

Supplemental Table 1. Targeted recessive genes in murine models with unilateral renal agenesis and respective phenotypes caused by recessive mutations in humans.

Gene Symbol	Mouse Model with unilateral renal agenesis ¹	Inh. in Mice	Inh. in Humans	Phenotype if mutated in Humans [OMIM#]	Renal Involvement	MGI short description of murine phenotype ²	Lit.
<i>BAG6</i>	<u><i>Bag6</i>^{tm1Pmc}/<i>Bag6</i>^{tm1Pmc}</u>	AR	n/a	none	no	"Targeted disruption of this gene results in either embryonic lethality following abnormal brain development or neonatal death associated with severe developmental defects in the lung and kidney. These developmental defects are associated with widespread aberrant apoptosis and proliferation."	1
<i>CTNNBIP1</i>	<u><i>Ctnnbip1</i>^{tm1Taki}/<i>Ctnnbip1</i>^{tm1Taki}</u>	AR	n/a	none	no	"Homozygous null mice display neonatal lethality associated with rupture of the gut, posteriorized neural cell fate within the neural plate, abnormal craniofacial morphology, and renal agenesis due to arrest of ureteric bud branching."	2
<i>DACT1</i>	<u><i>Dact1</i>^{tm1Yegc}/<i>Dact1</i>^{tm1Yegc}</u>	AR	n/a	none	no	"Mice homozygous for a knock-out allele exhibit neonatal lethality, abnormal embryogenesis, blind-ended colons, and abnormal renal/urinary system."	3, 4
<i>FRAS1</i>	<u><i>Fras1</i>^{bl}/<i>Fras1</i>^{bl}</u>	AR	AR	Fraser syndrome 1 [219000]	yes	"Mice homozygous for mutations at this locus display a significant amount of embryonic lethality due to hemorrhaging of embryonic blisters. Survival is variable on genetic backgrounds. Kidney development is severely affected and syndactyly is common."	5, 6
<i>FREM1</i>	<u><i>Frem1</i>^{eyes2}/<i>Frem1</i>^{eyes2}</u>	AR	AR	Bifid nose with or without anorectal and renal anomalies [608980] Manitoba oculotrichoanal syndrome [248450]	yes	"Homozygous mutation of this gene results in subepidermal blistering, cryptophthalmos, syndactyly, and renal agenesis."	7, 8
<i>FREM2</i>	No targeted allele caused unilateral renal agenesis.	AR	AR	Fraser syndrome 2 [219000]	yes	"Mice homozygous for mutations at this locus display a significant amount of embryonic lethality due to hemorrhaging of embryonic blisters. Kidney development is severely affected and syndactyly is common. Phenotypes of homozygous mutants are indistinguishable from those of <i>Fras1</i> homozygous mutant."	9
<i>GREM1</i>	<u><i>Grem1</i>^{ld}/<i>Grem1</i>^{ld}</u>	AR	n/a	none	no	"Homozygous null mice display neonatal lethality with bilateral agenesis of the kidneys and ureters, oligodactyly, limb skeletal malformations, cyanosis, dyspnea, and abnormal lung morphology."	10-12
<i>GRIP1</i>	<u><i>Grip1</i>^{eb}/<i>Grip1</i>^{eb}</u>	AR	AR	Fraser syndrome 3 [219000]	yes	"Homozygous ablation of gene function results in embryonic lethality and blistering skin lesions."	13
<i>ILK</i>	<u><i>Ilk</i>^{tm9.1Ref}/<i>Ilk</i>^{tm9.1Ref}</u>	AR	n/a	none	no	"Homozygous disruptions of this gene result in embryonic lethality. Homozygous mutant embryos fail to form a mature epiblast and die around time of implantation. Conditional deletion targeted specifically to chondrocytes lead to reduced cell proliferation, dwarfism, and shortened limbs."	14
<i>ITGA8</i>	<u><i>Itga8</i>^{tm1Lfr}/<i>Itga8</i>^{tm1Lfr}</u>	AR	n/a	none	no	"Mice homozygous for disruptions in this gene usually die by the end of the second day after birth. Those that do survive have reduced kidneys and abnormal stereocilia in the inner ear."	15
<i>LIN7C</i>	<u><i>Lin7c</i>^{tm1Dsb}/<i>Lin7c</i>^{tm1Dsb}</u>	AR	n/a	none	no	"Targeted disruption of this gene appears to have no phenotype, but when combined with <i>Lin7a</i> or <i>Lin7a</i> and <i>Lin7b</i> results in early postnatal lethality."	16, 17
<i>LRP4</i>	<u><i>Lrp4</i>^{mitt}/<i>Lrp4</i>^{mitt}</u>	AR	AR	Cenani-Lenz syndactyly syndrome [212780] Sclerosteosis 2 [614305]	no	"Homozygous mice have malformed digits on all 4 feet, some exhibiting brachydactyly, some syndactyly."	18, 19

¹Genotypes of mouse models (MGI allele symbols).

²Obtained from <http://www.informatics.jax.org/>

AR, autosomal recessive; Inh; mode of inheritance; Lit, literature.

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Supplemental Table 2: Demographics and epidemiologic characterization of 590 families with CAKUT.

Number of families	590
Number of affected individuals	672
CAKUT phenotype	Count
VUR	269
Renal hypodysplasia	101
Unilateral renal agenesis	80
Duplex system	80
Ureteropelvic junction obstruction	77
Renal ectopia	34
Multicystic dysplastic kidney	33
Posterior urethral valves	30
Ureterovesical junction obstruction	30
Hydronephrosis	25
Horseshoe kidney	18
“Multiple cysts”	17
Sum^a	794
Origin of affected individuals	Count
Macedonian	350
German	61
Kuwaiti	50
Indian	49
Albanian	48
Serbian	30
UK	16
Egyptian	9
USA	8
Romani	8
Hungarian	7
Somalia	6
Arabic	6
Turkish	6
Hispanic	4
Taiwanese	4
Jordanian	2
Caucasian	2
Europe	2
Swedish	1
Syrian	1
Asian	1
Bosnian	1
Sum	672

^a Sum of observed CAKUT-phenotypes exceeds the number of affected individuals due to presence of >1 phenotypes in 195/672 individuals.

Supplemental Table 3. Comparison of biallelic missense mutations in individuals with isolated CAKUT *versus* protein-truncating mutations in individuals with Fraser syndrome.

	Isolated CAKUT			Fraser Syndrome			
	M/M	M/T	T/T	M/M	M/T	T/T	Ref.
FRAS1	5 (7 a.)	1 (2 a.)	n/a	3 (4 a.)	n/a	15 (19 a.)	¹⁻⁶
FREM2	4 (5 a.)	n/a	n/a	3 (1 a.)	n/a	1 (1 a.)	^{7, 8}
GRIP1	1 (2 a.)	n/a	n/a	n/a	n/a	3 (2 a.)	⁹
FREM1	2 (1 a.)	n/a	n/a	3 (3 a.)	1 (2 a.)	11 (12 a.)	¹⁰⁻¹³

a., alleles; M/M, number of families with biallelic missense mutations; M/T, number of families with biallelic mutations including one protein-truncating allele; T/T, number of families with biallelic protein-truncating mutations; Ref., References.

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Supplemental Table 4: Comparison of truncating variants in 6,500 healthy individuals in the EVS Server in recessive genes mutated in individuals with isolated CAKUT *versus* autosomal recessive and autosomal dominant control genes. Note that 6,500 healthy control individuals have heterozygous truncating alleles in the genes recessively mutated in individuals with isolated CAKUT (upper panel). Note that the number of truncating alleles in these genes compares to the number of truncating alleles in other genes mutated in known recessive disorders (middle panel) whereas truncating alleles in genes mutated in autosomal dominant disorders are unusual (lower panel).

