Dyslipidemias are a clinically and genetically heterogenous group of disorders associated with abnormal levels of lipids and lipoproteins, including increased or decreased levels of LDL or HDL cholesterol or increased levels of triglycerides [1]. Dyslipidemias can have a monogenic cause, or may be associated with other conditions such as diabetes and thyroid disease, or lifestyle factors. The most common subset of monogenic dyslipidemia is familial hypercholesterolemia (FH), which has an estimated prevalence of 1 in 200 in the Caucasian population [2].

**Our Dyslipidemia Sequencing and Deletion/Duplication Panels include analysis of all 23 genes listed below.**

<table>
<thead>
<tr>
<th>Gene</th>
<th>OMIM#</th>
<th>Associated disorders</th>
<th>Dyslipidemia phenotype</th>
<th>Inheritance</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABCA1</td>
<td>600046</td>
<td>Tangier disease; High density lipoprotein (HDL) deficiency</td>
<td>Low HDL-C</td>
<td>Recessive; Dominant</td>
<td>[3, 4]</td>
</tr>
<tr>
<td>ABCG5</td>
<td>605459</td>
<td>Sitosterolemia</td>
<td>Hypercholesterolemia, hyperlipidemia</td>
<td>Recessive</td>
<td>[5]</td>
</tr>
<tr>
<td>ABCG8</td>
<td>605460</td>
<td>Sitosterolemia</td>
<td>Hypercholesterolemia, hyperlipidemia</td>
<td>Recessive</td>
<td>[5]</td>
</tr>
<tr>
<td>ANGPTL3</td>
<td>605019</td>
<td>Familial hypobetalipoproteinemia-2</td>
<td>Low LDL-C</td>
<td>Recessive</td>
<td>[6]</td>
</tr>
<tr>
<td>APOA1</td>
<td>107680</td>
<td>Apolipoprotein A-I deficiency; HDL deficiency</td>
<td>Low HDL-C</td>
<td>Recessive; Dominant</td>
<td>[7, 8]</td>
</tr>
<tr>
<td>APOA5</td>
<td>606368</td>
<td>Hyperchylomicronemia; Hypertriglyceridemia</td>
<td>Hypertriglyceridemia</td>
<td>Dominant/Recessive; Dominant</td>
<td>[9, 10]</td>
</tr>
<tr>
<td>APOB</td>
<td>107730</td>
<td>Familial hypercholesterolemia; hypobetalipoproteinemia</td>
<td>High LDL-C; Low LDL-C</td>
<td>Co-dominant</td>
<td>[1, 11]</td>
</tr>
<tr>
<td>APOC2</td>
<td>608083</td>
<td>Apolipoprotein C-II deficiency</td>
<td>Hypertriglyceridemia</td>
<td>Recessive</td>
<td>[12]</td>
</tr>
<tr>
<td>CETP</td>
<td>118470</td>
<td>Hyperalphalipoproteinemia</td>
<td>High HDL-C</td>
<td>Dominant/Recessive</td>
<td>[13, 14]</td>
</tr>
<tr>
<td>GPD1</td>
<td>138420</td>
<td>Transient infantile hypertriglyceridemia</td>
<td>Hypertriglyceridemia</td>
<td>Recessive</td>
<td>[15]</td>
</tr>
<tr>
<td>GPIHBP1</td>
<td>612757</td>
<td>Hyperlipoproteinemia 1D</td>
<td>Hypertriglyceridemia</td>
<td>Recessive</td>
<td>[16]</td>
</tr>
<tr>
<td>LCAT</td>
<td>609667</td>
<td>Familial LCAT deficiency</td>
<td>Low HDL-C</td>
<td>Recessive</td>
<td>[17]</td>
</tr>
<tr>
<td>LDLR</td>
<td>609645</td>
<td>Familial hypercholesterolemia</td>
<td>High LDL-C</td>
<td>Co-dominant</td>
<td>[1]</td>
</tr>
<tr>
<td>LDLRAP1</td>
<td>605747</td>
<td>Familial hypercholesterolemia</td>
<td>High LDL-C</td>
<td>Recessive</td>
<td>[1]</td>
</tr>
<tr>
<td>LIPA</td>
<td>613497</td>
<td>Cholesterol ester storage disease / Wolman disease</td>
<td>High LDL-C</td>
<td>Recessive</td>
<td>[18, 19]</td>
</tr>
<tr>
<td>LPC</td>
<td>151670</td>
<td>Hepatic lipase deficiency</td>
<td>High HDL-C</td>
<td>Dominant/Recessive</td>
<td>[20, 21]</td>
</tr>
<tr>
<td>LMF1</td>
<td>611761</td>
<td>Combined lipase deficiency</td>
<td>Hypertriglyceridemia</td>
<td>Recessive</td>
<td>[22, 23]</td>
</tr>
</tbody>
</table>
LPL  609708  Lipoprotein lipase deficiency; Familial combined hyperlipidemia  Hypertriglyceridemia  Recessive; Dominant  [24, 25]

MTTP  157147  Abetalipoproteinemia  Low LDL-C  Recessive  [26]

PCSK9  607786  Familial hypercholesterolemia; Hypobetalipoproteinemia  High LDL-C; Low LDL-C  Dominant  [1]

SAR1B  607690  Chylomicron retention disease  Low LDL-C  Recessive  [27]

SCARB1  601040  Scavenger receptor B1 deficiency  High HDL-C  Dominant/Recessive  [28, 29]

STAP1  604298  Familial hypercholesterolemia  High LDL-C  Dominant  [30]

Test methods:
Comprehensive sequence coverage of the coding regions and splice junctions of all genes in this panel is performed. Targets of interest are enriched and prepared for sequencing using the Agilent SureSelect system. Sequencing is performed using Illumina technology and reads are aligned to the reference sequence. Variants are identified and evaluated using a custom collection of bioinformatic tools and comprehensively interpreted by our team of directors and genetic counselors. All pathogenic and likely pathogenic variants are confirmed by Sanger sequencing. The technical sensitivity of this test is estimated to be >99% for single nucleotide changes and insertions and deletions of less than 20 bp.

Deletion/duplication analysis of the panel genes is performed by oligonucleotide array-CGH. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by array-CGH. Array-CGH will not detect low-level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of this assay may be reduced when DNA is extracted by an outside laboratory.

Dyslipidemia Sequencing Panel (23 genes sequence analysis)
- Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
- Cost: $3000
- CPT codes: 81407
- Turn-around time: 8 weeks

Dyslipidemia Deletion/Duplication Panel (23 genes deletion/duplication analysis)
- Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
- Cost: $2500
- CPT codes: 81407
- Turn-around time: 6 weeks

Results:
Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

For more information about our testing options, please visit our website at dnatesting.uchicago.edu or contact us at 773-834-0555.

References: