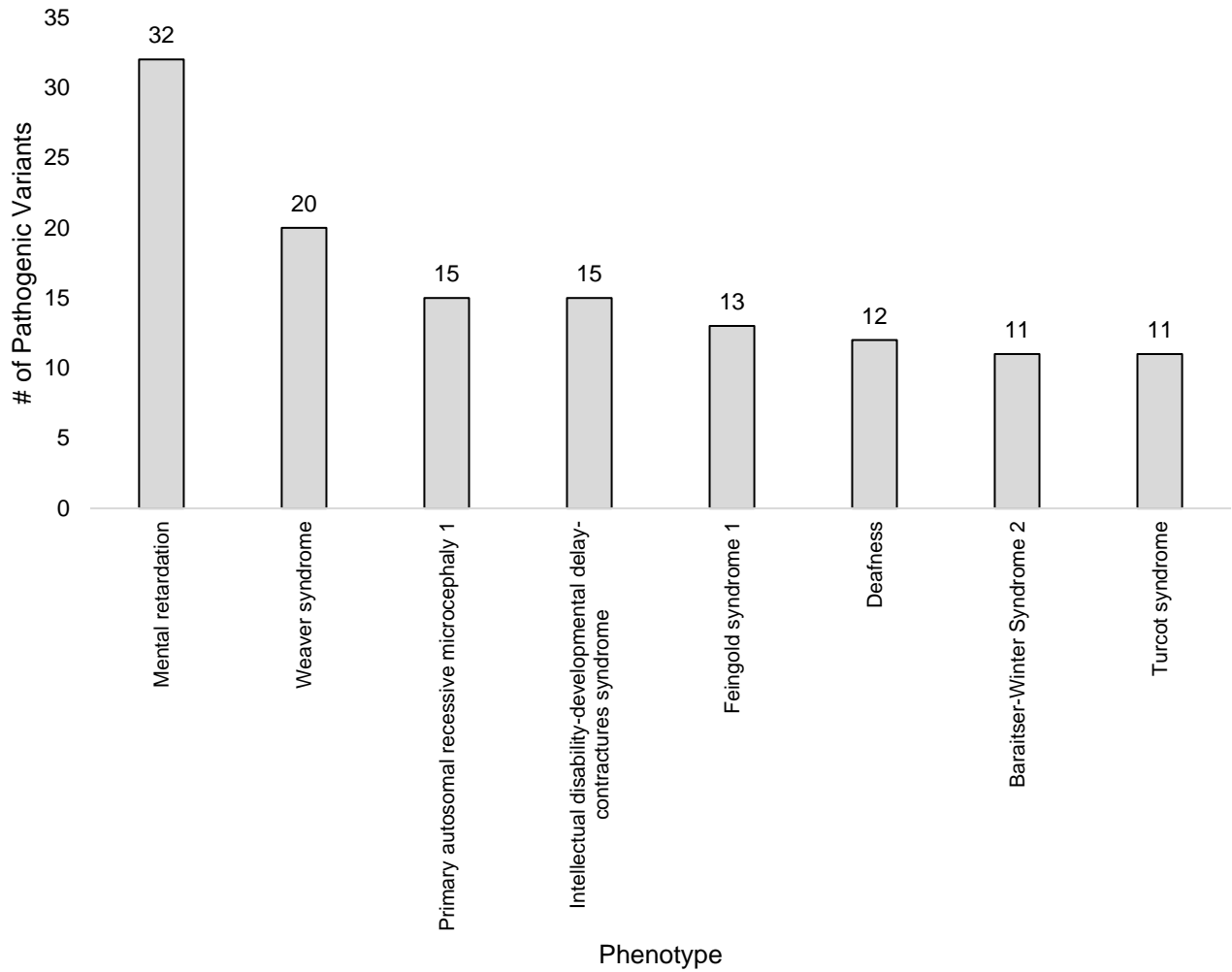


Figure S11 ClinVar of 0.9 R² *ODC1* correlated genes from Allen Brain Atlas Developmental Transcriptome. Genes from Figure S8 were extracted from ClinVar pathogenic annotations, pulling clinical annotations. Eight different neurological phenotypes are reported with the number of variants linked to each term shown.