AR genes in isolated CAKUT Human Disorder	<i>FRAS1</i> * Fraser 1		<i>FREM1</i> MOTA Syndr.		<i>FREM2</i> * Fraser 2		<i>GREM1</i> none		<i>GRIP1</i> Fraser 3		<i>ITGA8</i> none	
	# Var.	# Ind.	# Var.	# Ind.	# Var.	# Ind.	Var.	Ind.	# Var.	# Ind.	# Var.	# Ind.
Stop gained	4	5	8	10	4	4	0	0	1	1	1	1
Stop lost	0	0	0	0	0	0	0	0	0	0	0	0
Frameshift	3	3	3	4	5	5	0	0	0	0	1	1
Sum Trunc.	7	8	11	14	9	9	0	0	1	1	2	2
AAs # ¹	4012		2179		3169		184		1076		1063	

Control AR Known Human Disorder	<i>NPHP1</i> Nephronophthisis 1		<i>NPHS1</i> Cong. NS 1		<i>NPHS2</i> Cong. NS 2		<i>CFTR</i> Cystic Fibrosis		<i>ATP7B</i> Wilson Disease		<i>GALT</i> Galactosemia		<i>IDUA</i> MPS I (Hurler)		<i>FANCA</i> Fanconi Anemia A	
	# Var.	# Ind.	# Var.	# Ind.	# Var.	# Ind.	Var.	Ind.	# Var.	# Ind.	# Var.	# Ind.	# Var.	# Ind.	# Var.	# Ind.
Stop gained	2	2	5	5	0	0	12	41	7	12	0	0	2	13	3	3
Stop lost	0	0	3	3	0	0	0	0	0	0	0	0	0	0	0	0
Frameshift	0	0	0	0	1	234	16	60	3	5	1	1	2	54	4	33
Sum Trunc.	2	2	8	8	1	234	28	101	10	17	1	1	4	67	7	36
AAs #	733		1241		383		1480		1465		379		653		1455	

Control AD Known Human Disorder	<i>EYA1</i> BOR		<i>SALL1</i> Townes-Brocks		<i>PAX2</i> Papillorenal		<i>ROBO2</i> VUR 2		<i>HNF1B</i> Renal Cysts + Diabetes		<i>CREBBP</i> Rubinstein Taybi		<i>WT1</i> Denys-Drash		<i>APC</i> Familial Aden. Poliposis	
	# Var.	# Ind.	# Var.	# Ind.	# Var.	# Ind.	Var.	Ind.	# Var.	# Ind.	# Var.	# Ind.	# Var.	# Ind.	# Var.	# Ind.
Stop gained	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1
Stop lost	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Frameshift	0	0	0	0	3	174 ²	1	1	0	0	1	27	0	0	1	2
Sum Trunc.	0	0	0	0	3	174	1	1	0	0	2	28	0	0	2	3
AAs #	592		1324		431		1394		557		2442		517		2843	

¹ Amino acid number derived from the transcript mentioned in Table 1 or longest transcript/isoform.

² 3 of 3 frameshift variants in PAX2 are C-terminal after AA 397.

Trunc., truncating variant; AD, autosomal dominant; AR, autosomal recessive; cong., congenital; Ind., individuals with truncating variant in the EVS Server; Var., number of different truncating variants in the EVS Server.

*Note that in 6,500 individuals of the EVS-database, there are 8 and 9 individuals with protein-truncating variants in *FRAS1* and *FREM2*, respectively. The presence of rare protein-truncating variants in a large cohort of healthy individuals is acceptable for recessive genes but highly unusual in autosomal dominant genes. Hence, *FRAS1* and *FREM2* are unlikely to be autosomal dominant genes.

Supplemental Table 5. Exon-flanking oligo nucleotides primers for 12 CAKUT candidate genes and median coverage of targeted regions. Primers highlighted in red failed to generate PCR-products.

Gene	Amplicon	Sequence Forwar Primer	Sequence Reverse Primer	Length	Median Coverage
BAG6	BAG6_E25	CCTTGTGTGCTTGCTGGG	GTCCCTGTATGAGGAAGGG	200	2771.19
BAG6	BAG6_E24	TTGATCCTCTTTCCCTCCC	ACCCCTCCCACTAGACCATC	227	1424.92
BAG6	BAG6_E23	GGCAGCTGAAAGTCAAGGAC	TTGATTCCAGGCATGACG	219	2966.93
BAG6	BAG6_E22	TCTGAAGCCTGGCTCTTCC	GCCATGACCCACTGGATTAC	214	3488.00
BAG6	BAG6_E21	ATGGGGTCAGGGTACTTGAG	GTGTCAGATGGCGGGAAG	240	1630.87
BAG6	BAG6_E20	AGGTGGTTGAGGGTTTTGTG	AAGTACCCTGACCCCATCG	229	3128.62
BAG6	BAG6_E19	CATTCCCTCCTTGTATTTTGC	GCTAAGGATCTGGGGCTAGG	182	3617.43
BAG6	BAG6_E18	TTTGGGATCTTTGTGTATCTTG	CCTGCACATGCAACAGGC	184	3604.84
BAG6	BAG6_E17	TGGAAGCTTTGGGAGGACTG	AAGACTGGGAGTGGAGGAGG	183	4891.03
BAG6	BAG6_E16	TGCTAACATCTGCCCTTGTC	TGCAAAAGAGGAGAGTTCTGG	237	1898.34
BAG6	BAG6_E15.2	GGTCTTGAGAGCCTGTCACC	GGAGCAAGCCAAAGCATC	202	3972.00
BAG6	BAG6_E15.1	TGTGTCTTCATTCTCACCTCAC	ACACCCTGCACCACTGAG	224	587.61
BAG6	BAG6_E14.2	TCAACCCTCCATGGCTGATC	GTGAATGGCAAGCCAGC	196	5501.52
BAG6	BAG6_E14.1	ATGCTCAGCCAGCTTTC	CCCTAGCAGGTTCCCCAG	219	3764.07
BAG6	BAG6_E13	GCATGGAAGGGCAGGTC	AAACTCTGAGTGGGGAAGAATG	163	5991.61
BAG6	BAG6_E12	TTCGGTCTGTCTCTTCTGCC	TCTCTCCCTAGACTGTTACGCAC	188	3968.48
BAG6	BAG6_E11	TACCTCAGGGCCACTGTCTC	CAGCCCTTCCCTTTCTCTAC	169	4737.66
BAG6	BAG6_E10.1	ATGACAGGAAATGGGACTCG	ATGAACCTCCCTCATCATGC	283	1384.16
BAG6	BAG6_E10.2	GGAGGAGACTGGAACATGG	GGAGGTGCCTCTGCATTG	195	4515.49
BAG6	BAG6_E09	GACTCCAGCTTGATATTTCTGC	TCTCCCTCAGGCCAGACTC	280	1491.86
BAG6	BAG6_E08	AATCTGAGGAAGGCTTTGGC	CTGAGGAGAAAGGGCAGGG	211	3651.19
BAG6	BAG6_E07.2	GGAGCCAGTAGCCTTGAGC	ACTTAGGATTCCCCACCCAC	217	3757.24
BAG6	BAG6_E07.1	GCAGTCTTACCCTGCCTTTG	CGCTCCTCACTTCTTCTGC	201	3890.79
BAG6	BAG6_E06	ATGGCTGGGACCTGATTTAG	TATGAAGGCCAAACCCTGTG	264	1805.94
BAG6	BAG6_E05	CCAGAACAACCTCCCTTACCC	ATCTCTCAGCCAGGTCCACC	164	5309.60
BAG6	BAG6_E04	ACCTGTTTACTATGTTTTGGTG	CTACCACAAAAGCCCTCC	279	1382.85
BAG6	BAG6_E03	ATTCTGTGCATGCCTCTTC	TAGCCCCAACCTCTGAACCTG	183	3363.69
BAG6	BAG6_E02	TTTCGGGTACACTCTGGTCTG	AAAAGCTAAAGGTGTCTTCCAG	211	2771.87
CTNNBIP1	CTNNBIP1_E06	TCGGAAGTACTTTGTCTCAG	CAGATCTTTGGCCCTCAAC	246	2200.64
CTNNBIP1	CTNNBIP1_E05	AGGTGCCTTTTCAAGGAAACAG	GCTACGCTTTCTAAGGGAACC	229	2281.28
CTNNBIP1	CTNNBIP1_E04	TTTGATGCTGTTGCTTGCTC	GCCTGACACCCACAGG	169	4551.61
DACT1	DACT1_E01.1	GGTGACGGCTCTCGCTG	ACCAGCAGCTCTTGGCG	237	0.00
DACT1	DACT1_E01.2	GCGAGGCAGACACCGAG	AGCCGTGCTCCACCTTC	272	0.00
DACT1	DACT1_E02	CACCCTGTATGTTATGTTTTT	GTTAACCACAAGGGGCTGAG	242	1898.44
DACT1	DACT1_E03	GACATGATGTTAATTCCAACGG	GCCAAATAACCTTTTAAGGGC	263	1243.78
DACT1	DACT1_E04.1	TTCATTTCTTCAGAGTGACCTTAAC	CCCGTCAGACAAAGGAGAAAC	269	1592.39
DACT1	DACT1_E04.2	TCGCTATCCCAGTCCACTTC	ATGGGAAGCAGACCACAGAC	193	924.03
DACT1	DACT1_E04.3	AGTTCCTTACCCTCCCAAG	GTTACACTGTTGCCCTGTG	222	631.57
DACT1	DACT1_E04.4	AACCAAGAACCAGCGTGAAC	TGGCAGGTGCTTACTCTGAAG	290	1289.17
DACT1	DACT1_E04.5	CCTCAGGCGCTGCCTCC	TAGACAGCAGGGGAGGAGTG	253	1917.14
DACT1	DACT1_E04.6	CGCCGCAGGAGAACAAAG	AGGCTGGAGTTCTTCACGAC	265	2268.66
DACT1	DACT1_E04.7	TGGTCAAGGCCAGTTTATC	CGGGAACACCAGCCTCGG	270	991.79
DACT1	DACT1_E04.8	AGTGTGCTTCCCAGATGAC	GGGCCTTCTCGTAGGAAATC	240	556.22
DACT1	DACT1_E04.9	CACAAGCGAAGTACTACCG	CTCACACTGACTCGCTGTC	275	1704.55
DACT1	DACT1_E04.10	TTACACCACCAACTGCTTCG	TCACTCAAACCGTCGTCATC	272	1960.18
DACT1	DACT1_E04.11	CCGCTTTCCGTCTGGCTC	AAAGGCACTAGCATCCATACG	216	2240.32
FRAS1	FRAS1_E01	TCTTGGATGCTGAAGGCTG	AAACTGCACGATCACTCACAC	202	573.47
FRAS1	FRAS1_E02	TGGAAGAAGCTCATTTTCTCG	TCACTCAGGAACCTCAATCAAGC	226	707.60
FRAS1	FRAS1_E03	TGGGACTATTGATGGTGACG	AACCTGACCTTCACTGACTTTAC	246	569.29
FRAS1	FRAS1_E04	TCCATCTGTTGTGTACAC	CTCTGACACAGAAATCAACC	264	331.09
FRAS1	FRAS1_E05	ATGAAAGCCTGTGTTTGGC	GGGTCCCTTCTACAAGCTC	245	393.50
FRAS1	FRAS1_E06	AGTCAGCCCTGGGATCAAC	TGCCTGCCATAATCTCAGAAG	274	339.98
FRAS1	FRAS1_E07	GATGGATTGTTCTGTTCTGC	TGGCAGAGTCAGACATGAGG	221	867.52
FRAS1	FRAS1_E08	GACATTTGATTTTCCATGTTCTTC	CCCAGAAAAGAGCTTAAACAAG	188	859.51
FRAS1	FRAS1_E09	CTTGGGTGTTTACCCTGCTC	AACGTTCCAAATGGAAATGC	282	179.22
FRAS1	FRAS1_E10	TAACAGTGTGCCAGCGTTTC	AATGTTCCCTCATTAGATTAATTTG	273	93.26
FRAS1	FRAS1_E11	AAAGTTGCATGTTCTTGGG	AGTGCCATCAAATGTGGCTG	268	209.00
FRAS1	FRAS1_E12	TTCTTCAGCAGCAAGCTCTC	GGGGAAGAGGATCTCTGAGC	290	225.69
FRAS1	FRAS1_E13	GGAGTTCACAGATTCTCCCC	ACCTCTGGGTTGTCCACTTG	214	1010.63
FRAS1	FRAS1_E14	TAAGCACTGGCATGGGG	GGGAGCTGTCTTGGTAGCTG	261	579.62
FRAS1	FRAS1_E15	ACCAGTCCTTTCTGCCGTAG	AAAGGACACGTCAGCATCG	229	669.14
FRAS1	FRAS1_E16	TCTTTTGCTCACTATTGCCTTTC	GATGATGATGATGGTGACCC	220	876.71
FRAS1	FRAS1_E17	GCACTTTATTCACCATGTCC	TTGTGGGATAGCCTCTCAAG	236	562.07
FRAS1	FRAS1_E18	TGATCCTTGGATTATTTCTGC	AGATAAGCCCAGAGGCTACC	263	86.00
FRAS1	FRAS1_E19	TTTCTGATTGTCTCCTTTC	ATAGGCAATGTGCCTCAGC	212	548.99

