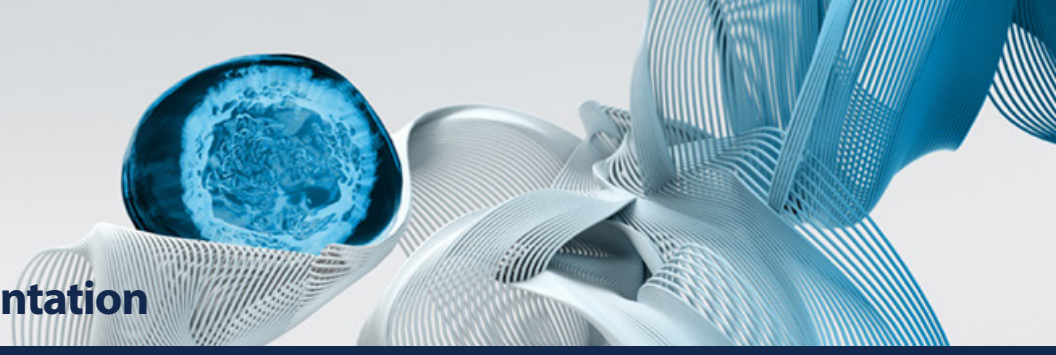
BioSkryb GENOMICS



AGBT 2021 Poster Presentation

Cells explored. Answers revealed.

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Accurate detection of small genomic variants, copy number alterations, and heteroplasmy in early human embryos.

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Technology Development Poster Session on Tuesday, March 2nd from 3:30pm-5:30pm ET

Preimplantation genetic testing (PGT) is currently applied clinically to screen for aneuploidy or common Mendelian diseases in embryos after in vitro fertilization (IVF). However, biopsies sampled from embryos have a limited quantity of DNA from approximately five cells requiring genome amplification prior to sequencing. Consequently, the accuracy of the results is currently limited by the fidelity of the whole-genome amplification (WGA) method employed. Moreover, due to the limitations of current WGA technologies, most PGT strategies either assess embryos for gross aneuploidy or perform targeted evaluations of a small number of disease-associated loci. We recently developed a new WGA method named primary template-directed amplification (PTA), which can be used to detect variants in single cells with much higher sensitivity and precision than existing methods. In the present study, we applied PTA to perform genome-wide evaluations of all classes of genomic variants in five embryos after IVF. We found that we can evenly cover 95.6% (mean value) of the genome, resulting in the detection of 94% (mean value) of the 3.2 million single-nucleotide variants (SNVs) found in the corresponding whole embryo with high precision. Further, we find distinct patterns of copy number variation (CNV) from two independent biopsies of the same embryo and identified a case of mosaicism in which CNV was identified in both biopsies but had a subclonal signal in the embryo. Finally, we highly cover the mitochondrial genome with PTA, which enabled us to identify an SNV in a subset of mitochondrial genomes from two independent biopsies from the same embryo. Taken together, this study established the feasibility of genome-wide PGT evaluations with PTA, which could be utilized to globally screen embryos for disease-causing genetic variation.