

**Table S3.** High confidence loss of hydroxylation sites with their associated disease.

Pro ID	AC	Variation	Site	Associated disease	Note
ABCA4_HUMAN	P78363	C1490Y	P1486	Cone-rod dystrophy 3 (CORD3) [MIM:604116]	i
AGAL_HUMAN	P06280	C378Y	P380	Fabry disease (FD) [MIM:301500]	c
ANDR_HUMAN	P10275	R615P	P612	Androgen insensitivity syndrome (AIS) [MIM:300068]	e
ANDR_HUMAN	P10275	L616P	P612	Androgen insensitivity syndrome (AIS) [MIM:300068]	e
ANDR_HUMAN	P10275	R617P	P612	Androgen insensitivity syndrome (AIS) [MIM:300068]	e
ASM_HUMAN	P17405	L225P	P224	Niemann-Pick disease B (NPDB) [MIM:607616]	b
C1QB_HUMAN	P02746	G42D	P41	Complement component C1q deficiency (C1QD) [MIM:613652]	e
C1QB_HUMAN	P02746	G42D	P38	Complement component C1q deficiency (C1QD) [MIM:613652]	e
CCBE1_HUMAN	Q6UXH8	G327R	P323	Hennekam lymphangiectasia-lymphedema syndrome 1 (HKLLS1) [MIM:235510]	d
CFAH_HUMAN	P08603	C325Y	P324	Hemolytic uremic syndrome atypical 1 (AHUS1) [MIM:235400]	c
CFAH_HUMAN	P08603	C1163W	P1166	Hemolytic uremic syndrome atypical 1 (AHUS1) [MIM:235400]	c
CHST6_HUMAN	Q9GZX3	S131P	P133	Macular corneal dystrophy 1 (MCD1) [MIM:217800]	i
CHST6_HUMAN	Q9GZX3	S131P	P132	Macular corneal dystrophy 1 (MCD1) [MIM:217800]	i
CHSTE_HUMAN	Q8NCH0	C289S	P288	Ehlers-danlos syndrome, musculocontractural type 1 (EDSMC1) [MIM:601776]	c
CO1A1_HUMAN	P02452	G350R	P346	Osteogenesis imperfecta 3 (OI3) [MIM:259420]	a
CO1A1_HUMAN	P02452	G1157D	P1159	Osteogenesis imperfecta 1 (OI1) [MIM:166200]	a
CO1A1_HUMAN	P02452	G548A	P544	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G533D	P529	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G560R	P556	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G1187V	P1183	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G1025R	P1024	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G338C	P343	Osteogenesis imperfecta 4 (OI4) [MIM:166220]	a
CO1A1_HUMAN	P02452	G581R	P583	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G977D	P976	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G197R	P196	Osteogenesis imperfecta 4 (OI4) [MIM:166220]	a
CO1A1_HUMAN	P02452	G287S	P289	Osteogenesis imperfecta 1 (OI1) [MIM:166200]	a
CO1A1_HUMAN	P02452	G980V	P976	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G368V	P373	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G257R	P262	Osteogenesis imperfecta 4 (OI4) [MIM:166220]	a
CO1A1_HUMAN	P02452	G977D	P973	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G476R	P475	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G1100D	K1096	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G1094S	K1096	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G1091S	K1096	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A1_HUMAN	P02452	G266E	K265	Osteogenesis imperfecta 1 (OI1) [MIM:166200]	a
CO1A1_HUMAN	P02452	G263R	K265	Osteogenesis imperfecta 1 (OI1) [MIM:166200]	a
CO1A2_HUMAN	P08123	G253D	P255	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A2_HUMAN	P08123	G1003D	K1008	Osteogenesis imperfecta 2 (OI2) [MIM:166210]	a
CO1A2_HUMAN	P08123	G1012S	K1008	Osteogenesis imperfecta 3 (OI3) [MIM:259420]	a
CO2A1_HUMAN	P02458	G510D	P506	Achondrogenesis 2 (ACG2) [MIM:200610]	a
CO2A1_HUMAN	P02458	G948D	P953	Achondrogenesis 2 (ACG2) [MIM:200610]	a
CO2A1_HUMAN	P02458	G894E	P899	Achondrogenesis 2 (ACG2) [MIM:200610]	a
CO2A1_HUMAN	P02458	G780R	P779	Achondrogenesis 2 (ACG2) [MIM:200610]	a
CO2A1_HUMAN	P02458	G303D	K308	Kniest dysplasia (KD) [MIM:156550]	a
CO2A1_HUMAN	P02458	G453V	K452	Achondrogenesis 2 (ACG2) [MIM:200610]	a
CO2A1_HUMAN	P02458	G282D	K287	Stickler syndrome 1 (STL1) [MIM:108300]	a
CO2A1_HUMAN	P02458	G453D	K452	Achondrogenesis 2 (ACG2) [MIM:200610]	a
CO2A1_HUMAN	P02458	G453A	K452	Stickler syndrome 1 (STL1) [MIM:108300]	a
CO2A1_HUMAN	P02458	D547V	K542	Achondrogenesis 2 (ACG2) [MIM:200610]	a
CO2A1_HUMAN	P02458	G375R	K374	Spondyloepiphyseal dysplasia congenital type (SEDC) [MIM:183900]	a
CO2A1_HUMAN	P02458	G447S	K452	Spondyloepiphyseal dysplasia congenital type (SEDC) [MIM:183900]	a
CO3A1_HUMAN	P02461	G879V	P875	Ehlers-Danlos syndrome 4 (EDS4) [MIM:130050]	a
CO3A1_HUMAN	P02461	G660D	P659	Ehlers-Danlos syndrome 4 (EDS4) [MIM:130050]	a
CO3A1_HUMAN	P02461	G657E	P659	Ehlers-Danlos syndrome 4 (EDS4) [MIM:130050]	a
CO3A1_HUMAN	P02461	G444R	P443	Ehlers-Danlos syndrome 4 (EDS4) [MIM:130050]	a

