KromaTiD

Direct Definitive Genomics

Directional Genomic Hybridization (dGH™): Single Cell Structural Genomics

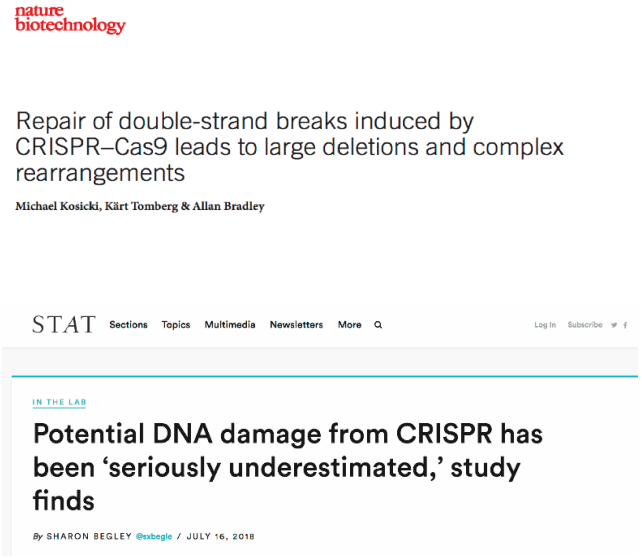
Strategic Partnering for Gene Editing and Undiagnosed Disease Markets

David P Sebesta, PhD
Chief Commercial Officer
January 7, 2019

The Unmet Need in Gene Editing: Discovery of Structural Errors

Regulatory Review for GT Products Incorporating GE

- Science-based approach
- Benefit-risk analysis
  - Potential to:
    - Correct or remove defective genes
    - Eliminate disease phenotype
    - Improve therapeutic effects
  - Risk of:
    - Off-target modifications in the genome
    - Genome instability caused by chromosomal translocations / rearrangements
  - Unknown long term outcomes from on- or off-target genome editing events or due to the delivery system (vector)



nature biotechnology

Repair of double-strand breaks induced by CRISPR–Cas9 leads to large deletions and complex rearrangements

Michael Kosicki, Kärt Tomberg & Allan Bradley

STAT Sections Topics Multimedia Newsletters More

IN THE LAB

Potential DNA damage from CRISPR has been 'seriously underestimated,' study finds

By SHARON BEGLEY @sxbegle / JULY 16, 2018

Editing Causes Errors:

For the promise of gene editing to be realized, there must be methods to measure and control these errors

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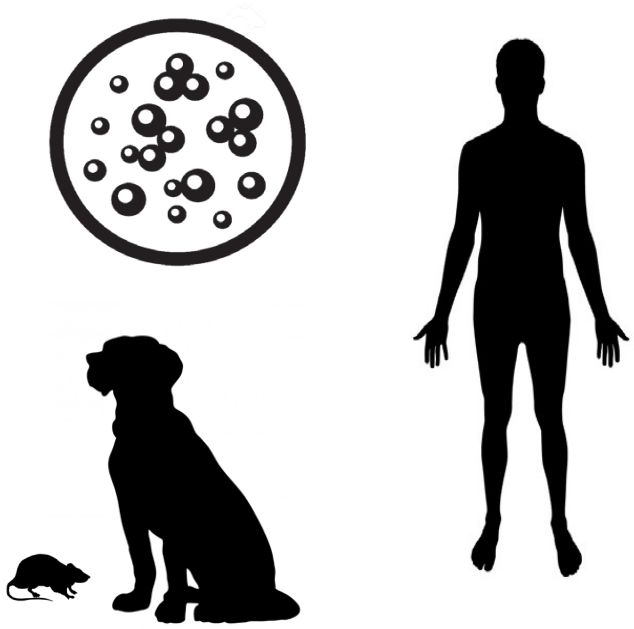
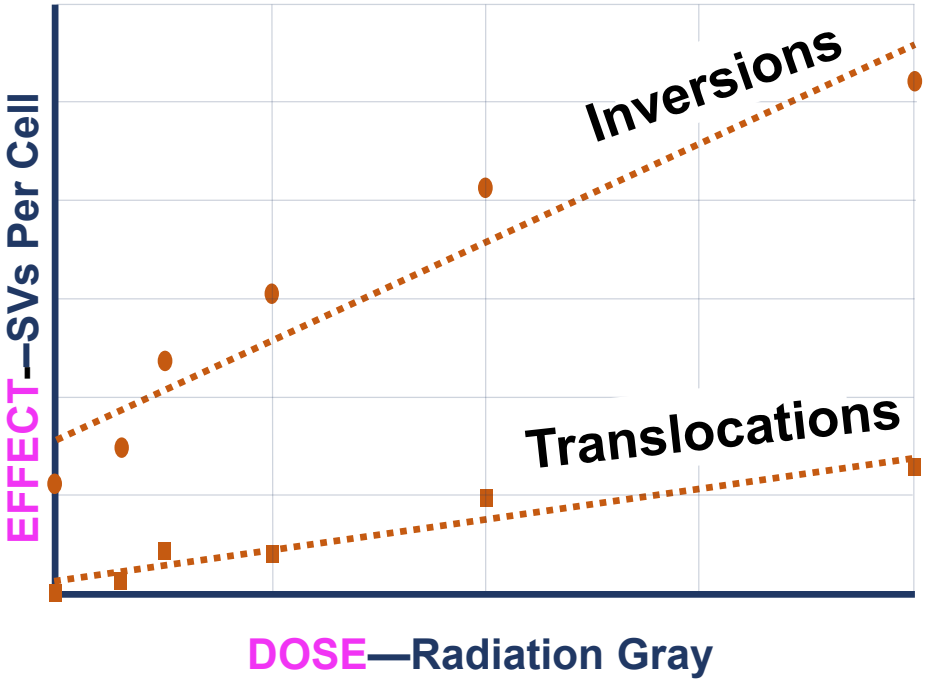
dGH: Robust Measurement of Structural Variation





Discovery, detection and quantitation of structural errors and **DNA mis-repair** for therapeutic Gene Editing, Global Pharma, and Research Institutions

Colorado State University

NASA

St. Jude Children's Research Hospital

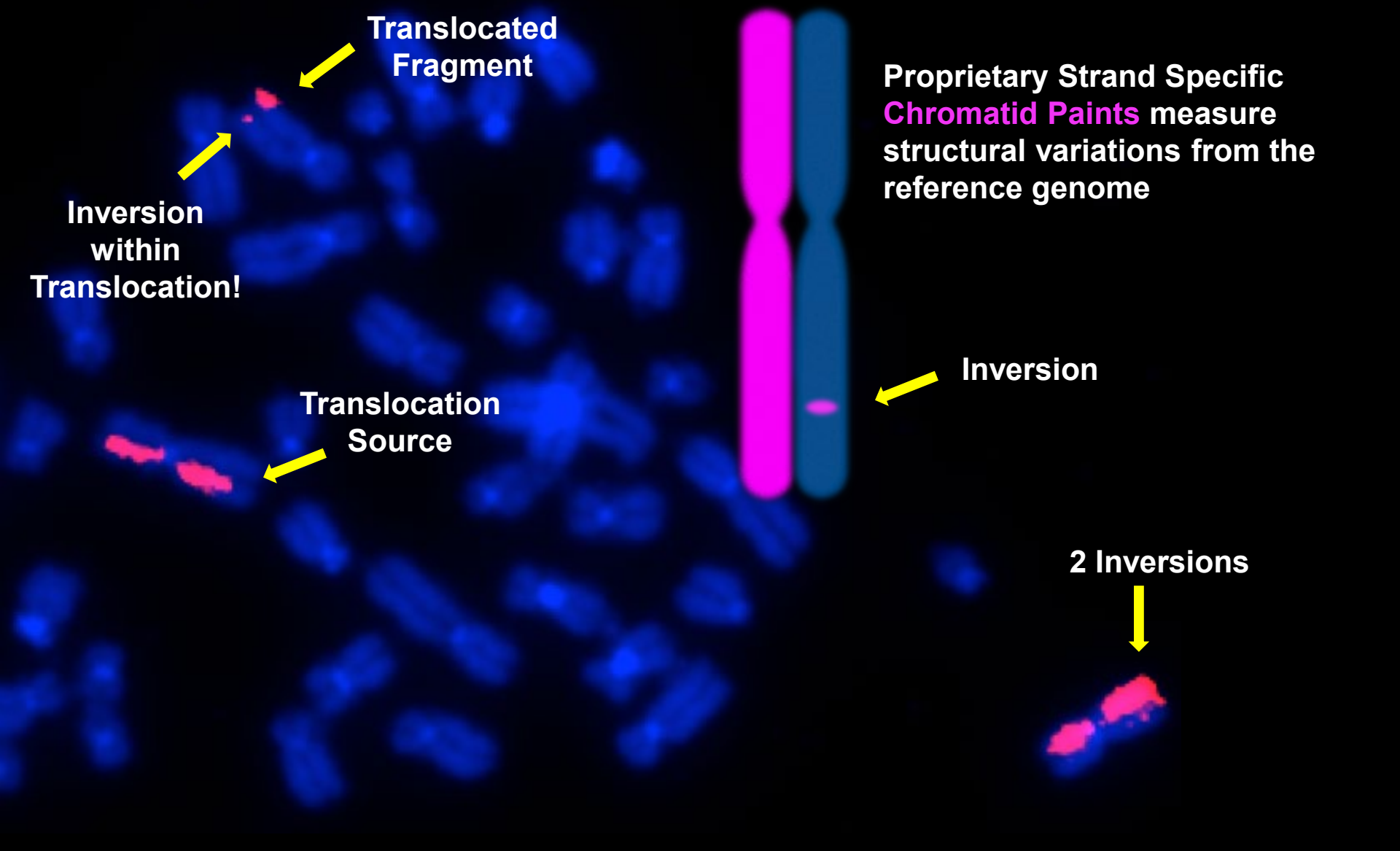
University of Colorado Cancer Center

FRED HUTCH CURES START HERE®

NIH National Human Genome Research Institute

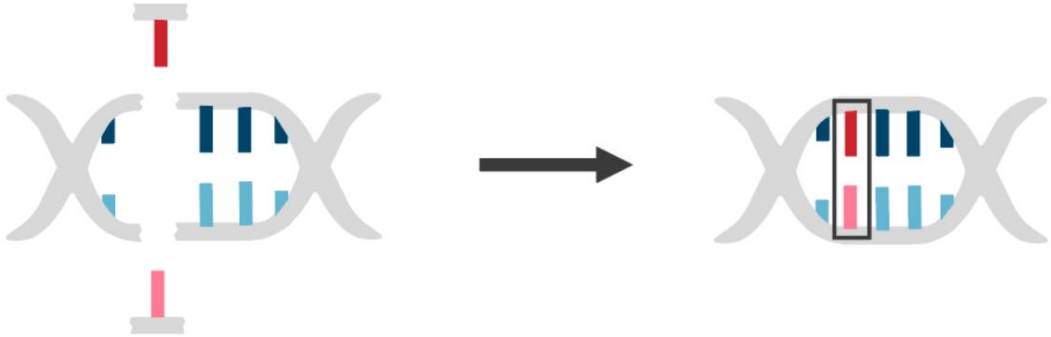
ARRAY

De Novo dGH


Translocated Fragment
Inversion within Translocation!
Translocation Source
Proprietary Strand Specific Chromatid Paints measure structural variations from the reference genome
Inversion
2 Inversions

Two Sources of Gene Editing Errors

Mis-edits: Measurable by Sequencing



Faulty edit + Accurate repair

Edit and homologous site Involvement

Generally small changes

Mis-repairs: Only Measurable by dGH

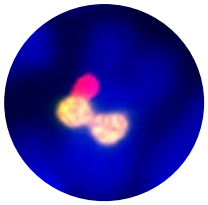
Repair of incorrect ends

Edit, homologous and random site involvement

Larger genomic changes

dGH: Empowering Clinical Gene Editing

The identification and control of structural errors are key concerns of the FDA.



Edit Site Inversion

Successful Edit

KromaTiD's dGH is **the only tool** for measuring all types of structural errors:

- **Pre-existing**
- Process associated

dGH could be a gold standard test for therapeutic CRISPR quality control (QC).

