

## Academic labs and Portfolio Leads work hand in hand.

Unlike traditional academic core labs, the Broad Institute's Genomics Platform (GP) is structured more like a biotech startup. We are nimble enough to support new technologies from our internal scientific community and industry partners alike. Over the past ten years, the GP has been the largest producer of human genomic information in the world. We hold ourselves to highest standards for sample processing and data quality. We look to our academic community of over 4,000 Internal members of the Broad and it's affiliates to help steer our technological roadmap.

In order to support such a large group, GP created two new roles in 2017- Germline and Somatic Portfolio Leads. The creation of these roles has allowed the platform to launch new products and improve existing capabilities.

A key driver for the germline portfolio is Broad's Medical and Populations Genetics (MPG) group. This group is a diverse community of experts with various areas of focus that include:

- Human Genetic Variation
- Metabolic Disease
- Psychiatric Genetics
- Rare Disease
- Inflammatory Disease
- Population Genetics
- Cancer Susceptibility
- Vertebrate Genome Biology

## Case Study 1: New Exome designed with mitochondrial research in mind.

One of GP's major efforts in late 2018, early 2019 was to launch a new Germline exome v6 product. The previous exome excluded regions of interest for some of our MPG research community.

When researching the requirements for the new exome, MPG investigators expressed a need for better mitochondrial coverage. Portfolio worked closely with MPG stakeholders and their analysis teams to hone our design and include mitochondrial genome coverage where our previous exome lost this coverage.

The final product maintains robust and even coverage across nuclear target regions, in addition, we now capture 100x more coverage over the mitochondrial genome.

