

Supplementary Table 1: Variants used to evaluate the performance of REVEL on loss of function (LoF) and gain of function (GoF) variants.

Diabetes includes neonatal diabetes and maturity onset diabetes of the young (MODY). HI; hyperinsulinism. Nomenclature is given according to the following transcripts: *ABCC8* NM_001287174.1, *GCK* NM_000162.3 and *KCNJ11* NM_000525.4.

Gene	Protein change	Nucleotide change	Genomic location (GRCh37)	REVEL score	GoF or LoF	Phenotype
<i>ABCC8</i>	p.(Val86Ala)	c.257T>C	11:17496466A>G	0.794	GoF	Diabetes
<i>ABCC8</i>	p.(Val86Gly)	c.257T>G	11:17496466A>C	0.97	GoF	Diabetes
<i>ABCC8</i>	p.(Phe132Leu)	c.394T>C	11:17491666A>G	0.89	GoF	Diabetes
<i>ABCC8</i>	p.(Phe132Val)	c.394T>G	11:17491666A>C	0.808	GoF	Diabetes
<i>ABCC8</i>	p.(Glu208Lys)	c.622G>A	11:17483330C>T	0.669	GoF	Diabetes
<i>ABCC8</i>	p.(Asp209Glu)	c.627C>A	11:17483325G>T	0.739	GoF	Diabetes
<i>ABCC8</i>	p.(Gln211Lys)	c.631C>A	11:17483321G>T	0.617	GoF	Diabetes
<i>ABCC8</i>	p.(Leu213Arg)	c.638T>G	11:17483314A>C	0.72	GoF	Diabetes
<i>ABCC8</i>	p.(Leu225Pro)	c.674T>C	11:17483278A>G	0.769	GoF	Diabetes
<i>ABCC8</i>	p.(Thr229Ile)	c.686C>T	11:17483266G>A	0.894	GoF	Diabetes
<i>ABCC8</i>	p.(Val324Met)	c.970G>A	11:17482076C>T	0.895	GoF	Diabetes
<i>ABCC8</i>	p.(Leu451Pro)	c.1352T>C	11:17464840A>G	0.936	GoF	Diabetes
<i>ABCC8</i>	p.(Leu582Val)	c.1744C>G	11:17452434G>C	0.839	GoF	Diabetes
<i>ABCC8</i>	p.(Arg826Trp)	c.2476C>T	11:17434943G>A	0.855	GoF	Diabetes
<i>ABCC8</i>	p.(His1024Tyr)	c.3070C>T	11:17428530G>A	0.687	GoF	Diabetes
<i>ABCC8</i>	p.(Asn1123Asp)	c.3367A>G	11:17427076T>C	0.896	GoF	Diabetes
<i>ABCC8</i>	p.(Arg1183Trp)	c.3547C>T	11:17426072G>A	0.885	GoF	Diabetes
<i>ABCC8</i>	p.(Arg1183Gln)	c.3548G>A	11:17426071C>T	0.767	GoF	Diabetes
<i>ABCC8</i>	p.(Arg1314His)	c.3941G>A	11:17418790C>T	0.933	GoF	Diabetes
<i>ABCC8</i>	p.(Arg1380Cys)	c.4138C>T	11:17417462G>A	0.953	GoF	Diabetes
<i>ABCC8</i>	p.(Arg1380His)	c.4139G>A	11:17417461C>T	0.964	GoF	Diabetes
<i>ABCC8</i>	p.(Arg1380Leu)	c.4139G>T	11:17417461C>A	0.959	GoF	Diabetes
<i>ABCC8</i>	p.(Ile1425Val)	c.4273A>G	11:17417194T>C	0.772	GoF	Diabetes

