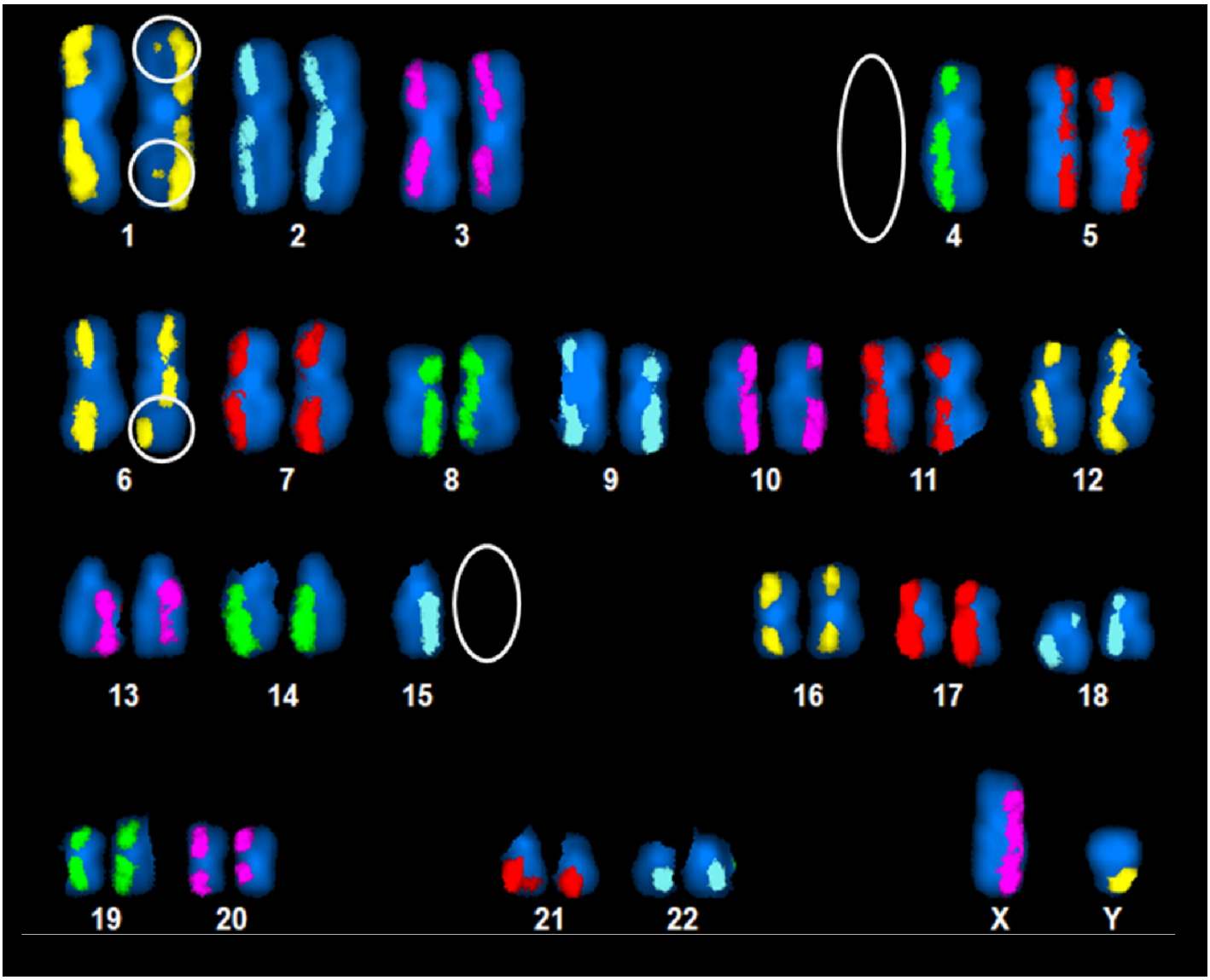
CSU DGH Technology Helps Detect Genomic Structural Variation, Health Risks

Colorado State University



Human karyotype illustrating five color whole genome dGH paints. Inversions are readily visualized as switch of fluoresent signal from one side (chromatid) to the other and back (chromosome 1, circles). Sister chromatid exchange (SCE) detected as single switch (chromosome 6, circle).

NASA's first One Year Mission attracted much media attention as the mission's astronaut, Scott Kelly, had an identical twin brother, Mark Kelly, who was also an astronaut and former Navy test pilot. The perfect "out-of-this world" experiment was conceived, with "Space twin" and "Earth twin" as the high-profile subjects – one spending a year in space aboard the International Space Station (ISS) and the other, similar in both nature and nurture, stuck on Earth serving as the perfect ground control. The landmark NASA Twins Study represented the most comprehensive investigation ever conducted on the response of the human body to space flight.

The Twins Study was also NASA's first integrated effort to launch human space life science research into the modern age of molecular- and "omics"-based studies. In addition to a variety of gene expression changes and dramatic shifts in telomere length dynamics, chromosomal signatures of space radiation exposure were also observed during spaceflight. For the first time in astronauts, directional Genomic Hybridization (dGH™) was employed as a direct "biodosimeter" to detect genomic structural variation, a potential cause of cancers or other genetic diseases, and importantly, providing NASA a better understanding of the inherent health risks of spaceflight. Directional Genomic Hybridization was originally invented in 2007 by faculty at Colorado State University in Fort Collins and UTMB to provide exactly this type of dosimetry data for NASA.

To date, eleven astronauts on one-year and six-month ISS missions have been analyzed with dGH (*Cell Reports*, Luxton et al., 2020a,b) and, consistent with chronic exposure to the radiation environment of near space, frequencies of structural changes known as inversions increased during spaceflight. Surprisingly, levels of inversions remained elevated after spaceflight, a finding potentially suggestive of damage to stem cells and/or genome instability, hallmarks of increased disease risk. Other exposed cohorts analyzed with dGH include WWII Atomic Veterans (*Radiation Research*, McKenna et al., 2019), and prostate cancer patients undergoing radiation therapy (*Journal of Personalized Medicine*, Luxton et al., 2021).

The dGH results will guide future studies and personalized approaches for evaluating health effects of individual astronauts, as we continue to partner with NASA to monitor the health effects of space flight for years to come.

Because of the human health impacts of structural variants, and the unique power of dGH, in 2007 the CSU inventors partnered with CSU Ventures, the TTO for Colorado State University, to launch the start-up KromaTiD, a company dedicated to developing and commercializing the platform. CSU Ventures provided the upfront costs for the initial invention patent filing through licensing, and provided the support and guidance to KromaTiD's founders. The TTO has continued to provide marketing, media support/dissemination, and assistance with company development, facilities, etc. during the early years of KromaTiD company formation.

With the support of CSU Ventures, NASA, and the NHGRI, KromaTiD developed dGH into the only comprehensive, whole genome, strand-specific, single-cell method for measuring complex structural variation on the market. Based on the foundation built from this and similar studies, KromaTiD today provides dGH structural variant assays throughout genomics, in particular for the emerging market of gene therapies. By leveraging cellular engineering techniques such as CRISPR/Cas9, other gene editing techniques, as well as viral-mediated genome modification approaches like AAV and lentiviral tools, gene therapies hold tremendous promise in the treatment of cancers, heritable genetic diseases and hematologic diseases. However, much like radiation exposure, the introduction of unwanted and unexpected structural variants represent real and uncontrolled risks to patients. KromaTiD's dGH products and services provide gene therapy innovators with a variety of targeted and unbiased tools for detection and measurement of genomic structural variants of all types.

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