From sample to diagnosis

Genetic testing with Blueprint Genetics

Blueprint Genetics

Genetic diagnostics provides answers

Monogenic diseases are caused by a single defective gene that occurs in all cells throughout the body. Geneticists have identified approximately 7,500 inherited diseases in humans that affect millions of people worldwide. Although the global prevalence is relatively rare, affecting roughly 5 in 100 people from birth, these diseases place a massive cost burden on national healthcare systems. Moreover, the impact on patients and the loss of life is profound. In many cases, early diagnosis and treatment can significantly improve a patient's quality of life and longevity.

If you suspect your patient has a specific inherited disorder, genetic testing provides answers to help you determine what's next on your patient's care path. In the case of cardiac diseases, for example, there are approximately 20 different genes associating with left ventricular hypertrophy (hypertrophic cardiomyopathy), and many of those genes require different treatments. Knowing the most suitable treatment could greatly impact your patient's outcome. Genetic testing can guide you to a definitive diagnosis, and by understanding the exact cause of the disease, you can find the most effective treatments and optimal clinical follow-up.

For terminal diseases, the answers provided by genetic testing are invaluable compared to other diagnostic tools. Alternatives, such as ultrasound, require repeat observations over a long period of time — time that your patient can't afford to lose. Furthermore, if the cause of a disease is genetic, the concern and need for a swift diagnosis extends beyond the patient to their family members as well.

Comprehensive, rapid, high-quality genetic diagnostics solutions

Blueprint Genetics provides high-coverage panels, high-resolution CNV detection, and comprehensive coverage of clinically relevant noncoding variants

Despite its obvious benefits, genetic testing has only recently come into use as a standard diagnostic tool. Previously, when considering genetic diagnostics as an option, clinicians faced the challenges of high costs, long turnaround times, and the difficulty of interpreting results for rare inherited diseases. Current state-of-the-art next-generation sequencing (NGS) technology enables rapid and cost-effective diagnostics for rare diseases. Many times genetic testing is the only solution to avoid a long diagnostic odyssey.

About 2% of the genome is actually encoding genes and only a subset of genes are known to be medically relevant.Blueprint Genetics' sequencing platform focuses on that portion of the genome that is clinically relevant, reducing the complexity of the sequencing process.

High-quality exome capture is performed using an in-house–designed WES platform (xGen Exome Research Panel with custom-designed capture probes, IDT) and the Illumina NovaSeq sequencing system to obtain deep and uniform sequencing data from coding exons, exon-intron boundary and over 1,500 selected noncoding deep intronic variants. Our careful oligo design, validated laboratory process and quality control, clinical-grade sequencing coverage, and proprietary bioinformatic pipeline enable high quality for detecting SNVs, indels and copy number aberrations. With improved sequencing coverage and sensitivity to detect clinically relevant mutations, we can provide higher diagnostic yield.

Blueprint Genetics uses custom whole exome sequencing assay and Illumina NovaSeq technology to offer you over 220 tests covering all medical specialties, and to deliver results within 28 days.

But how is it done? And how can a clinician use genetic testing to progress from a sample to a diagnosis?

Ordering and sample preparation

The order process begins when you provide your patient's medical history. This is done through Nucleus, our online portal, where you can order tests, track samples, and receive your test results. The entire process is transparent, showing you at every stage what is happening with your patient's sample.

When we receive the sample, we first check to ensure it meets the quality criteria required to produce an accurate result. If the sample is blood or saliva, it's run through an extraction robot to acquire the DNA. We then perform a series of molecular biology techniques to prepare the sample DNA for sequencing.

First, the DNA is sheared into fragments, each comprised of about 300 nucleotides. Next, a synthetic DNA sequence is added to both ends of each DNA fragment during adapter ligation. These synthetic ends allow the DNA fragment to interact with the sequencing system, while also tagging the DNA to a specific patient sample. Finally, the adapted DNA fragments are copied multiple times in a process called enrichment. Once the NGS libraries are generated, clinically relevant portions of the genome are targeted using an exome capture method and further enriched.