CO3A1_HUMAN	P02461	G1098V	K1094	Ehlers-Danlos syndrome 4 (EDS4) [MIM:130050]	a
CO3A1_HUMAN	P02461	G1098D	K1094	Ehlers-Danlos syndrome 4 (EDS4) [MIM:130050]	a
CO3A1_HUMAN	P02461	G1101E	K1106	Ehlers-Danlos syndrome 4 (EDS4) [MIM:130050]	a
CO3A1_HUMAN	P02461	G1104A	K1106	Ehlers-Danlos syndrome 4 (EDS4) [MIM:130050]	a
CO3A1_HUMAN	P02461	G264R	K263	Ehlers-Danlos syndrome 4 (EDS4) [MIM:130050]	a
CO3A1_HUMAN	P02461	G1089D	K1094	Ehlers-Danlos syndrome 4 (EDS4) [MIM:130050]	a
CO3A1_HUMAN	P02461	G267V	K263	Ehlers-Danlos syndrome 4 (EDS4) [MIM:130050]	a
CO4A3_HUMAN	Q01955	G532D	K537	Alport syndrome, autosomal recessive (APSAR) [MIM:203780]	a
CO4A5_HUMAN	P29400	G796R	P795	Alport syndrome, X-linked (APSX) [MIM:301050]	a
CO4A5_HUMAN	P29400	G204V	P200	Alport syndrome, X-linked (APSX) [MIM:301050]	a
CO4A5_HUMAN	P29400	E633K	K634	Alport syndrome, X-linked (APSX) [MIM:301050]	a
CO4A5_HUMAN	P29400	G638V	K634	Alport syndrome, X-linked (APSX) [MIM:301050]	a
CO4A5_HUMAN	P29400	G638S	K634	Alport syndrome, X-linked (APSX) [MIM:301050]	a
CO4A5_HUMAN	P29400	G635D	K634	Alport syndrome, X-linked (APSX) [MIM:301050]	a
CO4A5_HUMAN	P29400	G638A	K634	Alport syndrome, X-linked (APSX) [MIM:301050]	a
CO4A5_HUMAN	P29400	G629D	K634	Alport syndrome, X-linked (APSX) [MIM:301050]	a
CO4A5_HUMAN	P29400	G230R	K229	Alport syndrome, X-linked (APSX) [MIM:301050]	a
CO4A5_HUMAN	P29400	G325E	K330	Alport syndrome, X-linked (APSX) [MIM:301050]	a
CO7A1_HUMAN	Q02388	G2674D	P2673	Epidermolysis bullosa dystrophica, autosomal recessive (RDEB) [MIM:226600]	a
CO7A1_HUMAN	Q02388	G2671V	P2667	Epidermolysis bullosa dystrophica, autosomal recessive (RDEB) [MIM:226600]	a
CO7A1_HUMAN	Q02388	G2674R	P2673	Epidermolysis bullosa dystrophica, autosomal recessive (RDEB) [MIM:226600]	a
CO7A1_HUMAN	Q02388	G2623C	K2625	Epidermolysis bullosa dystrophica, pretibial type (PR-DEB) [MIM:131850]	a
COBA2_HUMAN	P13942	G808E	K810	Deafness, autosomal dominant, 13 (DFNA13) [MIM:601868]	a
COLQ_HUMAN	Q9Y215	C444Y	P450	Myasthenic syndrome, congenital, Engel type (CMSE) [MIM:603034]	b
CRUM1_HUMAN	P82279	C195F	P194	Retinitis pigmentosa 12 (RP12) [MIM:600105]	i
CXA1_HUMAN	P17302	H194P	P193	Oculodentodigital dysplasia (ODDD) [MIM:164200]	i
CXA1_HUMAN	P17302	H194P	P191	Oculodentodigital dysplasia (ODDD) [MIM:164200]	i
CXB1_HUMAN	P08034	C173R	P172	Charcot-marie-tooth disease, x-linked dominant, 1 (CMTX1) [MIM:302800]	b
DCR1C_HUMAN	Q96SD1	H35D	K40	Omenn syndrome (OS) [MIM:603554]	d
F13B_HUMAN	P05160	C450F	P453	Factor XIII subunit B deficiency (FA13BD) [MIM:613235]	c
FA7_HUMAN	P08709	S120P	P114	Factor VII deficiency (FA7D) [MIM:227500]	c
FBN1_HUMAN	P35555	C1733Y	P1732	Geleophysic dysplasia 2 (GPHYSD2) [MIM:614185]	a
FBN1_HUMAN	P35555	C1577G	P1573	Stiff skin syndrome (SSKS) [MIM:184900]	a
FBN1_HUMAN	P35555	R1137P	P1142	Marfan syndrome (MFS) [MIM:154700]	i
FBN1_HUMAN	P35555	C890R	P886	Marfan syndrome (MFS) [MIM:154700]	i
FKRP_HUMAN	Q9H9S5	C318Y	P316	Muscular dystrophy-dystroglycanopathy congenital with brain and eye anomalies A5 (MDDGA5) [MIM:613153]	i
GRM6_HUMAN	O15303	C522Y	P521	Night blindness, congenital stationary, 1B (CSNB1B) [MIM:257270]	i
HEMH_HUMAN	P22830	C406S	P404	Erythropoietic protoporphyria (EPP) [MIM:177000]	c
HEMH_HUMAN	P22830	C406Y	P404	Erythropoietic protoporphyria (EPP) [MIM:177000]	c
IDS_HUMAN	P22304	H159P	K164	Mucopolysaccharidosis 2 (MPS2) [MIM:309900]	h
KCNH2_HUMAN	Q12809	T65P	P63	Long QT syndrome 2 (LQT2) [MIM:613688]	c
MIS_HUMAN	P03971	C525Y	P524	Persistent Muellerian duct syndrome 1 (PMDS1) [MIM:261550]	g
MIS_HUMAN	P03971	C525Y	P523	Persistent Muellerian duct syndrome 1 (PMDS1) [MIM:261550]	g
NDP_HUMAN	Q00604	S92P	P98	Norrie disease (ND) [MIM:310600]	i
NDP_HUMAN	Q00604	R97P	P98	Norrie disease (ND) [MIM:310600]	i
NDP_HUMAN	Q00604	C96W	P98	Norrie disease (ND) [MIM:310600]	i
NMDE1_HUMAN	Q12879	C436R	P435	Epilepsy, focal, with speech disorder and with or without mental retardation (FESD) [MIM:245570]	b
NOTC3_HUMAN	Q9UM47	C123F	P122	Cerebral arteriopathy with subcortical infarcts and leukoencephalopathy, autosomal dominant (CADASIL) [MIM:125310]	c
NOTC3_HUMAN	Q9UM47	C201Y	P197	Cerebral arteriopathy with subcortical infarcts and leukoencephalopathy, autosomal dominant (CADASIL) [MIM:125310]	c
NOTC3_HUMAN	Q9UM47	C123Y	P122	Cerebral arteriopathy with subcortical infarcts and leukoencephalopathy, autosomal dominant (CADASIL)	c

