Weill Cornell Medicine

Single Sperm Sequencing Assay for Prediction of Autism Risk

Lead Inventors:

Christopher E. Mason, Ph.D.

Professor of Neuroscience, Brain and Mind Research Institute, Weill Cornell Medical College
Professor of Physiology and Biophysics, Weill Cornell Medical College
Professor of Computational Genomics in Computational Biomedicine, Institute for Computational Biomedicine, Weill Cornell Medical College

Jeffrey R. Rosenfeld, Ph.D.

Assistant Professor of Pathology and Laboratory Medicine, Robert Wood Johnson Medical School, Rutgers University

Business Development Contact:

Louise Sarup

Associate Director, Business Development and Licensing

(646) 962-3523

lss248@cornell.edu

Single Sperm Sequencing Assay for Prediction of Autism Risk

Background & Unmet Need

- Investigating RNA and mutations in sperm is an important tool for predicting risk of diseases such as autism spectrum disorders (ASD), which have been correlated with advanced paternal age

- Most studies have focused on the assessment of bulk sperm, where only high-frequency variants are detected

- Single-cell RNA sequencing (scRNA-seq) allows for the discovery and investigation of many cellular subtypes, but is difficult to apply to human germline tissues due to transcriptional and morphological differences from somatic cells

- **Unmet Need:** Methods to analyze sperm on a single-cell level to improve prediction of ASD and other diseases

Technology Overview

- **The Technology:** Single cell sperm sequencing assay for offspring disease risk assessments and IVF sperm sampling procedures

- Using the 10x Genomics Chromium platform, the inventors performed single-cell RNA sequencing on six donor sperm samples (scSperm-RNA-seq)

- **PoC Data:** Differences between the ASD and control samples revealed distinct expression landscapes and pathways that have potential to be used as biomarkers for sperm health or function

- ASD samples exhibited enrichment of genes for mTOR signaling, which has been shown to be a potential target for autism, and eIF2 signaling, which is involved in the inhibition of CREB, a transcription factor being investigated in connection with multiple neurodegenerative disorders

- This method could also be used to replace manual sperm analysis procedures performed as part of an infertility evaluation

Inventors:
Christopher Mason
Jeffrey Rosenfeld
Delia Tomoiaga

Patents:
EP Patent 3,583,213
US Patent Application

Publications:
Tomoiaga et al. *NPJ Genom Med.* 2020.

Biz Dev Contact:
Louise Sarup
(646) 962-3523
lss248@cornell.edu

Cornell Reference:
D-7698

Weill Cornell Medicine

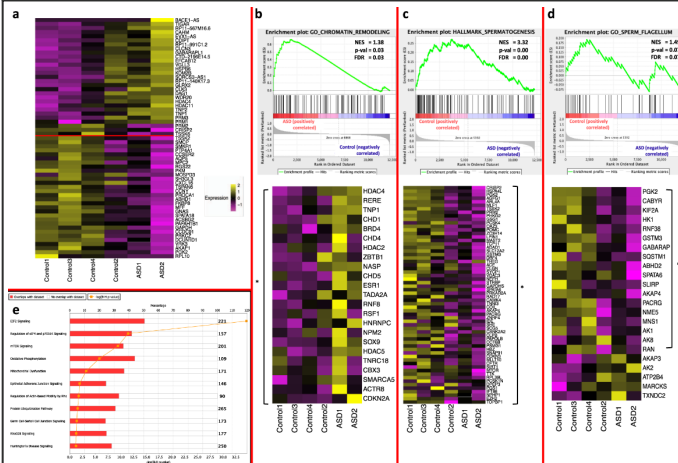# Single Sperm Sequencing Assay for Prediction of Autism Risk

Technology Applications

- Can be used to assess risk of autism and other diseases in future offspring
- Sperm sample assessment in fertility clinics
- Sperm analysis for animal husbandry

Technology Advantages

- Automated and accurate analysis
- Cost-effective
- Enables genetic analysis of single sperm cells

Supporting Data / Figures

Figure 1: **A:** Heatmap of representative DEGs (aligned set) from the top and bottom of the list ranked by average log fold change, between the ASD and the Control samples. **B–D:** GSEA enrichment plots showing: (b) Chromatin remodeling (c) Spermatogenesis (d) Flagellum. **E:** Canonical pathways enrichment analysis in Qiagen IPA, the red bar represents the ratio of the # of DEGs in the pathway to total genes in the pathway.