ABCC8	p.(Gly7Arg)	c.19G>C	11:17498305C>G	0.954	LoF	HI
ABCC8	p.(Val21Asp)	c.62T>A	11:17498262A>T	0.863	LoF	HI
ABCC8	p.(Asn24Lys)	c.72C>A	11:17498252G>T	0.858	LoF	HI
ABCC8	p.(Arg74Trp)	c.220C>T	11:17496503G>A	0.976	LoF	HI
ABCC8	p.(Gly111Trp)	c.331G>T	11:17491729C>A	0.636	LoF	HI
ABCC8	p.(His125Gln)	c.375C>G	11:17491685G>C	0.888	LoF	HI
ABCC8	p.(Val187Asp)	c.560T>A	11:17485004A>T	0.815	LoF	HI
ABCC8	p.(Gly228Asp)	c.683G>A	11:17483269C>T	0.614	LoF	HI
ABCC8	p.(Asp310Asn)	c.928G>A	11:17482118C>T	0.833	LoF	HI
ABCC8	p.(Arg370Gly)	c.1108A>G	11:17474734T>C	0.644	LoF	HI
ABCC8	p.(Arg370Ser)	c.1110G>C	11:17474732C>G	0.559	LoF	HI
ABCC8	p.(Arg495Gln)	c.1484G>A	11:17464413C>T	0.872	LoF	HI
ABCC8	p.(Arg1215Trp)	c.3643C>T	11:17424218G>A	0.964	LoF	HI
ABCC8	p.(Arg1353His)	c.4058G>A	11:17418527C>T	0.934	LoF	HI
ABCC8	p.(Lys1374Arg)	c.4121A>G	11:17418464T>C	0.868	LoF	HI
ABCC8	p.(Ser1386Pro)	c.4156T>C	11:17417444A>G	0.979	LoF	HI
ABCC8	p.(Gly1478Val)	c.4433G>T	11:17415928C>A	0.88	LoF	HI
ABCC8	p.(Gly1479Arg)	c.4435G>A	11:17415926C>T	0.939	LoF	HI
ABCC8	p.(Arg1494Trp)	c.4480C>T	11:17415881G>A	0.93	LoF	HI
ABCC8	p.(Arg1494Gln)	c.4481G>A	11:17415880C>T	0.979	LoF	HI
ABCC8	p.(Glu1507Lys)	c.4519G>A	11:17415842C>T	0.963	LoF	HI
ABCC8	p.(Ile1512Thr)	c.4535T>C	11:17415826A>G	0.927	LoF	HI
ABCC8	p.(Arg1539Gln)	c.4616G>A	11:17414671C>T	0.877	LoF	HI
ABCC8	p.(Leu1544Pro)	c.4631T>C	11:17414656A>G	0.915	LoF	HI
GCK	p.(Ser64Tyr)	c.191C>A	7:44192917G>T	0.984	GoF	HI
GCK	p.(Thr65Ile)	c.194C>T	7:44192914G>A	0.82	GoF	HI
GCK	p.(Gly68Val)	c.203G>T	7:44192905C>A	0.993	GoF	HI

<i>GCK</i>	p.(Trp99Arg)	c.295T>C	7:44191938A>G	0.753	GoF	HI
<i>GCK</i>	p.(Tyr214Cys)	c.641A>G	7:44189397T>C	0.706	GoF	HI
<i>GCK</i>	p.(Val452Leu)	c.1354G>C	7:44184779C>G	0.601	GoF	HI
<i>GCK</i>	p.(Val455Met)	c.1363G>A	7:44184770C>T	0.853	GoF	HI
<i>GCK</i>	p.(Ala456Val)	c.1367C>T	7:44184766G>A	0.883	GoF	HI
<i>GCK</i>	p.(Gly44Ser)	c.130G>A	7:44192978C>T	0.962	LoF	Diabetes
<i>GCK</i>	p.(Gly44Asp)	c.131G>A	7:44192977C>T	0.995	LoF	Diabetes
<i>GCK</i>	p.(Tyr108His)	c.322T>C	7:44191911A>G	0.949	LoF	Diabetes
<i>GCK</i>	p.(Cys129Tyr)	c.386G>A	7:44190652C>T	0.97	LoF	Diabetes
<i>GCK</i>	p.(Phe150Ser)	c.449T>C	7:44190589A>G	0.983	LoF	Diabetes
<i>GCK</i>	p.(Asp160Asn)	c.478G>A	7:44190560C>T	0.712	LoF	Diabetes
<i>GCK</i>	p.(Asn180Lys)	c.540T>G	7:44189607A>C	0.751	LoF	Diabetes
<i>GCK</i>	p.(Val182Met)	c.544G>A	7:44189603C>T	0.937	LoF	Diabetes
<i>GCK</i>	p.(Ala188Thr)	c.562G>A	7:44189585C>T	0.933	LoF	Diabetes
<i>GCK</i>	p.(Arg191Trp)	c.571C>T	7:44189576G>A	0.936	LoF	Diabetes
<i>GCK</i>	p.(Ala201Ser)	c.601G>T	7:44189437C>A	0.929	LoF	Diabetes
<i>GCK</i>	p.(Val203Ala)	c.608T>C	7:44189430A>G	0.946	LoF	Diabetes
<i>GCK</i>	p.(Gly223Ser)	c.667G>A	7:44189371C>T	0.943	LoF	Diabetes
<i>GCK</i>	p.(Gly261Arg)	c.781G>A	7:44187331C>T	0.914	LoF	Diabetes
<i>GCK</i>	p.(Glu265Lys)	c.793G>A	7:44187319C>T	0.728	LoF	Diabetes
<i>GCK</i>	p.(Asp278Glu)	c.834C>A	7:44187278G>T	0.896	LoF	Diabetes
<i>GCK</i>	p.(Ser340Ile)	c.1019G>T	7:44186062C>A	0.792	LoF	Diabetes
<i>GCK</i>	p.(Met381Thr)	c.1142T>C	7:44185207A>G	0.93	LoF	Diabetes
<i>GCK</i>	p.(Arg392Cys)	c.1174C>T	7:44185175G>A	0.911	LoF	Diabetes
<i>GCK</i>	p.(Arg397Leu)	c.1190G>T	7:44185159C>A	0.925	LoF	Diabetes
<i>KCNJ11</i>	p.(Ser3Cys)	c.8C>G	11:17409631G>C	0.658	GoF	Diabetes
<i>KCNJ11</i>	p.(His46Tyr)	c.136C>T	11:17409503G>A	0.845	GoF	Diabetes

