Personalis ACE Clinical Exome

The First Test to Combine an Enhanced Clinical Exome with Genome-Scale Structural Variant Detection

Personalis, Inc. 1350 Willow Road, Suite 202, Menlo Park, California 94025 • info@personalis.com • 1.855.GENOME4 • 1.650.752.1300

www.personalis.com

Personalis ACE Clinical Exome™

The First Test to Combine an Enhanced Clinical Exome with Genome-Scale Structural Variant Detection

- Combines high accuracy exome sequencing with genome-wide structural variant detection for improved sensitivity and diagnostic yield.
- Includes the most complete and accurate coverage of medically interpretable regions inside and outside the exome.
- Leverages a comprehensive collection of curated variant and phenotype associations for superior disease-phenotype analysis.
- Presents intuitive and actionable reports created by clinicians, for clinicians.
- Provides accurate, timely results with operational excellence and support from experts.

Indications for Testing

The Personalis ACE™ Clinical Exome is appropriate when a patient's medical history and physical exam suggest a syndrome of unknown genetic etiology.

This includes patients with:

- An ongoing "diagnostic odyssey" where other genetic testing has failed.
- A clinical presentation where traditional single gene/panel testing is of low yield.
- A broad differential diagnosis where comprehensive initial testing can enable more rapid, cost-effective diagnosis

Test Description

- **A "One-Stop" Test That Combines Enhanced Exome Sequencing and Genome-Wide Structural Variant Detection to Increase Diagnostic Yield**

  Founded by leaders in sequencing, genomics, and clinical medicine, Personalis' goal is to improve diagnostic yield while decreasing overall cost and turn-around time compared with traditional serial genetic testing.

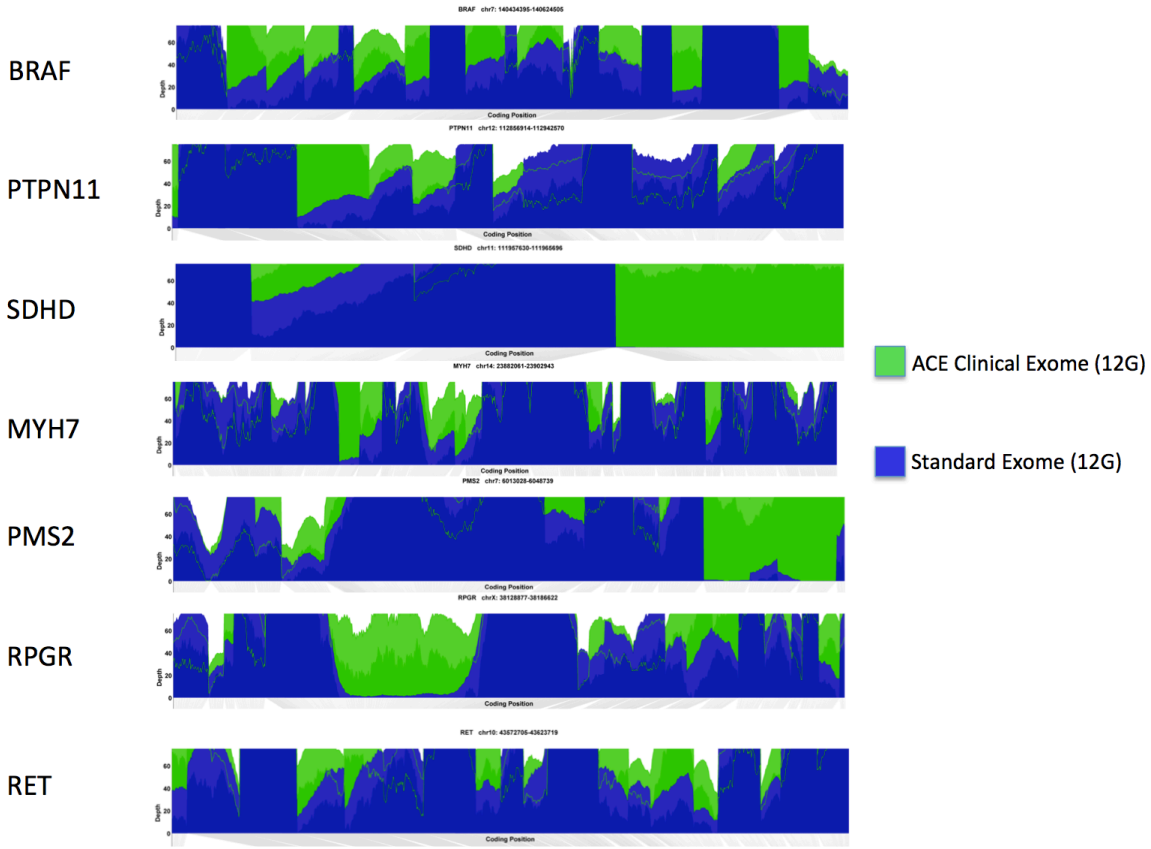
  Until now separate testing has been required for exome small variant detection and genome-wide structural variant detection, but the Personalis ACE™ Clinical Exome combines these into a single, convenient test. Our enhanced clinical-grade ACE™ Exome includes a new sequencing-based structural variant assay to provide a "one-stop" test that detects small variants exome-wide and large deletions and duplications genome-wide.

