Enlis Genomics

Report Date: **January 15, 2017**
Software Annotation Version: **8**

Genome Summary

Name: **(unknown)**
Genome ID:
genome_Karen_Allen_v4_Full_20160921154018

Sequencing Provider: **23andMe**
Sequencing Type: **Genotyping SNP Array**

Sequencing Coverage:

Full Genome	Genes	Exons	Protein-coding
0.019%	0.023%	0.071%	0.139%
589,093 bases	380,071 bases	74,174 bases	56,233 bases

Variation Counts:

Total number of variations:	375,534
Heterozygous:	167,000
Homozygous (x2):	104,267
Rare variations (MAF <1%):	1,939
SNV:	375,518
MNV:	0
Insertion:	5
Deletion:	11

Nonsense:	69
Frameshift:	14
Misstart:	17
Nonstop:	16
Inframe Ins/Del:	1
Missense:	5,909
Splice site:	700
Coding synonymous:	2,802
mRNA untranslated:	11,273
Intron:	190,278

Known Phenotype Summary:

42,032 variations known to affect a disease or trait were assessed

151 disease or trait variations are found in this genome

Phenotype variation coverage

32.9%
Successfully sequenced **13,841** phenotype variations
Missing data for **28,191** phenotype variations

Clinical classification:

Pathogenic	40
Likely pathogenic	2
Risk factor	66
Drug response	11
Association	22
Protective	10

Selected Phenotype Variation Details:

- **Chr1: 147,380,823 T>G** — **Pathogenic**

  Phenotype: Cataract 1

  Zygosity: Heterozygous (x1) dbSNP ID: rs80358202

  Population Allele Frequency: 0.32%

  Gene Impact: **GJA8** MISSENSE I-247-M

  Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/11846744

  Phenotype Description:

  Mutations in the GJA8 gene have been found to cause several types of autosomal dominant cataract, which have been described as congenital, zonular pulverulent, nuclear progressive, nuclear pulverulent, stellate nuclear, nuclear total, total, and posterior subcapsular. Cataract associated with microcornea, sometimes called the cataract-microcornea syndrome, is also caused by mutation in the GJA8 gene. Before it was known that mutation in the GJB8 gene caused multiple types of cataract, this entry was titled 'Cataract, zonular pulverulent, 1,' with the symbols CZP1, CZP, and CAE1.

  Modes of inheritance*: Autosomal Dominant

- **Chr1: 155,210,452 INS C** — **Pathogenic**

  Phenotype: Gaucher's disease, type 1

  Zygosity: Heterozygous (x1) dbSNP ID: rs387906315

  Population Allele Frequency: <0.01%

  Gene Impact: **GBA** FRAMESHIFT L-29-AS
  INTRON

  Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/8432537
  http://www.ncbi.nlm.nih.gov/pubmed/7789963
  http://www.ncbi.nlm.nih.gov/pubmed/1961718

  Phenotype Description:

  Gaucher disease (GD) encompasses a continuum of clinical findings from a perinatal lethal disorder to an asymptomatic type. The identification of three major clinical types (1, 2, and 3) and two other subtypes (perinatal-lethal and cardiovascular) is useful in determining prognosis and management. GD type 1 is characterized by the presence of clinical or radiographic evidence of bone disease (osteopenia, focal lytic or sclerotic lesions, and osteonecrosis), hepatosplenomegaly, anemia and thrombocytopenia, lung disease, and the absence of primary central nervous system disease. GD types 2 and 3 are characterized by the presence of primary neurologic disease; in the past, they were distinguished by age of onset and rate of disease progression, but these distinctions are not absolute. Disease with onset before age two years, limited psychomotor development, and a rapidly progressive course with death by age two to four years is classified as GD type 2. Individuals with GD type 3 may have onset before age two years, but often have a more slowly progressive course, with survival into the third or fourth decade. The perinatal-lethal form is associated with ichthyosiform or collodion skin abnormalities or with nonimmune hydrops fetalis. The cardiovascular form is characterized by calcification of the aortic and mitral valves, mild splenomegaly, corneal opacities, and supranuclear ophthalmoplegia. Cardiopulmonary complications have been described with all the clinical subtypes, although varying in frequency and severity.