FRAS1	FRAS1_E20	CATGCTGAGCTGCTAATTCC	CCAGTGATTTCGAGGAGTC	228	986.87
FRAS1	FRAS1_E21	CTTCTCTGTGCTCCCCCTCC	AAGAGAACCTCAGGTGGCAG	231	624.03
FRAS1	FRAS1_E22	GACATCATGGTTTCTGTGTGTC	GAAAGGAGAGAAGGTTTATTGG	218	583.90
FRAS1	FRAS1_E23	CATCTGTCTAGGTTTGATCAGTC	AAAGTGGTACTACTGTGTAAGAATC	277	556.39
FRAS1	FRAS1_E24	TCTGAGGGTGGACAGAAAGG	ACAATCAGAGGTGGCCAAG	249	312.02
FRAS1	FRAS1_E25	AAGCCACACAGATTCTTGATG	CTGCCCTCACTTCTTCCAG	226	287.74
FRAS1	FRAS1_E26	CTGGTGTGCTTGATTGAG	TTACCAGACCATCTGAGG	220	516.80
FRAS1	FRAS1_E27.01	CATAAGCTTGACCTTTGGATT	TCCAGCTGAACCTCTTTTCC	231	1009.33
FRAS1	FRAS1_E27.02	CCTCTGAATGTCCAAGACC	GATGGAAGGAGGCAGGAAG	235	958.21
FRAS1	FRAS1_E28	TTTTCTTATTCTTTCTTTGGGAC	AAACCTAGATTTCTGTCTTGAG	186	175.39
FRAS1	FRAS1_E29.01	TGTCCTTTCTTTCCCTCTTAACTG	GCCTCTAGAGAGTTTCATCCAGC	262	256.92
FRAS1	FRAS1_E29.02	CCGGCAACCCCTATCTATC	TGACTACCCATATCTTAACTTTGTGAG	264	382.21
FRAS1	FRAS1_E30	CAACAACAGAAGTGGATAACTTATGTG	GCTGAATGCAACGATGAAAC	287	160.77
FRAS1	FRAS1_E31	CACCTAATGTGGCCTGTGC	GAGCGATTGGATTATTGGATT	265	433.48
FRAS1	FRAS1_E32	CCACGTACTAACATGCTCTGC	TGCTGTGTGCTCCTCTAAG	231	843.69
FRAS1	FRAS1_E33	TGACTAATTTAAAGCCAGAGC	TCACTCAAAGATCATTTACTGCAC	258	75.00
FRAS1	FRAS1_E34	CCCACCAACAAGAAGAGCAG	TGCCTCAAAGCAGAGAGGAG	259	369.69
FRAS1	FRAS1_E35	TTCTAACCTCTGCCCTTTG	TGATGGGAACAAAAGAAAGAAC	200	427.91
FRAS1	FRAS1_E36	AAGAGGACCACTACAAGTTG	ATCCCATTTCCAAAGCCATG	272	162.65
FRAS1	FRAS1_E37	TCTACCAACGCTTCTCTCTC	TCCAAGCAGTCACTGACAG	197	336.00
FRAS1	FRAS1_E38.01	GAAAAGCATTATTTCCAGAAGC	CGGTCTTCTGACAGGGACAC	211	1372.25
FRAS1	FRAS1_E38.02	CATGATGGTTCCTCTACCCG	CATCAGAAGATGCGGCG	249	1341.42
FRAS1	FRAS1_E39	CATGTCCTGCCTCATGTTTG	AACAGAGCTACAACCAGTTGCTG	258	317.21
FRAS1	FRAS1_E40	TTACCTGGCTTGTATCGTG	CATTACTACGGATTCCAGCTCTC	278	173.20
FRAS1	FRAS1_E41	TGTGAAATCACCAAGGACTCTC	CCCTCCCTTCTCTCAAGGTC	224	270.91
FRAS1	FRAS1_E42.01	TTCAGCCTAGTAAGCAGGAATTG	TCCAACCTTCAAAGCTTTACCTC	274	245.60
FRAS1	FRAS1_E42.02	ATGAAAGCATTGAGCCAACC	ACTCAAGCCTTCCCCAAATG	283	211.80
FRAS1	FRAS1_E43	TGCATTTTCTTTCTTCTTAAATATCTG	TGTTTATTCTAACAGCCCATCG	277	44.30
FRAS1	FRAS1_E44.01	CCTCTGAGGCATTTGACATTC	AGGCCATCAGTGAGGGAGAAC	290	224.56
FRAS1	FRAS1_E44.02	CTGGCATGGTCTGGATG	TGGAAGAAAGTACTGCATCTGG	221	821.22
FRAS1	FRAS1_E45	GGAAATGTTGGGGAATAACC	GTAGGTGCAGTCCACGGAAG	281	355.38
FRAS1	FRAS1_E46	CAGAAAGCACTAATAGCAAATCTTG	GAGCCTCGAGGTGAACAAAG	250	271.00
FRAS1	FRAS1_E47	GAGAAGATCCCATTTCAAATCAC	TGGCTGCCCTCAATACTTAC	287	193.77
FRAS1	FRAS1_E48	GAGAGTATGACACTTCCCTAGCC	ACTCTGCCTACTCCACTCAAAG	283	198.54
FRAS1	FRAS1_E49	TGGGTAGGTGCTAGGGACAG	AGAGAACCTATGGGAAGAAG	221	532.57
FRAS1	FRAS1_E50.01	CAATTGGGCATCACTCACTC	GGGTTTGTCCCATCAGAAAC	271	705.58
FRAS1	FRAS1_E50.02	CCATCGAGCGAACCAGC	GTGCTAGGCTACCTCCTCCAG	219	921.07
FRAS1	FRAS1_E51	CTTCAGGTACTTGTGAATGATGAG	TGGTGTGAACATGACAGAGG	195	801.54
FRAS1	FRAS1_E52	TCCTGCTTTATTTCCACCTC	TCTCCCATTTCTAAGTTCCCAG	235	417.97
FRAS1	FRAS1_E53	CATCCCTGGGTAAATTCACAG	TGATTTCTCAAGAAGGAAAGCAC	237	441.66
FRAS1	FRAS1_E54	TTTCATAACCATGGGGCATAG	ATTGCTGCAGCCATGTAC	282	64.76
FRAS1	FRAS1_E55.01	CTATGATGCCCTGGGGAAG	TAATGTGGGTTCATCCTCGG	251	733.33
FRAS1	FRAS1_E55.02	GAATTCACCCAGGCGAAG	TGGGAACCAATGAGTTAATAAGTG	263	583.39
FRAS1	FRAS1_E56.01	GGAGGGACCAAGCTCATTAAC	GACATCACAGGTGGACATGG	257	1303.41
FRAS1	FRAS1_E56.02	TCCCTAAGTCAGCTATGGGAAG	GCCAAGGCAATCTCAAACCT	184	2155.25
FRAS1	FRAS1_E56.03	TGTCCACCTGTGATGTCATG	CAGGAGACAGGTGAAGGAAAC	236	1002.94
FRAS1	FRAS1_E57	AAACCTCGCTGATTTTCTGG	TCACAAACCGACCTGTCAAC	272	295.73
FRAS1	FRAS1_E58	CACCAAAGACAGGCAAGTTG	GACCTACCAGCTGGCATCC	276	269.76
FRAS1	FRAS1_E59.01	AACCATGCTTTGGAATCTGC	TCACTGATGACTCATAGCTCAGG	271	387.44
FRAS1	FRAS1_E59.02	CTAGTGCCCAAGCATGCAG	TCTCATCTTTTCAAGCCACCAC	242	545.70
FRAS1	FRAS1_E60	AGCAATCACTGATATCTTGCTG	TGTCCTCTCAACCTAAGAGTAAC	259	437.56
FRAS1	FRAS1_E61	ACTGGCTCTTGTCTTCTAACC	AACCCACAGATTGAGGTTGG	266	363.22
FRAS1	FRAS1_E62	AAGCTGCACTCTCTTGGGTG	AAACAGCAATCCTTTGGGTC	287	211.72
FRAS1	FRAS1_E63.01	GCCTAGTTCTCTGACCTTGCC	ACTTCCCAGCTGAAGTGCAC	252	591.63
FRAS1	FRAS1_E63.02	CCCTGCGACCCCTCATTT	GCATGGACCATAAGGAATTTG	275	586.78
FRAS1	FRAS1_E64.01	TGAACCATCATGTAAGGAGC	CCTGGAAGCCTCTGGATGTC	242	1316.65
FRAS1	FRAS1_E64.02	GACACAGGTGGGCCATGTG	TCCTGGGAAACACACAAAGG	246	1257.62
FRAS1	FRAS1_E65	TTGACCATTTATAGCAGTCAGC	CTGGGCTAGCATGGAAAGAC	258	283.33
FRAS1	FRAS1_E66.01	AGTAGGGTCTCAGGTGATTGAAAG	ACATAATAAGCATCAAAGGTCCAC	281	347.97
FRAS1	FRAS1_E66.02	TTCTGGATGATGTGGTCTATG	TTCAGGAACAAACAAGGTTGAC	276	313.07
FRAS1	FRAS1_E67	AAATGGAACCAAGATGTGGTG	ATCTTGCTTGAGTGAGGCC	289	163.20
FRAS1	FRAS1_E68	CCATGCCCTAGCATTTTCTC	CATGGATGTATAGCAAATGTTAATC	270	41.89
FRAS1	FRAS1_E69	TTTTGTGGGGCTCTACCAG	TGGAAAACCATTCAGCTCTACC	290	95.65
FRAS1	FRAS1_E70	GGGTAAGCCAGCAACCTATC	CCATGTTGATTTGGGGGTTAC	274	87.45
FRAS1	FRAS1_E71	AGCTGACCCTGCTCTCAAAG	AGAGCCTCTTTCTGCAGGTG	248	460.06
FRAS1	FRAS1_E72	AAGGGAGCATGTTAAACCCC	GAAGTCATAGCTGAGGAAATCTG	256	36.93
FRAS1	FRAS1_E73	CACCTACCAATATAGTGAACCATC	TTGGTCTTAAGCTTCTGTTCTTCTC	245	159.92
FRAS1	FRAS1_E74.01	TCTTCAGAGGTGGTCTGTGG	GCTCTACCAGGTCCCTTCG	181	2098.43
FRAS1	FRAS1_E74.02	GTCCAGCGCTCTCTCACAG	TGTGACAGGGACGCAGCTAC	185	851.42
FRAS1	FRAS1_E74.03	AATGGCACCAATATGAAGTCC	CAGTGCAGTAGTGTCTATTACG	283	388.72
FRAS1	FRAS1_E74.04	GAAGAAGAAGCCCGCAGAG	AAAAAATACACATAGGTCTCCTCC	264	496.51

FRAS1	FRAS1 E74.05	TGCTAAAGTCAAAAGACTGAATC	GCTGTCTGCCACTCAAAGC	190	445.48
FREM1	FREM1 E38	ACGCAATAAAAGTAATTGGTACATTC	TGACAAACTCCAGGTGGC	281	123.90
FREM1	FREM1 E37	GCAGAAATGTTAACTGCTTGTG	AAGGAAGTAGCAGGGTGGTG	220	487.41
FREM1	FREM1 E36	TCCTTATGCTGAACCAACTCC	CCGCTTCCATGAGCAAATAG	254	279.89
FREM1	FREM1 E35	TTGCTAAATTGCCTTTCCTTC	GAATAAAGGTGCTTGGCTGC	192	645.01
FREM1	FREM1 E34	GAATTGCTCATTTTTTTGTTTG	GCAAACAACCTGTTATAAGGTGAG	289	90.77
FREM1	FREM1 E33	TTGGTGGTTTTACCTATTGC	AATAGCTTCATTAAATACTTGCATCC	187	425.62
FREM1	FREM1 E32	CTGCCATCTTGCATGCC	TCATTCCCAGAAGGTCCC	289	180.31
FREM1	FREM1 E31	CCTAGGTGATTGAAATAGCAATTAAG	AGCAGTTGGCTGTTGAAG	280	196.44
FREM1	FREM1 E30	TTTAAGAGCATGAGTTTAGTCCAG	TCTACAATCTCCAGACATGCCTAC	250	116.70
FREM1	FREM1 E29	CCCTATAGGCATATACTATGCATTCTC	TGAAATTTCTTGGTCACTCTG	290	58.58
FREM1	FREM1 E28	TATTTAATGTTTTGTTTGATTACCC	CATTTCACTTTCCTAATATTTCAGATAC	271	5.40
FREM1	FREM1 E27	GAGGGGCTTTGGACAAC	GGCAATTGTAAGGATTAAGGAGG	276	192.23
FREM1	FREM1 E26.02	CACCTTCCTCTTGGTTCAGC	TTACATCTCTGGCAAATGAAC	272	368.58
FREM1	FREM1 E26.01	AGAATCCATGCTGAAGGCTG	CCCACGGTAGAGCTGGC	272	418.48
FREM1	FREM1 E25.02	TGCTCTATGTCATCACCTCCC	CCAAAGAAGGGGTTTGAAAAG	194	981.65
FREM1	FREM1 E25.01	TCTGCCTTTGCTTGAC	TTGGCTGAAGTTTGTAAATGGG	263	569.63
FREM1	FREM1 E24	GCAGCTGACTAACTCTGGCTC	CCCAGTAAACCTTGGTAGACG	254	493.93
FREM1	FREM1 E23	TCAATATAAGTGTCCCCTACTAAAGG	ATTGAGAAGATTTATACCTGCTACG	274	62.00
FREM1	FREM1 E22	TTAAGACATTATCTGTGACATATGTC	GAATTGTATAGAAATCTGAAAGGG	266	14.00
FREM1	FREM1 E21	TATGCATTGTTGACTTTTCTCATG	ACAAATGCATGGAAGTGGAAAC	290	192.59
FREM1	FREM1 E20	GGAAAAATTTTTTTTTTATTTATCTG	GATAAAGAGAAATGGAACATTTG	282	0.00
FREM1	FREM1 E19	GGATTTTCATGCTAAGTTGTAATTGTG	AGGGAGTCATTGCTGGTGAC	264	220.39
FREM1	FREM1 E18	GGCAGGTTTCAGCTATAGTTGTG	TGAACCACGGTATGACACTAGG	287	215.98
FREM1	FREM1 E17.02	TGCTACTGATGTGGACAGCG	TCTCATGTTGCTTGCATTCC	196	1441.11
FREM1	FREM1 E17.01	GAGCAATGGATTACCTGTCAAAG	TGACTCCAGCTCTCCTCACC	268	858.73
FREM1	FREM1 E16	AGTGAACACATGGCCAAAGC	TATGGCAGCACAAAACAGAC	252	510.75
FREM1	FREM1 E15	GGCTTTGAATGTTTCCTTCC	CTAAAGCATGTAAATAAAAAACCATG	282	113.93
FREM1	FREM1 E14	CAAGTCAGCACCCACATATCC	AGTTACCATTCTAGTAGGTCTTCAAG	287	234.21
FREM1	FREM1 E13	TTCTTCTCACATGAAGTCTTTTCAG	TCTAAGGCGACACTTGCATC	245	234.66
FREM1	FREM1 E12	TTTGGTATTTCAAATTAATGGTACAG	GAAGTAGTAGCCCAAATGGTGAC	272	60.98
FREM1	FREM1 E11	CAAAAGTATGTGGTGTTTTATGGAC	ACCTGTGCACAAGACTTTGG	221	582.86
FREM1	FREM1 E10.02	AATTCCCCATCAACGTCTTG	CATTCAAATGATCTTAAGTCCG	245	842.37
FREM1	FREM1 E10.01	TGCTCAATCTGCTCCATCTC	CCCTCTCCAGTTCATCAC	246	716.93
FREM1	FREM1 E09	GTGTATATGTGCCTCATTTTCTTATC	CTTTGGATTCTTGTAGGTTACC	241	353.46
FREM1	FREM1 E08	TTCAGTGTGTGGCTCCTTTG	TTCCCTTCAGGGCTATGTTG	191	490.69
FREM1	FREM1 E07.02	TCCTTGACTACATCAGTTCTGGAC	GCTGGAAGCTTTGTCTCTCC	240	452.94
FREM1	FREM1 E07.01	TTAGCCCTGTATGATATCACCTC	GAGTCACATAGCCCTGGAGC	278	274.86
FREM1	FREM1 E06	GTGACTCTCTTAATCCAGTGCTG	GGGCACCCACACATAACC	259	321.83
FREM1	FREM1 E05.02	TGAATTCATGGCTGTGCTCC	CCCAGAAAGGCATTAAAGAC	225	746.51
FREM1	FREM1 E05.01	CCAATTAATATTGCTTTTGCCC	TCCAGGCTAGCCATCCTATC	216	916.71
FREM1	FREM1 E04	TCTCCTGGCAAATGTAAATC	TGGTACTTGGCAGCAAATG	209	803.42
FREM1	FREM1 E03	GAGTTGGGCCCTGTGACG	TGAACAGAAATCGCAGATAGG	280	193.19
FREM2	FREM2 E01.01	CTCAGGCTGACCTGTCCAAG	CCAGCACTATGGCCTCCTC	259	400.06
FREM2	FREM2 E01.02	GCTGTCCCCTGGTCTCG	GCCCAGGTGAGAGTAGCG	262	303.56
FREM2	FREM2 E01.03	CTTCCCGTGCAGATTG	ACTCCTCTGTCTCGGGCTG	269	347.95
FREM2	FREM2 E01.04	TTGTGACTCGGAATTGCC	CGGCTGTGTGGCGATAG	270	301.61
FREM2	FREM2 E01.05	AGCTTTCAGGAAGTAGGCG	AGCATGTCTGGGGTCAGG	258	560.05
FREM2	FREM2 E01.06	AAGCCAGTTTCGTGGC	AAAGAGGCGCTCCTGGTC	270	402.62
FREM2	FREM2 E01.07	GGCTCCTGAAGATTGCCTAC	TCGCTGATGACCAAGTTTTG	250	142.86
FREM2	FREM2 E01.08	CTATGAGGGTCAGTCTCGGC	GCGAAGCACAGGTTGTC	259	229.17
FREM2	FREM2 E01.09	CAGCATGATGACAGAGACGG	ATGCCCGTAGTTAAGAAGG	270	521.57
FREM2	FREM2 E01.10	CCTGAGTGCAACTGACATGG	TGTGAACTGGTCTGTGACTGG	265	431.93
FREM2	FREM2 E01.11	AACAGAGGGCAGGCTGTTT	TCTCGGTCATCTGTGTCCAG	267	436.41
FREM2	FREM2 E01.12	AATCCCAGCTCACACCACTG	AACTGGAAGTGGGGCACTC	268	237.34
FREM2	FREM2 E01.13	GACCCCGGGTCAAGAAC	CTCTCATGTGGCCATGTTTG	276	268.45
FREM2	FREM2 E01.14	AGAGTTGCACGTGAATGATG	CTGGCCGGACATTTACTCTG	257	410.73
FREM2	FREM2 E01.15	CCCTGACTGATAGCTGCTCC	CTGCTGGAATGCCATTGAC	279	260.81
FREM2	FREM2 E01.16	TGACTTTCCTCTTGAAGATCC	GCTATCAACAGGCAGGATGG	251	395.93
FREM2	FREM2 E01.17	TGGTGGCAATACTATCCAAGG	TATGGCAATCCCTGCTCTTG	265	310.06
FREM2	FREM2 E01.18	TTGAAAACATTTCTCCAGCAC	GACTCATGCCTTCCATCACC	273	263.63
FREM2	FREM2 E01.19	TTCCACCAATGATGAACAG	AACTGTCTTCTGGGTCTCG	279	247.68
FREM2	FREM2 E01.20	TGGTCGAAAGCTTCACCTTG	AAACCAAAGATTTGTCTTCTGAATC	279	256.01
FREM2	FREM2 E01.21	GGACTAGAAATAGAAATTGGGGATAC	ATTAGGTCCCGAATGCCCTC	251	387.20
FREM2	FREM2 E01.22	CCCAGGATGAAGTAGACAGAAAC	GCCCTGGTGATGGTAAAAAC	277	262.41
FREM2	FREM2 E01.23	AGCACTAGTGACTTGAACAGTCC	TGTCACATCGCTAATGGAG	259	486.20
FREM2	FREM2 E01.24	AGTACCGATGGACGTAACC	TGCTTGGTAAAAACCATGACAG	255	510.29
FREM2	FREM2 E01.25	ACCCAGGTGCCTATTTCATGG	TTATTCACTGCGATTGGGG	269	405.34
FREM2	FREM2 E01.26	GATCCAGTCTTGGCTGTTG	AACAAGGATAACCAAGAAAGAAAC	275	258.74
FREM2	FREM2 E02	CATAATGAATCATCAATTTTACTCTGG	CTCTCCTTGGCGTCACTACC	190	1550.14
FREM2	FREM2 E03	TGAAGATCACTCATTCAAGAAAGC	AATCACTGTAGAATTATAAACCTTTGC	275	6.00