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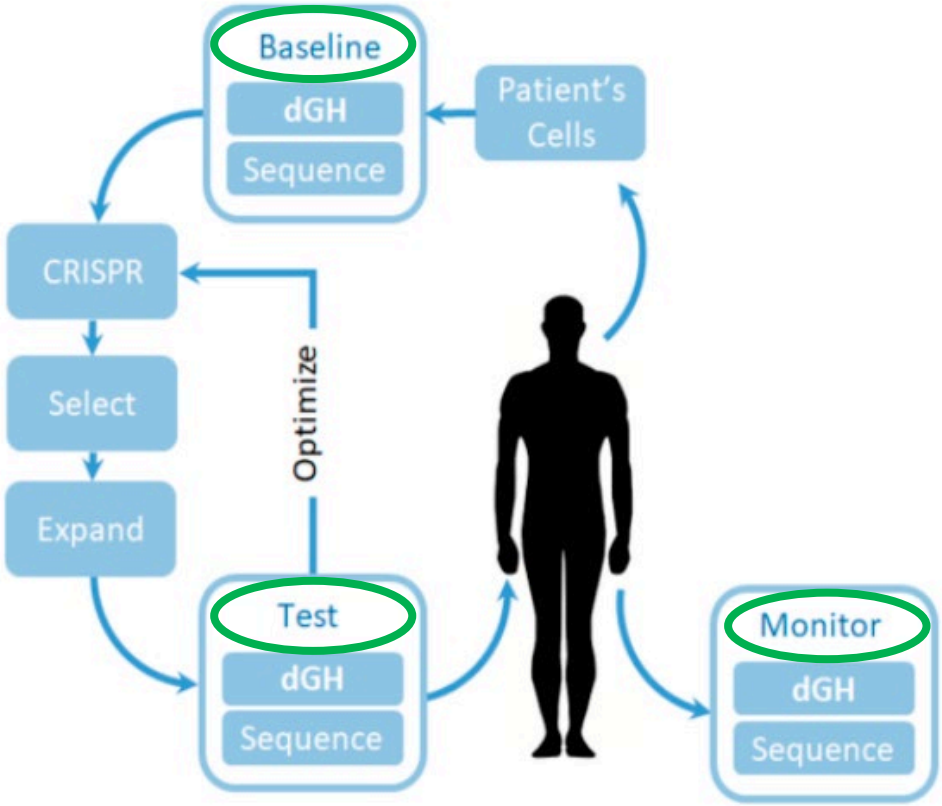
Essential Use Cases for Clinical Gene Editing

Quantitate individual on-and off-target variations:

- Structural variation-based specifications
- **Reduce regulatory risk**
- Accelerate therapeutic gene editing programs to the market



dGH: Measuring structural variation in **1000's of single cells**

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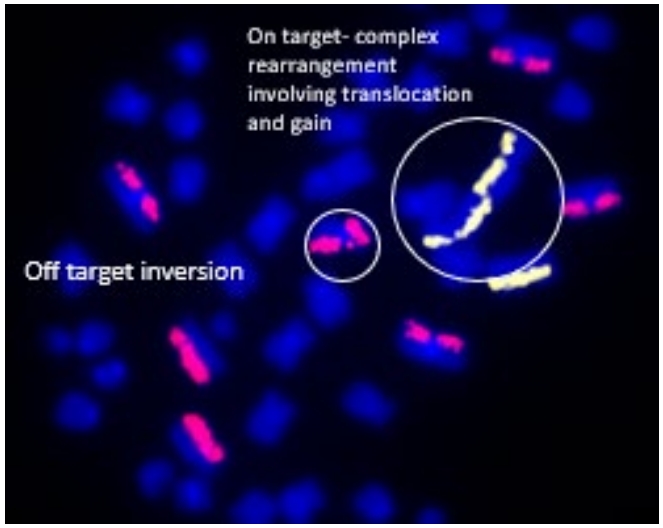
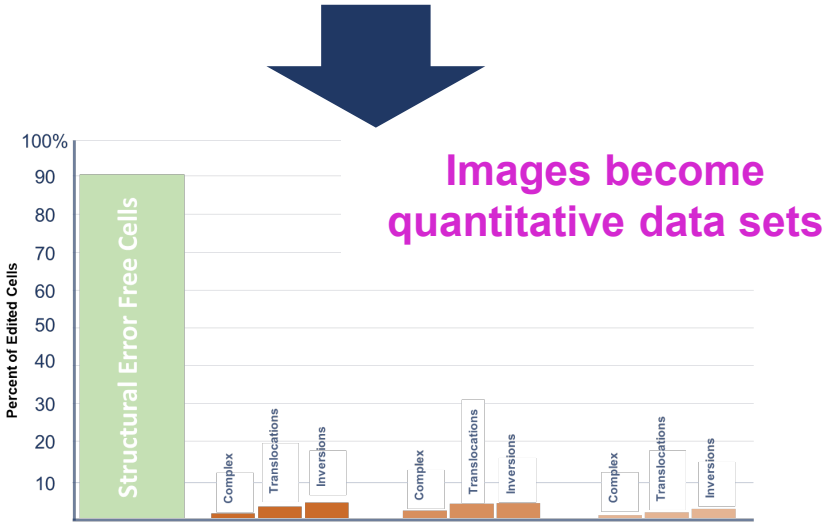
Structural Genomic-Based Specifications

- Mechanistic insights
- Quantitative assays (Regulator ready)
- Pre-existing variation prior to editing
- Genome-wide longitudinal monitoring after editing





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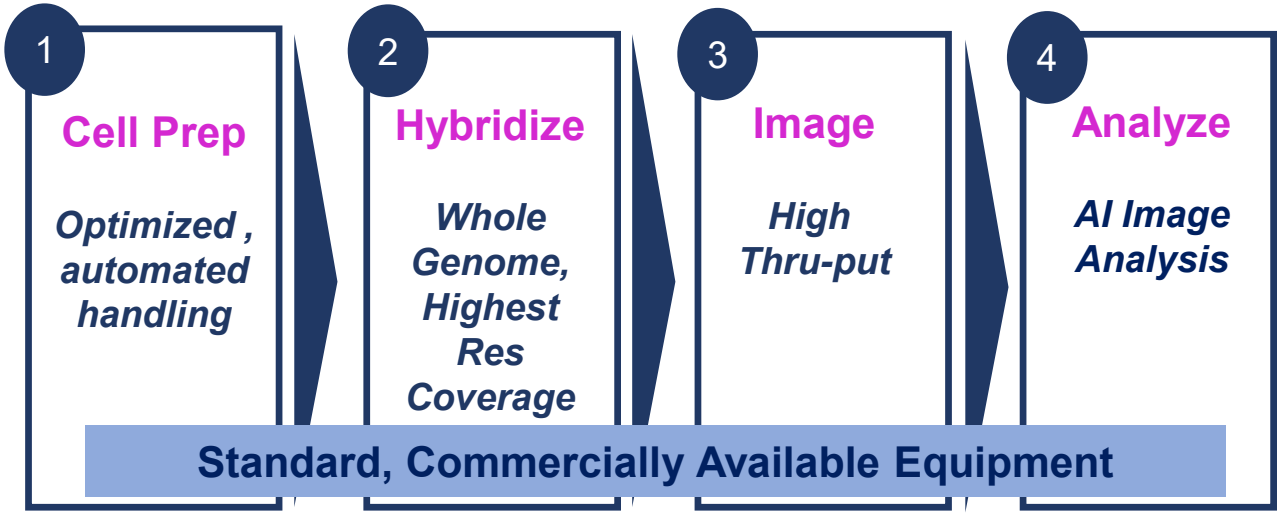
dGH 2.0: High-Throughput, Whole Genome



High Res Structural Genomics for:

Development
Qualification
Optimization
Screening
Control…

$1/cell analyzed!