  Modes of inheritance*: Autosomal Recessive

- **Chr6: 32,007,587 T>A** — **Pathogenic**

  Phenotype: 21-hydroxylase deficiency
  21-hydroxylase deficiency

Zygosity: Homozygous (x2) dbSNP ID: rs12530380

Population Allele Frequency: 0.00%

Gene Impact: **CYP21A2** MISSENSE V-238-E
MISSENSE V-208-E

Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/15623806
http://www.ncbi.nlm.nih.gov/pubmed/2845408
http://www.ncbi.nlm.nih.gov/pubmed/2249999

Phenotype Description:

21-hydroxylase deficiency (21-OHD) is the most common cause of congenital adrenal hyperplasia (CAH), a family of autosomal recessive disorders involving impaired synthesis of cortisol from cholesterol by the adrenal cortex. In 21-OHD CAH, excessive adrenal androgen biosynthesis results in virilization in all individuals and salt wasting in some individuals. A classic form with severe enzyme deficiency and prenatal onset of virilization is distinguished from a non-classic form with mild enzyme deficiency and postnatal onset. The classic form is further divided into the simple virilizing form (~25% of affected individuals) and the salt-wasting form, in which aldosterone production is inadequate (=75% of individuals). Newborns with salt-wasting 21-OHD CAH are at risk for life-threatening salt-wasting crises. Individuals with the non-classic form of 21-OHD CAH present postnatally with signs of hyperandrogenism; females with the non-classic form are not virilized at birth.

Modes of inheritance*: Autosomal Recessive

• Chr12: 103,288,579-103,288,581 DEL TGA

Pathogenic ★☆☆☆†

Phenotype: Phenylketonuria

Zygosity: Heterozygous (x1) dbSNP ID: rs62508727

Population Allele Frequency: <0.01%

Gene Impact: **PAH** DELETE+ IK-95-K
DELETE+ IK-90-K

Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/17630668
http://www.ncbi.nlm.nih.gov/pubmed/1709636

Phenotype Description:

Phenylalanine hydroxylase (PAH) deficiency results in intolerance to the dietary intake of the essential amino acid phenylalanine and produces a spectrum of disorders including phenylketonuria (PKU), non-PKU hyperphenylalaninemia (non-PKU HPA), and variant PKU. Classic PKU is caused by a complete or near-complete deficiency of phenylalanine hydroxylase activity; without dietary restriction of phenylalanine, most children with PKU develop profound and irreversible intellectual disability. Non-PKU HPA is associated with a much lower risk of impaired cognitive development in the absence of treatment.

Modes of inheritance*: Autosomal Recessive

The remaining known phenotype variations affect the following traits and diseases:

Obesity, association with • Encephalopathy, acute, infection-induced, 4, susceptibility to • Inflammatory bowel disease 17, protection against • Macular degeneration, age-related, 2, susceptibility to • Lumbar disc herniation, susceptibility to • Low density lipoprotein cholesterol level quantitative trait locus 6 • Serum level of interleukin-6 soluble receptor • Lupus nephritis, susceptibility to • Neutrophil-specific antigens na1/na2 • Trimethylaminuria, mild • Trimethylaminuria • Prostate cancer, susceptibility to • Age-related macular degeneration 4 • Thyrotoxic periodic paralysis • Chitotriosidase deficiency • Lymphoproliferative disorders, susceptibility to • Fasting plasma glucose level quantitative trait locus 5 • Ovarian response to FSH stimulation • Prostate cancer, hereditary, 12 • Asthma, susceptibility to • Febrile seizures, familial, 3a • Hashimoto thyroiditis, susceptibility to • Autosomal recessive congenital ichthyosis 4B • Insulin resistance, susceptibility to • Inflammatory bowel disease 10, susceptibility to • Gilbert syndrome, susceptibility to • Bilirubin, serum level of, quantitative trait locus 1 • Obesity, age at onset of • Atrial fibrillation • Human immunodeficiency virus type 1, rapid progression to AIDS • Schizophrenia, susceptibility to • Transferrin variant c1/c2 • Hypertension, essential, susceptibility to • Calcium oxalate urolithiasis • Leanness, susceptibility to • Recombination rate quantitative trait locus 1 • Hypertension, salt-sensitive essential, susceptibility to • Diabetes mellitus, noninsulin-dependent, association with • Leprosy, protection against • Alcoholism, susceptibility to • Alcohol dependence • Metabolic syndrome, protection against • Prekallikrein deficiency • Neural tube defects, folate-sensitive, susceptibility to • Severe combined immunodeficiency, autosomal recessive, T cell-negative, B cell-positive, NK cell-positive • Atopy, susceptibility to • Skin/hair/eye pigmentation, variation in, 8 • Age-related macular degeneration 14 • NamedVar: Factor B fast/slow polymorphism • Microvascular complications of diabetes 1 ... **and more...**