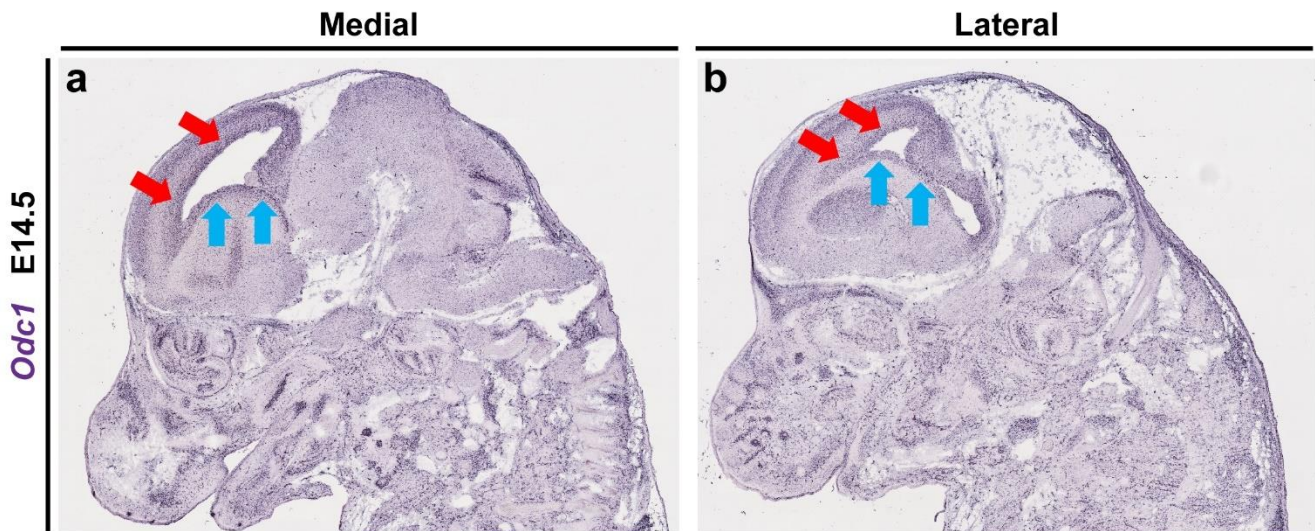


Figure S12 *Odc1* expression is elevated in embryonic telencephalic progenitor domains of mouse brain development. Embryonic day (E)14.5 sagittal sections acquired from Genepaint showing mRNA expression of the *Odc1* transcript in mice. While expression is enriched in different brain regions (darker signal), the progenitor domains of the telencephalon have consistent elevated mRNA levels in both medial and lateral tissue sections (a, b). Arrows denote different progenitor domains that give rise to Glutamatergic neurons and cortical glia (Red) and GABAergic neurons (Blue).

