Is autism genetic?

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February 21, 2017
What we know about autism
Autism is complex. It is not a single condition, and many individuals have related challenges.
Twin studies suggest that genes are important in some individuals with autism

Identical Twins 77%
Fraternal Twins 31%
Siblings 20%
General Population 1%

Concordance for autism differs by family relationship and is correlated with genetic similarity.
There are many causes of autism, but for most individuals we do not yet know the cause.
The ABCs of DNA: An overview of genetics
The collection of all your DNA is your genome and codes for the instructions for your body in 20,000 genes.
We are all different, and some of these differences are coded in our genes
Recipes provide the instructions for baking

Chocolate chip cookies

- 1 cup sugar
- 1/2 cup butter
- 2 cups flour
- 2 eggs
- 2 cups chocolate chips
- 1/2 tsp baking soda
- 1 tsp vanilla
Substituting raisins makes a different type of cookie

Chocolate chip cookies

- 1 cup sugar
- 1/2 cup butter
- 2 cups flour
- 2 eggs
- 2 cups chocolate chips
- 1/2 tsp baking soda
- 1 tsp vanilla
Substituting salt for sugar makes a cookie that no longer tastes like a cookie

Chocolate chip cookies

- salt
- 1 cup sugar
- 1/2 cup butter
- 2 cups flour
- 2 eggs
- 2 cups chocolate chips
- 1/2 tsp baking soda
- 1 tsp vanilla
Our genes are encoded in pieces called exons
The exons are separated by DNA of unclear function

- wpod?am fkw cu.gjhklf four sjckfo qu score
- and void m$%d jkkk yp@mvjckd fkkseo
- cbqw.oiwjfm du seven years ago dllffk*wqm
- fkkd xmmenfyruuci our skkdj$fmvjkjdfk&%wo
- qppalfdkkf qa.q.d eiidty forefathers brought jjd
- qpoooekfjk vbzxx dsg forth a
Having biological parents available for comparison is essential to identify new genetic differences.
How genetic variants get passed down in families
De novo (new) genetic variants start in the child with autism

De novo genetic changes

Genetic change in the egg or sperm

Child with genetic change in autism gene
X-linked genetic variants are commonly passed down from the mother and more commonly affect boys.
Autosomal recessive genetic variants are passed down from the mother and the father.
SPARK and autism research
SPARK processes for genetic studies

Process: saliva collection/analysis and return of results

1. Consent to share your data and saliva
2. Saliva kits mailed to you
3. Provide saliva samples and mail back saliva kit
4. DNA extraction and exome analysis
5. REANALYSIS EVERY YEAR
6. Identify participants with known genetic causes of ASD
7. Notify participant and designated provider of a genetic finding from the clinical lab ready for return
8. Return of genetic results

SPARK genetics committee defines autism gene list
SPARK processes for genetic studies: genetic information will be re-analyzed each year

Process: saliva collection/analysis and return of results

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REANALYSIS EVERY YEAR
As new autism genes are identified, additional genetic results will be returned.
Autism research milestones

1943
Leo Kanner, psychiatrist, is the first to describe autism as a syndrome.

1977
Michael Rutter, psychologist, publishes first study of twins with autism and concludes that autism is at least partially genetic in some cases.

1987
Ivar Lovaas, researcher, is the first to suggest that autism is treatable with applied behavioral methods.

1991
Changes in the FMR1 gene were identified and shown to cause Fragile X syndrome.

1999
Huda Zoghbi and colleagues discover that variants in the MecP2 gene cause Rett’s syndrome.

2006
FDA approves use of risperidone for treatment and irritability in autism.

2016
SPARK begins recruitment for the largest autism study to date.

2007
Michael Wigler and colleagues discover that the de novo mutations are a more significant contributor to autism than previously recognized.
How many families will get a genetic answer?

5-10% of families enrolled in SPARK are expected to receive results in the first analysis.

This will grow over time as we learn more.
What will it mean for us if we receive genetic diagnosis?
A genetic diagnosis is important because it helps to...

1. End the diagnostic journey and minimize additional tests
2. Understand recurrence risk for families
3. Provide a roadmap for the future
4. Identify opportunities to network with similar participants
5. Learn about clinical trials and/or treatments specific to your diagnosis
How can I learn about my/my child’s genetic condition?

- Talk to your doctor
- Talk to a genetic counselor through SPARK
- Read the SPARK materials that come with your report
- Talk with other families through Simons VIP (SimonsVIPconnect.org)
What does it mean if I do not get notified about a genetic result right away?

- This does NOT rule out genetic causes
- This genetic evaluation cannot evaluate all genetic causes of autism
- This study does not replace a consultation with a medical geneticist or clinical genetic testing
- You may be notified in the future as we learn more about what genes cause autism
How will I know that you have analyzed my sample?

- Check your SPARK Dashboard to see the status of your saliva kit
- Because we can perform better genetic analyses on complete families, those with samples from all family members, (mom, dad and person with autism) will be analyzed first
Will you tell me about other genetic conditions besides autism?

- Unlikely, because we are not actively looking
- If we stumble upon genetic information that could be life-saving, and you have asked to receive this information, we will provide it to you
- Example: gene for sudden cardiac death
Summary

- Autism has known and unknown genetic & environmental causes

- Many types of genetic changes can lead to autism

- By participating in SPARK, you can find out if you (or your family member) has a genetic cause in a known autism gene

- Identifying a genetic cause of autism can be helpful to a family even if it does not change treatment today

- Knowing the genetic cause of autism in your family may inform you about future research studies