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Automated Analysis v0.1

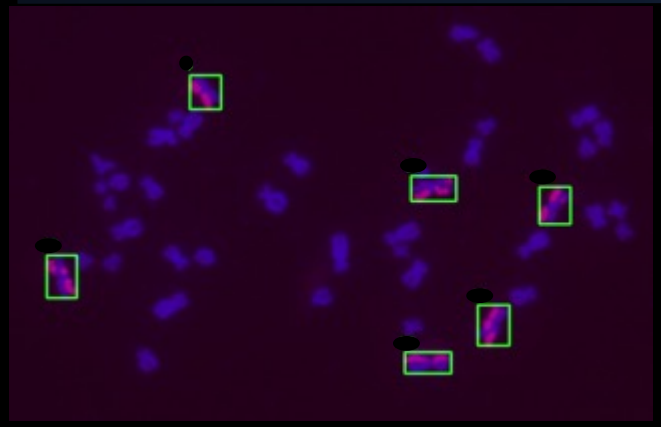
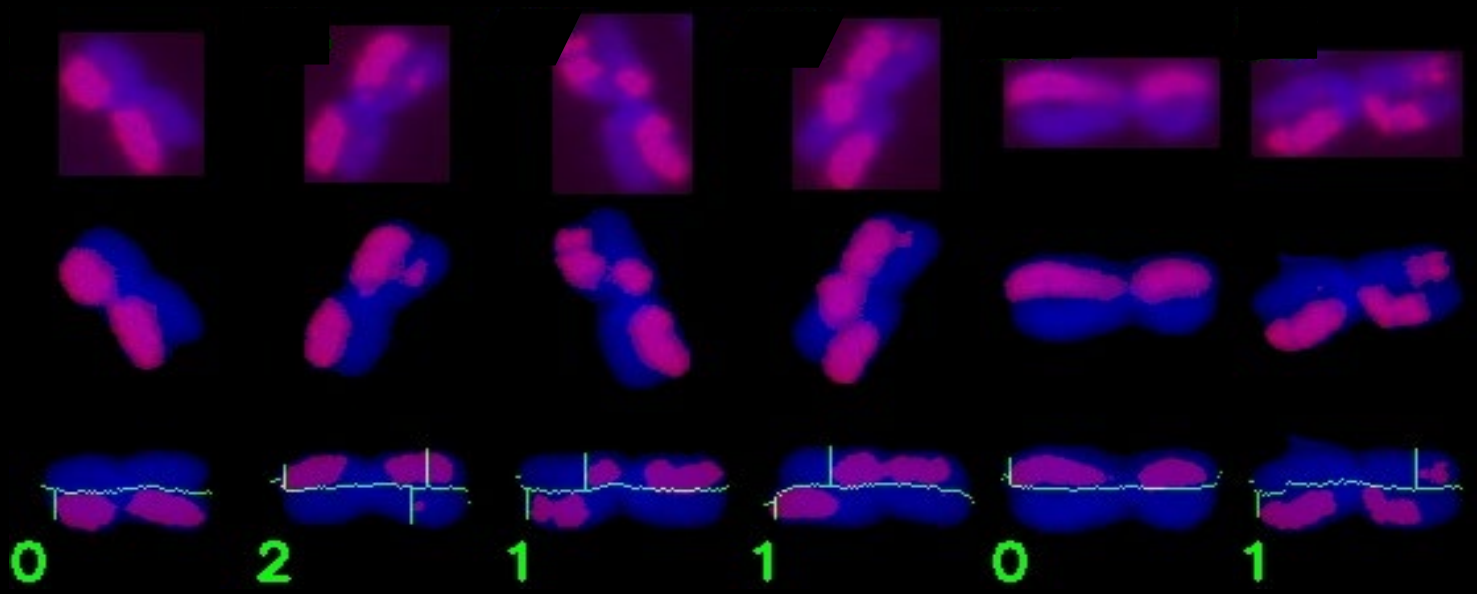


Image Optimized and Breakpoints Determined by KromaTiD Machine Learning Algorithms



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dGH 2.0 Strategic Partnering Goals

KromaTiD is seeking strategic partners to tailor and accelerate the development of the platform:

- **Imaging and automation**-Build the core of dGH 2.0 using World class image scanning and automation

- **Gene editing**-Support the development of de Novo, Whole Genome dGH 2.0 to meet the unique structural genomic and throughput requirements of gene editing

- **Rare/undiagnosed diseases and oncology**-Partners to exploit dGH 2.0 for other genomic applications
    - Small inversions as biomarkers and drivers of disease
    - **$1/cell will open large markets for screening and disease-specific biomarker discovery**

Business Model Overview

Funding

Services revenue ✓
- Research program support ✓
- Custom assay development
- Clinical testing ***(CLIA lab-2020)***

Proprietary products revenue ✓
- Chromosome paints ✓
- Custom assay supply
- License fees ***(2020)***

Strategic partnerships
- Tech development ***(coming Jan 2019)***
- Clinical and CDx programs ***(2020)***

Grant funded research ✓
- Technology development
- KOL relationships ***(submissions planned for 2019)***

Equity/Debt ✓
- Capital line of credit
- Bridging round ***(Q12019)***
- Series B round? ***(2019/20)***

Markets

Gene editing ✓
- Therapeutics ✓
- Target validation/ research cell lines ***(2020)***