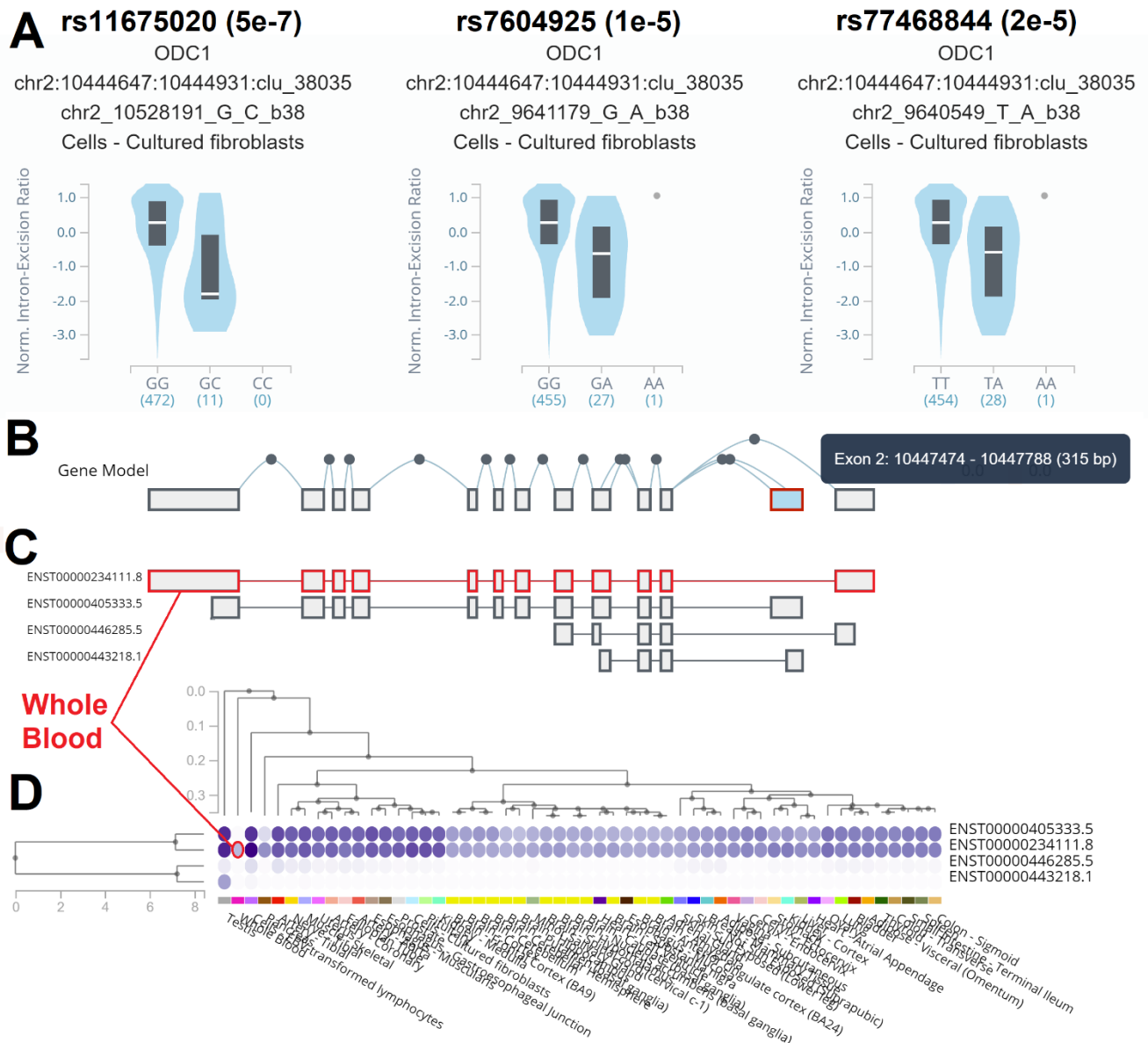


Figure S13 Splicing QTL for *ODC1*. **A**) Violin plots for three SNPs (with p-value) for exon1/exon2 to exon 3 splicing QTL of *ODC1* from GTEx v8. **B**) Splicing site changes with the red and blue exon changed in panel A. **C**) Known isoforms for *ODC1* with the isoform of panel A shown in red. **D**) Expression heatmap for multiple tissues (x-axis) of four isoforms of *ODC1* with whole blood utilizing the isoform of panel A sQTL.