Get full details on the remaining 147 known phenotype variations within the Enlis Genome software.

Interesting Variations of Uncertain Significance:

Filter steps:

- **Protein-disrupting variations** (Nonsense, Frameshift, Misstart, Splice Disrupt)
- **Phenotype Genes** - Within a gene already implicated in a disease or trait
- Global allele frequency < 1%
- Uncertain clinical significance

Results:

Variation	Gene	Impact	Allele Freq.	Gene Phenotype
Chr5: 138,658,285 A>C	**MATR3**	SPLICE DISRUPT	0.00%	Amyotrophic lateral sclerosis
Chr7: 117,170,991 DEL A	**CFTR**	FRAMESHIFT	0.01%	Bronchiectasis • Congenital bilateral absence of vas deferens • Cystic fibrosis • Hypertrypsinemia • Pancreatitis • Sweat chloride elevation
Chr7: 117,304,816 INS A	**CFTR**	FRAMESHIFT	0.00%	Bronchiectasis • Congenital bilateral absence of vas deferens • Cystic fibrosis • Hypertrypsinemia • Pancreatitis • Sweat chloride elevation
Chr12: 133,196,338 T>C	**P2RX2**	SPLICE DISRUPT	0.02%	Deafness
Chr13: 32,900,419 INS G	**BRCA2**	FRAMESHIFT	0.00%	Breast cancer • Breast-ovarian cancer • Fanconi anemia • Glioblastoma • Medulloblastoma • Pancreatic cancer • Pre-B-cell acute lymphoblastic leukemia • Prostate cancer • Wilms tumor

+ 6 additional variations

Filter steps:

- **Predicted deleterious variations**
- **Phenotype Genes** - Within a gene already implicated in a disease or trait
- Global allele frequency < 1%
- Uncertain clinical significance

Results:

Variation	Gene	Impact	Allele Freq.	Gene Phenotype
Chr3: 33,155,769 T>C	**CRTAP**	MISSENSE	0.00%	Osteogenesis imperfecta
Chr12: 6,128,067 G>A	**VWF**	MISSENSE	0.00%	von Willebrand disease
Chr12: 121,174,903 T>C	**ACADS**	MISSENSE	0.00%	Acyl-CoA dehydrogenase deficiency
Chr13: 52,542,693 A>G	**ATP7B**	MISSENSE	0.00%	Wilson disease
Chr14: 23,887,588 G>A	**MYH7**	NONSENSE	0.00%	Cardiomyopathy • Left ventricular noncompaction • Liang distal myopathy • Myopathy • Scapuloperoneal syndrome

+ 2 additional variations

Notes

* Mode of inheritance defintions:

Autosomal Dominant
Autosomal dominant inheritance refers to genetic conditions that occur when a mutation is present in one copy of a given gene (i.e., the person is heterozygous).

Autosomal Recessive
Autosomal recessive inheritance refers to genetic conditions that occur only when mutations are present in both copies of a given gene (i.e., the person is homozygous for a mutation, or carries two different mutations of the same gene, a state referred to as compound heterozygosity).