All of the methods used in this preparatory phase are tested and trusted methods of DNA sequencing preparation. A reference DNA is also prepared alongside the samples to serve as the control during sequencing. Because the sequencing results for the reference DNA are already known, it provides a way to ensure all the results are reliable.

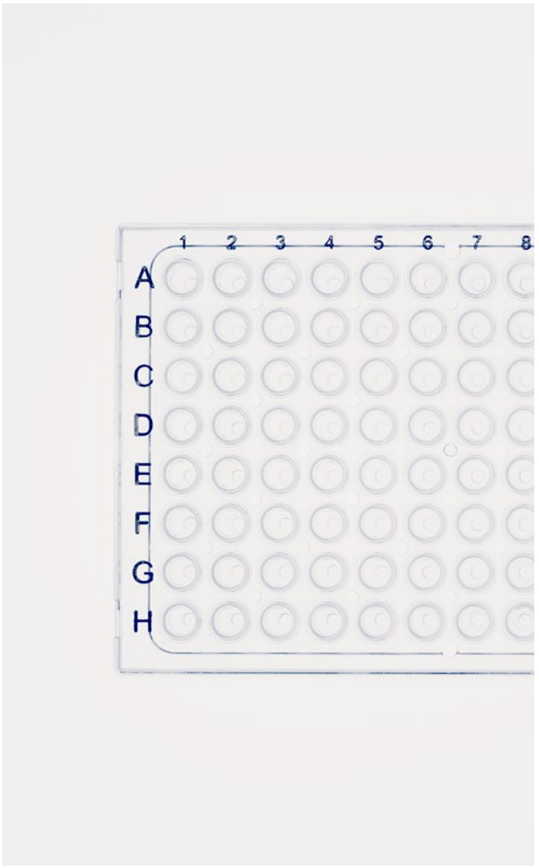
For more detailed information on sample requirements and ordering, please visit blueprintgenetics.com

High-quality NGS sequencing

Only a specific, targeted portion of the genome is sequenced, making the process very fast and efficient

The prepared DNA library mixture is loaded into the NovaSeq sequencing instrument. DNA fragments are mixed with reagents and immobilized inside the flow cells containing billions of nanowells at fixed locations. Sequencing analysis is performed on each nanowell simultaneously. Inside the nanowells, DNA segments are clustered and fluorescent nucleotides latch onto the exposed ligated ends of the DNA strands. After the nucleotides are attached, an image of the flow cell surface is taken. Once the image capture is complete, fresh fluorescent nucleotides are added and the imaging process is repeated. The images reveal all the bases (and their order) which comprise the sequences. The captured information is extracted from the images, converted to raw data, and exported as a text file.

For details on the sequencing depth and sensitivity, please visit blueprintgenetics.com



Data analysis and interpretation

More than just results — we provide expert clinical interpretation services

Sequencing creates a massive amount of raw data, which require heavy processing to become clinically relevant information. The proprietary automated bioinformatics pipeline developed and used by Blueprint Genetics produces fast, reliable results. All of the software, equipment, and algorithms used are industry-standard in the field of molecular genetics, but specific parameters have been adjusted and other customizations have been made to improve data processing and analysis.

The first step in analyzing the results is quality filtering on the raw sequencing reads. This allows any uncertain nucleotides to be trimmed out of the data pool. Once the highest-quality reads have been isolated, they are aligned with the human reference genome so variant calling can begin. Variants are differences from the reference genome. Hundreds may be found in any patient's DNA, but not all the variants will be clinically relevant to the suspected disease diagnosis.

To aid in variant interpretation, Blueprint Genetics uses a comprehensive, proprietary mutation database containing only disease-related mutations. This database is comprised of information from more than 2,500 scientific publications and publicly available genetic databases. The output of the bioinformatics pipeline is a Sequence Analysis Report, which contains the detailed results of the test, related literature links, the pathogenicity evaluation, and the quality assessment.

