Enlis Genomics

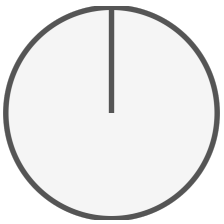
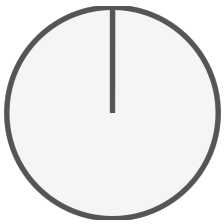
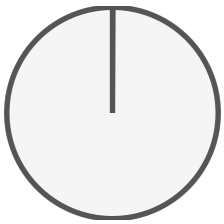
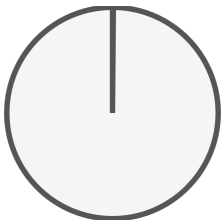
Report Date: **August 20, 2015**
Software Annotation Version: **8**

Genome Summary

Name: **Greg Mendel**
Genome ID: **genome_Greg_Mendel_Dad**

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

Sequencing Coverage:

Full Genome	Genes	Exons	Protein-coding
			
0.019%	0.023%	0.070%	0.137%
588,028 bases	378,924 bases	73,277 bases	55,269 bases

Variation Counts:

Total number of variations:	367,818
Heterozygous:	168,276
Homozygous (x2):	99,771
Rare variations (MAF <1%):	1,997
SNV:	367,818
MNV:	0
Insertion:	0
Deletion:	0

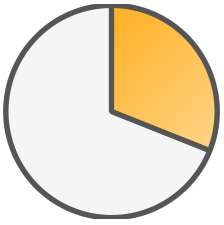
Nonsense:	66
Frameshift:	0
Misstart:	11
Nonstop:	12
Inframe Ins/Del:	0
Missense:	5,797
Splice site:	674
Coding synonymous:	2,740
mRNA untranslated:	11,070
Intron:	186,893

Known Phenotype Summary:

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

131 disease or trait variations are found in this genome

Phenotype variation coverage



31.0%
Successfully sequenced **13,033** phenotype variations
Missing data for **28,999** phenotype variations

Clinical classification:

Pathogenic	29
Likely pathogenic	2
Risk factor	61
Drug response	10
Association	24
Protective	5

Selected Phenotype Variation Details:

- **Chr6: 137,219,380 G>C** — **Pathogenic** ★★☆☆†

  Phenotype: Rhizomelic chondrodysplasia punctata type 1

  Zygosity: Heterozygous (x1) dbSNP ID: rs148591292

  Population Allele Frequency: <0.01%

  Gene Impact: **PEX7** SPLICE DISRUPT

  Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/12325024

  Phenotype Description:

  Rhizomelic chondrodysplasia punctata type 1 (RCDP1) classic type, a peroxisome biogenesis disorder (PBD), is characterized by proximal shortening of the humerus and to a lesser degree the femur (rhizomelia), punctate calcifications in cartilage with epiphyseal and metaphyseal abnormalities (chondrodysplasia punctata, or CDP), coronal clefts of the vertebral bodies, and cataracts that are usually present at birth or appear in the first few months of life. Birth weight, length, and head circumference are often at the lower range of normal; postnatal growth deficiency is profound. Intellectual disability is severe, and the majority of children develop seizures. Most affected children do not survive the first decade of life; a proportion die in the neonatal period. A milder phenotype in which all affected individuals have congenital cataracts and chondrodysplasia is now recognized; some do not have rhizomelia, and some have less severe intellectual disability and growth deficiency.

  Modes of inheritance*: Autosomal Recessive

- **Chr7: 150,648,790 A>G** — **Pathogenic** ★☆☆☆†

  Phenotype: Congenital long QT syndrome

  Zygosity: Homozygous (x2) dbSNP ID: rs199472924

  Population Allele Frequency: 0.00%

  Gene Impact: **KCNH2** MISSENSE L-224-P
  MISSENSE L-468-P
  MISSENSE L-564-P

  Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/10744792

  Phenotype Description:

  None available

  Modes of inheritance*: Autosomal Recessive
  Autosomal Dominant

- **Chr9: 80,919,758 A>C** — **Pathogenic** ★☆☆☆†

  Phenotype: Phosphoserine aminotransferase deficiency

  Zygosity: Heterozygous (x1) dbSNP ID: rs118203967

  Population Allele Frequency: 0.00%

  Gene Impact: **PSAT1** MISSENSE D-100-A

  Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/17436247

Phenotype Description:

Deficiency of phosphoserine aminotransferase (PSAT; EC 2.6.1.52) is characterized biochemically by low plasma and cerebrospinal fluid (CSF) concentrations of serine and glycine and clinically by intractable seizures, acquired microcephaly, hypertonia, and psychomotor retardation. Outcome is poor once the individual becomes symptomatic, but treatment with serine and glycine supplementation from birth can lead to a normal outcome (Hart et al., 2007).

