Exome sequencing solutions
Rapid, accurate and simple

Ion Torrent™
Exome sequencing applications

Exome sequencing is a targeted sequencing approach that is restricted to the protein-coding regions of genomes. The exome is estimated to encompass approximately 1% of the genome, yet contains approximately 85% of disease-causing mutations [1]. For genetic researchers trying to identify the genes implicated in over 6,800 rare diseases [2], exome sequencing enables the identification of common single nucleotide variants (SNVs), copy number variations (CNVs), and small insertions or deletions (indels), as well as rare de novo mutations that may explain the heritability of Mendelian and complex disorders [3].

Exome for copy number variation analysis
Copy number variations (CNVs) represent a class of genomic variation in which large regions of the genome (>1 kb) are duplicated or deleted. Until recently, researchers mainly employed methods such as array comparative genomic hybridization (aCGH) or fluorescence in situ hybridization (FISH) to detect CNVs and other types of genomic alterations. However, microarray-based methods are limited by the requirement of array design, have limited dynamic range compared with other methods, and depending on array design, only gross-level changes can be detected while smaller variations might be missed. The Ion AmpliSeq™ Exome RDY Kit not only allows discovery of novel copy number variants but also provides important genetic information such as single-nucleotide variants (SNVs) and small insertion/deletions (indels) that link variants to biological pathways found in disease research. Coupled with specific CNV workflows within the Ion Reporter™ Software, the kit enables simultaneous identification of SNVs, small indels, and now, gene-level CNVs up to aneuploidies within one sample in a single day.

Exome for Mendelian disorders
The causes of most Mendelian disorders, or single-gene disorders, have been found in the exonic regions of the causative gene. Traditional approaches such as linkage mapping and Sanger sequencing of candidate genes have contributed to the discovery of causative variants for Mendelian disorders. However, these approaches are often costly or time-consuming, or have limited power due to small sample sizes. Through affected archived sample trio analysis, exome sequencing can be a powerful approach for identifying the causative variation responsible for Mendelian disorders in your research. The Ion AmpliSeq™ Exome RDY Kit enriches only the exonic regions of the genome. The Ion AmpliSeq™ exome trio workflow in the Ion Reporter™ Software uses exome sequencing data from the trio to characterize variant alleles in the proband (affected child) that may account for the Mendelian disorder.
Exome for complex disorders

Genome-wide association studies (GWAS) have identified a large number of variants that contribute to heritability of complex traits. These studies often have challenges in differentiating the functional consequences of the identified common variants, and in most studies the loci identified only partially explain heritability—this has become known as the “missing heritability” of common or complex multigenic disorders. The role of rare alleles in the heritability of complex disorders is not fully understood.

To this end, the Ion AmpliSeq™ Exome RDY Kit enables accurate detection of rare and common variants in the protein-coding regions of the genome, making it a cost-effective method for elucidating the causes of complex disorders in your research. The detection and discovery of unknown variants in multiple samples per chip reduces total cost and time, enabling researchers to gain comprehensive insight into complex disorders.

Exome for tumor genomics

Exome sequencing enables cancer researchers to detect germline genetic alterations that may predispose cells to cancer in the future. The goal of sequencing the exome is to identify coding variants and mutations critical in the development of tumors. The Ion AmpliSeq™ Exome RDY Kit enables researchers to focus on the protein-coding regions of genomes to identify the mutations, deletions, or copy number variations that can help provide important insights into tumor genetic pathways. The kit offers a simple and flexible workflow that targets ~33 Mb of coding exons—greater than 97% of coding regions as described by consensus coding sequence (CCDS) annotation. The kit offers the advantages of low DNA input, with as little as 50 ng required for each individual library.

Exome analysis for whole-genome sequencing

While whole-genome sequencing (WGS) is the most comprehensive approach for genome-wide variant detection, it is often cost-prohibitive for large samples, and many of the detected variants have not been well characterized. The variants detected by WGS often need to be analyzed by another method, such as Sanger sequencing. This could be very time-consuming and not feasible for more than a few variants. Research using the Ion AmpliSeq™ Exome RDY Kit helps to improve variant calling of critical regions of the genome to analyze and augment WGS data, giving greater confidence that the variants found with WGS are indeed true variants.
The Ion AmpliSeq™ Exome RDY solution enables you to:

**FAST**
Whole-exome enrichment with the simplicity, specificity, and speed of PCR with less than 50 minutes of hands-on time

**ROBUST**
Enables high coverage with >90% of targeted bases covered at 20x

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**Ion Torrent™ semiconductor sequencing**

The Ion Proton™ System makes affordable, high-quality next-generation sequencing accessible to scientists around the world. The Ion Proton™ System is a reliable sequencing platform that combines simple sample preparation and data analysis solutions with flexible chip output for ultimate project flexibility. Human disease researchers can perform applications such as exome sequencing to elucidate variants important for the heritability found in cancer research as well as Mendelian and complex disorders.

“Ion AmpliSeq™ Exome RDY provides the simplest exome enrichment. The dried-down primers reduce the number of pipetting steps and allow preparation of reproducible libraries that sequence with high uniformity. The straightforward workflow—similar to PCR—allows for someone with little to no next-generation sequencing experience to successfully perform the protocol.”

**RICHARD ALLCOCK**
DIRECTOR, LOTTERYWEST STATE BIOMEDICAL FACILITY
GENOMICS SCHOOL OF PATHOLOGY AND LABORATORY MEDICINE
THE UNIVERSITY OF WESTERN AUSTRALIA
ACCURATE
Highly accurate variant calling performance, providing greater insights into the discovery of disease-causing mutations

SIMPLE
Integrated bioinformatics through point-and-click run setup and data analysis

CALL VARIANTS WITH CONFIDENCE
Helps reduce orthogonal confirmation due to superior accuracy of the Ion Proton™ Hi-Q™ Sequencing Solution

EASILY IDENTIFY RELEVANT VARIANTS
Integrated software and pipeline delivers a focused list of annotated variants

SIMPLIFY YOUR EXOME ENRICHMENT
Whole-exome enrichment with the simplicity of PCR and with less than 50 minutes of hands-on time
Exome sequencing workflow

The Ion AmpliSeq™ Exome RDY research solution offers the simplest exome enrichment approach with less than 50 minutes of hands-on time, and a low cost per sample on a benchtop sequencer—with flexible throughput from 1 to 3 exomes per run or up to 24 exomes per week. The Ion Proton™ System, combined with Ion AmpliSeq™ technology and an integrated data analysis solution, offers fast and high-quality exome sequencing that scales with your research needs.

The Ion AmpliSeq™ Exome RDY Kit enables enrichment and library construction for 1 to 8 samples in less than 6 hours. The kit requires less hands-on time when compared with other exome enrichment technologies, and as little as 50 ng of input DNA can be used. Leveraging the ultrahigh-multiplex PCR approach of Ion AmpliSeq™ technology with the Ion Proton™ System, the Ion AmpliSeq™ Exome RDY Kit allows for rapid exome sequencing, going from DNA to annotated variants in less than 2 days.
The Ion Community allows researchers to openly share methods and data, to both evaluate the technology and build on it. We have opened our protocols, datasets, and source code to the world to enable the community to drive application development.
Exome sequencing with the Ion AmpliSeq™ Exome RDY solution

**Accurate variant calling:**
Highly accurate variant calling performance that helps reduce the amount of time and labor spent on confirmatory testing with orthogonal technologies

**Rapid, easy exome enrichment:**
Simplicity, specificity, and speed of PCR, with less than 50 minutes of hands-on time with dried-down primers. Go from DNA to variants in less than 2 days.

**On-demand exome sequencing:**
Flexible throughput of 1 to 3 exomes per run, or up to 24 exomes per week

**Integrated bioinformatics:**
Integrated software workflow delivers a focused list of annotated variants

Learn more about exome sequencing using the Ion Proton™ System at lifetechnologies.com/ionexome

References
2. National Institutes of Health, Office of Rare Diseases Research.