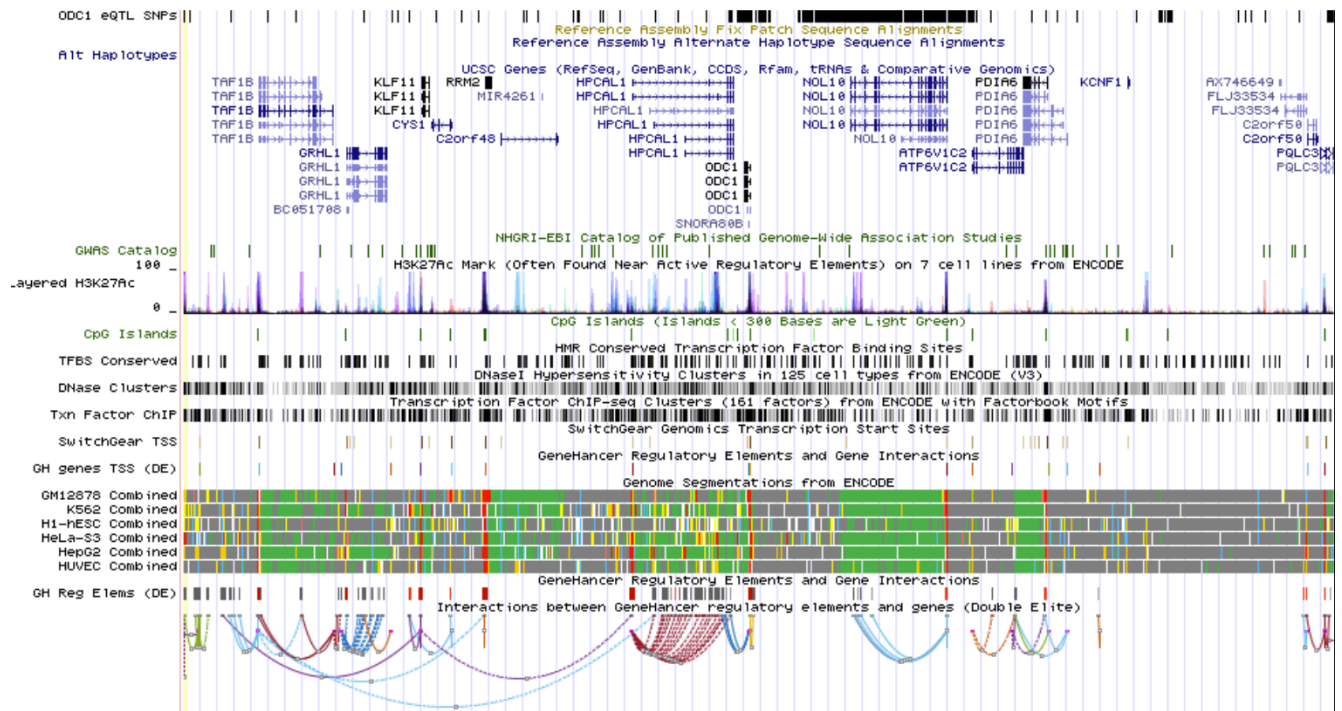


Figure S14 Genomic regions for eQTLs connected to *ODC1* levels. Shown on the top are all of the eQTL LD SNPs. This is followed by genome tracts for genes, GWAS linked SNPs, H2K27Ac data, CpG islands, conserved transcription factor binding sites, DNaseI hypersensitivity, ENCODE ChIP-Seq, SwitchGear start sites, GeneHancer locations, genome annotated segmentation for ENCODE cell lines, and GeneHancer looping data. These tracts were extracted for integrative analysis of each *ODC1* associated eQTL.

