IntegraNews

HELPING YOU TO FIND™

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WELCOME TO IntegraNews.

The goal of this newsletter is to provide an update on the latest service offers, news and events at IntegraGen Genomics.

INTEGRAGEN GENOMICS

2018 will certainly be a key year for IntegraGen Genomics and therefore for the management of your projects. Our offering now extends to new areas and recent partnerships will ensure the continuity of the quality service which makes IntegraGen proud.

Online bioinformatics solutions have now become significant offerings for the company with the launch of our two new software tools. SIRIUS and MERCURY both enable clinicians, pathologists and genome researchers to benefit from the breadth and depth of data and knowledge resulting from large scale genomic analysis. Both software tools also provide automated access to the informative parts of genome data within minutes via an extremely intuitive interface, enabling large scale genomics to be utilized as a clinically operational tool. They also provide researchers with the ability to extract the "juicy bits" of their data in an extremely rapid manner.

On the bench side, we have implemented 10x Genomics technology in our lab and have recently partnered with Twist Bioscience for exome sequencing. These are only two of the several events making our offerings more attractive.

Please join us in Nantes for the 9th Assises de Génétique to receive more details about these exciting happenings at IntegraGen Genomics.

IN THIS ISSUE:

100% COVERAGE OF EXOMES IS NOW POSSIBLE WITH INTEGRAGEN

Announced mid-January 2018, IntegraGen has partnered with Twist Bioscience and is the first service provider to offer Twist Bioscience Human Core Exome Enrichment System as a service.

Whole exome sequencing has always been considered as the fastest and least expensive way to explore the entire knowledgeable genome, both for research applications, and more recently, for clinical research purposes in rare disease investigations and tumor profiling. Unfortunately, the lack of homogeneity in sequence coverage led to the need to over sequence in order to reach the expected mean depth among the genome. This led to considering the whole genome as the best exome possible, however, this approach is unaffordable for most projects and studies.

Introducing a new way of DNA synthesis

Twist Bioscience has developed a solution which creates the ability to generate an extremely homogeneous capture kit enabling homogeneous coverage across the exome. This produces the ability to achieve 100% target coverage above 25X with less data generated than previously needed with competitor's reagents (see Figure).

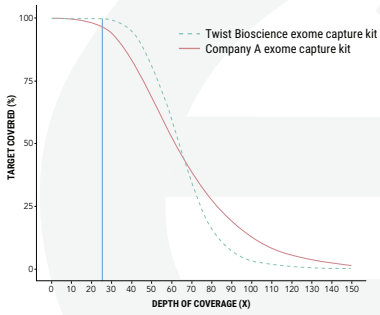

Figure - Percentage of the targeted exome as a function of depth, for Twist Bioscience exome kit and other company's kit as a reference.

Based on these exciting preliminary results, IntegraGen has decided to be one of the first genomic service providers to offer Twist Bioscience's solution to its customers. Our customers will experience two benefits from this solution:

- **Money saving - 100% coverage at 25X with up to 30% less data**
- **Increased mean depth of exome and a gain in sensitivity for somatic variant detection or mosaicism studies**

Twist Bioscience exome system is immediately available through IntegraGen Genomics with the first available kit covering the entire human CCDS.

In conjunction with this new partnership, Twist Bioscience will also add IntegraGen's Sirius™ and Mercury™ software tools for sequencing analysis to its catalogue.

INTEGRAGEN LAUNCHES MERCURY™ - A NEW TOOL FOR MOLECULAR TUMOR PROFILING IN ONCOLOGY

MERCURY is a cloud-based single workspace tool that seamlessly manages data by **transforming raw sequencing data into a clinical molecular report for oncology patients.** Mercury was developed based on efforts by IntegraGen as a part of the ICE (Interpretation of Clinical Exome) Project. **MERCURY minimizes the complexity, time, and cost associated with determining clinical significant and actionable NGS variants.**

MERCURY is designed to be integrated into the bioinformatics pipeline to support both exome and transcriptome analysis for molecular tumor profiling. Whole genome and large panel modules for MERCURY are currently under development and are expected within the coming months.

MERCURY
CLINICAL COMPUTING FOR MOLECULAR TUMOR PROFILING

MERCURY is a highly scalable cloud-based tool that delivers an extensive analysis of tumor DNA and RNA, including somatic variants, tumor load, molecular signature, copy number analysis, fusion transcript detection and annotation.

Additional modules with clinical implication will be added in the next months.

The data analysis performed by MERCURY is intended to assist oncologists and biologists with clinical interpretation and decision making such as clinical diagnostics, treatment determination, and clinical trial identification that best fit the comprehensive molecular profiling of a cancer patient. This software tool enables the rapid generation of customized reports with an extensive amount of information clinicians can utilize to make informed decisions.

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INTEGRAGEN ACQUIRES THE CHROMIUM™ SYSTEM FROM 10x GENOMICS®

The technology powered in the Chromium™ system enables to deeper explore the genome or transcriptome profile. The system combines microfluidics with molecular barcoding enabling to isolate cells or partitioning long DNA molecules. All the fragments produced within a partition share a common barcode. Re-assembly of tagged fragments into long reads is facilitated and provides a more comprehensive view of the genome.

