Genomic Sequencing in Support of the Gabriella Miller Kids First Pediatric Research Program

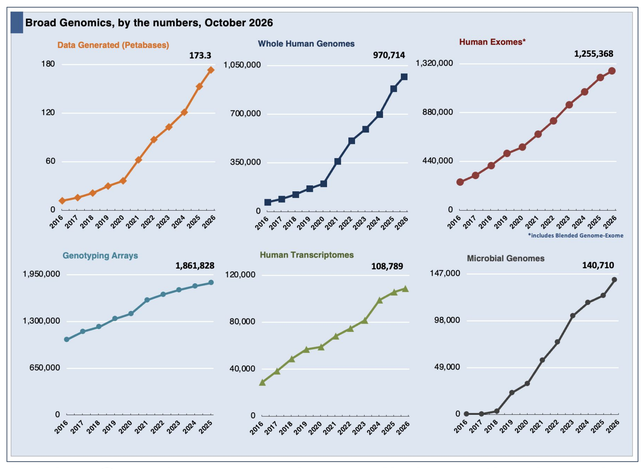
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Broad Platforms - Scalable Services

The genomics group within the Broad Platforms Scalable Services organization has a 30-year track record of delivering on transformative projects in the field of genomics. With over 173 Petabytes of data generated to date, our data generation and analysis is finely tuned to provide data of the highest quality.

Figure 1: Data Generation at Broad Platforms Scalable Services



Broad Platforms Scalable Services works collaboratively with scientific and clinical research communities to design, implement, and validate genomic services rapidly and at scale, always keeping in mind the mission to advance our understanding of the biology and treatment of human disease, and to help lay the groundwork for a new generation of therapies.

GMKF X01 Sequencing Center and Data Delivery

As a designated sequencing center for the Gabriella Miller Kids First Pediatric Research Program (GMKF), the Broad Institute has processed over 47,000 WGS to date (with over 99% of data meeting or exceeding 30X coverage). We also perform multiple complementary sequencing applications spanning RNASeq (50M and 75M reads), EPIC methylation array, long read RNA and whole genome sequencing (PacBio) and high coverage srWGS for tumor DNA (60X depth). Table 1 summarizes all the X01 samples we have sequenced thus far, and noting the current year awardees in Table 2.

Table 1: Summary of GMKF 2016-2025 (Y1-10) X01 Samples Sequenced at the Broad

Year	# of X01 Collaborators	Samples Seq Complete
1	4	4,363
2	4	3,685
3	9	5,446
4	6	6,118
5	3	3,745
6	8	11,694
7	5	6,045
8	8	8,810
9	9	11,450
10	10	6,741
Total		68,097

GMKF X01 and Kids First Long Read Analysis Support

Collaboration with GMKF X01 investigators continues for analysis and gene discovery activities, facilitated by the Broad analysis platform seqr.

- Seqr analysis by the Engle group of 899 individuals' genomes (270 families) representing six major classes of CCDDs solved 25 cases, provided partial diagnoses for 13 cases and identified 440 candidate variants in 348 novel genes.

The KF LR Working Group, with participation from the Broad, CHOP DRC, X01 labs and X01 investigators focuses on three key areas:

- Manuscript development resulting in a commentary manuscript with significant engagement across the group. This has been submitted for review.
- Pipeline and methods implementation, including alignment, variant and SV calling, and the development of de novo variant discovery workflows
- Invited speaker series exploring topics relevant to LRS for rare disease

Table 2: 2026-2027 (Y11) GMKF X01 Awardees

Collaborator	Disease
Dr. Wendy Chung *Boston Children's Hospital*	Congenital Diaphragmatic Hernia (CDH)
Dr. Joseph Gleeson *University of California San Diego*	Neural Tube Defects (NTD)
Dr. Ingo Helbig *Children's Hospital of Philadelphia*	Structural Epilepsies
Dr. Elizabeth Leslie *Emory University*	Orofacial Clefts Birth Defects
Dr. Philip Lupo *Emory University*	Pediatric Cancer Predisposition Syndrome
Dr. Erin Peckham-Gregory *Baylor College of Medicine*	Langerhans Cell Histiocytosis (LCH)
Dr. Jenny Poynter *University of Minnesota*	Germ Cell Tumors
Dr. Adam Resnick *Children's Hospital of Philadelphia*	Pediatric Brain Cancer
Dr. David Teachey *Children's Hospital of Philadelphia*	T-Cell Acute Lymphoblastic Leukemia (T-ALL)
Dr. Michael Wagner *Cincinnati Children's Hospital*	Congenital Heart Defects (CHD)