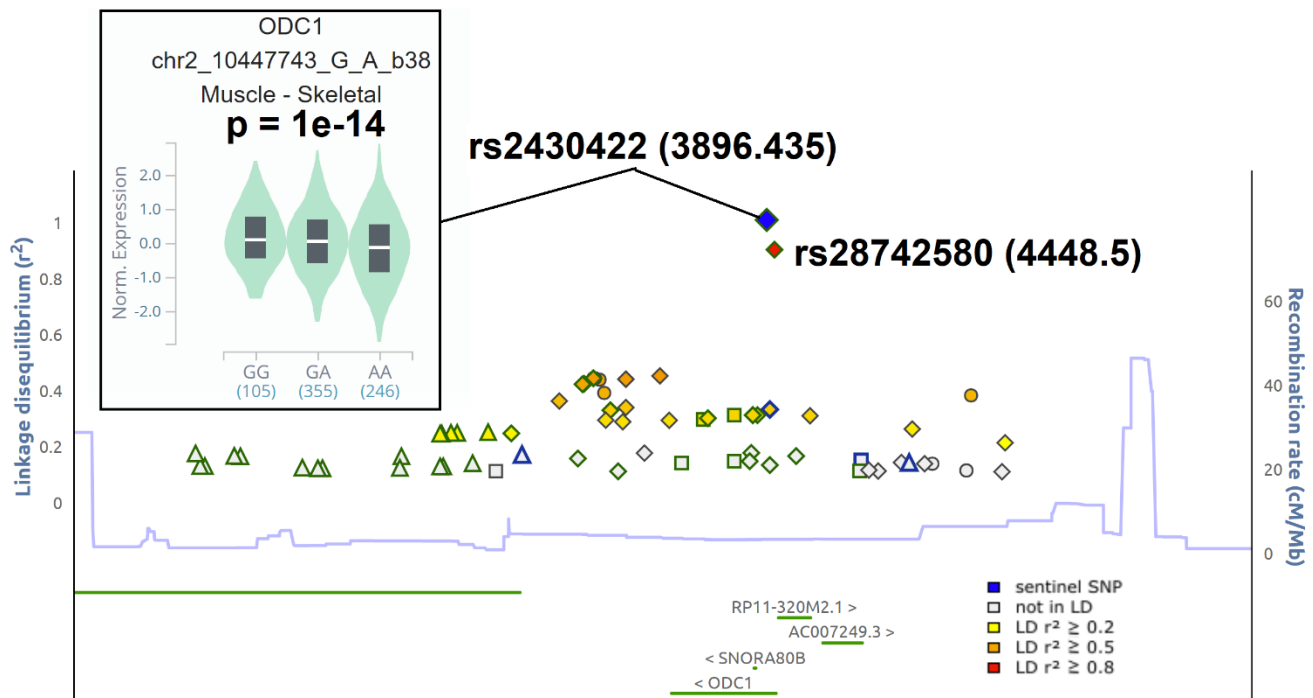


Figure S15 rs2430422 Linkage disequilibrium SNPs. rs2430422 is marked in blue with all LD SNPs with $>0.8R^2$ SNP (rs28742580) in red. Next to each SNP is the annotated score and called out is shown the violin plot for eQTLs of rs2430422 for skeletal muscle. Shown on the bottom is the map of genes.

