Method for Assessing Risk of Genetic Defects in Children by Identifying De Novo Mutations in Male Sperm

Tech ID: 29526 / UC Case 2017-181-0

BACKGROUND

In general, the risk of having a child with autism spectrum disorder (ASD) is about 1 in 68, or 1.5%. But the risk goes up for families who already have a child with ASD. If a family has one child with ASD, the chance of the next child having ASD is about 20%. If the next child is a boy, the risk is 26%, whereas if it's a girl the risk is 10%. About 47% of families had more than one child with autism. Currently if a child has a birth defect or autism, the emerging trend is to perform whole exome sequencing to identify genetic mutations. These mutations overwhelmingly come from the father, because sperm cells but not egg cells continue to divide through the life of adults. Once the mutation is identified, the diagnosis can be made in the child, but the parents are left wondering if this genetic event could recur in future children.

Currently there is no genetic assessment of sperm available commercially, and no publications on the application of using sperm as a way to assess risk of childhood disease, nor is there a risk assessment available for couples that have had a child with a genetic disease due to de novo genetic mutation.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have an invention that predicts the risk of autism or other *de novo* mutation diseases arising from male sperm. By assessing the sperm of males planning to have children using high read depth sequencing or single-molecule genotyping by Droplet Digital PCR (ddPCR,) we can assess the risk that a fetus will receive a mutation that is present in the father's sperm but not present in the rest of his body. In this way, sampling the sperm is the most direct way of detecting the personalized risk of having a child with a disease.

APPLICATIONS

This method can work with specific mutations (i.e. alleles), or a panel of genes contributing to a specific disease (i.e. the 'autism-ome') or a complete panel of genes that produce birth defects due to haploinsufficiency or other diseases when one copy of the gene is defective (i.e. 'haploinsufficiency-ome'). Our invention produces an individualized risk assessment that can help couples decide whether to conceive naturally or through artificial insemination, through preimplantation genetic diagnosis, or through adoption.

ADVANTAGES

We utilize well accepted methods from the cancer and human genetics field including ddPCR, panel deep sequencing, and risk assessment of candidate mutations. ddPCR methodology genotypes a particular allele in 10,000 parallelized PCR reactions, separated by droplets in in a single PCR reaction tube, to allow for high sensitivity and specificity of the mutation from a mixture of cells.

STATE OF DEVELOPMENT

Presently, the invention is at a stage where we could accept human samples for testing of specific genetic mutations in sperm samples in a research setting. To date, for disease alleles, we have tested variants in ~20 patients with a primary diagnosis of ASD and could detect mosaic variants in 4.

INTELLECTUAL PROPERTY INFO

A provisional patent has been submitted and the technology is available for licensing.

PATENT STATUS

Country	Type	Number	Dated	Case
Patent Cooperation Treaty	Published Application	2018183525	10/04/2018	2017-181

Additional Patent Pending

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OTHER INFORMATION

KEYWORDS

Autism, birth defects, de novo mutations, germ cells prenatal testing, single cell, sequencing, sperm, testes, aging related genetic risk

CATEGORIZED AS

- **Medical**
  - Diagnostics
  - Disease: Genetic Diseases and Dysmorphic Syndromes
  - Screening

RELATED CASES

2017-181-0

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