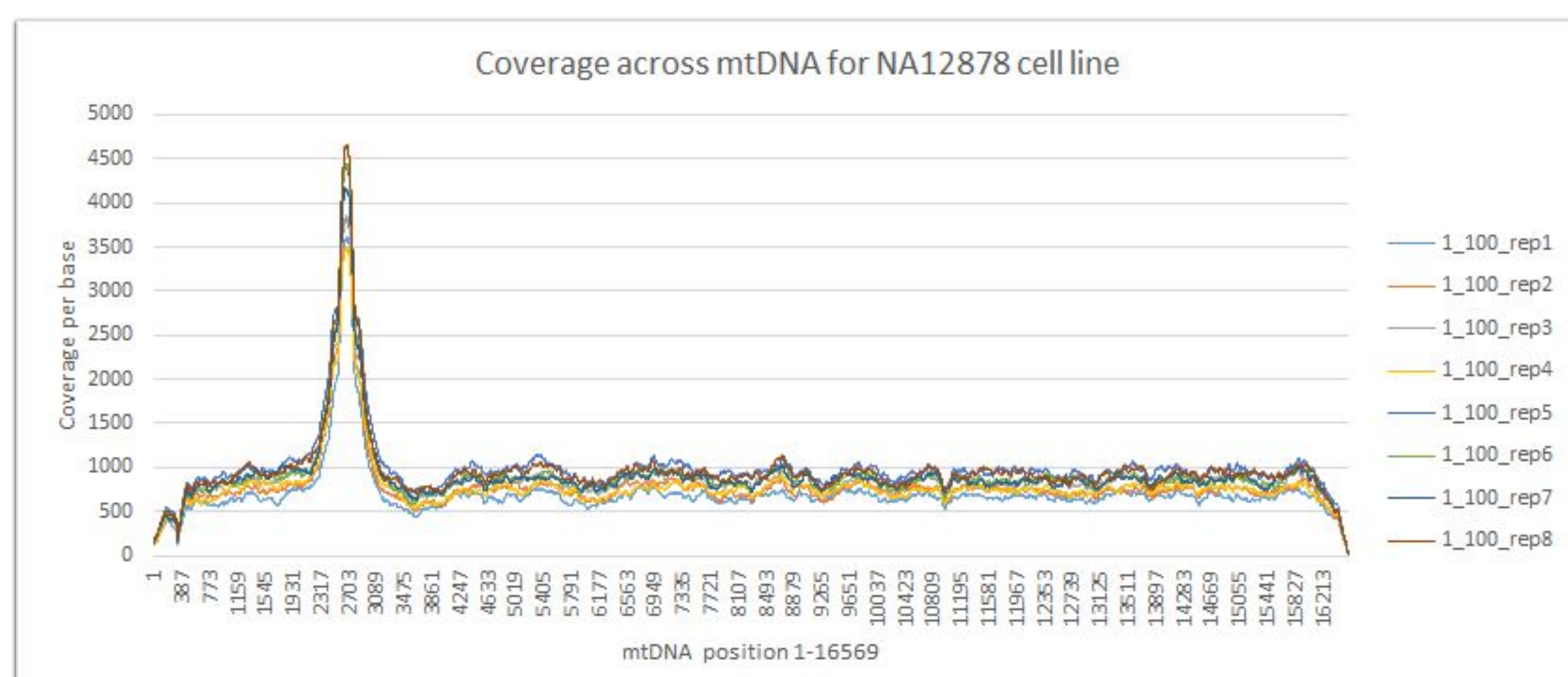


Figure: Shows coverage of NA12878 with different mito spike-ins.

## Case Study 2: More researchers have access to single cell sequencing.

The Klarman Cell Observatory (KCO) has a scientific mission to understand the human body at the cellular level. To meet the tremendous demand of collaborations they were interested in handing off production-like activities to the Genomics Platform.

Portfolio led the effort to meet with stakeholders on all sides to gather requirements, understand the scientific use cases and technical elements. As a result of these efforts, KCO transferred the SmartSeq2M protocol as well as methods and pipeline development to the GP.

With the addition of this new product, more researchers have access to sequence single cell or populations for their full-length transcript capture methods.