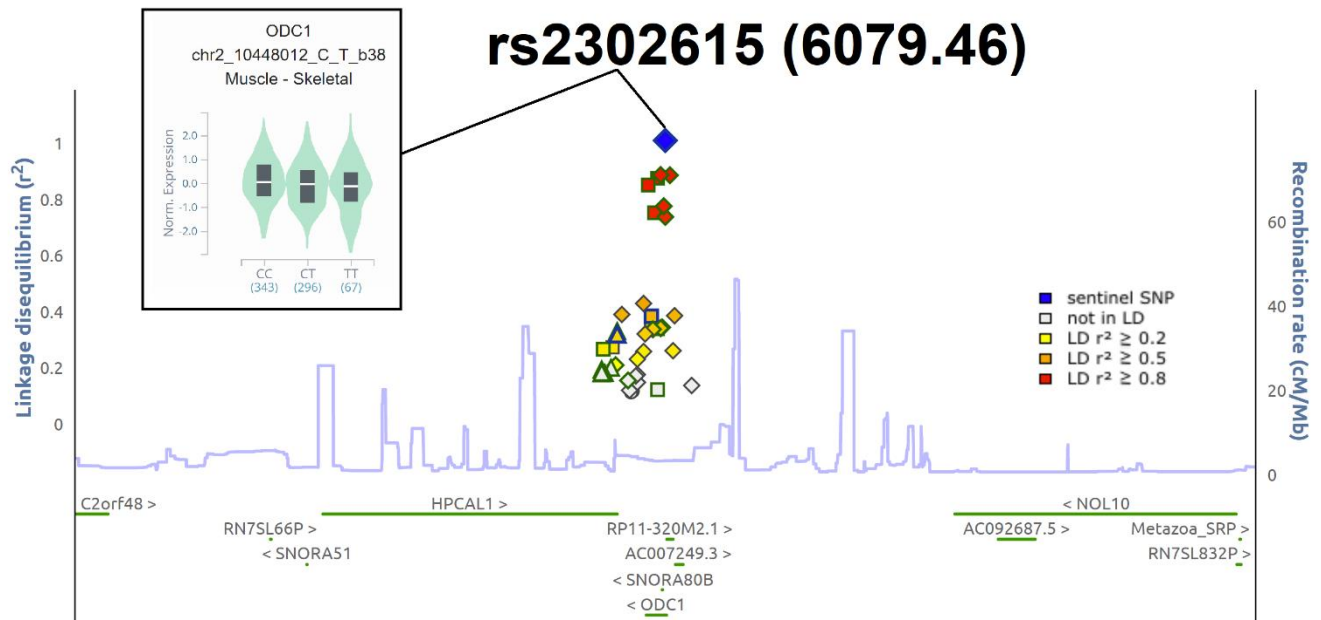


Figure S16 rs2302615 Linkage disequilibrium SNPs. rs2302615 is marked in blue with all LD SNPs with $>0.8R^2$ SNP in red. Next to rs2302615 is the annotated score and called out is shown the violin plot for eQTLs of rs2302615 for skeletal muscle. Shown on the bottom is the map of genes.

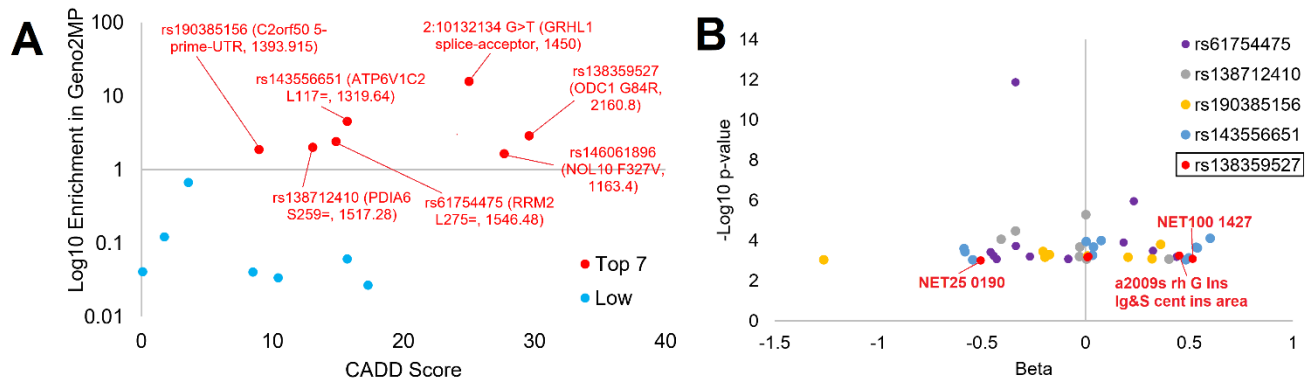


Figure S17 Enriched SNPs with high impact from Geno2MP in *ODC1* associated genomic region. **A)** The seven highest ranked Geno2MP SNPs (red) within the *ODC1* eQTL linked genomic region showing CADD score (x-axis) and the Log10 enrichment (y-axis), observed frequency within Geno2MP vs expected frequency based on gnomAD. Each SNP is labeled with rsID, gene, variant annotation, and combined score. Shown in blue are seven SNPs of low enrichment with at least 10 occurrences within Geno2MP. **B)** PheWAS returns for Beta (x-axis) and $-\log_{10}$ p-value (y-axis) for top SNPs in panel A. Details of traits are shown in Table S9. Neurological traits connected to rs138359527 are labeled in red.