SUPPLEMENTAL FILE FOR: A comparative medical genomics approach may facilitate the interpretation of rare missense variation

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Supplemental Table 1. Non-human animal missense variants (n=339) extracted from OMIA and studied in humans. See text for details.

Gene Symbol	Chr	Genomic Position (hg19)	Ref Allele	Alt Allele	Classification of Orthologous Human Variant in ClinVar	gnomAD Allele Frequency (v2.1.1)[1]		phyloP Score[2]	REVEL Score[3]	AlphaMissense Score[4]
						Genome seq	Exome seq			
ABCA1	9	107646745	C	T	ABSENT	0	0	0.935	0.911	0.9782
ABCA12	2	215815679	A	G	ABSENT	0	0	1.199	0.949	0.9935
ACSL5	10	114168275	C	G	ABSENT	0	0	0.927	0.195	0.1602
ACVR1	2	158630626	C	T	LP/P	0	0	0.935	0.948	0.9581
ADAMTS10	19	8654389	C	T	ABSENT	0	4E-06	0.852	0.859	0.9977
ADAMTS10	19	8661222	C	T	ABSENT	0	0	0.935	0.785	0.9425
ADAMTS17	15	100673442	C	T	ABSENT	0	0	0.847	0.732	0.9738
ADAMTS2	5	178552032	C	T	VUS	0	1.2E-05	0.852	0.275	0.1486
ADAMTSL2	9	136406102	C	T	LP/P	0	0	0.852	0.467	0.5975
ADAMTSL4	1	150530585	G	A	ABSENT	0	7.6E-05	0.154	0.033	0.0752
AGTPBP1	9	88201870	C	G	ABSENT	0	0	0.935	0.688	0.999
AGXT	2	241810860	G	A	LP/P	0	0	0.887	0.945	0.975
AGXT	2	241808659	G	A	ABSENT	0	0	0.898	0.837	0.275
ALDH5A1	6	24523122	G	A	ABSENT	0	0	1.045	0.888	0.9058
ALMS1	2	73777489	G	C	ABSENT	0	0	1.048	0.368	NA
ALPL	1	21903126	T	G	ABSENT	0	0	1.058	0.8	0.1902
AR	X	66931514	G	C	ABSENT	0	0	1.047	0.955	0.9995
AR	X	66937392	C	T	ABSENT	0	0	0.85	0.912	0.9575
ARSB	5	78181645	C	T	VUS	3.2E-05	8E-06	0.935	0.984	0.9611
ARSB	5	78076401	A	G	ABSENT	0	0	1.088	0.977	0.9935
ARSB	5	78076270	C	T	ABSENT	0	0	0.852	0.633	0.3668

ARSG	17	66339822	G	A	VUS	0	2.4E-05	1.048	0.621	0.6041
ASIP	20	32856947	T	A	ABSENT	0	0	0.9	0.636	0.8136
ASIP	20	32856863	C	T	ABSENT	0	0	0.795	0.183	0.3526
ASPA	17	3402296	G	C	ABSENT	0	0	0.998	0.926	0.9502
ASPRV1	2	70187847	A	G	ABSENT	0	0	1.088	0.173	0.9158
ATF2	2	175986219	A	C	ABSENT	0	0	1.136	0.695	0.9988
ATG4D	19	10663609	G	A	ABSENT	0	0	0.065	0.037	0.0944
ATP13A2	1	17323577	G	A	ABSENT	0	0	1.048	0.871	0.9491
ATP2A1	16	28909686	C	T	ABSENT	0	3.2E-05	0.848	0.935	0.9987
ATP2A1	16	28898747	G	T	ABSENT	0	0	0.953	0.964	0.9902
ATP2A1	16	28898972	G	T	ABSENT	0	0	0.902	0.858	0.8338
ATP7A	X	77245098	C	T	ABSENT	0	0	0.852	0.594	0.1894
BCKDHA	19	41930425	C	T	ABSENT	0	0	0.935	0.56	0.4864
BEST1	11	61724316	G	A	ABSENT	0	0	1.048	0.985	0.9659
BMP15	X	50659434	A	C	ABSENT	0	5.5E-06	0.211	0.612	0.2127
BMP15	X	50659387	G	A	ABSENT	0	0	0.953	0.97	0.9852
BMP15	X	50659525	G	T	ABSENT	0	0	0.127	0.711	0.929
BMP15	X	50659375	C	T	ABSENT	0	0	0.044	0.303	0.1591
BMP3	4	81974618	C	A	ABSENT	0	0	0.935	0.815	0.993
BMPR1B	4	96051173	A	G	ABSENT	0	4E-06	1.199	0.704	0.7864
BRAF	7	140453136	A	T	LP/P	0	4E-06	1.193	0.931	0.9927
CAD	2	27447710	A	G	VUS	3.2E-05	2.8E-05	1.199	0.949	0.7597
CAPN1	11	64950951	G	A	ABSENT	0	0	1.048	0.881	0.9997
CAT	11	34478287	G	A	ABSENT	0	0	1.048	0.673	0.1547
CD320	19	8368785	G	C	ABSENT	0	4.3E-06	-0.309	0.88	0.9404
CDH23	10	73330622	C	T	ABSENT	0	0	0.934	0.846	NA
CHAT	10	50827789	G	A	CIP	0.0002	0.00004	0.953	0.804	0.5351
CHST6	16	75512976	G	T	ABSENT	0	0	0.813	0.779	0.2157

CLCN1	7	143016944	G	A	ABSENT	0	4E-06	1.048	0.342	0.0716
CLCN1	7	143021535	C	G	ABSENT	0	0	0.935	0.892	0.8213
CLCN1	7	143039214	A	C	ABSENT	0	0	1.187	0.666	0.4716
CLCN1	7	143048744	G	C	ABSENT	0	0	0.953	0.628	0.8425
CLN6	15	68510888	G	A	CIP	0	8E-06	1.048	0.926	0.9585
CLN6	15	68500588	A	G	ABSENT	0	0	1.088	0.863	0.9949
CNGA3	2	99012861	C	T	LP/P	0	4E-05	0.935	0.846	0.3505
CNGA3	X	150912464	G	A	ABSENT	0	0	1.045	0.972	0.9862
CNGB3	8	87679206	C	T	ABSENT	0	1.2E-05	0.935	0.796	0.6972
CNGB3	8	87679206	C	T	ABSENT	0	1.2E-05	0.935	0.796	0.6972
CNTNAP1	17	40845375	G	A	ABSENT	0	8E-06	1.048	0.821	0.9682
COL10A1	6	116441496	C	T	ABSENT	0	0	0.935	0.925	0.8733
COL11A2	6	33157186	C	G	ABSENT	0	0	-0.001	0.095	0.5283
COL1A1	17	48273017	C	T	ABSENT	0	0	0.935	0.976	0.7926
COL1A1	17	48272838	C	G	ABSENT	0	0	0.935	0.961	0.807
COL1A1	17	48263763	A	T	ABSENT	0	0	1.028	0.662	0.618
COL2A1	12	48376666	C	T	ABSENT	0	0	0.935	0.991	0.9204
COL2A1	12	48372397	C	T	ABSENT	0	0	0.935	0.995	0.9777
COL2A1	12	48378812	C	T	ABSENT	0	0	0.935	0.993	0.9994
COL2A1	12	48371210	C	T	ABSENT	0	0	0.852	0.993	0.9423
COL2A1	12	48372091	C	T	ABSENT	0	0	0.935	0.942	0.8857
COL5A1	9	137707826	G	A	VUS	0	0	0.943	0.969	0.9945
COL5A2	2	189921724	C	A	ABSENT	0	0	0.892	0.947	0.9838
COL6A3	2	238274501	G	A	VUS	0.0002	4E-05	0.953	0.131	0.108
COL7A1	3	48613963	C	T	ABSENT	0	0	0.892	0.771	0.1912
COLQ	3	15498031	A	G	LP/P	0	0	1.199	0.845	0.8338
COLQ	3	15497411	C	T	ABSENT	0	0	0.87	0.894	0.9472
COLQ	3	15499767	C	T	ABSENT	0	0	0.935	0.285	0.1033