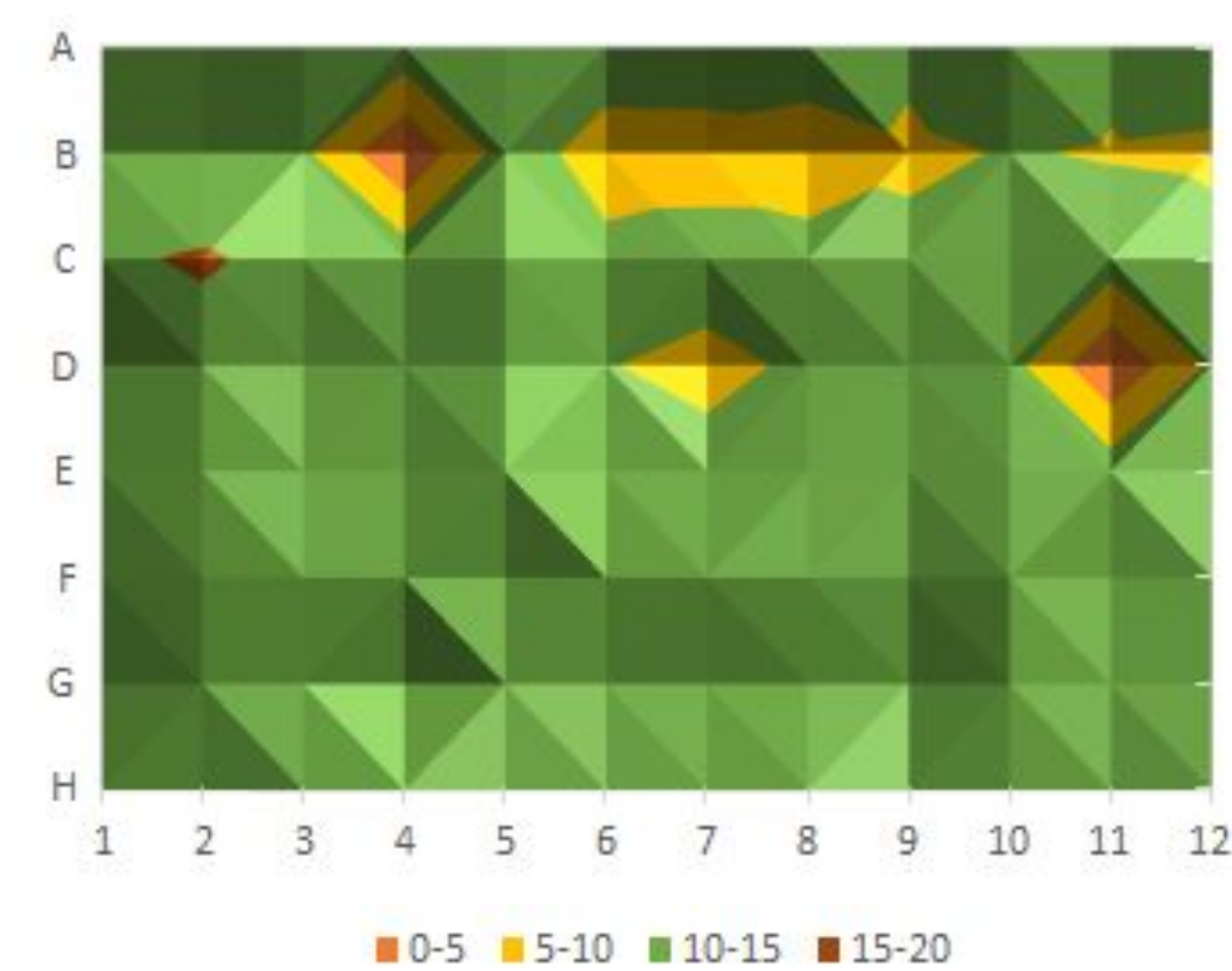


Figure 1. Plate heat map of millions of reads per cell population by well position, illustrating evenness of coverage. Note well D11 is a negative control.

## Case Study 3: Working to implement long reads sequencing at scale.

As a suite of long read sequencing products are being developed by GP, Portfolio has created a Long Read User Group. This group meets monthly to share best practices and overall ideas on these technologies. Through these meetings, GP decided to bring PacBio into our fleet of sequencing instruments.

The GP was part of PacBio's early access program to evaluate the Sequel II instrument with higher yielding 8M SMRT cells and longer run times. In GP's hands, the Sequel II has delivered raw average read lengths of ~50 kb with 50% of reads being >140 kb. GP now has added PacBio our it's catalog of products and services.

Additionally, researchers expressed to Portfolio they are interested in nanopore technology. We recently began evaluating Oxford Nanopore Technology's latest high throughput instrument, PromethION 48.

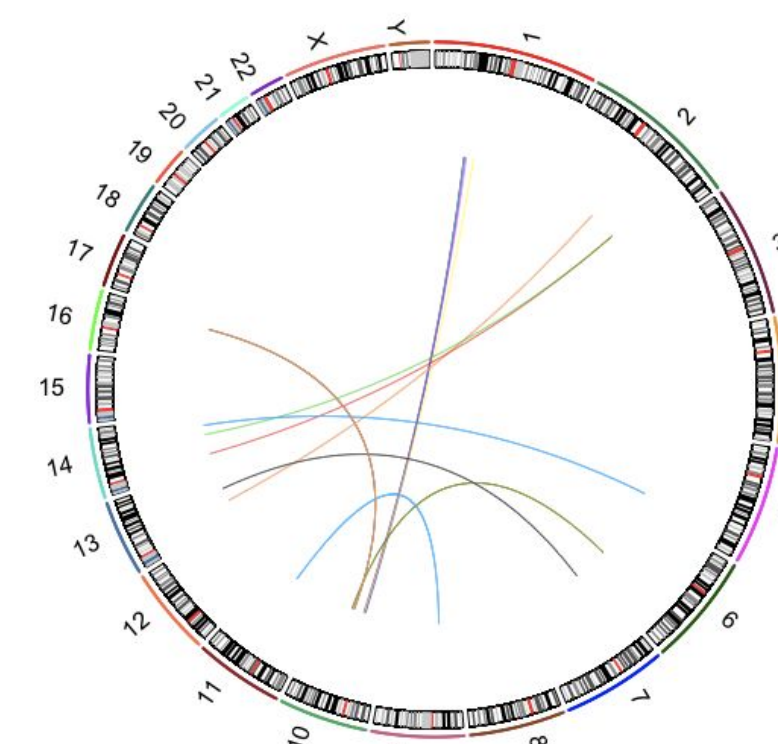


Figure: Circos plot is representing putative translocation events in a clinical research sample.



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Sequel II

## Acknowledgments



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