FREM2	FREM2_E04.01	TCCAAGCGAAAATGAACTAAG	TCAGACTGCTCATGCTCCC	189	1445.04
FREM2	FREM2_E04.02	AGTTCAACCCAGGCCAGAC	CATAAACCCAGTTGACGATGGC	189	1695.20
FREM2	FREM2_E05	AATGCTTGCAATTGTGTTTT	TCATGGTAAATGTTATGGCTCC	243	243.23
FREM2	FREM2_E06.01	TGCTGTGTATGAAAATAATTGTGTC	GCTCAGAAGGACATGGAAGG	263	386.77
FREM2	FREM2_E06.02	GGGAGAACTGTGTGCGATAG	TCCTGATGTTGATCTTCCCG	203	904.91
FREM2	FREM2_E07	TGGAAGCATGTCAATAGAGTTTG	AAAAGAGCCGAGTGGGAAAC	250	363.06
FREM2	FREM2_E08	CCAACTGAATATTTTTTTG	TATGATTTCAATTATCATTG	288	0.00
FREM2	FREM2_E09	GAAATTTCTGTTCACTTTAATCCTTTG	TGAGTAAAAATTCGGCTTCTTC	290	191.38
FREM2	FREM2_E10	TCCTATGGGATGTGATTGACC	TTGGCTGGATTTTAGTTTCTAATTTAC	262	430.05
FREM2	FREM2_E11	TTTGCTTTTGTITCCCAC	GGCATGATCCATCAGGAGAC	249	218.74
FREM2	FREM2_E12	TTAAATCTGTGATGTTAC	CATGAATTTACATACACATTAC	188	0.00
FREM2	FREM2_E13	GCCAGGGATCGTGAGTATTG	TTTCCTCAATTTTGTGAATCTCC	277	192.73
FREM2	FREM2_E14.01	AGAATGCGTTCACCTGTTC	GCCAGGCTGAAAGTATATGGAG	268	677.37
FREM2	FREM2_E14.02	CCAGCCATGAGAGAAGTGG	TGATCTTCAGGGGAAAATGG	211	982.12
FREM2	FREM2_E15	CCTTCTTTTCGCATAAATATGGTC	TTCCATGAGATTGCTTACCC	202	480.87
FREM2	FREM2_E16.01	TTTAAAGTGTCAAATTTCTTGGC	AGCGCAAGGTAGTGGAAAC	289	256.29
FREM2	FREM2_E16.02	GTGAAGACTCATTATGGTTTCTTG	CCAATTGGTTTATCCAGTGACC	266	396.51
FREM2	FREM2_E17	TTAGGCCCACTTAGTTAACTG	AACTATAGAATTTTCCAAGTCTTCTG	284	162.31
FREM2	FREM2_E18	GGAAGGAATCTGTACATAAGGGG	CGCTGAAATGTGTGAAGATG	250	164.55
FREM2	FREM2_E19	ATGCACTCTTTTAATTGAACCAC	TAATCAGATGGCAGCAGCAG	237	249.72
FREM2	FREM2_E20	GCTGCTGCCATCTGATTACAC	ACAAAGTGGGATTCTGCAAG	248	312.21
FREM2	FREM2_E21	TTGTGCACCATCAGAACCAC	CAGAGCATCCCTCTCATTG	212	340.81
FREM2	FREM2_E22	ATAACATTTCCACATCTC	GCTCATTTTTTGGGTCAAAG	241	8.00
FREM2	FREM2_E23	GAGAACATGCTGTCCTGGC	GGCATATAAATGTTCCATACTTGC	287	138.58
FREM2	FREM2_E24.01	TGCTTGCAAGAGCTGTGG	TTTTTCAGCACCAATCTCCC	275	367.42
FREM2	FREM2_E24.02	CGGAAGAAGAGAGAGATCAGG	AGGCAGATGGTGAGTAACCC	233	921.05
FREM2	FREM2_E24.03	CTGCAGTCAGCCTGGTCAC	GGCACTTACGGAAAAGGTTG	228	782.03
GREM1	GREM1_E02.01	GTGTCTTCCCCTCTCTGTGC	TGGACTCCAGCACCTCCTC	263	238.17
GREM1	GREM1_E02.02	CAGACTCAGTCGCCCCAG	GATGTGCCTGGGGATGTAG	258	460.66
GREM1	GREM1_E02.03	ACAGTCGCACCATCATCAAC	TATCTAGGACATGCTGGGTG	264	492.68
GRIP1	GRIP1_E25	ACCCACTGGCTTCACAGAAG	CCTGTGCTTGCAGTTAATGCC	255	2715.51
GRIP1	GRIP1_E24	CGGGTTTTGGGAATTATGG	TGTTCTGTTCACTCCAATCTCC	219	3950.93
GRIP1	GRIP1_E23	GCTAAATATTCACATCCCATTTC	GCTCCCAGTGAGAAATTAATTG	233	2097.47
GRIP1	GRIP1_E22.2	AGCTTCAGGAGCGCAG	ATGCTATGCAGAATGGCTGCC	215	4435.68
GRIP1	GRIP1_E22.1	TTAGTCCATGGCTTAATTGTTTC	CACATCTGAAGGCAGGGTG	197	5250.27
GRIP1	GRIP1_E21	GGTAGCCTTGGTCTGTCTAC	TTGCTGTCCAGAAGGCAAG	230	1706.03
GRIP1	GRIP1_E20	CTGGCAAGTTCCTAACCCAG	GAAACAATAAAAGTAAGTAGCAGGACC	187	4707.71
GRIP1	GRIP1_E19	GGGCCCAATGCTAACAC	TGACCATGCAGTCATCTTGG	238	2356.17
GRIP1	GRIP1_E18	TTTACTCTGATACTTAACTCCTTTC	TGGGCTTCAACAATGACAAG	281	895.07
GRIP1	GRIP1_E17	AGGTATGTGAGGGAATTTATATTCAG	TCAAGGAAGAAAATGCACTGG	272	860.55
GRIP1	GRIP1_E16	TGAATCTATGCATCTTACTCTTTTGC	GTTGTGAGGAAGGAAGCCC	276	16.39
GRIP1	GRIP1_E15	TCATCATTAGTCATGTGTTACTTTGC	ATCTTTGGTGACAGATGGGC	244	1973.34
GRIP1	GRIP1_E14	GGGAAATGTACAGTAAGGGGTG	CTTTGGGTGTGGAAGGTGTC	214	2197.20
GRIP1	GRIP1_E13	TGCTCCAGTCCTCAGTGTTT	CCTGCAAACCATTTGACAAC	205	1108.43
GRIP1	GRIP1_E12	ACAACCTCTCACATGTGGTTC	CCAATATAACTCACATGCAGTCC	222	8.81
GRIP1	GRIP1_E11	TGCTTGCTCCAACCTAAAGTC	ACGCAGAGCAGAAAATGATG	273	1501.33
GRIP1	GRIP1_E10	CACCTGAGAGTGCTCTGTGC	CCAAATGCCATTGGCTGTC	227	3055.19
GRIP1	GRIP1_E9b	CTTATTTTTTCATCATCACTTCATATG	ACCAGGAGGAGAAAGCATGG	215	2094.48
GRIP1	GRIP1_E09	GGCACTGCCCTTACCAG	TGCTAGAGGGAGCAACACTG	269	2144.42
GRIP1	GRIP1_E08	TTTACTCTTTCTTTGTCTCTTTG	CGGAAAAGTAGGCACTTTCTAC	249	858.47
GRIP1	GRIP1_E07	GACTATTAATACTAAGCCCTATTATGC	AGACAGTGCAGTTCTGGTGC	262	1865.84
GRIP1	GRIP1_E06	CAATGAAAGCAGTTTAAAGCTCTG	TCAACTTCTATGTTAAAGTCCCCAG	189	3516.80
GRIP1	GRIP1_E05	TTTTATGCCACATTGAATGATTAG	AACCAAATACCCAAATACCACC	245	1083.07
GRIP1	GRIP1_E04	GGTCTGTTGAAACAACATTGTC	CACTGGGGGTCTTGAATG	232	1807.61
GRIP1	GRIP1_E03	AGGAGAAATGACATTGGTGATTC	TGTTCTTTTCACTAGATTTCCCC	235	1765.73
GRIP1	GRIP1_E02	TGGAAATTAACCAACGCTTC	TTTGAATCACCAATAACAGGATTC	183	3980.81
GRIP1	GRIP1_E01	CACCTGGGACTACCTTTCTCCTG	TCGCTGAGGGAATAACAAGG	202	4091.27
ILK	ILK_E02	CCACAGTCCTCAGGCTTCC	CTTCTCTCATCCACCAACC	173	4746.99
ILK	ILK_E03	TTCAGGAATCAAAACCTTTGTC	TGATGTGGATGACGAAGGAG	262	1552.36
ILK	ILK_E04	CTGACTGTACTTTCTGCCTCTTC	CCATCTCAGGAATTAAGGGC	174	5730.83
ILK	ILK_E05	AGTGACTGCCAGCGAGGTAG	TGAGATTCTGGCCCATCTTC	276	2487.87
ILK	ILK_E06	CCTAGCTTGTGTCTCTCG	TACCACTTCAACCCTAACCC	243	3402.81
ILK	ILK_E07	AATAATCCTGGCCTCTTGGG	CCTTGCCCACTAACTGGAGG	247	2142.15
ILK	ILK_E8-13.1	CAAGCCTCCTAACCCCTACC	ACTGGGAGCACATTTGGATG	273	1958.29
ILK	ILK_E8-13.2	CAACCACTCCCTCCCTCTTC	CTCTGGTCCACGACGAAATC	254	2537.07
ILK	ILK_E8-13.3	GGGAGCCTCTCTGAACATTTTG	TAATTCGGGCACTCATGTCC	280	1393.54
ILK	ILK_E8-13.4	TCTGTTTTCTCTCTCAGATTG	ACATGTCTGCTGAGCGTCTG	279	1407.31
ILK	ILK_E8-13.5	CCCTATCTCTCCAGCTCTGC	GCCCTTGGGACAGGATTAC	265	1830.13
ILK	ILK_E8-13.6	TTGGCTCTCACATATTTGTTT	TGCTCTGCATCTTCTCAAGG	258	2169.26
ILK	ILK_E8-13.7	GAATGAAGACCCTGCAAAGC	GGCTGGGGTAGTACCATGAC	286	4075.45
ITGA8	ITGA8_E30	TTCACAGGTTCCAGAAATGAC	GAACAGGACCAGTGTGTTGAGG	185	4712.22