COPA	1	160302256	G	A	ABSENT	0	0	1.048	0.704	0.9882
CORIN	4	47625754	G	A	ABSENT	0	2.4E-05	0.998	0.268	0.1958
CORIN	4	47695070	C	T	ABSENT	0	0	0.888	0.974	0.9822
CPT1C	19	50200599	G	A	ABSENT	0	0	1.036	0.734	0.5224
CSNK1G2	19	1978903	G	C	ABSENT	0	0	0.859	0.932	1
CTSD	11	1775313	C	T	ABSENT	0	0	0.852	0.856	0.9981
CTSD	11	1778655	C	T	ABSENT	0	0	0.881	0.376	0.9648
CYB5R3	22	43027384	C	T	ABSENT	3.2E-05	1.3E-05	0.852	0.908	0.891
CYB5R3	22	43023363	T	G	ABSENT	0	0	0.076	0.441	0.2783
CYP26C1	10	94822610	T	C	ABSENT	0	0	0.828	0.901	0.927
DKK4	8	42233272	C	T	ABSENT	0	0	0.826	0.661	0.9281
DKK4	8	42234511	G	A	ABSENT	0	0	1.048	0.038	0.339
DMD	X	32360270	G	A	CIP	0	2.8E-05	1.048	0.212	0.1353
DNM1	9	130982538	G	T	ABSENT	0	0	1.048	0.715	0.9167
DNM2	19	10909219	C	T	LP/P	0	0	-0.035	0.83	0.9079
DPYS	8	105405152	C	T	LP/P	0	8E-06	0.935	0.872	0.9731
DSP	6	7584358	C	A	ABSENT	0	0	0.935	0.72	0.9988
DUOX2	15	45401730	T	C	ABSENT	0	0	1.011	0.764	0.8356
EDN2	1	41949787	C	T	ABSENT	0	0	0.852	0.928	0.984
EDNRA	4	148461045	G	A	ABSENT	0	8E-06	0.953	0.536	0.6778
EDNRA	4	148453825	G	T	ABSENT	0	0	1.048	0.795	0.9977
ENAM	4	71507856	C	T	ABSENT	0	0	0.935	0.166	0.1776
ENTREP2	15	29428645	T	C	ABSENT	0	1.3E-05	0.913	0.18	0.085
ETFDH	4	159616656	T	G	ABSENT	0	0	0.964	0.925	0.9203
F11	4	187207634	G	A	VUS	0	2.8E-05	1.048	0.903	0.4246
F12	5	176829582	C	G	ABSENT	0	0	0.785	0.782	0.5487
F8	X	154189400	G	C	ABSENT	0	0	1.048	0.991	0.9594
F8	X	154091390	A	T	ABSENT	0	0	1.199	0.936	0.9645

F8	X	154185266	C	T	ABSENT	0	0	0.852	0.925	0.9961
F9	X	138644124	G	A	ABSENT	0	0	1.048	0.993	0.9893
FAM20C	7	295908	C	T	ABSENT	0	7.1E-06	0.883	0.754	0.8671
FAM83G	17	18907200	C	G	ABSENT	0	0	-0.012	0.21	0.7512
FBN1	15	48777685	C	T	ABSENT	0	0	0.935	0.933	0.9807
FGF5	4	81207591	C	T	ABSENT	0	4E-06	0.935	0.893	0.9937
FGF5	4	81188256	G	T	ABSENT	0	0	1.048	0.907	0.998
FGF5	4	81207590	G	A	ABSENT	0	0	1.048	0.875	0.9793
FGF5	4	81207488	A	C	ABSENT	0	0	1.199	0.044	0.8405
FGFR2	10	123279562	C	A	LP/P	0	0	0.892	0.982	0.9999
FGFR3	4	1808341	T	A	ABSENT	0	0	1.049	0.802	0.988
FLCN	17	17125830	T	C	ABSENT	0	0	1.061	0.957	0.9979
FZD7	2	202900611	G	C	ABSENT	0	4E-06	1.048	0.791	0.9477
G6PC1	17	41059562	G	C	ABSENT	0	0	0.953	0.899	0.9664
GALC	14	88450799	T	G	ABSENT	0	0	1.011	0.931	0.8029
GART	21	34900853	T	G	ABSENT	0	0	0.964	0.65	0.8083
GDF9	5	132197700	G	A	LP/P	0	8E-06	0.712	0.484	0.1934
GDF9	5	132197364	T	G	ABSENT	0	0	1.061	0.875	0.9922
GDF9	5	132197459	G	A	ABSENT	0	0	1.048	0.85	0.8223
GDF9	5	132197532	C	T	ABSENT	0	0	0.935	0.5	0.468
GDF9	5	132197609	A	C	ABSENT	0	0	1.199	0.393	0.6187
GDF9	5	132199997	G	A	ABSENT	0	0	1.04	0.192	0.1105
GFAP	17	42990701	C	T	LP/P	0	0	0.935	0.902	0.5695
GLB1	3	33114105	C	T	LP/P	0	3.6E-05	0.892	0.941	0.5309
GLB1	3	33058235	C	G	ABSENT	0	0	0.932	0.942	0.9874
GLB1	3	33099625	C	A	ABSENT	0	0	0.807	0.901	0.8685
GUSB	7	65441045	G	A	CIP	0	8E-06	0.912	0.945	0.9131
GUSB	7	65435316	G	A	ABSENT	0	2E-05	1.048	0.934	0.8431

GUSB	7	65439917	C	T	ABSENT	0	0	0.847	0.95	0.9274
GUSB	7	65435319	A	C	ABSENT	0	0	0.158	0.282	0.1253
HCRTR2	6	55039545	G	A	ABSENT	0	0	0.953	0.448	0.9166
HES7	17	8027398	A	G	ABSENT	0	0	1.199	0.346	0.4372
HEXA	15	72637818	G	A	LP/P	0	4E-06	1.048	0.888	0.9397
HEXA	15	72641439	C	T	ABSENT	0	0	0.935	0.964	0.9063
HMBS	11	118959966	G	A	ABSENT	0	0	1.048	0.837	0.6996
IARS1	9	95050449	C	G	ABSENT	0	0	0.935	0.474	0.9716
IFT122	3	129234353	G	A	ABSENT	0	1.6E-05	0.94	0.663	0.7181
ITGA2B	17	42460879	C	G	ABSENT	0	0	-0.774	0.586	0.7564
ITGA3	17	48148681	C	T	ABSENT	0	4E-06	0.935	0.407	0.2516
ITGB2	21	46323396	T	C	ABSENT	0	0	0.964	0.982	0.9936
ITGB2	21	46330239	C	G	ABSENT	0	0	0.935	0.939	0.9935
KCNG1	20	49620870	C	A	ABSENT	0	0	0.932	0.952	0.9963
KCNJ10	1	160011337	A	G	ABSENT	0	0	1.199	0.663	0.8078
KDM2B	12	121880815	C	T	ABSENT	0	0	0.935	0.053	0.3299
KDSR	18	61018135	C	T	ABSENT	0	0	0.935	0.31	0.1947
KIF1C	17	4905937	G	A	ABSENT	0	8E-06	1.048	0.916	0.9635
KIF3B	20	30898580	G	A	ABSENT	0	0	1.048	0.868	0.9116
KIT	4	55575645	A	G	VUS	0	1.2E-05	1.199	0.359	0.0986
KIT	4	55604682	G	A	VUS	0	2E-05	1.048	0.108	0.0642
KIT	4	55595543	T	C	ABSENT	0	0	1.061	0.976	0.9999
KIT	4	55595543	T	A	ABSENT	0	0	1.061	0.971	0.9995
KIT	4	55599304	T	A	ABSENT	0	0	0.113	0.927	1
KIT	4	55598160	A	T	ABSENT	0	0	1.14	0.898	0.926
KIT	4	55595523	A	T	ABSENT	0	0	0.238	0.872	0.9886
KIT	4	55594269	G	A	ABSENT	0	0	1.048	0.847	0.9997
KIT	4	55565844	T	C	ABSENT	0	0	1.061	0.761	0.9745

KIT	4	55594031	C	T	ABSENT	0	0	0.935	0.679	0.9983
KIT	4	55569989	G	A	ABSENT	0	0	1.048	0.451	0.7469
KIT	4	55589840	A	G	ABSENT	0	0	1.199	0.329	0.4299
KLKB1	4	187172760	T	A	ABSENT	0	0	0.963	0.753	0.6779
KRT25	17	38911258	C	T	ABSENT	0	4E-06	0.935	0.937	0.3718
KRT27	17	38938470	G	C	ABSENT	0	0	-0.64	0.774	0.9798
KRT5	12	52910431	C	T	LP/P	0	0	0.935	0.895	0.9786
KRT71	12	52944024	G	A	ABSENT	0	2.8E-05	1.048	0.769	0.6363
L2HGDH	14	50713867	T	C	ABSENT	0	0	1.061	0.904	0.9751
LAMA3	18	21512141	A	T	ABSENT	0	0	1.199	0.604	0.973
LAMB3	1	209801494	A	G	ABSENT	0	0	1.194	0.956	0.9723
LAMP3	3	182841997	C	T	ABSENT	0	0	0.789	0.418	0.3219
LDLR	19	11215925	C	T	LP/P	0	2.8E-05	0.888	0.81	0.4117
LOXHD1	18	44085947	C	G	ABSENT	0	0	0.935	0.859	0.9255
LRP4	11	46897459	C	T	ABSENT	0	0	0.919	0.953	0.674
LRP4	11	46903348	C	T	ABSENT	0	0	0.919	0.95	0.9967
LVRN	5	115298993	G	A	ABSENT	0	0	0.949	0.194	0.1824
LYST	1	235929441	T	C	ABSENT	0	0	1.011	0.851	0.966
MAN2B1	19	12772142	A	G	ABSENT	0	0	1.088	0.881	0.9961
MAN2B1	19	12774621	C	T	ABSENT	0	0	0.935	0.811	0.7674
MARS2	2	198571682	G	A	ABSENT	0	0	0.953	0.445	0.5059
MC1R	16	89985962	T	C	VUS	0	4E-06	0.964	0.207	0.315
MC1R	16	89985962	T	C	VUS	0	4E-06	0.964	0.207	0.315
MC1R	16	89985916	G	A	LB/B	3.2E-05	4E-06	0.953	0.601	0.2372
MC1R	16	89985916	G	A	ABSENT	3.2E-05	4E-06	0.953	0.601	0.2372
MC1R	16	89986384	G	A	ABSENT	3.2E-05	3.6E-05	0.039	0.514	0.0924
MC1R	16	89986148	C	T	ABSENT	3.2E-05	3.7E-05	0.852	0.085	0.1252
MC1R	16	89986090	C	T	ABSENT	6.4E-05	2.9E-05	0.014	0.857	0.1787