				[MIM:125310]	
NPC2_HUMAN	P61916	C47F	P46	Niemann-Pick disease C2 (NPC2) [MIM:607625]	b
PERT_HUMAN	P07202	C808R	P806	Thyroid dyshormonogenesis 2A (TDH2A) [MIM:274500]	e
PKD1_HUMAN	P98161	L727P	P733	Polycystic kidney disease 1 (PKD1) [MIM:173900]	e
PRKN2_HUMAN	O60260	C418R	P417	Parkinson disease 2 (PARK2) [MIM:600116]	b
SCN5A_HUMAN	Q14524	H681P	P685	Brugada syndrome 1 (BRGDA1) [MIM:601144]	c
SCN5A_HUMAN	Q14524	H681P	P684	Brugada syndrome 1 (BRGDA1) [MIM:601144]	c
STS_HUMAN	P08842	Q560P	P564	Ichthyosis, X-linked (IXL) [MIM:308100]	e
THAP1_HUMAN	Q9NVV9	Q187K	K190	Dystonia 6,torsion (DYT6) [MIM:602629]	a
TNR11_HUMAN	Q9Y6Q6	C175R	P171	Osteopetrosis, autosomal recessive 7 (OPTB7) [MIM:612301]	a
TSC2_HUMAN	P49815	R261P	P255	Tuberous sclerosis 2 (TSC2) [MIM:613254]	h
UROM_HUMAN	P07911	C223Y	P219	Familial juvenile hyperuricemic nephropathy 1 (HNFJ1) [MIM:162000]	c
UROM_HUMAN	P07911	C217R	P219	Familial juvenile hyperuricemic nephropathy 1 (HNFJ1) [MIM:162000]	c

Note: a. Dysplasia of skeleton, joint, muscle or skin; b. Malfunction of neurologic system; c. Abnormalities of cardiovascular, cerebrovascular, arteries or blood; d. Immunodeficiency; e. Kidney disease; f. Malfunction of endocrine system; g. Abnormalities of reproductive system; h. Multisystem disorder; i. Dysplasia of eyes or areas. There are 111 different disease-associated variations in all in this table that were predicted to cause 117 different high-confidence loss of hydroxylation sites.