Modes of inheritance*: Autosomal Recessive
Autosomal Dominant

- **Chr11: 111,635,566 C>T** — **Pathogenic** ★☆☆☆†

Phenotype: Lung cancer

Zygosity: Heterozygous (x1) dbSNP ID: rs1805076

Population Allele Frequency: 0.63%

Gene Impact: **PPP2R1B** MISSENSE G-90-D
INTRON
UTR5

Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/11996789
http://www.ncbi.nlm.nih.gov/pubmed/9765152

Phenotype Description:

Lung cancer is the leading cause of cancer deaths in the U.S. and worldwide. The 2 major forms of lung cancer are nonsmall cell lung cancer and small cell lung cancer (see 182280), which account for 85% and 15% of all lung cancers, respectively. Nonsmall cell lung cancer can be divided into 3 major histologic subtypes: squamous cell carcinoma, adenocarcinoma, and large cell lung cancer. Cigarette smoking causes all types of lung cancer, but it is most strongly linked with small cell lung cancer and squamous cell carcinoma. Adenocarcinoma is the most common type in patients who have never smoked. Nonsmall cell lung cancer is often diagnosed at an advanced stage and has a poor prognosis (summary by Herbst et al., 2008).

Modes of inheritance*: Autosomal Recessive

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

MTHFR deficiency, thermolabile type • Drug addiction, susceptibility to • Encephalopathy, acute, infection-induced, 4, susceptibility to • Myocardial infarction 1 • Homocysteine, total plasma, elevated • Lumbar disc herniation, susceptibility to • Low density lipoprotein cholesterol level quantitative trait locus 6 • Serum level of interleukin-6 soluble receptor • Familial medullary thyroid carcinoma • Spherocytosis, type 3, autosomal recessive • Lupus nephritis, susceptibility to • Neutrophil-specific antigens na1/na2 • Trimethylaminuria, mild • Prostate cancer, susceptibility to • Lymphoproliferative disorders, susceptibility to • Rhizomelic chondrodysplasia punctata type 2 • Fasting plasma glucose level quantitative trait locus 5 • Ovarian response to FSH stimulation • Fetal hemoglobin quantitative trait locus 5 • Prostate cancer, hereditary, 12 • Gastric cancer susceptibility after h. pylori infection • Febrile seizures, familial, 3a • Breast cancer, protection against • Autosomal recessive congenital ichthyosis 4B • Inflammatory bowel disease 10, susceptibility to • Gilbert syndrome, susceptibility to • Bilirubin, serum level of, quantitative trait locus 1 • Diabetes mellitus type 2 • Human immunodeficiency virus type 1, rapid progression to AIDS • Schizophrenia, susceptibility to • Hypertension, essential, susceptibility to • Leanness, susceptibility to • Recombination rate quantitative trait locus 1 • Leprosy, protection against • Systemic lupus erythmatosus, association with • Venous thromboembolism, susceptibility to • Prekallikrein deficiency • Severe combined immunodeficiency, autosomal recessive, T cell-negative, B cell-positive, NK cell-positive • Familial hypercholesterolemia • Asthma, susceptibility to • Atopy, susceptibility to • Memory quantitative trait locus • Skin/hair/eye pigmentation, variation in, 8 • High density lipoprotein cholesterol level quantitative trait locus 7 • Hemochromatosis type 1 • Age-related macular degeneration 14 • NamedVar: Factor B fast/slow polymorphism • Atherosclerosis, susceptibility to • Microvascular complications of diabetes 1 • Asthma and atopy, susceptibility to ... **and more...**

Get full details on the remaining 127 known phenotype variations within the Enlis Genome Research 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: 112,162,854 T>G	**APC**	NONSENSE	0.00%	Adenoma • Adenomatous polyposis coli • Brain tumor-polyposis syndrome • Colon cancer • Desmoid disease • Gardner syndrome • Gastric cancer • Hepatoblastoma

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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:

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Chr5: 112,162,854 T>G	**APC**	NONSENSE	0.00%	Adenoma • Adenomatous polyposis coli • Brain tumor-polyposis syndrome • Colon cancer • Desmoid disease • Gardner syndrome • Gastric cancer • Hepatoblastoma
Chr16: 2,166,918 A>G	**PKD1**	MISSENSE	0.00%	Polycystic kidney disease
Chr22: 42,523,897 G>A	**CYP2D6**	MISSENSE	0.01%	Codeine sensitivity • Debrisoquine sensitivity

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

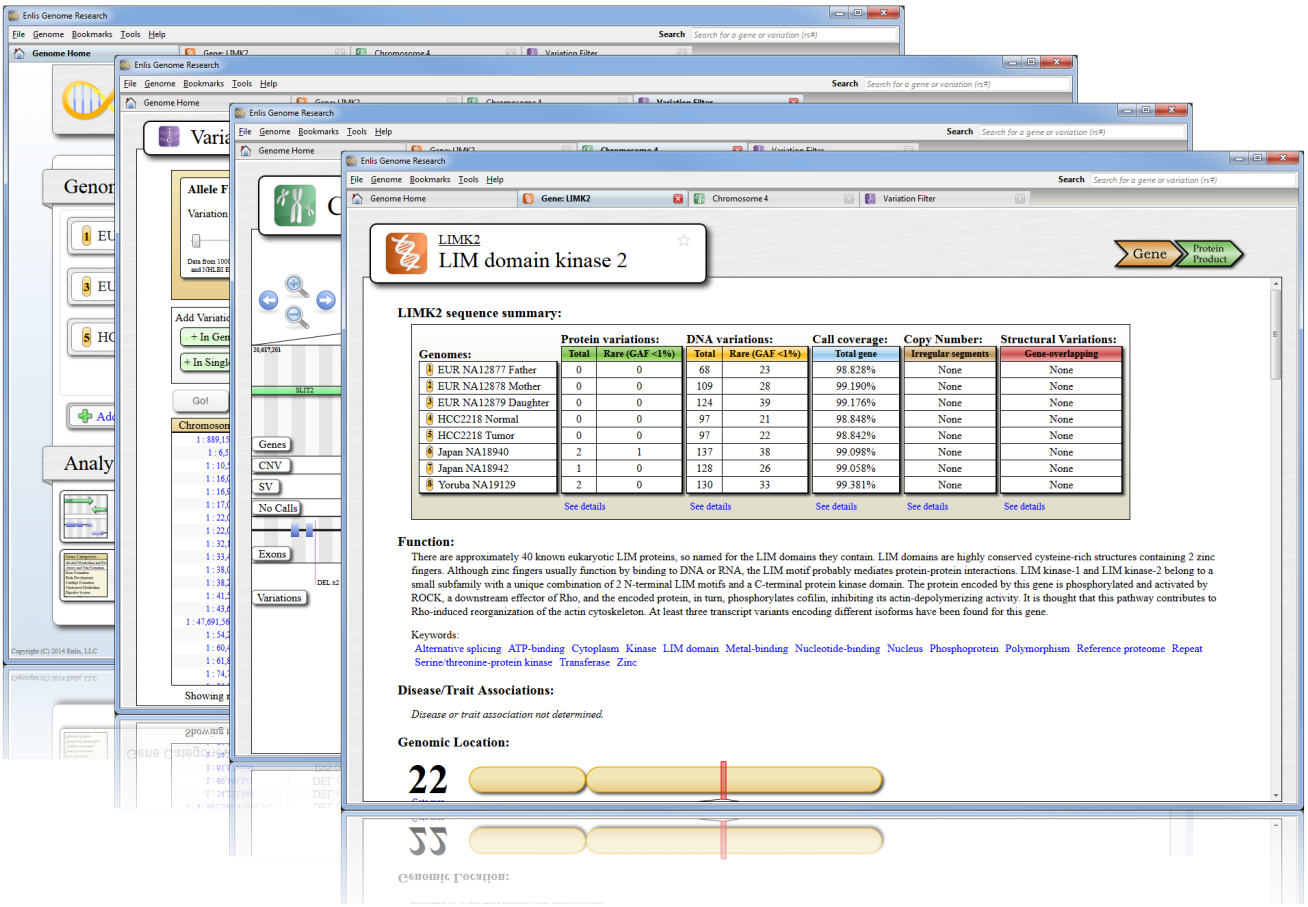

Review Status: Classified by multiple submitters


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