<i>KCNJ11</i>	p.(Arg50Gln)	c.149G>A	11:17409490C>T	0.831	GoF	Diabetes
<i>KCNJ11</i>	p.(Arg50Pro)	c.149G>C	11:17409490C>G	0.887	GoF	Diabetes
<i>KCNJ11</i>	p.(Glu51Ala)	c.152A>C	11:17409487T>G	0.907	GoF	Diabetes
<i>KCNJ11</i>	p.(Gln52Arg)	c.155A>G	11:17409484T>C	0.811	GoF	Diabetes
<i>KCNJ11</i>	p.(Gly53Ser)	c.157G>A	11:17409482C>T	0.794	GoF	Diabetes
<i>KCNJ11</i>	p.(Gly53Arg)	c.157G>C	11:17409482C>G	0.817	GoF	Diabetes
<i>KCNJ11</i>	p.(Gly53Asp)	c.158G>A	11:17409481C>T	0.841	GoF	Diabetes
<i>KCNJ11</i>	p.(Val59Met)	c.175G>A	11:17409464C>T	0.766	GoF	Diabetes
<i>KCNJ11</i>	p.(Val59Gly)	c.176T>G	11:17409463A>C	0.939	GoF	Diabetes
<i>KCNJ11</i>	p.(Leu164Pro)	c.491T>C	11:17409148A>G	0.973	GoF	Diabetes
<i>KCNJ11</i>	p.(Cys166Tyr)	c.497G>A	11:17409142C>T	0.954	GoF	Diabetes
<i>KCNJ11</i>	p.(Cys166Phe)	c.497G>T	11:17409142C>A	0.944	GoF	Diabetes
<i>KCNJ11</i>	p.(Ile167Leu)	c.499A>C	11:17409140T>G	0.828	GoF	Diabetes
<i>KCNJ11</i>	p.(Lys170Thr)	c.509A>C	11:17409130T>G	0.99	GoF	Diabetes
<i>KCNJ11</i>	p.(Lys170Arg)	c.509A>G	11:17409130T>C	0.946	GoF	Diabetes
<i>KCNJ11</i>	p.(Lys170Asn)	c.510G>C	11:17409129C>G	0.886	GoF	Diabetes
<i>KCNJ11</i>	p.(Glu179Ala)	c.536A>C	11:17409103T>G	0.945	GoF	Diabetes
<i>KCNJ11</i>	p.(Ile182Val)	c.544A>G	11:17409095T>C	0.786	GoF	Diabetes
<i>KCNJ11</i>	p.(Arg201Ser)	c.601C>A	11:17409038G>T	0.969	GoF	Diabetes
<i>KCNJ11</i>	p.(Arg201Cys)	c.601C>T	11:17409038G>A	0.977	GoF	Diabetes
<i>KCNJ11</i>	p.(Arg201His)	c.602G>A	11:17409037C>T	0.982	GoF	Diabetes
<i>KCNJ11</i>	p.(Arg201Leu)	c.602G>T	11:17409037C>A	0.986	GoF	Diabetes
<i>KCNJ11</i>	p.(Glu227Lys)	c.679G>A	11:17408960C>T	0.972	GoF	Diabetes
<i>KCNJ11</i>	p.(Glu229Lys)	c.685G>A	11:17408954C>T	0.981	GoF	Diabetes
<i>KCNJ11</i>	p.(Leu233Phe)	c.697C>T	11:17408942G>A	0.752	GoF	Diabetes
<i>KCNJ11</i>	p.(Val252Met)	c.754G>A	11:17408885C>T	0.918	GoF	Diabetes
<i>KCNJ11</i>	p.(Val252Gly)	c.755T>G	11:17408884A>C	0.97	GoF	Diabetes