MC1R	16	89985940	G	A	ABSENT	0.0763	0.0781	-0.333	0.039	0.1201
MC1R	16	89986070	T	A	ABSENT	0	0	0.964	0.898	0.3537
MC1R	16	89986316	A	C	ABSENT	0	0	1.028	0.702	0.2547
MC1R	16	89986467	C	G	ABSENT	0	0	0.069	0.594	0.6414
MC1R	16	89985929	G	A	ABSENT	0	0	0.953	0.349	0.6499
MC1R	16	89986027	G	A	ABSENT	0	0	0.953	0.317	0.2437
MC1R	16	89986027	G	A	ABSENT	0	0	0.953	0.317	0.2437
MC1R	16	89985884	T	A	ABSENT	0	0	0.089	0.289	0.2335
MC1R	16	89985946	G	A	ABSENT	0	0	0.953	0.275	0.3161
MC1R	16	89985884	T	C	ABSENT	0	0	0.089	0.139	0.0876
MC4R	18	58038691	C	T	ABSENT	6.4E-05	8E-06	0.935	0.371	0.9448
MITF	3	70008453	T	C	VUS	0	0	1.061	0.963	1
MITF	3	70001032	A	G	CIP	0	0	1.199	0.824	0.9979
MITF	3	70008444	G	A	LP/P	0	0	1.048	0.882	1
MITF	3	70005618	G	T	ABSENT	0	0	1.048	0.966	1
MLPH	2	238402172	C	T	LP/P	3.2E-05	2.4E-05	-2.117	0.623	0.5533
MLPH	2	238428672	G	C	ABSENT	0	0	1.034	0.13	0.2153
MOCOS	18	33767639	T	C	ABSENT	0	0	0.935	0.446	0.7402
MRC2	17	60754698	T	G	ABSENT	0	0	0.954	0.739	0.9821
MSTN	2	190922174	C	T	ABSENT	0	0	0.807	0.974	0.9998
MSTN	2	190927132	A	G	ABSENT	0	0	1.199	0.889	0.9993
MSTN	2	190924991	C	T	ABSENT	0	0	0.935	0.181	0.0885
MSTN	2	190927009	G	C	ABSENT	0	0	1.048	0.171	0.1811
MTBP	8	121534921	G	A	ABSENT	0	0	1.044	0.378	0.1765
MTM1	X	149826391	A	C	ABSENT	0	0	1.14	0.95	0.9863
MTM1	X	149807426	C	T	ABSENT	0	0	0.935	0.893	0.8038
MX1	21	42830462	G	A	ABSENT	0	0	-0.317	0.122	0.1559
MYBPC1	12	102036319	T	G	LP/P	0	0	1.061	0.823	0.5828

MYBPC3	11	47359086	G	A	CIP	0	4E-06	0.076	0.65	0.8113
MYBPC3	11	47372991	C	G	ABSENT	0	0	0.892	0.489	0.9726
MYH1	17	10416047	T	C	ABSENT	0	0	1.061	0.777	0.5552
MYH7	14	23883224	C	T	VUS	3.2E-05	0	0.932	0.879	0.7712
MYO7A	11	76901153	G	A	LP/P	0	7.5E-05	0.988	0.951	0.9982
NAGLU	17	40695378	G	A	LP/P	0	1.2E-05	0.092	0.653	0.6898
NAPEPLD	7	102760427	C	G	ABSENT	0	0	0.892	0.842	0.994
NDRG1	8	134274323	C	A	ABSENT	0	0	0.935	0.792	0.9983
NECAP1	12	8245519	G	A	ABSENT	0	0	1.036	0.237	0.4966
NHLRC2	10	115644032	T	C	ABSENT	0	0	1.006	0.877	0.6448
NPC1	18	21118578	G	C	ABSENT	0	0	1.048	0.954	0.9103
NPC1	18	21119363	C	G	ABSENT	0	0	0.935	0.728	0.9946
NPC1	18	21136211	T	G	ABSENT	0	0	1.061	0.664	0.6993
NSDHL	X	152036164	G	A	ABSENT	0	0	1.048	0.941	0.9867
NSDHL	X	152031158	A	G	ABSENT	0	0	1.199	0.89	0.8701
NUBPL	14	32142695	C	A	ABSENT	0	0	0.935	0.663	0.9915
P3H2	3	189688652	C	G	ABSENT	0	0	0.927	0.07	0.1412
PAX3	2	223161809	C	T	ABSENT	0	0	0.935	0.982	0.9999
PAX3	2	223161923	G	C	ABSENT	0	0	1.048	0.675	0.9683
PCDH15	10	55780104	G	C	ABSENT	0	0	1.048	0.152	0.1347
PFAS	17	8172081	C	T	ABSENT	0	2E-05	0.925	0.454	0.3573
PFKM	12	48527220	C	T	ABSENT	9.6E-05	3.2E-05	0.02	0.842	0.9917
PIGN	18	59824406	G	A	ABSENT	0	0	1.048	0.583	0.646
PITX3	10	103990842	C	G	ABSENT	3.2E-05	0	0.769	0.934	0.9998
PKD1	16	2150031	C	T	ABSENT	0	0	0.846	0.255	0.9036
PKLR	1	155264148	C	T	LP/P	9.6E-05	5.6E-05	0.932	0.959	0.568
PKLR	1	155264390	A	G	ABSENT	0	0	1.136	0.812	0.6757
PLN	6	118880110	G	A	CIP	3.2E-05	8E-06	0.953	0.906	0.1589

PLOD1	1	12034713	G	A	CIP	0	2.8E-05	1.045	0.893	0.989
PLP1	X	103040616	A	C	ABSENT	0	0	1.199	0.936	0.9787
PLP2	X	49028397	C	T	ABSENT	0	0	0.764	0.125	0.2719
PMEL	12	56359732	C	T	ABSENT	0	0	0.031	0.036	0.1947
PNKP	19	50370313	T	C	ABSENT	0	0	1.061	0.33	0.8662
PNPLA8	7	108128384	C	T	ABSENT	0	0	0.892	0.688	0.9964
PPARD	6	35378959	G	A	ABSENT	0	0	0.953	0.457	0.076
PPIB	15	64455071	C	T	ABSENT	0	0	0.865	0.433	0.9798
PRCD	17	74536228	G	A	LP/P	0	0	1.048	0.825	0.8828
PRKAG3	2	219693283	C	T	VUS	0	1.6E-05	0.935	0.9	0.8395
PRL	6	22287660	A	C	ABSENT	0	0	1.199	0.976	0.959
PRNP	20	4680464	G	A	LP/P	0	4E-06	0.953	0.761	0.7744
PRNP	20	4680245	G	A	LP/P	0	4E-06	0.953	0.812	0.5322
PRNP	20	4680318	G	A	ABSENT	6.4E-05	2.8E-05	0.953	0.625	0.2165
PRNP	20	4680318	G	A	ABSENT	6.4E-05	2.8E-05	0.953	0.625	0.2165
PRNP	20	4680264	C	T	ABSENT	0	0	0.852	0.717	0.1883
PRNP	20	4680285	A	G	ABSENT	0	0	1.088	0.659	0.1437
PRNP	20	4680283	A	G	ABSENT	0	0	-1.629	0.341	0.0863
PSMB7	9	127177131	A	C	ABSENT	0	0	1.199	0.562	0.849
PYGM	11	64520595	G	A	ABSENT	0	8E-06	1.048	0.892	0.9789
RAB24	5	176730177	T	G	ABSENT	0	0	0.831	0.755	0.7662
RABGGTB	1	76257870	A	G	ABSENT	0	4E-06	1.199	0.777	0.9368
RASGRP2	11	64506944	A	G	ABSENT	0	0	1.088	0.737	0.9993
RDH5	12	56115704	G	T	ABSENT	0	0	1.048	0.77	0.7757
RETREG1	5	16479075	G	A	ABSENT	0	0	1.048	0.734	0.7485
RHO	3	129247587	C	G	ABSENT	0	0	0.892	0.754	0.436
RYR1	19	38948185	C	T	LP/P	0.0003	8.7E-05	0.852	0.927	0.9627
RYR1	19	38991282	C	G	ABSENT	0	0	0.796	0.893	0.9797