Multi-Omic and Clinical Sequencing Capabilities

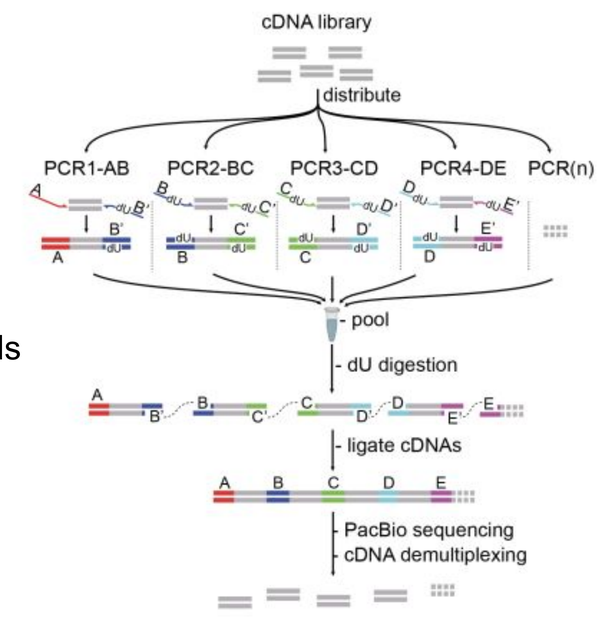
Recent additions to product offerings

- Kinnex full-length mRNA sequencing (Figure 2) accurately characterizes alternative splice site isoforms at high resolution using PacBio's Revio platform.
- Spatial transcriptomics using the 10x Genomics Xenium platform offers high plex capacity with 10x or custom panels as well as histology services
- CLIA-certified and CAP-accredited clinical whole genome sequencing via Broad Clinical Labs

In product development

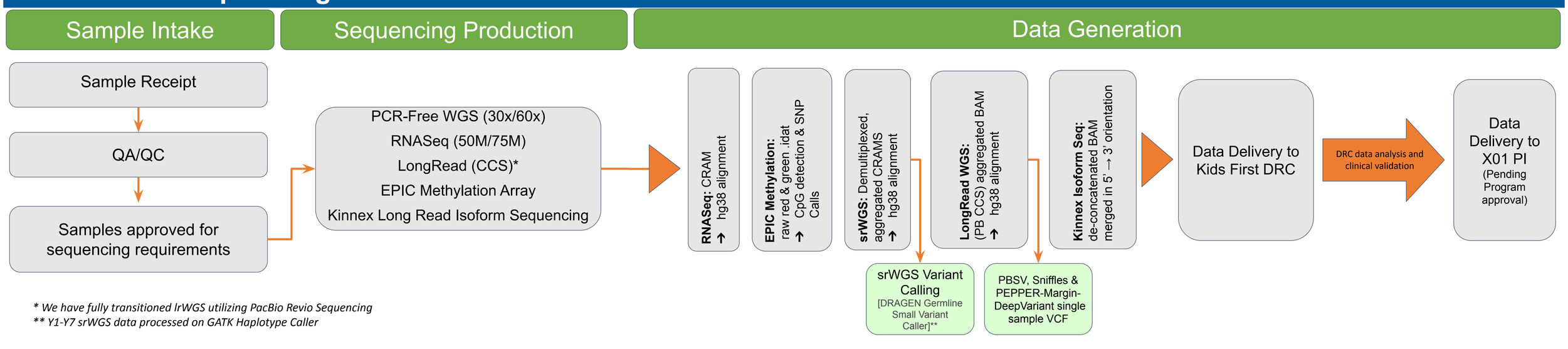
- WGS methylation with Illumina 5-Base
- Rapid whole genome sequencing

Figure 2: Schematic of Kinnex MAS-seq workflow



Additional assay and pipeline resources:

GMKF X01 Sequencing Center Workflow



** We have fully transitioned lrWGS utilizing PacBio Revio Sequencing*
*** Y1-Y7 srWGS data processed on GATK Haplotype Caller*