Genomic Unity™ Test

Information sheet

Genomic Unity™ test is intended to help physicians diagnose the molecular cause of single gene as well as complex, oftentimes multifactorial, diseases in patients that present with unclear or heterogeneous phenotypes that cannot readily be linked to a clinical diagnosis. Genetic testing can be performed on the patient alone or as a trio where the patient's genomic variation is compared to his or her parents, enabling use of more powerful data analysis methods.

What is Genomic Unity™ test?

Genomic Unity™ is like an exome test, with additional benefits. It detects single nucleotide variants and small indels, but it does so with higher sensitivity and specificity. It also detects structural variants, including copy number variants, tandem repeat expansions and mitochondrial variants. Thus this single test replaces the need for separate exome analysis, chromosomal microarray analysis, repeat expansion analysis and mitochondrial variant analysis.

How is Genomic Unity™ better than traditional exome tests?

Genomic Unity™ uses in-silico exome analysis based on whole genome sequencing (WGS) technology. WGS provides the most comprehensive view of an individual's genome, covering the entire genome including the exons, relevent non-coding regions and the mitochondrial genome. Because WGS does not rely on PCR amplification, it is less susceptible to introduced errors while generating consistent read depth across the entire genome. The result is better coverage which leads to higher sensitivity and specificity for exonic variants as well as the ability to detect additional variant types not detectable through exome sequencing alone.

Better coverage of exonic variants

Better exonic variant coverage is accomplished by sequencing the entire genome using a PCR-free protocol that avoids the bias of probe- or amplicon-based separation kits. The result is more comprehensive and consistent coverage of all exons which are subsequently analysed as an in-silico exome[1,2,3]. An in-silico exome means that the exons are isolated for analysis after sequencing using computer-driven methods as opposed to isolating the exons as part of the DNA preparation prior to sequencing.

Identification of additional variant types as part of a single assay

Using WGS as the underlying technology enables detection of additional variant types that are not detectable when using exome sequencing technology: large structural variants[4], including copy number variants and tandem repeat expansions.

These variant types are detected using a combination of read depth and break point analysis that is enabled by WGS's consistent and comprehensive genome-wide coverage.

Mitochondrial variants, which are tested for by some exome vendors using a concurrent assay, are also detected as part of the Genomic Unity™ test. Due to WGS's inherently deep mitochondrial coverage, variants are detected at heteroplasmy levels down to 4%.

What about incidental findings?

Variantyx reports on findings that are directly related to the reason(s) for testing the patient, or that fall within genes evaluated for their association with the reason(s) for testing. Incidental findings are only provided for the patient when specifically opted in. Incidental findings are limited to the set of 59 genes recommended by the American College of Medical Geneticists for WES and WGS reporting[5]. Only pathogenic and likely pathogenic incidental findings are reported.

What if a diagnosis is not made?

Because WGS covers an individuals entire genome it is not biased by current knowledge of disease-variant or disease-gene associations. WGS results can easily be reanalyzed as more information becomes available, or as variant calling algorithms become even more sophisticated. As the pool of disease knowledge continues to grow, Variantyx can rerun the analysis for unsolved cases and can automatically alert you if relevant new findings arise.

References

1. Zhang et al. Non-coding genetic variants in human disease. Hum Mol Genet. 2015 Oct 15;24(R1):R102-10.
2. Meienberg et al. Clinical sequencing: is WGS the better WES? Hum Genet. 2016 Mar;135(3):359-62.
3. Belkadi et al. Whole-genome sequencing is more powerful than whole-exome sequencing for detecting exome variants. Proc Natl Acad Sci U S A. 2015 Apr 28;112(17):5473-8.
4. Liang et al. Clinical application of whole-genome low-coverage next-generation sequencing to detect and characterize balanced chromosomal translocations. Clin Genet. 2017 Apr;91(4):605-610.
5. Kalia et al. Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): a policy statement of the American College of Medical Genetics and Genomics. Genet Med. 2017 19, 249–255.