RYR1	19	38946154	T	C	ABSENT	0	0	0.945	0.757	0.9841
SCN8A	12	52200168	G	T	ABSENT	0	0	1.048	0.893	0.9569
SEL1L	14	81950643	A	G	ABSENT	0	0	1.199	0.531	0.9982
SERPINH1	11	75282848	T	C	ABSENT	0	0	1.061	0.949	0.9809
SGSH	17	78188504	G	A	CIP	3.2E-05	8E-06	0.951	0.942	0.4445
SLC12A1	15	48527101	C	T	ABSENT	0	0	0.892	0.973	0.9063
SLC24A5	15	48414204	T	A	ABSENT	0	0	1.061	0.734	0.4384
SLC25A12	2	172669974	A	G	ABSENT	0	0	1.022	0.939	0.9999
SLC25A46	5	110079477	C	T	ABSENT	0	0	0.935	0.773	0.9609
SLC2A9	4	9982268	C	A	ABSENT	0	0	0.841	0.826	0.9382
SLC35A3	1	100459183	C	A	ABSENT	0	4E-06	0.935	0.624	0.9961
SLC35A3	1	100476990	G	T	ABSENT	0	0	0.998	0.741	0.9849
SLC36A1	5	150843158	C	G	ABSENT	0	0	0.935	0.556	0.9524
SLC39A4	8	145639765	C	G	ABSENT	0	0	0.877	0.505	NA
SLC3A1	2	44539746	C	T	LP/P	3.2E-05	8.4E-05	-0.017	0.943	0.6546
SLC45A2	5	33963887	T	C	ABSENT	0	4E-06	1.061	0.035	0.0778
SLC45A2	5	33944868	C	T	ABSENT	0	8E-06	0.935	0.742	0.7432
SLC45A2	5	33984384	C	T	ABSENT	0	2E-05	0.798	0.917	0.8041
SLC45A2	5	33982446	C	T	ABSENT	0	0	0.927	0.834	0.9482
SLC45A2	5	33954510	C	T	ABSENT	0	0	0.935	0.795	0.7387
SLC45A2	5	33954504	G	T	ABSENT	0	0	1.048	0.161	0.4745
SLC5A3	21	35468849	C	T	ABSENT	0	4E-06	0.935	0.877	0.9716
SLC6A5	11	20628679	T	C	ABSENT	0	0	1.061	0.872	0.9984
SLC7A9	19	33333132	G	A	LP/P	3.2E-05	1.6E-05	1.048	0.871	0.5122
SLC7A9	19	33349368	C	T	ABSENT	0	0	0.935	0.917	0.993
SLC7A9	19	33350748	A	T	ABSENT	0	0	1.199	0.942	0.8032
SLC7A9	19	33353031	C	T	ABSENT	0	0	0.935	0.536	0.837
SMC2	9	106900433	T	C	ABSENT	0	0	1.061	0.768	0.9916

SOD1	21	33036151	G	A	ABSENT	0	0	1.045	0.449	0.1248
SOWAHB	4	77817829	G	T	ABSENT	0	0	0.953	0.096	0.1298
SPAST	2	32370074	G	A	LP/P	0	0	0.953	0.889	0.9887
STAT5B	17	40359728	T	G	ABSENT	0	0	1.061	0.758	0.9917
SUGT1	13	53261902	T	C	ABSENT	0	0	1.061	0.833	0.9998
SUV39H2	10	14941660	T	G	ABSENT	0	0	-0.219	0.876	0.9995
TBXT	6	166580884	T	C	ABSENT	0	0	1.011	0.953	0.9999
TBXT	6	166580891	G	C	ABSENT	0	0	0.12	0.852	0.997
TECPR2	14	102963981	C	T	VUS	3.2E-05	5.1E-05	0.067	0.608	0.9679
TNXB	6	32053766	C	T	ABSENT	0	0	0.935	0.139	0.2902
TPO	2	1491745	C	T	ABSENT	0	1.2E-05	0.807	0.906	0.8571
TPO	2	1440068	G	A	ABSENT	0	0	0.902	0.504	0.4515
TRPV4	12	110236547	C	A	LP/P	0	0	0.935	0.442	0.8876
TSEN54	17	73513639	G	A	ABSENT	0	0	1.048	0.909	0.9089
TUBB1	20	57594582	G	A	ABSENT	0	8E-06	1.048	0.637	0.8966
TUBB1	20	57599227	G	A	ABSENT	0	0	1.048	0.739	0.8421
TUBD1	17	57955604	T	C	ABSENT	0	0	0.955	0.667	0.1455
TUBGCP5	15	22840245	C	A	ABSENT	0	0	NA	0.283	0.3493
TYR	11	88911351	G	A	LP/P	0.0001	8.4E-05	1.048	0.877	0.6493
TYR	11	88961072	C	A	LP/P	0.0004	0.0003	0.852	0.708	0.7055
TYR	11	88924454	G	A	ABSENT	0	0	1.048	0.851	0.4958
TYRP1	9	12695772	C	A	ABSENT	0	4E-06	0.892	0.925	0.9884
TYRP1	9	12698611	G	T	ABSENT	0	1.2E-05	1.048	0.721	0.9872
TYRP1	9	12702382	T	G	ABSENT	0	0	1.009	0.984	0.9639
TYRP1	9	12694117	T	A	ABSENT	0	0	1.061	0.96	0.9824
TYRP1	9	12708035	C	T	ABSENT	0	0	0.892	0.947	0.9104
TYRP1	9	12694121	G	A	ABSENT	0	0	1.048	0.943	0.9489
UCHL1	4	41270049	G	A	ABSENT	0	0	1.048	0.486	0.9341

UNC93B1	11	67759230	G	T	ABSENT	0	0	NA	NA	NA
UROD	1	45479381	T	C	ABSENT	0	0	1.061	0.969	0.8853
UROS	10	127496045	C	T	ABSENT	0	0	0.935	0.786	0.208
UROS	10	127504753	G	A	ABSENT	0	0	1.048	0.29	0.1585
VPS11	11	118951867	A	G	ABSENT	0	0	1.199	NA	NA
VWF	12	6167087	A	C	ABSENT	0	0	1.053	0.649	0.8761
VWF	12	6127647	T	C	ABSENT	0	0	0.083	0.079	0.0809
WIF1	12	65460443	G	C	ABSENT	0	4E-06	1.048	0.186	0.9735
WWP1	8	87440033	G	A	ABSENT	3.2E-05	0	1.048	0.498	0.883
YARS2	12	32903702	C	T	ABSENT	0	0	0.931	0.501	0.834

Supplemental Table 2. Human genes (n=220) orthologous to the genes with non-human animal missense variants extracted from OMIA and included in this study. See Supplemental Table 1 for details. An asterisk next to a gene symbol indicates that the gene is included in the HRT Atlas v1.0 database list of human housekeeping genes.[5] OMIM, Online Mendelian Inheritance in Man (https://www.omim.org/, accessed 2023).

Gene symbol	OMIM phenotype
ABCA1	HDL deficiency, type 2;Tangier disease, Autosomal recessive
ABCA12	Ichthyosis, congenital, autosomal recessive 4A, Autosomal recessive;Ichthyosis, congenital, autosomal recessive 4B (harlequin), Autosomal recessive
ACSL5	No Mendelian disease association in OMIM
ACVR1	Fibrodysplasia ossificans progressiva, Autosomal dominant
ADAMTS10	Weill-Marchesani syndrome 1, recessive, Autosomal recessive
ADAMTS17	Weill-Marchesani-like syndrome, Autosomal recessive
ADAMTS2	Ehlers-Danlos syndrome, type VIIC, Autosomal recessive
ADAMTSL2	Geleophysic dysplasia 1, Autosomal recessive
ADAMTSL4	Ectopia lentis et pupillae, Autosomal recessive;Ectopia lentis, isolated, autosomal recessive, Autosomal recessive
AGTPBP1	No Mendelian disease association in OMIM
AGXT	Hyperoxaluria, primary, type 1, Autosomal recessive
ALDH5A1	Succinic semialdehyde dehydrogenase deficiency, Autosomal recessive
ALMS1	Alstrom syndrome, Autosomal recessive
ALPL	Hypophosphatasia, adult, Autosomal recessive, Autosomal dominant;Hypophosphatasia, childhood, Autosomal recessive;Hypophosphatasia, infantile, Autosomal recessive;Odontohypophosphatasia, Autosomal recessive, Autosomal dominant
AR	Androgen insensitivity, X-linked recessive;Androgen insensitivity, partial, with or without breast cancer, X-linked recessive;Hypospadias 1, X-linked, X-linked recessive;Spinal and bulbar muscular atrophy of Kennedy, X-linked recessive

ARSB	Mucopolysaccharidosis type VI (Maroteaux-Lamy), Autosomal recessive
ARSG	Usher syndrome, type IV
ASIP	No Mendelian disease association in OMIM
ASPA	Canavan disease, Autosomal recessive
ASPRV1	No Mendelian disease association in OMIM
ATF2	No Mendelian disease association in OMIM
ATG4D	No Mendelian disease association in OMIM
ATP13A2	Kufor-Rakeb syndrome, Autosomal recessive;Spastic paraplegia 78, autosomal recessive, Autosomal recessive
ATP2A1	Brody myopathy, Autosomal recessive
ATP7A	Menkes disease, X-linked recessive;Occipital horn syndrome, X-linked recessive;Spinal muscular atrophy, distal, X-linked 3, X-linked recessive
BCKDHA	Maple syrup urine disease, type Ia, Autosomal recessive
BEST1	Bestrophinopathy, autosomal recessive;Macular dystrophy, vitelliform, 2, Autosomal dominant;Microcornea, rod-cone dystrophy, cataract, and posterior staphyloma, Autosomal dominant;Retinitis pigmentosa, concentric;Retinitis pigmentosa-50;Vitreoretinochoroidopathy, Autosomal dominant
BMP15	Ovarian dysgenesis 2;Premature ovarian failure 4
BMP3	No Mendelian disease association in OMIM
BMPR1B	Acromesomelic dysplasia, Demirhan type, Autosomal recessive;Brachydactyly, type A1, D, Autosomal dominant;Brachydactyly, type A2, Autosomal dominant
BRAF	Cardiofaciocutaneous syndrome, Autosomal dominant;Colorectal cancer, somatic (3);LEOPARD syndrome 3, Autosomal dominant;Melanoma, malignant, somatic (3);Nonsmall cell lung cancer, somatic (3);Noonan syndrome 7, Autosomal dominant
CAD	Epileptic encephalopathy, early infantile, 50, Autosomal recessive
CAPN1	Spastic paraplegia 76, autosomal recessive, Autosomal recessive
CAT	Acatalasemia

