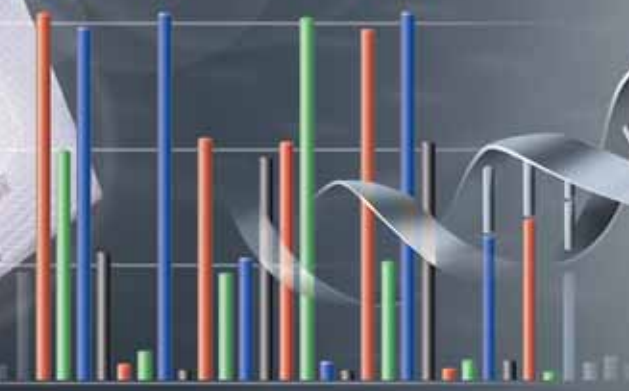


The Genome Sequencer FLX System

Human Genetics and Genomics



Human variation detection on the Genome Sequencer FLX System

Get the complete picture – from SNPs to structural variations

The recent sequencing of individual human genomes clearly revealed the large degree of variation in human populations. Within a single human genome there exist approximately 3 million single nucleotide polymorphisms (SNPs), over 200,000 smaller insertions and deletions, and 1,000 larger structural rearrangements.

The Genome Sequencer FLX System provides the most complete picture of human genetic variation, on both the genome and the transcriptome level. Learn how 454 Sequencing systems can help you answer your research questions.

Whole human genomes

Whole exome resequencing

Disease associated regions



Promotor methylation patterns

Ultra deep exon resequencing



Whole genome epigenetics

Expression profiling



Whole human genomes – Get the complete picture from SNPs to large structural variations

- Perform unbiased sequencing with approximately 99% genome coverage
- Use GS FLX Titanium series reagents to identify the entire range of human genetic variation including SNPs, insertions, deletions and structural variations
- Combine long single reads (>400 bp) and long-tag paired end reads (>100 bp each) at different insert lengths (3-20 kb)
- Detect 99% of all heterozygotes at 12x oversampling

Disease associated regions – Comprehensively analyze megabase size regions in days

- Employ sequencing of long range PCR products or enrich target regions with NimbleGen's Sequence Capture arrays (Figure 1)
- Sequence as many as eight 1 MB captured regions on a single GS FLX Titanium run
- Use the GS Reference Mapper software for comprehensive variant detection and visualization

Ultra-deep exon resequencing – Identify and quantify both known and novel DNA variants

- Perform ultra-deep amplicon sequencing for the quantification of somatic mutations
- Detect minor frequency variants with ultra-high sensitivity in as little as 0.02% of the population
- Cover entire PCR fragments with a single read for accurate haplotype calling
- Use the GS Amplicon Variant Analyzer software for straightforward variant detection and quantification

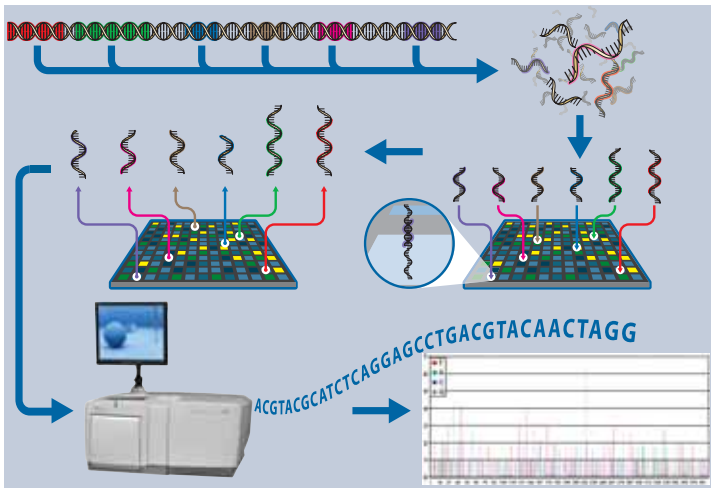


Figure 1: NimbleGen Sequence Capture in combination with the Genome Sequencer FLX System. Genetic material is fragmented and targeted sequences are captured by hybridization to the sequence capture microarray. Captured DNA fragments are eluted from the array and sequenced on the GS FLX System.

Exome resequencing – From hundreds of exons to the entire human exome

- Enrich and sequence all human exons stored in the CCDS database with NimbleGen's Sequence Capture arrays (Figure 1)
- Benefit from long reads, enabling haplotyping of >400 bp and straightforward identification of insertions and deletions
- Use the GS Reference Mapper software for comprehensive variant detection and visualization

Transcriptome sequencing – Analyze genetic variations in expressed genes

- Sequence cDNA libraries to detect genetic variations including SNPs, insertions, deletions and structural variations in the coding genome
- Generate a working database with only approximately 250 MB of shotgun data per individual genome
- Obtain an unbiased gene expression profile using methods such as SuperSAGE ditag sequencing

Methylation patterns, ncRNA detection, splice variant analysis, SuperSAGE expression profiling, epigenetics and many more.

The Genome Sequencer FLX Bioinformatic Tools

1. Reference Mapper: Accurate assembly and comparison with a given reference sequence
2. Amplicon Variant Analyzer: Identification and quantification of known and novel DNA variants (e.g. rare alleles) by Ultra Deep Sequencing coverage of targeted regions of interest.
3. 454 FusionPrimer design software and custom primers from IDT:
<http://www.idtdna.com/Catalog/fusionprimers/Page1.aspx>

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More references can be found at www.454.com

“We had the privilege of being the first early access site for the new GS FLX Titanium series reagents, and are happy to say that its performance is as 454 Life Sciences promised it would be. The new chemistry effectively replaces Sanger Sequencing and we are in the process of implementing it on our ten Genome Sequencer FLX instruments.”

— **Dr. Richard Gibbs, Professor and Director,
Human Genome Sequencing Center,
Baylor College of Medicine**



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