- **Finishing the Clinical Exome, Providing Confidence in Gene Coverage**

  Standard exome sequencing approaches leave gaps in coverage of critical, medically important genes due to systematic sequencing and sample-preparation biases.

  Our ACE™ Clinical Exome provides additional targeted sequencing to fill in gaps and problem regions, including additional coverage for more than 7,000 genes related to disease. ACE™ Clinical Exome finishes thousands more of these clinically important genes (99% of all bases covered to a **minimum** depth of 20x) than an exome without our accuracy and content

enhancement (ACE™). The graphs below show examples of coverage over all exons in each gene spliced together using a 12G standard exome (blue) versus a 12G ACE clinical exome (green):



- **Comprehensive Analysis to Improve Diagnostic Yield**

  Our state-of-the-art informatics pipeline improves overall accuracy and sensitivity for calling single nucleotide variants, indels, and structural variants. Our bioinformatics and clinical team analyze variant results leveraging both proprietary and external variant databases. We systematically identify and prioritize candidate genes based on clinical phenotype/features, and employ tools to analyze both common and rare inheritance patterns, consanguinity, aneuploidy, and regions identical by descent. Unconventional explanations for disease such as *de novo* events in the context of all inheritance patterns, and non-penetrance are also considered.

- **Intuitive and Actionable Reports, Created by Clinicians for Clinicians**

  Each prioritized variant is examined in detail by Personalis' clinical team of physicians, genetic counselors, bioinformaticians, and laboratory directors who determine if any of the variants identified are likely to be causally related to the clinical presentation. Results are compiled in a clear, intuitive report so providers can rapidly understand and assess the results.

- **Accurate, Timely Results with Operational Excellence and Support**

  Our services are provided by a world-class operational and clinical team operating a CLIA-certified lab. We will deliver the highest quality results in a core report to clinicians within 8-12 weeks during our early access program. Our genetic counselors and clinical team are readily available to assist with test selection, case reviews, and results interpretation.

Submission Requirements

Samples (for proband only or trios)

- Recommended: Blood (2-5mL whole blood in EDTA, shipped overnight at ambient temperature, with cool pack in hot weather)
- Alternatively: Purified DNA sample from each individual (5ug with minimum concentration of 30ng/ul)
- Alternatively: Saliva (with approved saliva collection kits)

Forms and Clinical Information

- A test requisition form must be filled out for all cases.
- A completed Personalis consent form must be received for each individual submitting a specimen including the affected individual and parents (if available).
  - Consent form allows the family to "opt-out" of receiving our ACMG report for incidental findings.
- Clinical records and prior genetic testing results for affected individual(s) should be provided when available.

Reporting of Results

Personalis will provide a core report detailing variants in the patient's DNA sequence in genes relevant to similar disease presentations. Our interpretation is focused on over 7000 genes reasonably expected to cause human disease based on literature based databases including OMIM, HGMD, Personalis' Disease Variant Database, HPO and other sources. Single nucleotide variants and small indels identified as causative in this report will be confirmed under CLIA by capillary Sanger sequencing, quantitative PCR, or as appropriate to the genomic region and variant type, another second sequence detection method.

Additionally, we will provide a report based on current ACMG guidelines for reporting of incidental findings, unless the requesting physician and/or patient have opted-out. This report may exclude genes recommended by the ACMG that have significant associated intellectual property. In our standard offering, we do not report variants in genes not included in the ACMG recommended incidental findings list.

The report(s) from this test will be delivered to the ordering physician.

Turn Around Time

For our early access program, our core report turnaround time for ACE™ Clinical Exome is 8-12 weeks from receipt of sample and phenotypic/clinical information. If a report of ACMG incidental findings is requisitioned additional time from issue of the core report is required.

Reanalysis Policy

Upon physician request, we will offer a re-analysis service for all samples processed in our early access program within one year for a nominal processing fee.

Pricing

Please discuss pricing with a Personalis representative.