CD320 *	Methylmalonic aciduria, transient, due to transcobalamin receptor defect
CDH23	Deafness, autosomal recessive 12, Autosomal recessive;Usher syndrome, type 1D, Autosomal recessive, Digenic recessive;Usher syndrome, type 1D/F digenic, Autosomal recessive, Digenic recessive
CHAT	Myasthenic syndrome, congenital, 6, presynaptic, Autosomal recessive
CHST6	Macular corneal dystrophy, Autosomal recessive
CLCN1	Myotonia congenita, dominant, Autosomal dominant;Myotonia congenita, recessive, Autosomal recessive;Myotonia levior, recessive (3)
CLN6	Ceroid lipofuscinosis, neuronal, 6, Autosomal recessive;Ceroid lipofuscinosis, neuronal, Kufs type, adult onset, Autosomal recessive
CNGA3	Achromatopsia 2, Autosomal recessive
CNGB3	Achromatopsia 3, Autosomal recessive;Macular degeneration, juvenile, Autosomal recessive
CNTNAP1	Lethal congenital contracture syndrome 7, Autosomal recessive
COL10A1	Metaphyseal chondrodysplasia, Schmid type, Autosomal dominant
COL11A2	Deafness, autosomal dominant 13, Autosomal dominant;Deafness, autosomal recessive 53, Autosomal recessive;Fibrochondrogenesis 2, Autosomal recessive, Autosomal dominant;Otospondylomegaepiphyseal dysplasia, Autosomal recessive;Stickler syndrome, type III, Autosomal dominant;Weissenbacher-Zweymuller syndrome, Autosomal dominant
COL1A1	Caffey disease, Autosomal dominant;Ehlers-Danlos syndrome, classic, Autosomal dominant;Ehlers-Danlos syndrome, type VIIA, Autosomal dominant;Osteogenesis imperfecta, type I, Autosomal dominant;Osteogenesis imperfecta, type II, Autosomal dominant;Osteogenesis imperfecta, type III, Autosomal dominant;Osteogenesis imperfecta, type IV, Autosomal dominant
COL2A1	Achondrogenesis, type II or hypochondrogenesis, Autosomal dominant;Avascular necrosis of the femoral head, Autosomal dominant;Czech dysplasia, Autosomal dominant;Epiphyseal dysplasia, multiple, with myopia and deafness, Autosomal dominant;Kniest dysplasia, Autosomal dominant;Legg-Calve-Perthes disease, Autosomal dominant;Osteoarthritis with mild chondrodysplasia, Autosomal dominant;Otospondylomegaepiphyseal dysplasia, Autosomal recessive;Platyspondylic skeletal dysplasia, Torrance type, Autosomal dominant;SED congenita, Autosomal dominant;SMED Strudwick type, Autosomal dominant;Spondyloepiphyseal dysplasia, Stanescu type, Autosomal dominant;Spondyloperipheral dysplasia, Autosomal dominant;Stickler sydrome, type I, nonsyndromic ocular, Autosomal dominant;Stickler syndrome, type I, Autosomal dominant;Vitreoretinopathy with phalangeal epiphyseal dysplasia (3)

COL5A1	Ehlers-Danlos syndrome, classic type, Autosomal dominant
COL5A2	Ehlers-Danlos syndrome, classic type, Autosomal dominant
COL6A3	Bethlem myopathy 1, Autosomal recessive, Autosomal dominant;Dystonia 27, Autosomal recessive;Ullrich congenital muscular dystrophy 1, Autosomal recessive, Autosomal dominant
COL7A1	EBD inversa, Autosomal recessive;EBD, Bart type, Autosomal dominant;EBD, localisata variant (3);Epidermolysis bullosa dystrophica, AD, Autosomal dominant;Epidermolysis bullosa dystrophica, AR, Autosomal recessive;Epidermolysis bullosa pruriginosa, Autosomal recessive, Autosomal dominant;Epidermolysis bullosa, pretibial, Autosomal recessive, Autosomal dominant;Toenail dystrophy, isolated, Autosomal dominant;Transient bullous of the newborn, Autosomal recessive, Autosomal dominant
COLQ	Myasthenic syndrome, congenital, 5, Autosomal recessive
COPA *	No Mendelian disease association in OMIM
CORIN	Preeclampsia/eclampsia 5
CPT1C	No Mendelian disease association in OMIM
CSNK1G2 *	No Mendelian disease association in OMIM
CTSD *	Ceroid lipofuscinosis, neuronal, 10, Autosomal recessive
CYB5R3 *	Methemoglobinemia, type I, Autosomal recessive;Methemoglobinemia, type II, Autosomal recessive
CYP26C1	Focal facial dermal dysplasia 4, Autosomal recessive
DKK4	No Mendelian disease association in OMIM
DMD	Becker muscular dystrophy, X-linked recessive;Cardiomyopathy, dilated, 3B, X-linked;Duchenne muscular dystrophy, X-linked recessive
DNM1	Epileptic encephalopathy, early infantile, 31, Autosomal dominant
DNM2	Charcot-Marie-Tooth disease, axonal, type 2M, Autosomal dominant;Charcot-Marie-Tooth disease, dominant intermediate B, Autosomal dominant;Lethal congenital contracture syndrome 5, Autosomal recessive;Myopathy, centronuclear, Autosomal dominant
DPYS	Dihydropyrimidinuria, Autosomal recessive
DSP	Arrhythmogenic right ventricular dysplasia 8, Autosomal dominant;Cardiomyopathy, dilated, with woolly hair and keratoderma,

	Autosomal recessive;Dilated cardiomyopathy with woolly hair, keratoderma, and tooth agenesis, Autosomal dominant;Epidermolysis bullosa, lethal acantholytic, Autosomal recessive;Keratosis palmoplantaris striata II;Skin fragility-woolly hair syndrome, Autosomal recessive
DUOX2	Thyroid dyshormonogenesis 6, Autosomal recessive
EDN2	No Mendelian disease association in OMIM
EDNRA	Mandibulofacial dysostosis with alopecia, Autosomal dominant
ENAM	Amelogenesis imperfecta, type IB, Autosomal dominant;Amelogenesis imperfecta, type IC, Autosomal recessive
ENTREP2	No Mendelian disease association in OMIM
ETFDH	Glutaric acidemia IIC, Autosomal recessive
F11	Factor XI deficiency, autosomal dominant;Factor XI deficiency, autosomal recessive
F12	Angioedema, hereditary, type III, Autosomal dominant;Factor XII deficiency, Autosomal recessive
F8	Hemophilia A, X-linked recessive
F9	Hemophilia B, X-linked recessive;Thrombophilia, X-linked, due to factor IX defect
FAM20C	Raine syndrome, Autosomal recessive
FAM83G	No Mendelian disease association in OMIM
FBN1	Acromicric dysplasia, Autosomal dominant;Ectopia lentis, familial, Autosomal dominant;Geleophysic dysplasia 2, Autosomal dominant;MASS syndrome;Marfan lipodystrophy syndrome, Autosomal dominant;Marfan syndrome, Autosomal dominant;Stiff skin syndrome, Autosomal dominant;Weill-Marchesani syndrome 2, dominant, Autosomal dominant
FGF5	Trichomegaly, Autosomal recessive
FGFR2	Antley-Bixler syndrome without genital anomalies or disordered steroidogenesis, Autosomal recessive;Apert syndrome, Autosomal dominant;Beare-Stevenson cutis gyrata syndrome, Autosomal dominant;Bent bone dysplasia syndrome, Autosomal dominant;Craniofacial-skeletal-dermatologic dysplasia, Autosomal dominant;Craniosynostosis, nonspecific (3);Crouzon syndrome, Autosomal dominant;Gastric cancer, somatic;Jackson-Weiss syndrome, Autosomal dominant;LADD syndrome, Autosomal dominant;Pfeiffer syndrome, Autosomal dominant;Saethre-Chotzen syndrome, Autosomal dominant;Scaphocephaly and Axenfeld-Rieger anomaly (3);Scaphocephaly, maxillary retrusion, and mental retardation

FGFR3	Achondroplasia, Autosomal dominant;Bladder cancer, somatic;CATSHL syndrome, Autosomal recessive, Autosomal dominant;Cervical cancer, somatic;Colorectal cancer, somatic;Crouzon syndrome with acanthosis nigricans, Autosomal dominant;Hypochondroplasia, Autosomal dominant;LADD syndrome, Autosomal dominant;Muenke syndrome, Autosomal dominant;Nevus, epidermal, somatic;SADDAN, Autosomal dominant;Spermatocytic seminoma, somatic;Thanatophoric dysplasia, type I, Autosomal dominant;Thanatophoric dysplasia, type II, Autosomal dominant
FLCN *	Birt-Hogg-Dube syndrome, Autosomal dominant;Colorectal cancer, somatic;Pneumothorax, primary spontaneous, Autosomal dominant;Renal carcinoma, chromophobe, somatic
FZD7	No Mendelian disease association in OMIM
G6PC1	Glycogen storage disease Ia, Autosomal recessive
GALC	Krabbe disease, Autosomal recessive
GART	No Mendelian disease association in OMIM
GDF9	No associated disease in OMIM
GFAP	Alexander disease, Autosomal dominant
GLB1	GM1-gangliosidosis, type I, Autosomal recessive;GM1-gangliosidosis, type II, Autosomal recessive;GM1-gangliosidosis, type III, Autosomal recessive;Mucopolysaccharidosis type IVB (Morquio), Autosomal recessive
GUSB	Mucopolysaccharidosis VII, Autosomal recessive
HCRTR2	No Mendelian disease association in OMIM
HES7	Spondylocostal dysostosis 4, autosomal recessive, Autosomal recessive
HEXA	GM2-gangliosidosis, several forms, Autosomal recessive;Tay-Sachs disease, Autosomal recessive
HMBS	Porphyria, acute intermittent, Autosomal dominant;Porphyria, acute intermittent, nonerythroid variant, Autosomal dominant
IARS1	No Mendelian disease association in OMIM
IFT122	Cranioectodermal dysplasia 1, Autosomal recessive
ITGA2B	Bleeding disorder, platelet-type, 16, autosomal dominant, Autosomal dominant;Glanzmann thrombasthenia, Autosomal recessive;Thrombocytopenia, neonatal alloimmune, BAK antigen related (3)

ITGA3	Interstitial lung disease, nephrotic syndrome, and epidermolysis bullosa, congenital, Autosomal recessive
ITGB2	Leukocyte adhesion deficiency, Autosomal recessive
KCNG1	No Mendelian disease association in OMIM
KCNJ10	Enlarged vestibular aqueduct, digenic, Autosomal recessive;SESAME syndrome, Autosomal recessive
KDM2B	No Mendelian disease association in OMIM
KDSR	Lymphoma/leukemia, B-cell, variant (1)
KIF1C	Spastic ataxia 2, autosomal recessive, Autosomal recessive
KIF3B	No Mendelian disease association in OMIM
KIT	Gastrointestinal stromal tumor, familial, Autosomal dominant, Isolated cases;Germ cell tumors, Somatic mutation;Leukemia, acute myeloid, Autosomal dominant;Mast cell disease, Autosomal dominant;Piebaldism, Autosomal dominant
KLKB1	Fletcher factor (prekallikrein) deficiency, Autosomal recessive
KRT25	Woolly hair, autosomal recessive 3, Autosomal recessive
KRT27	No Mendelian disease association in OMIM
KRT5	Dowling-Degos disease 1, Autosomal dominant;Epidermolysis bullosa simplex, Dowling-Meara type, Autosomal dominant;Epidermolysis bullosa simplex, Koebner type, Autosomal dominant;Epidermolysis bullosa simplex, Weber-Cockayne type, Autosomal dominant;Epidermolysis bullosa simplex, recessive 1, Autosomal recessive;Epidermolysis bullosa simplex-MP, Autosomal dominant;Epidermylysis bullosa simplex-MCR
KRT71	No Mendelian disease association in OMIM
L2HGDH	L-2-hydroxyglutaric aciduria, Autosomal recessive
LAMA3	Epidermolysis bullosa, generalized atrophic benign, Autosomal recessive;Epidermolysis bullosa, junctional, Herlitz type, Autosomal recessive;Laryngoonychocutaneous syndrome, Autosomal recessive
LAMB3	Amelogenesis imperfecta, type IA, Autosomal dominant;Epidermolysis bullosa, junctional, Herlitz type, Autosomal recessive;Epidermolysis bullosa, junctional, non-Herlitz type, Autosomal recessive
LAMP3	No Mendelian disease association in OMIM

LDLR	Hypercholesterolemia, familial, Autosomal dominant;LDL cholesterol level QTL2, Autosomal dominant
LOXHD1	Deafness, autosomal recessive 77, Autosomal recessive
LRP4	Cenani-Lenz syndactyly syndrome, Autosomal recessive;Sclerosteosis 2, Autosomal recessive, Autosomal dominant
LVRN	No Mendelian disease association in OMIM
LYST	Chediak-Higashi syndrome, Autosomal recessive
MAN2B1	Mannosidosis, alpha-, types I and II, Autosomal recessive
MARS2	Spastic ataxia 3, autosomal recessive, Autosomal recessive
MC1R	Skin/hair/eye pigmentation
MC4R	Obesity, autosomal dominant, Autosomal recessive, Autosomal dominant, Multifactorial
MITF	COMMAD syndrome, Autosomal recessive;Tietz albinism-deafness syndrome, Autosomal dominant;Waardenburg syndrome, type 2A, Autosomal dominant;Waardenburg syndrome/ocular albinism, digenic, Autosomal dominant
MLPH	Griscelli syndrome, type 3, Autosomal recessive
MOCOS	Xanthinuria, type II, Autosomal recessive
MRC2	No Mendelian disease association in OMIM
MSTN	Muscle hypertrophy
MTBP	No Mendelian disease association in OMIM
MTM1	Myotubular myopathy, X-linked, X-linked recessive
MX1	No Mendelian disease association in OMIM
MYBPC1	Congenital myopathy 16
MYBPC3	Cardiomyopathy, dilated, 1MM, Autosomal dominant;Cardiomyopathy, hypertrophic, 4, Autosomal dominant;Left ventricular noncompaction 10, Autosomal dominant
MYH1	No Mendelian disease association in OMIM

MYH7	Cardiomyopathy, dilated, 1S, Autosomal dominant;Cardiomyopathy, hypertrophic, 1, Autosomal dominant;Laing distal myopathy, Autosomal dominant;Left ventricular noncompaction 5, Autosomal dominant;Myopathy, myosin storage, autosomal dominant, Autosomal dominant;Myopathy, myosin storage, autosomal recessive, Autosomal recessive;Scapuloperoneal syndrome, myopathic type, Autosomal dominant
MYO7A	Deafness, autosomal dominant 11, Autosomal dominant;Deafness, autosomal recessive 2, Autosomal recessive;Usher syndrome, type 1B, Autosomal recessive
NAGLU	Mucopolysaccharidosis type IIIB (Sanfilippo B), Autosomal recessive
NAPEPLD	No Mendelian disease association in OMIM
NDRG1	Charcot-Marie-Tooth disease, type 4D, Autosomal recessive
NECAP1	No Mendelian disease association in OMIM
NHLRC2	No Mendelian disease association in OMIM
NPC1	Niemann-Pick disease, type C1, Autosomal recessive;Niemann-Pick disease, type D, Autosomal recessive
NSDHL	CHILD syndrome, X-linked dominant;CK syndrome, X-linked recessive
NUBPL	Mitochondrial complex I deficiency, Autosomal recessive, X-linked dominant, Mitochondrial
P3H2	Myopia, high, with cataract and vitreoretinal degeneration, Autosomal recessive
PAX3	Craniofacial-deafness-hand syndrome, Autosomal dominant;Rhabdomyosarcoma 2, alveolar, Autosomal recessive;Waardenburg syndrome, type 1, Autosomal dominant;Waardenburg syndrome, type 3, Autosomal recessive, Autosomal dominant
PCDH15	Deafness, autosomal recessive 23, Autosomal recessive;Usher syndrome, type 1D/F digenic, Autosomal recessive, Digenic recessive;Usher syndrome, type 1F, Autosomal recessive
PFAS	No Mendelian disease association in OMIM
PFKM	Glycogen storage disease VII, Autosomal recessive
PIGN	Multiple congenital anomalies-hypotonia-seizures syndrome 1, Autosomal recessive
PITX3	Anterior segment dysgenesis 1, multiple subtypes, Autosomal dominant;Cataract 11, multiple types, Autosomal dominant;Cataract 11, syndromic, Autosomal dominant

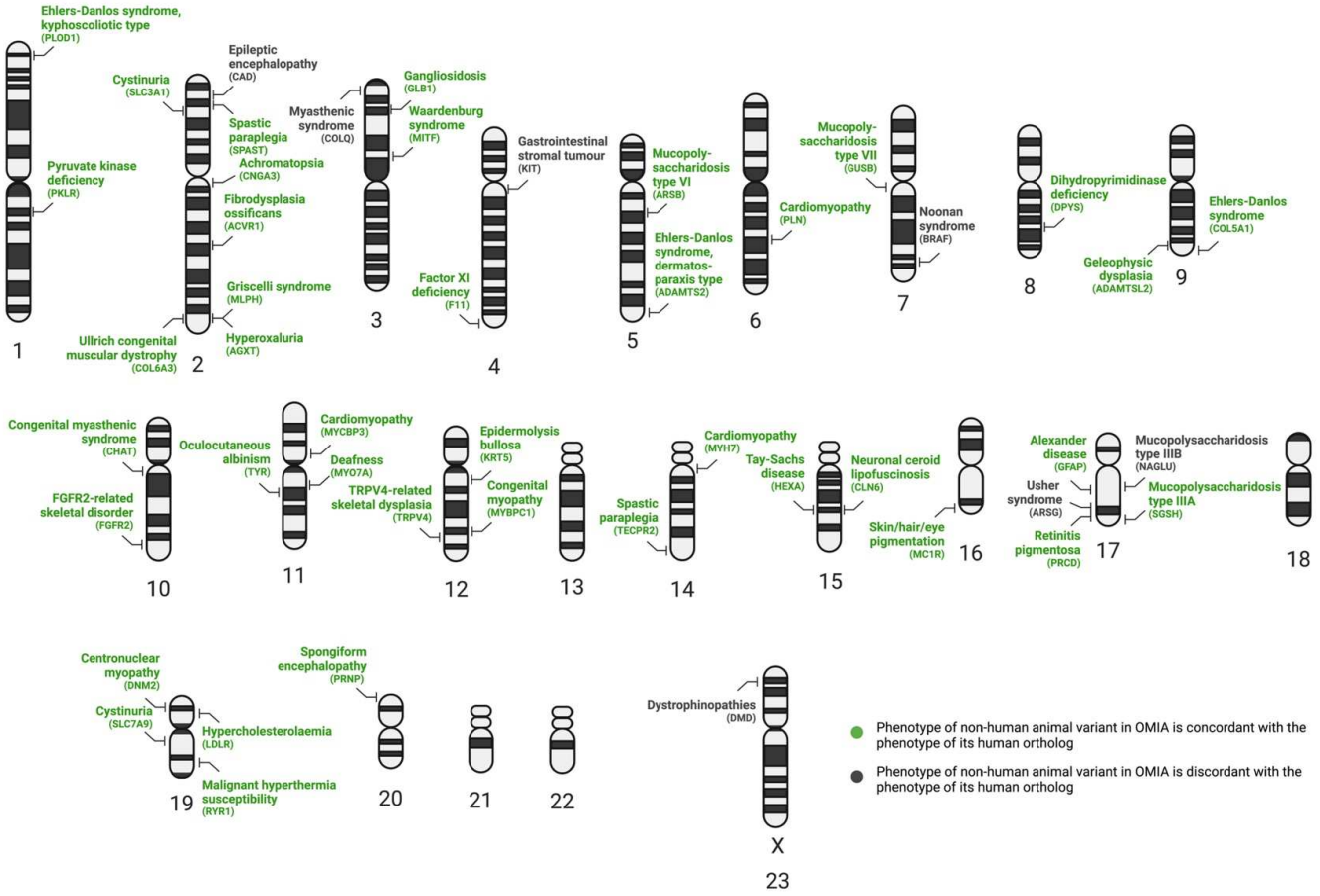
PKD1	Polycystic kidney disease, adult type I, Autosomal dominant
PKLR	Adenosine triphosphate, elevated, of erythrocytes, Autosomal dominant;Pyruvate kinase deficiency, Autosomal recessive
PLN	Cardiomyopathy, dilated, 1P;Cardiomyopathy, hypertrophic, 18, Autosomal dominant
PLOD1 *	Ehlers-Danlos syndrome, type VI, Autosomal recessive
PLP1	Pelizaeus-Merzbacher disease, X-linked recessive;Spastic paraplegia 2, X-linked, X-linked recessive
PLP2	No Mendelian disease association in OMIM
PMEL	No Mendelian disease association in OMIM
PNKP	Ataxia-oculomotor apraxia 4, Autosomal recessive;Microcephaly, seizures, and developmental delay, Autosomal recessive
PNPLA8	No Mendelian disease association in OMIM
PPARD	No Mendelian disease association in OMIM
PPIB *	Osteogenesis imperfecta, type IX, Autosomal recessive
PRCD	Retinitis pigmentosa 36
PRKAG3	[No associated Mendelian disease in OMIM] Skeletal muscle glycogen content and metabolism trait locus
PRL	No Mendelian disease association in OMIM
PRNP	Cerebral amyloid angiopathy, PRNP-related, Autosomal dominant;Creutzfeldt-Jakob disease, Autosomal dominant;Gerstmann-Straussler disease, Autosomal dominant;Huntington disease-like 1, Autosomal dominant;Insomnia, fatal familial, Autosomal dominant;Prion disease with protracted course, Autosomal dominant
PSMB7 *	No Mendelian disease association in OMIM
PYGM	McArdle disease, Autosomal recessive
RAB24	No Mendelian disease association in OMIM
RABGGTB *	No Mendelian disease association in OMIM
RASGRP2	No Mendelian disease association in OMIM

RDH5	Fundus albipunctatus, Autosomal recessive, Autosomal dominant
RETREG1	Neuropathy, hereditary sensory and autonomic, type IIB, Autosomal recessive
RHO	Night blindness, congenital stationary, autosomal dominant 1;Retinitis pigmentosa 4, autosomal dominant or recessive, Autosomal recessive, Autosomal dominant;Retinitis punctata albescens, Autosomal recessive, Autosomal dominant
RYR1	Central core disease, Autosomal recessive, Autosomal dominant;King-Denborough syndrome, Autosomal dominant;Minicore myopathy with external ophthalmoplegia, Autosomal recessive;Neuromuscular disease, congenital, with uniform type 1 fiber, Autosomal recessive, Autosomal dominant
SCN8A	Epileptic encephalopathy, early infantile, 13, Autosomal dominant;Seizures, benign familial infantile, 5, Autosomal dominant
SEL1L *	No Mendelian disease association in OMIM
SERPINH1	Osteogenesis imperfecta, type X, Autosomal recessive
SGSH	Mucopolysaccharidosis type IIIA (Sanfilippo A), Autosomal recessive
SLC12A1	Bartter syndrome, type 1, Autosomal recessive
SLC24A5	Albinism, oculocutaneous, type VI, Autosomal recessive
SLC25A12	Epileptic encephalopathy, early infantile, 39, Autosomal recessive
SLC25A46	Neuropathy, hereditary motor and sensory, type VIB, Autosomal recessive
SLC2A9	Hypouricemia, renal, 2, Autosomal recessive, Autosomal dominant
SLC35A3	No Mendelian disease association in OMIM
SLC36A1	No Mendelian disease association in OMIM
SLC39A4	Acrodermatitis enteropathica, Autosomal recessive
SLC3A1	Cystinuria, Autosomal recessive, Autosomal dominant
SLC45A2	Albinism, oculocutaneous, type IV
SLC5A3	No Mendelian disease association in OMIM

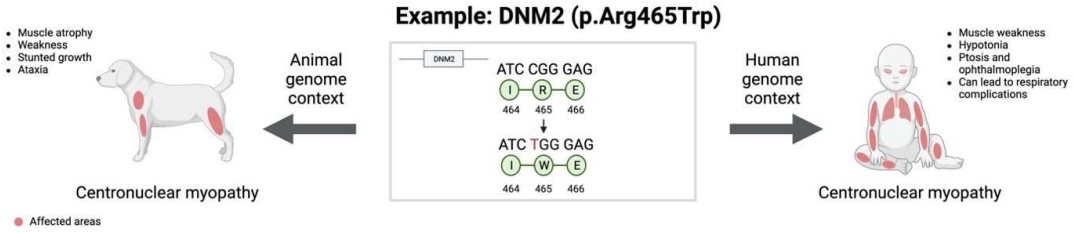
SLC6A5	Hyperekplexia 3, Autosomal recessive, Autosomal dominant
SLC7A9	Cystinuria, Autosomal recessive, Autosomal dominant
SMC2	No Mendelian disease association in OMIM
SOD1 *	Amyotrophic lateral sclerosis 1, Autosomal recessive, Autosomal dominant
SOWAHB	No Mendelian disease association in OMIM
SPAST	Spastic paraplegia 4, autosomal dominant, Autosomal dominant
STAT5B *	Growth hormone insensitivity with immunodeficiency;Leukemia, acute promyelocytic, somatic
SUGT1 *	No Mendelian disease association in OMIM
SUV39H2	No Mendelian disease association in OMIM
TBXT	No Mendelian disease association in OMIM
TECPR2	Spastic paraplegia 49, autosomal recessive, Autosomal recessive
TNXB	Ehlers-Danlos syndrome due to tenascin X deficiency, Autosomal recessive;Vesicoureteral reflux 8, Autosomal dominant
TPO	Thyroid dyshormonogenesis 2A, Autosomal recessive
TRPV4	Brachyolmia type 3, Autosomal dominant;Digital arthropathy-brachydactyly, familial, Autosomal dominant;Hereditary motor and sensory neuropathy, type IIc, Autosomal dominant;Metatropic dysplasia, Autosomal dominant;Parastremmatic dwarfism, Autosomal dominant;SED, Maroteaux type, Autosomal dominant;Scapuloperoneal spinal muscular atrophy, Autosomal dominant;Spinal muscular atrophy, distal, congenital nonprogressive, Autosomal dominant;Spondylometaphyseal dysplasia, Kozlowski type, Autosomal dominant
TSEN54	Pontocerebellar hypoplasia type 2A, Autosomal recessive;Pontocerebellar hypoplasia type 4, Autosomal recessive
TUBB1	Macrothrombocytopenia, autosomal dominant, TUBB1-related, Autosomal dominant
TUBD1	No Mendelian disease association in OMIM
TUBGCP5	No Mendelian disease association in OMIM

