Preface:
The Otogenetics Inherited Disease Panel allows for the identification of gene variants associated with known clinical phenotypes based on Human Gene Mutation Database (HGMD).

There are ~7,000 rare inherited diseases known. Many of which are severe recessive, pediatric disorders. The number of germline mutations associated with these inherited diseases now exceed 100,000 and are focused in multiple gene regions.

The Inherited Disease Gene Panel focuses on sequencing the regions of ~4,500 genes and ~180 SNPs (single nucleotide polymorphisms) to identify the underlying mutations of the specific diseases, regardless of syndromic physiological conditions.

Testing Rationale:
The Inherited Disease Gene Panel was designed to cover the most commonly requested clinical diagnostic assays and allows diagnosis with one comprehensive test.

Benefits of Testing:
The Otogenetics Inherited Diseases Panel can aid in genetic consultation of familial disorders and can also aid in potentially life-saving treatment. Testing could also prove beneficial not only for the affected patient, but also for related family members.

These tests provide:
- Very high depth of coverage to detect common and rare mutations.
- Capability to detect somatic point mutations, indels, gene fusions, and copy number variations (CNV).

Methodology:
The Otogenetics Inherited Disease Panel is performed by high throughput next generation sequencing; using Otogenetics' targeted enrichment systems. Select coding regions are sequenced at >100 fold average coverage.

Clinically significant variants are identified using the Burrows-Wheeler Aligner (BWA) and may be confirmed by Sanger sequencing.

Reporting Results:
Each Otogenetics Inherited Disease Gene Panel report includes a detailed explanation of all clinically-relevant variants.

Example of Data Quality

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Order #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inherited Disease</td>
<td>Oto-IDv1</td>
</tr>
</tbody>
</table>

Turn-Around-Time:
Approximately 5-6 weeks (Expedited service available)

Specimen Requirement:
- 2-5ml whole blood in EDTA or citric collection tubes
- Saliva in saliva collection kit
- Genomic DNA
Partial List of Inherited Disease Coverage

The Otogenetics Inherited Diseases Panel allows for the identification of gene variants with known risk association with hereditary diseases. The genetic test can aid in genetic consultation of familial disorders and potentially be life-saving, not only for the affected patient, but also for family members.

This is an important part of hereditary diseases risk evaluation, and identification of specific genetic variants provides important information for at-risk patients. Below is a partial list of diseases the panel covers.

- Autism Spectrum Disorders
- Cardiomyopathy
  - Arrhythmias
  - Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy
  - Brugada Syndrome
  - Dilated Cardiomyopathy
  - Hypertrophic Cardiomyopathy
  - Long and Short QT Syndrome
  - Pulmonary Arterial Hypertension
  - Sudden Cardiac Arrest
  - Thoracic Aortic Aneurysm & Dissection and Related Disorders
- Ciliopathies
- Congenital Disorders of Glycosylation
- Congenital Myasthenic Syndromes
- Epilepsy and Seizure Disorders
- Eye Disorders
  - Achromatopsia, Cone, and Cone-Rod Dystrophy
  - Albinism
  - Anophthalmia/Microphthalmia/Anterior Segment Dysgenesis/Anomaly
  - Bardet-Biedl Syndrome
  - Congenital Stationary Night Blindness
  - Flecked-Retina Disorders
  - Joubert Syndrome
  - Leber Congenital Amaurosis
- Macular Dystrophy/Degeneration/Stargardt Disease
- Neuronal Ceroid Lipofuscinoses
- Optic Atrophy
- Retinitis Pigmentosa
- Senior Loken Syndrome
- Stickler Syndrome
- Usher Syndrome
- Vitreoretinopathy
- Comprehensive Glycogen Storage Disorders
  - Glycogen Storage Disorders: Liver
  - Glycogen Storage Disorders: Muscle
- Hearing Loss
- Hereditary Cancer Syndrome
- Hereditary Periodic Fever Syndromes
- Inflammatory Bowel Disease
- Lysosomal Storage Disorders
- Maturity Onset Diabetes of the Young
- Multiple Epiphyseal Dysplasia
- Neuromuscular Disorders
  - Congenital Muscular Dystrophy
  - Limb-Girdle Muscular Dystrophy
- Noonan Syndrome and Related Disorders
- Peroxisome Biogenesis Disorders, Zellweger Syndrome Spectrum
- Short Stature Panel
- Skeletal Dysplasia
- X-Linked Intellectual Disability

Gene lists can be viewed at www.otogenetics.com