ITGA8	ITGA8_E29	GATCCTTTTCAGATCAACTTCCG	TAAATTCCTCAACAGCCCC	280	1204.59
ITGA8	ITGA8_E28	TGCCTTGAAATGCAAAACAC	GCCTAGCACAAAGCTAGACAGTG	282	23.56
ITGA8	ITGA8_E27	TCTGACGTGTTCCCACTGC	AGCAGTGTGTATGTGCTTCTG	177	5027.83
ITGA8	ITGA8_E26	GAAATGTAGCAACTGTTTCATGTG	AAGCCACTCATTTCCCTCAG	233	1841.75
ITGA8	ITGA8_E25	GCCTTCTGCTGGGTCATTAG	TCAACAAAGCCACTGATTAGAC	234	1898.57
ITGA8	ITGA8_E24	TTACCTGGGCCATTGCTAAC	CCCCTAACACAACCTTAACACAG	186	4097.25
ITGA8	ITGA8_E23	TGTAATAATACTCCTGAGCAGATAG	AATGCATCAGGAAAATTCCAC	218	954.04
ITGA8	ITGA8_E22	TTACAGTGATCCAGGGTGGG	GTGAGCTTTTAAGGCCAAGG	278	681.25
ITGA8	ITGA8_E21	GATGTCAATTTTCTCTGCCCC	TCCATTTGTTCCCTGTGAAG	205	3439.02
ITGA8	ITGA8_E20	AAGAAGTAGAGTACCTAATCCTTC	GCTCTTGACTTCAAACAATTTGC	224	1391.12
ITGA8	ITGA8_E19	AGAGGAAAGCTCTGGTTCCG	TGTAATTCATTAGATAGAAAGTACAC	221	1560.36
ITGA8	ITGA8_E18	TTGCAGCTATTTTCATGGAGC	TGCTTGAGAAAATGCCGTC	227	2812.87
ITGA8	ITGA8_E17	AGAGCACTGTGTTCACTGAATAC	AGGCCAGAGAAGTCTTTCTGG	237	503.99
ITGA8	ITGA8_E16	TCTGGGATTAGGTAAGGAAGG	TGGTCTGTGCAGAGAAATGG	210	2004.49
ITGA8	ITGA8_E15	AGTGAAGTGGGCTTCTGCC	GAGTTTGAGCAAGCACCGGAC	208	3392.24
ITGA8	ITGA8_E14	GCATGTAGGGGTATTCTATGTGC	TCCCCAGAATAAATCGTTGG	244	1614.44
ITGA8	ITGA8_E13	TACACATAAAACATGTTTTATGTCTG	CTCTCACGTGGGAAAAGAAAG	256	486.76
ITGA8	ITGA8_E12.2	GAATTTGAGAGCAACCCACG	AAATGACTTCCACGCTTTGG	193	5482.62
ITGA8	ITGA8_E12.1	GTGCTGAGCTGCTTTCTTTG	TACCGAATCTCCCAACGTC	191	6140.17
ITGA8	ITGA8_E11	TGTACCACAATGAGATGAATCTTTC	GTTGAGGCAATAAGGAAGGG	250	1142.57
ITGA8	ITGA8_E10	AATAAGATCATTCCTGGGGC	GTCTACTGGTAACCCAGAGTG	266	764.21
ITGA8	ITGA8_E09	AGTAATTCCTCTCTAAATGGC	TGTAATTCATCAAGGAGCAC	150	5301.76
ITGA8	ITGA8_E08	ACCATGGTAGCCCTTTCAC	ATGCCATTTTACCATTTC	195	1757.62
ITGA8	ITGA8_E07	CCTGCCCTCTTGCTTTCATTC	AAACCACAAATGTCTTGG	207	1256.75
ITGA8	ITGA8_E06	GGTTGCTGTTGCTGTTTCTG	AACCGTTCATTTGAGAACTATG	209	2264.00
ITGA8	ITGA8_E05	TTCTAGAGAAAATAACATAATATCCTG	TCAGATTAAATATTAGGAAGTCCGAG	197	34.45
ITGA8	ITGA8_E04	CAATTAATTCACCCAATAATTTAACAG	ACTTGAGCTAATGTCAGTTTCAAG	276	317.52
ITGA8	ITGA8_E03	CCACATTTTACAAATTATTAACCTTTC	AAATGCCAACAGCCTTATCG	277	725.85
ITGA8	ITGA8_E02	GCCCAAAGAGTGACTTTCTCC	TGGTCTCTCAAACCCAGG	218	1438.13
ITGA8	ITGA8_E01.2	GGGGATGTTGCTGTGGTC	AGCCGCTGGGACCTGAC	196	1383.70
ITGA8	ITGA8_E01.1	GGTAGCAGCCACCCACC	CTGTGAGCTTTTCCACGTCC	172	527.77
LIN7C	LIN7C_E05	AACTTAGATATTAGTGTATGGTTGGTTG	TTCTCTAGCTAAAACGCAAAATG	245	1240.99
LIN7C	LIN7C_E04	AGTCATATTTTTAATATGTAACCTTTC	CACTACAAATAGAAATAAAATTCATCC	275	1.10
LIN7C	LIN7C_E03	AAACCAGTCCCTCTCATTTTTG	TAATTTTGAAGAATTCCTACTTTTTGG	247	87.20
LIN7C	LIN7C_E02	AGGCATTGAGAAACCTTTG	TGAAACCAATTTAGAGTATTATCTG	245	640.29
LIN7C	LIN7C_E01	TACTCACTTTTCCGGCTTCC	GATCTCAGAGCCTGGGTCAC	221	273.95
LRP4	LRP4_E38.2	ATGCATGAAGACAGACACGG	AAGGAGAAGGAACAGGCAGG	237	3421.08
LRP4	LRP4_E38.1	TGACCATATCTGCCACTCTC	TGCTCCGTCTCTGTGTATC	235	2546.54
LRP4	LRP4_E37	TTTCTCATCACCTTCCCTCC	CTCGCCAAAAAGACCTTG	207	2728.07
LRP4	LRP4_E36	GCTAGAAAGTTGTGCGGTGGC	GTGGCCCTGTAGCAAGAC	166	6108.98
LRP4	LRP4_E35	CCTGAAAGCCCCCACTTAC	GTTTCAGCAACCCAGAGTCC	273	1855.05
LRP4	LRP4_E34	GTTTATGGTTCAGTGGCCC	CCATGATCCTGCATTGAACC	207	3920.26
LRP4	LRP4_E33	TGGGAGACCTGATTCTGTCC	GTGGCTCCAGCCATACAGTC	193	5077.53
LRP4	LRP4_E32	TTGGGCTTCCCTGTTG	TCCCACAGATGTTAAGGAAGC	211	2576.18
LRP4	LRP4_E31	CTGGGCTCCCTGGCAAG	CATCCCAGTCAAGGAGGTTTAG	207	4196.53
LRP4	LRP4_E30	CTTCCCATGCCTTGATGATG	GATTTCCAGGAGGCTGTTTG	210	3121.57
LRP4	LRP4_E29	ATCCAACACTGGGCTCTCC	TCTCTTCTGCTGGCCATAAAC	268	1631.63
LRP4	LRP4_E28.2	GACCTGTGATCCCTCTCCTG	TCTGGAGGTTTCAGTGTTC	218	2215.68
LRP4	LRP4_E28.1	GATGTTCCAGGCTAGGTGTG	CAGTGAGATACGCCGGATG	226	3601.35
LRP4	LRP4_E27	ACCTCTCCTTCTCTGTC	CAGAGGCTCTGACTCACAG	286	1247.11
LRP4	LRP4_E26	TGTGGTAGCTGTGAATAAC	GAAGCAGCAGGGACACG	242	2506.62
LRP4	LRP4_E25	CCAGTGTGCTCTTTTGACTTC	CCTTTACCCCGTCATAACCC	269	1521.45
LRP4	LRP4_E24	CGGTGAGGGTCTAGGTTGAG	CAGACAGGTGGTCCCTGG	162	4298.15
LRP4	LRP4_E23	TTAATGGCTGTGCTCGAGTG	AAGGCCAGGTGGGAAGAG	221	2990.82
LRP4	LRP4_E22	CATTGAACATCCCCTCTCTC	ATTGCCCCCTCCCAGAG	211	3573.09
LRP4	LRP4_E21	GTTGAAGATGACACAGTGTGG	TAGGGCATAGGAGGGCCAC	274	1630.08
LRP4	LRP4_E20	GTAAGACCTGCCTTGCCCTTG	AGATGTTTTAGTGCCACCCTTACC	279	1852.53
LRP4	LRP4_E19	CAAGACTAGAATTAATCTCTGTATCCC	ATGGAGCTCATTCCCAAGG	175	4900.62
LRP4	LRP4_E18	TGGTGATACAGCTTTGCTTCC	GAATCCCAGGGAGCCAG	153	3712.14
LRP4	LRP4_E17	TAAAAGAAGACCCCTTTCGGC	TTCAACCTCCCCACGCTG	266	2064.37
LRP4	LRP4_E16	GACCTTCGCTGATCCTCTTG	CCATGGAGGCTGGTGTG	193	1158.33
LRP4	LRP4_E15	TCCAGACTGAGGTCTTCTCTG	GAGGCTACTTTGGCTCACCC	246	2374.93
LRP4	LRP4_E14	CTGCCCCTTCCCAATTTAC	ATGAAGGAGACTGAAGGAAGG	280	1499.09
LRP4	LRP4_E13	GCCTGGGTTGACTCCTTG	AGAAAGTTCTGGGAGCCTGAG	233	2899.83
LRP4	LRP4_E12.2	TGCTGCTTAACAACCTGGAG	TCCATGGGGCCTTGTTT	178	5836.93
LRP4	LRP4_E12.1	CGGCTCTGAAACCCAGTG	GACCAGAAGACAAGCTCGC	191	6371.07
LRP4	LRP4_E11	GAGTGGGAGGACGACAGAAG	AGCCAAAGTGCCAACAGCC	200	3922.73
LRP4	LRP4_E10	CAACTCCCACTCTGGCTTG	CTCAGAACCCCGACTCTGC	206	904.30
LRP4	LRP4_E09	TTGCTATGACCTGACCTCC	GGGGTTCGGCCACAAAC	206	3767.51
LRP4	LRP4_E08	CACCTTTCATTAAGCCTTTGC	CTATAGGCTAAGGGTTCTGG	196	3206.88
LRP4	LRP4_E07	GGGACACTGCACAGACTGG	GCCCAACCTAATTCATTTC	197	3802.13

<i>LRP4</i>	LRP4_E06	ATCCAGGCCTGAGTGTGTG	ACCCAAGCAGTTCTTCCCAG	234	336.44
<i>LRP4</i>	LRP4_E05	CCCTCAGAACTGCTGTCCC	AACCCAACAGCCTGAGGTC	183	4256.40
<i>LRP4</i>	LRP4_E04	GCAGCCTGACTGCTCTGTG	ACCCACTGGCCACCTTG	185	1652.85
<i>LRP4</i>	LRP4_E03	CTGGCCTAGTTGAGCCTGAG	CTTTCCCAGTGGAACAATG	236	1369.94
<i>LRP4</i>	LRP4_E02	ACTGATTCCTTTTCCCTCCG	CAGGTCCCTCTCCACCAC	218	2327.22
<i>LRP4</i>	LRP4_E01	TGCACCCGGGACGCTTC	CGGACCCAGGGACAAAC	193	0.00

Supplemental Table 6: Genotype comparison of compound heterozygous alleles identified in three individuals with CAKUT in individuals of the 1000 Genomes Project (<http://browser.1000genomes.org/>) demonstrates that these alleles are in *trans*.

Individual, Sex, Origin	1 st allele	2 nd allele
A3975-2.1, M, GER	FRAS1 A1387L (EVS: 13/12487)	FRAS1 R3269Q (EVS: 88/12570)
NA19700, M, ASW	WT	G/A (het)
NA12413, M, CEU	WT	G/A (het)
HG00177, F, FIN	WT	G/A (het)
HG00104, F, GBR	WT	G/A (het)
HG00123, F, GBR	WT	G/A (het)
HG00134, F, GBR	WT	G/A (het)
NA20533, F, TSI	WT	G/A (het)
NA20757, F, TSI	WT	G/A (het)
A1023-2.1, M, IND	FREM2 R1344H (EVS: 25/12981)	FREM2 R2512H (EVS: 10/12996)
NA18635, M, CHB	A/G (het)	WT
HG00280, M, FIN	A/G (het)	WT
HG00284, M, FIN	A/G (het)	WT

ASW, Americans of African ancestry in Southwestern US; CEU, Utah residents with Northern or Western European ancestry; CHB, Han Chinese in Beijing, China; CLM, Colombians from Medellin, Columbia; EVS, Exome Variant Server; FIN, Finnish in Finland; GBR, British in England and Scotland; GER, German; IND, Indian; M, male; MAC, Macedonian; TSI, Toscani in Italy.

Supplemental Table 7. Evaluation workflow applied to Next Generation Sequencing-based mutation-analysis in 12 murine candidate genes in 672 individuals with CAKUT.

Applied Quality Control Filters ➤ Exclude variant if variant frequency in NGS-reads $\leq$ 20% ➤ Exclude variant if coverage $\leq$ 10x
Applied Variant Filters ➤ Exclude variant if present in common dnSNP132 (MAF >1%) ➤ Exclude variant if present in $\geq$ 5% of subjects ➤ Exclude variant if synonymous or not splice-site affecting ➤ Exclude single heterozygous variants in one gene
Variants were considered disease-causing and reported in Table 1 if: ➤ Confirmed in Sanger sequencing ➤ Positive segregation analysis ➤ Protein-truncating variants ➤ Affected amino acid residue is evolutionary conserved in vertebrates ➤ Variant is not present in a homozygous state in the EVS server and its minor allele frequency (MAF) is less than 1% in 13,000 control chromosomes (EVS). ➤ Variant prediction software do not unanimously predict the variant to be benign (PolyPhen2 Hum Var, SIFT, Mutation Taster).