Major applications validated at IntegraGen to date include:

Single cell 3' RNA-sequencing

The technology enables comprehensive study of cell subpopulations within a heterogeneous population, or comparison between different cell populations.

- From 100 to 10000 cells barcoded per sample in one library
- 50 000 reads per cell

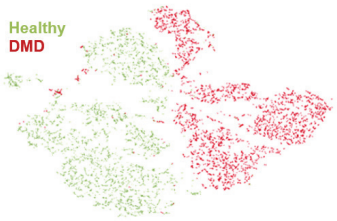


Figure shows PCA on 10X single cell RNA-Seq analysis showing clear distinction between DMD cells and healthy cells in iPS.

- courtesy of C. Pinset and V. Mournetas, I-Stem, France

Applications include stem cell biology, tumor heterogeneity, rare cell detection, immunology.

Whole Genome Sequencing

The technology allows to reveal a larger spectrum of variants in diploid genome like SNVs, InDels and large-scale structural rearrangements. Linked reads help to resolve genic phasing and to reveal structural variations.

- **Complex rearrangement solving**
- **Haplotype reconstruction**
- **De novo genome sequencing**

Applications includes oncology, genetic disorder, metagenomic.

REDUCED REPRESENTATION BISULFITE SEQUENCING - RRBS

A precise and affordable solution for methylation analysis

DNA methylation is a key epigenetic mechanism with important regulatory functions in development and disease like metabolism diseases and cancer. Methylation at these regulating regions, which are often located at gene promoters, is most likely to influence gene expression.

Bisulfite treated DNA samples sequencing enables the detection of cytosine methylation at **single-base resolution**. Reduced Representation Bisulfite Sequencing (RRBS) represents a **cost-effective** alternative to whole genome bisulfite sequencing and an efficient method to analyze DNA methylation in the most relevant genomic regions.

The RRBS protocol IntegraGen Genomics uses enables to start with **only 100 ng** of double stranded DNA. DNA is digested with the restriction enzyme MspI which specifically recognizes CCGG sites. A fragment size selection will enrich for the most CpG-rich regions, including CpG islands. Sequencing of the corresponding libraries allows to quantitatively measure the methylation status on **1.5 to 2 million CpG sites** providing a genome wide screening.

Based on sequencing, RRBS is more **precise** than fluorescence detection obtained from microarrays, therefore more **sensitive** for differential methylation analysis.

In conjunction with our GeCo solution, customers receive access to a full RRBS data analysis including quality control and alignment against the reference genome, methylation quantification, differential methylation analysis and gene set enrichment analysis. A complete report with detailed Material & Methods is provided as the study results. This technique is not restricted to human genome and can apply to small number of samples or large sample collection at affordable price.

SIRIUS™ - A NEW BIG DATA SOLUTION FOR RAPID ANALYSIS OF EXOME AND GENE PANEL DATA

FAST – Reduce significantly the time you spend to analyze your exome data

SIRIUS is an online big data solution designed for rapid analysis of SNP variants and CNV whatever the number of samples. A single click allows you to test familial transmission hypothesis (de novo, recessive, dominant) or to filter somatic variants. Analysis parameters can be saved as favorites and re-used for new analysis.

EXTENSIVE – Access to full annotation

SIRIUS gives access to the most relevant external databases to facilitate accurate interpretation of genetic variants (SNP and Indels) and CNV. Additionally, users can annotate variants and apply their own classification and visualize them with IGV browser online version.

SIRIUS
SHINE THE LIGHT ON YOUR DNA-SEQ

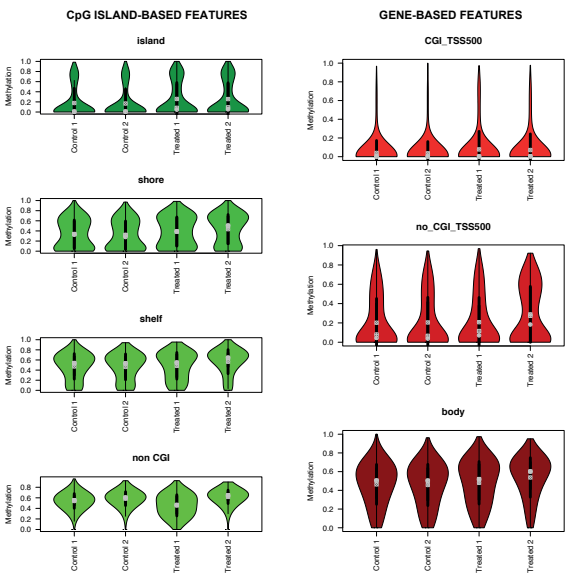
FLEXIBLE AND SECURED – Easily manage your exome projects with a unique online interface

SIRIUS is a unique interface for managing all your projects and create, merge or modify existing projects. This facilitates comparison of patients or families analyzed over time.

Several users can access to a common secured space and share lists of favorite genes and hotspots.

TRACEABILITY – Keep the trace of your analysis

Thanks to SIRIUS, you have access to complete quality report for each sample of each project. Bioinformatic methods and pipelines are described and versioned. Your analysis parameters can be saved and are registrable for each analysis.



References:

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Bock et al. Premium RRBS technology: cost-effective DNA methylation mapping with superior coverage. *Nature Methods. 2016.*

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