FAMILIAL HYPERCHOLESTEROLEMIA (FH)

About 1 in 50 people with high cholesterol are born with Familial Hypercholesterolemia (FH), a hereditary disorder that causes very high cholesterol. People with high cholesterol and FH are 22 times more likely to develop coronary heart disease (CHD) than those with normal cholesterol and no FH. FH is a common cause of premature cardiovascular disease and is often undiagnosed in young people.

Too Many: 1 in 250 people have familial hypercholesterolemia.

Too Young: FH is responsible for an estimated 20% of myocardial infarctions before age 45 and 5% between age 45 and 60.

Too Predictable: Each first-degree relative of an individual with FH has a 50% chance of having a genetic mutation. Circulogene FH genetic test can confirm clinical diagnosis of FH and facilitate family testing (cascade screening), which can further improve treatment management in children, adolescents and young adults.

CIRCULOGENE FH GENETIC TESTING

- One tube, one week, complete results, with insurance coverage providing a comprehensive analysis of the four genes associated with FH: LDLR, APOB, PCSK9 and LDLRAP1.
- Individuals with unexplained elevated cholesterol or early cardiovascular disease could benefit from the confirmation of an FH diagnosis through our testing to enable appropriate medical management and more targeted therapy.
- Early and appropriate medical intervention can reduce the risk of cardiovascular events. Through our FH full-gene sequencing analysis, at-risk relatives could be identified and preventive therapy could be initiated.
- Guideline-based cardiovascular risk reductions could include targeted therapy to reduce LDL cholesterol (i.e., Statins, Ezetimibe, PCSK9 inhibitors).

Data Analysis & Interpretation

Sequenced data analysis, annotated and pre-classified variants, and 200,000 community variant call consensus offer you the best tool for the most accurate results.

Variant Report

All the variants are called in different pathogenicity classes, i.e., from pathogenic to benign. This AI machine-learning pre-classification significantly simplifies interpreting variants and allows you to systematically evaluate each variant.

Any reportable pathogenic, likely pathogenic or VUS variant will be confirmed by high-sensitivity, allele-specific, real-time PCR when: (1) the variant depth of coverage is <300X; and (2) the variant frequency is between 10-25% or 70-85%, where the allele zyosity status can’t be clearly determined.
THE ONE-AND-DONE CIRCULOGENE BIOINFORMATICS ADVANTAGE

In hereditary cancers, insight into genomic risk factors helps steer improved patient care. Circulogene’s cutting-edge bioinformatics applies artificial intelligence, machine-learning and database-driven algorithms to deliver highest quality and most accurate SNV, INDEL and structural variant analysis and classification to clinic.

Aggregated Data From Diverse, First-Class Sources

- Automated, validated and up to date with built-in quality systems
- Data from diverse, first-class data sources aggregated, organized, aligned, annotated and classified
- Constant variant reclassification every 3 weeks

Advanced and Fully Integrated AI Greatly Enhances Confident Calls.

- Machine-educated variant calling of pathogenic, likely pathogenic, VUS variants, including automatic pre-classification
- Approx. 200,000 “global inter-lab” calling data sets, on top of eight major public databases to achieve unparalleled accuracy

Big Data-Sharing With Global Medical Community

- Fast, accurate raw data analysis and data sharing with variant calling and annotation
- Regular upload of our reported variants to share with broader medical community

Comprehensive Intuitive Report

- Variant details
- Clinically relevant and actionable information
- Follows ACMG and AMP guidelines for all mutation types
- Simplified data mining correlates millions of internal and external medical data sources, (both public & private)

Complete End-to-End Solution

- Patient centric
- Data analysis
- Classification
- Interpretation and reporting

Security and Privacy

- HIPAA compliant
- Long-term cloud storage
- Clinical grade security, privacy and compliance

OVER 2 MILLION VARIANT CALL DATA

Unlike most labs that use free, public databases, or rely on their own public-inaccessible databases, Circulogene has built a proprietary aggregate integrating the 8 largest public databases with a global community variant-calling atlas.

HUMAN GENETIC VARIANT DATABASES:

- **The Genome Aggregation Database (gnomAD)**
  Variants of 15,496 genomes and 123,136 exomes from seven populations worldwide
- **ClinVar**
  Currently holds >160,000 submitted interpretations, representing >130,000 variants, affecting >26,000 genes
- **COSMIC**
  >170,000 mutations, >2.9 million experiments, >500,000 tumors
- **ExAC**
  60,706 exomes from seven populations
- **ESP**
  6,503 exomes from European Americans and African Americans
- **1000 Genomes Project**
  Genomic data for 2,504 individuals from five populations
- **CG69**
  69 individuals with complete genomes
- **dbNSFP**
  83,422,341 nsSNVs and ssSNVs (splicing-site SNVs)