† Confidence Star Levels:


Review Status: Classified by single submitter with no evidence provided, or multiple conficting interpretations


Review Status: Classified by single submitter with evidence

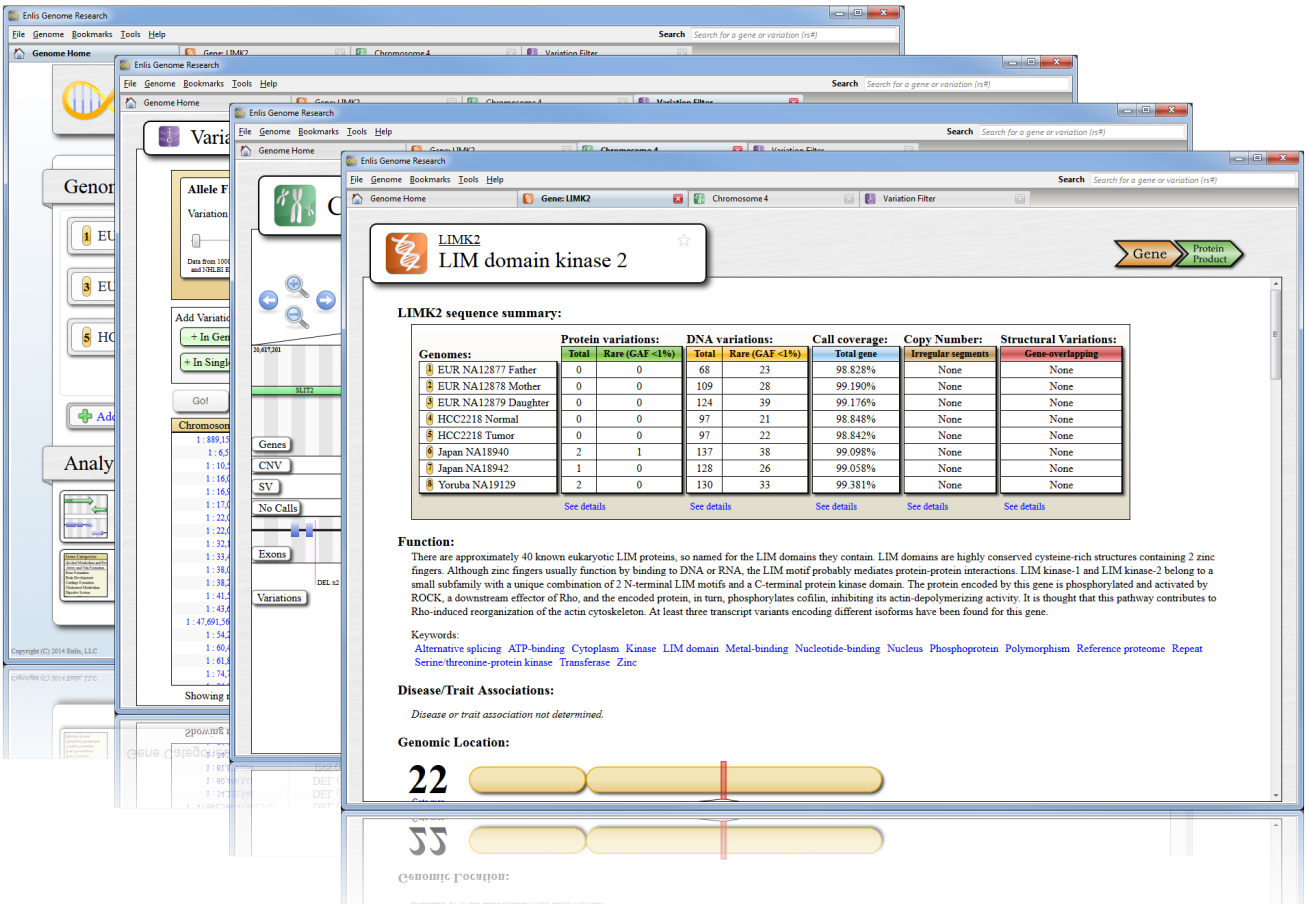

Review Status: Classified by multiple submitters


Review Status: Reviewed by expert panel


Review Status: Reviewed by professional society

Human genome reference version: HomoSapiens_GRCh37

Discover more with Enlis Genome software:



Your data has been converted. It is now ready for analysis with the award-winning Enlis Genome software!

- Comprehensive variation annotation
- Phenotype Explorer Tool - connect your data and generate PDF reports on over 6,000 diseases and traits
- Variation Filter - highly optimized with a point-and-click interface
- Gene Categories and Pathway Tool - evaluate over 20,000 built-in gene categories
- Homozygous Region Tool - to find regions associated with recessive disease

and much more...

Get started at: http://www.enlis.com