While other genetic testing companies might end the process with delivery of the results, Blueprint Genetics goes a step further by providing expert clinical interpretation services. This is the phase where the information is put into the knowledgeable hands of world-class geneticists and clinicians. The clinical evaluation team start by assessing the findings.

Assisted by our Clinical Interpretation Platform, our team can instantly query millions of genetic and medical sources.

Variants classified as likely pathogenic or pathogenic are confirmed using the conventional and reliable Sanger sequencing method, in use for over 25 years. Variant(s) fulfilling the following criteria are not Sanger confirmed: the variant quality score is above the internal threshold for a true positive call, and visual check-up of the variant at IGV is in-line with the variant call. Reported VUS's are confirmed with bi-directional Sanger sequencing only if the quality score is below our internally defined quality score for true positive call. Reported copy number variations with a size <10 exons are confirmed by orthogonal methods such as qPCR if the specific CNV has been seen less than three times at Blueprint Genetics.

The patient's clinical history and any identified variants are reviewed alongside the relevant medical and genetic literature.

For detailed information on Blueprint Genetics' variant classification scheme, please visit blueprintgenetics.com

A comprehensive clinical report

The final phase of Blueprint Genetics' all-inclusive process is the geneticist's statement, supported by the insight of a specialized clinician. For positive results, the report generally includes valuable insights into potential treatments while highlighting any risks the disease presents to the patient. The concluding statement is delivered to you through Nucleus, by mail, or by fax, depending on your preferences.

If the results are negative, the statement helps move toward a potential future diagnosis by ruling out one or more possibilities. The geneticist's statement may also include recommendations for a different, more comprehensive panel when deemed beneficial. In this event, Blueprint Genetics does not generally require a new sample to run the different panel, so it's easy for you to order a new panel if needed.

To see an example of a clinical report, please visit blueprintgenetics.com

Life-changing genetic knowledge

Our clinical statement will help you decide what to do next for your patient.

From start to finish, the genetic testing process followed by Blueprint Genetics is not only very fast and efficient, it's also very accurate due to the extreme care and checks performed throughout. The results you get provide reliable answers for both you and your patients.

Our report will help you decide what to do next for your patient, whether it's a treatment plan or reevaluating your suspected diagnosis. Due to the rarity of monogenic diseases, many doctors will see these cases only once in their entire careers. An informative, detailed interpretation of the results is incredibly beneficial in helping you decide how to treat diseases with which you may have little or no previous experience. Additionally, the fast turnaround time (21-28 days, or 10 days with our Express Service) and cost-efficient pricing of OS-Seq genetic testing, coupled with our patient-friendly billing policy, make it easier than ever to use use our services.

Your patient may also find comfort in knowing the answers. With your guidance, the results will help them identify and reduce risks and make any relevant lifestyle changes. They will benefit from a personalized treatment plan, developed by you, to facilitate their well-being and quality of life. Beyond the patient, the results also open the door to family screening, where you can help family members to minimize risks or begin pre-emptive treatment plans.

Our commitment to the genetic community

We help improve worldwide collective knowledge about genetic diseases.

Our testing not only helps individuals. When an unknown or new mutation with uncertain pathogenic relevance is found, the clinical evaluation team at Blueprint Genetics reports the anonymized finding to a public database. Documenting this information improves worldwide collective knowledge of genetic diseases, and helps further determine if an extremely rare variant could be clinically relevant to a particular disease.

Not every genetic testing company shares their discoveries with the public, but Blueprint Genetics is one diagnostics company that does. In this way, our fast, cost-efficient and accurate new genetic testing service can benefit you, your patients, and the world.

To view our full catalog of test panels and to order, please visit blueprintgenetics.com

We are continuously developing our services and offering. We may amend service descriptions from time to time by posting new versions on our website. For up-to-date information, please visit blueprintgenetics.com.

From start to finish, our genetic testing process is not only very fast and efficient, it's also very accurate.

Blueprint Genetics

Find out how to order or contact our customer support at blueprintgenetics.com with any questions about our services. We're here to help!

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