Ambry Genetics®
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FHNext Product Summary | September 2018

COMPREHENSIVE GENETIC ANALYSIS FOR FAMILIAL HYPERCHOLESTEROLEMIA

Why Order This Test?

- To confirm a diagnosis of familial hypercholesterolemia (FH)
- To allow for individualized disease management and treatment (*e.g.* avoiding/adjusting simvastatin use based on *SLCO1B1* genotype)
- To confirm personal risks for coronary artery disease
- To use genetic testing in cascade screening of family members, as supported by data and clinical practice guidelines to increase the detection of FH.[1]

Who should be tested with FHNext?[2]

GENETIC TESTING FOR FH	PROBAND (INDEX CASE)	LDL LEVEL (MG/DL)*	PERSONAL/FAMILY HISTORY
Should be offered	Children	≥160	≥1 first-degree relative similarly affected or with premature CAD OR Family history info not available
	Adults	≥190	
	Children	≥190	No additional family history required
	Adults	≥250	
May be considered	Children	≥160	≥1 parent with LDL ≥190 mg/dL OR Family history of hypercholesterolemia and premature CAD
	Adults	No pre-treatment LDL levels available	Personal history of premature CAD AND Family history of hypercholesterolemia and CAD
		≥160	Family history of hypercholesterolemia AND Either personal or family history of premature CAD

**Pre-treatment LDL Levels*

Cascade Testing for At-Risk Relatives Recommended[2]:

- When a patient is identified to have a mutation, genetic testing for the identified variant should be offered to all 1st-degree relatives (*i.e.* parents, siblings, children)
- Cascade testing should extend throughout the whole family until everyone at-risk has been assessed

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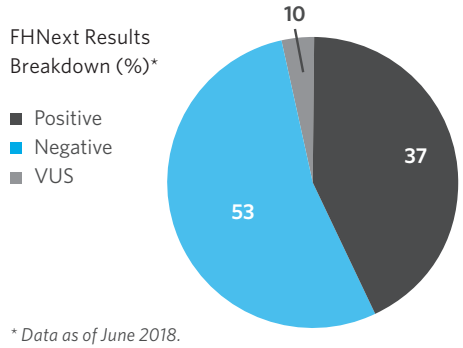
TEST DETAILS

- NGS panel of *LDLR, APOB, PCSK9, LDLRAP1* genes
- Del/dup analysis of *LDLR, APOB, PCSK9* genes
- Optional analysis of pharmacogenetic c.521T>C SNP in *SLCO1B1* gene

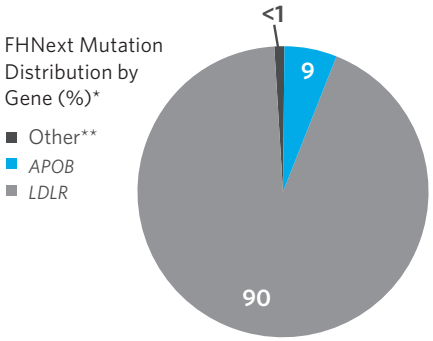
FHNEXT PERFORMANCE*

FHNext has one of the highest diagnostic yields of any test Ambry offers, with 37% of total cases yielding a positive result. The rate of genetic variants of unknown significance (VUS) is low at only 10%.

FHNext Results Breakdown (%)*



FHNext Mutation Distribution by Gene (%)*



** Data as of June 2018.*
*** LDLR/APOB compound heterozygous*

DID YOU KNOW?

Patients with FH may be asymptomatic and experience complications like angina, myocardial infarction, or stroke without warning. Studies suggest that only 10% of those with FH are aware of their condition and receiving the care they need. Additionally, 1-5% of those treated with statins experience myalgia; this can be related to a specific pharmacogenetic marker.[3]

TEST NAME	TEST CODE	YIELD	GENES	TAT
FHNext	8680	37%	*APOB, LDLR, PCSK9, LDLRAP1* + optional pharmacogenetic c.521T>C SNP in *SLCO1B1*	2-3 weeks

References

1. Goldberg AC, *et al.*, J Clin Lipidol., 2011.
2. Sturm, Amy C., *et al.*, Clinical Genetic Testing for Familial Hypercholesterolemia. Journal of the American College of Cardiology. 72 (2018) 662-680.
3. Ramsey LB, *et al.*, Clin Pharmacol Ther., 2014.

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