Inventors:

Christopher Mason

Jeffrey Rosenfeld

Delia Tomoiaga

Patents:

EP Patent 3,583,213

US Patent Application

Publications:

Tomoiaga et al. *NPJ Genom Med.* 2020.

Biz Dev Contact:

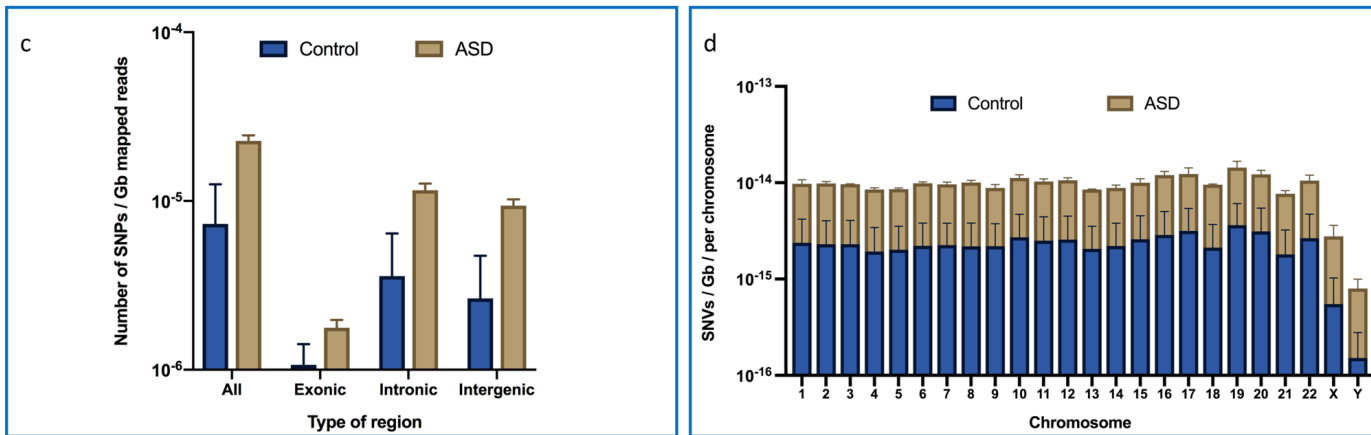Louise Sarup

(646) 962-3523

lss248@cornell.edu

Cornell Reference:

D-7698

Weill Cornell Medicine

Single Sperm Sequencing Assay for Prediction of Autism Risk

Supporting Data / Figures

Figure 2: A: The number of SNVs found in exonic, intronic, intergenic, and all three regions for the bulk RNA-seq analysis, normalized to the number of reads mapped to the transcriptome by the size of the read. **B:** The number of SNVs found in the bulk RNA-seq analysis with an allele frequency < 0.001 in gnomAD per chromosome, normalized to the total number of reads mapped to the transcriptome by the size of the read and to the chromosome length. Values are shown in a log10 scale.

Inventors:

Christopher Mason

Jeffrey Rosenfeld

Delia Tomoiaga

Patents:

EP Patent 3,583,213

US Patent Application

Publications:

Tomoiaga et al. *NPJ Genom Med.* 2020.

Biz Dev Contact:

Louise Sarup

(646) 962-3523

lss248@cornell.edu

Cornell Reference:

D-7698

Weill Cornell Medicine