Genetic diseases screening
- Research ✓
- Clinical ***(2020)***

Oncology
- Research ✓
- Clinical ***(2019)***

Other areas
- Dosimetry ✓
- Recombinant protein cell lines R&D ✓

Customers

Gene editing therapeutic
- Multiple Top US companies

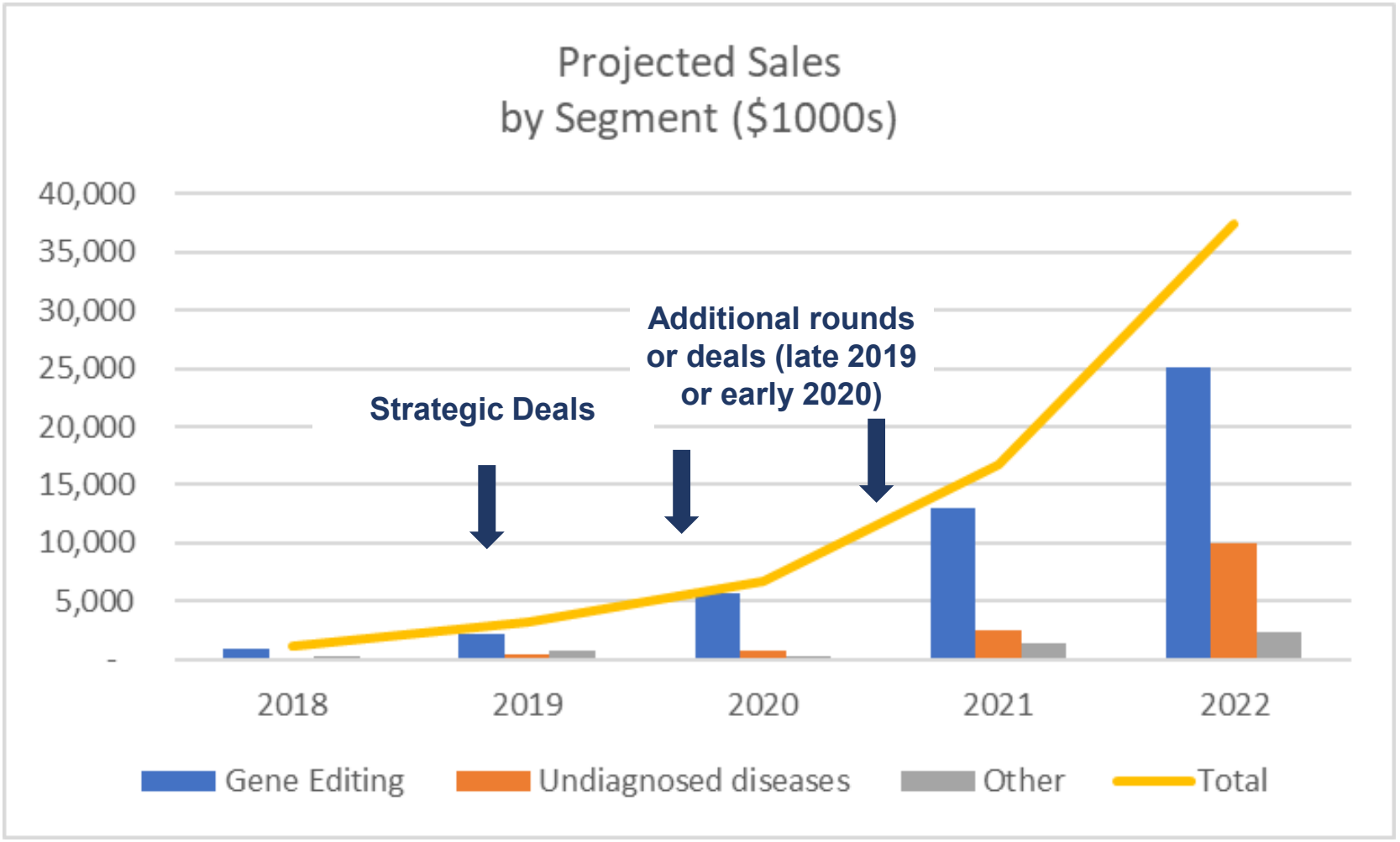
Pharma
- Multiple Top 20

Biopharma
- Oncology

Grants
- NHGRI
- State of CO
- (NCI)
- (NASA)

Clinical labs and core facilities *(2020)*

Why We're So Excited



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Thanks!

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For more information:

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Or reach out to
Christopher Tompkins
Or David P Sebesta on Linkedin