TYR	Albinism, oculocutaneous, type IA, Autosomal recessive;Albinism, oculocutaneous, type IB;Waardenburg syndrome/albinism, digenic, Autosomal dominant
TYRP1	Albinism, oculocutaneous, type III, Autosomal recessive
UCHL1	Spastic paraplegia 79, autosomal recessive, Autosomal recessive
UNC93B1	No Mendelian disease association in OMIM
UROD *	Porphyria cutanea tarda, Autosomal dominant;Porphyria, hepatoerythropoietic, Autosomal dominant
UROS	Porphyria, congenital erythropoietic, Autosomal recessive
VPS11	Leukodystrophy, hypomyelinating, 12, Autosomal recessive
VWF	von Willebrand disease, type 1, Autosomal dominant;von Willebrand disease, types 2A, 2B, 2M, and 2N, Autosomal recessive, Autosomal dominant;von Willibrand disease, type 3, Autosomal recessive
WIF1	No Mendelian disease association in OMIM
WWP1	No Mendelian disease association in OMIM
YARS2	Myopathy, lactic acidosis, and sideroblastic anemia 2, Autosomal recessive

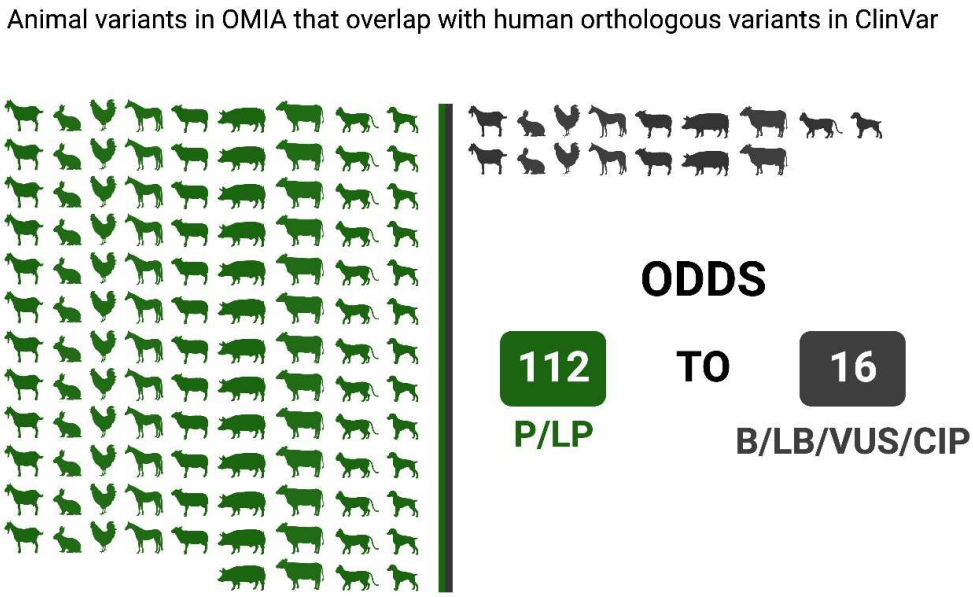
Supplemental Figure 1. Human karyogram indicating Mendelian diseases and the associated genes, where orthologous variants were observed in both non-human animals (OMIA) and humans (ClinVar). See text for details. Positions are approximate. Created with BioRender.com.



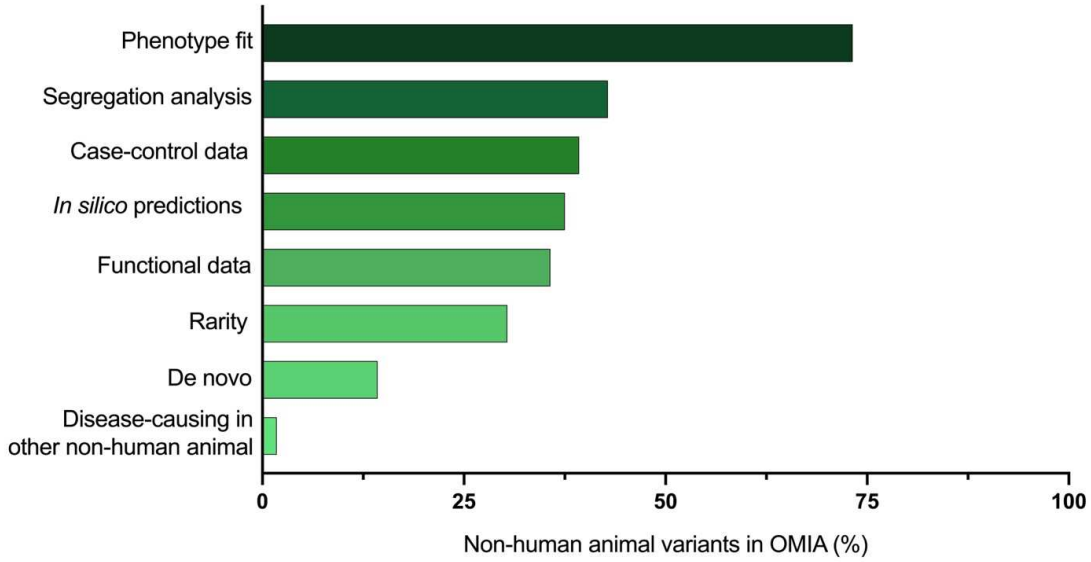
Supplemental Figure 2. An example of orthologous germline missense variants in *DNM2* (NM_001005361.3:c.1393C>T) affecting the conserved wild-type arginine residue [p.(Arg465Trp)] and causing centronuclear myopathy in both dogs and humans.[6 7] Created with BioRender.com.



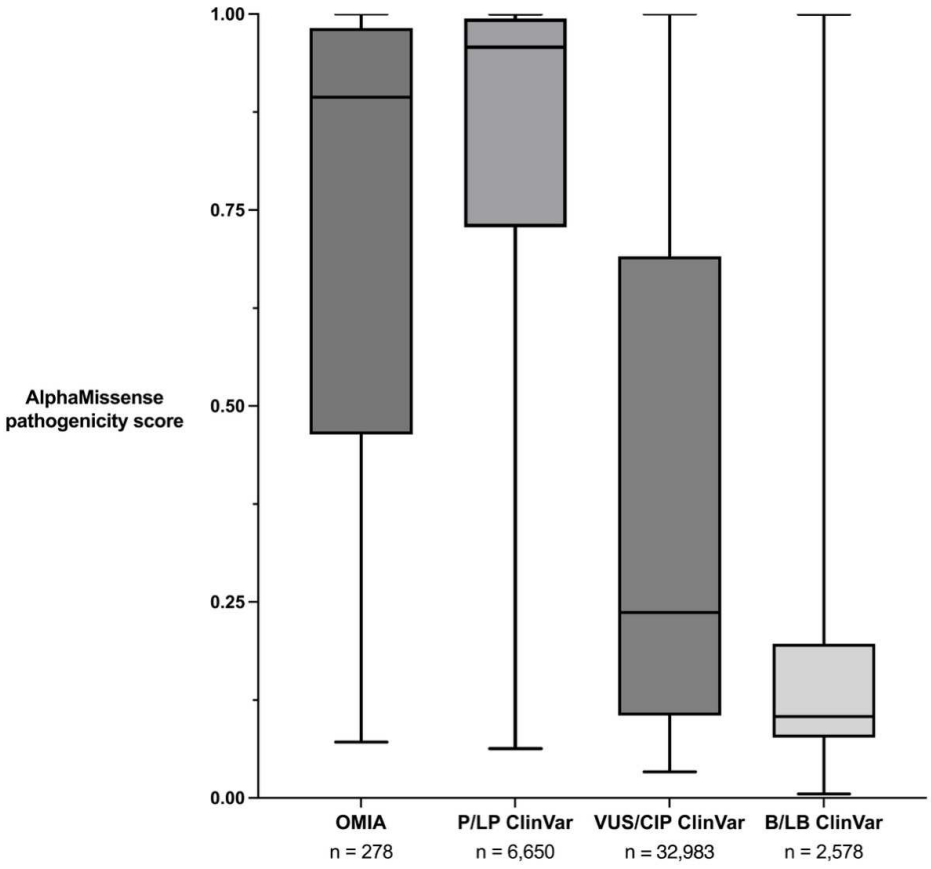
Supplemental Figure 3. Odds of the missense variants in non-human animal species extracted from OMIA for which orthologous human variants appear in ClinVar to have been classified in the latter as pathogenic/likely pathogenic (P/LP), compared to benign/likely benign/variant of uncertain significance/conflicting interpretations of pathogenicity (B/LB/VUS/CIP). Created with BioRender.com.



Supplemental Figure 4. Bar chart summarizing the evidence type(s) used in publications describing the initial association between a specific missense variant and a phenotype in a non-human animal species, for all variants in OMIA for which orthologous human variants were classified in ClinVar (n=56). Figure created with GraphPad Software.



Supplemental Figure 5. Boxplots of AlphaMissense[4] pathogenicity scores for the OMIA missense variants absent from ClinVar, comparing with other missense variation in ClinVar in the same gene set. B/LB, Benign/Likely benign; P/LP, Pathogenic/Likely pathogenic; VUS/CIP, variant of uncertain significance/conflicting interpretations of pathogenicity.



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