<i>KCNJ11</i>	p.(Thr293Asn)	c.878C>A	11:17408761G>T	0.832	GoF	Diabetes
<i>KCNJ11</i>	p.(Ile296Leu)	c.886A>C	11:17408753T>G	0.834	GoF	Diabetes
<i>KCNJ11</i>	p.(Glu322Lys)	c.964G>A	11:17408675C>T	0.911	GoF	Diabetes
<i>KCNJ11</i>	p.(Tyr330Ser)	c.989A>C	11:17408650T>G	0.981	GoF	Diabetes
<i>KCNJ11</i>	p.(Gly334Asp)	c.1001G>A	11:17408638C>T	0.787	GoF	Diabetes
<i>KCNJ11</i>	p.(Arg34His)	c.101G>A	11:17409538C>T	0.965	LoF	HI
<i>KCNJ11</i>	p.(Gly40Asp)	c.119G>A	11:17409520C>T	0.988	LoF	HI
<i>KCNJ11</i>	p.(Phe55Leu)	c.165C>A	11:17409474G>T	0.924	LoF	HI
<i>KCNJ11</i>	p.(Thr62Met)	c.185C>T	11:17409454G>A	0.952	LoF	HI
<i>KCNJ11</i>	p.(Lys67Asn)	c.201G>C	11:17409438C>G	0.815	LoF	HI
<i>KCNJ11</i>	p.(Trp91Arg)	c.271T>C	11:17409368A>G	0.953	LoF	HI
<i>KCNJ11</i>	p.(Ala101Asp)	c.302C>A	11:17409337G>T	0.467	LoF	HI
<i>KCNJ11</i>	p.(Ser116Pro)	c.346T>C	11:17409293A>G	0.93	LoF	HI
<i>KCNJ11</i>	p.(Gly134Ala)	c.401G>C	11:17409238C>G	0.976	LoF	HI
<i>KCNJ11</i>	p.(Arg136Leu)	c.407G>T	11:17409232C>A	0.984	LoF	HI
<i>KCNJ11</i>	p.(Gly156Arg)	c.466G>A	11:17409173C>T	0.99	LoF	HI
<i>KCNJ11</i>	p.(Asp204Glu)	c.612C>A	11:17409027G>T	0.948	LoF	HI
<i>KCNJ11</i>	p.(Ala213Thr)	c.637G>A	11:17409002C>T	0.954	LoF	HI
<i>KCNJ11</i>	p.(Pro254Leu)	c.761C>T	11:17408878G>A	0.971	LoF	HI
<i>KCNJ11</i>	p.(His259Arg)	c.776A>G	11:17408863T>C	0.993	LoF	HI
<i>KCNJ11</i>	p.(Pro266Leu)	c.797C>T	11:17408842G>A	0.979	LoF	HI
<i>KCNJ11</i>	p.(Glu282Lys)	c.844G>A	11:17408795C>T	0.961	LoF	HI
<i>KCNJ11</i>	p.(Thr294Met)	c.881C>T	11:17408758G>A	0.958	LoF	HI
<i>KCNJ11</i>	p.(Arg301Gly)	c.901C>G	11:17408738G>C	0.946	LoF	HI
<i>KCNJ11</i>	p.(Arg301Cys)	c.901C>T	11:17408738G>A	0.94	LoF	HI
<i>KCNJ11</i>	p.(Arg301His)	c.902G>A	11:17408737C>T	0.972	LoF	HI
<i>KCNJ11</i>	p.(Arg301Pro)	c.902G>C	11:17408737C>G	0.984	LoF	HI

