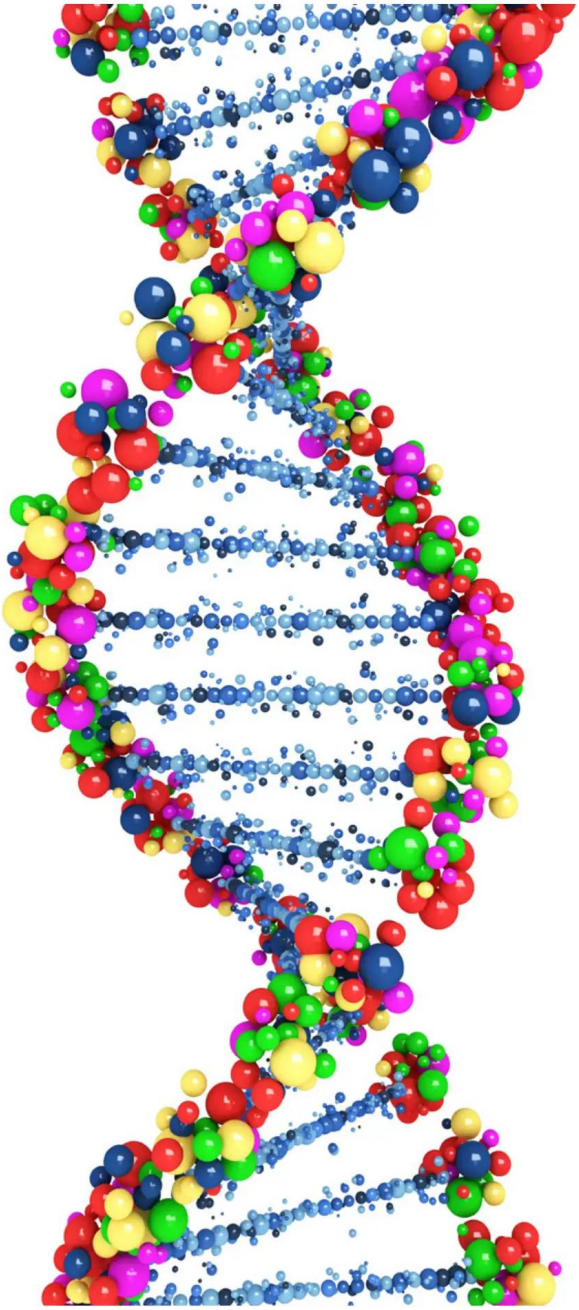
Groundbreaking New Genetic Discoveries in Autism

By **Jan Stewart**

New genetic research identifies specific autism genes and provides hope for new treatments.

Is it true that genetics is the most important determinant of autism? That four times as many boys as girls are diagnosed with autism? Groundbreaking new genetic research is validating these facts and identifying specific genes associated with autism.

In turn, this research is positioned to point the way towards novel diagnostic and treatment approaches.



Early beliefs about the causes of autism

Throughout the first half of the 20th century, parents were widely believed to be the cause of their child's autism. The "Refrigerator Mom" theory postulated that autism was due to emotionally cold and unempathetic parents.

It wasn't until 1964 when American psychologist Bernard Rimland challenged this assumption and pointed to biological genetic causes. Additional studies confirmed the importance of biological and genetic factors in autism.

In the 1970s, for example, a famous study at London's Institute of Psychiatry studied 21 pairs of identical twins and found that more than one-third of them shared autism. Several other family stories followed, supporting a significant role in genetics.

Discovery of genetic variants in autism

In the early 2000s, Dr. Stephen Scherer, now the Chief of Research at Toronto's world-famous SickKids Hospital, helped found the hospital's human genome research center. He had been working in the famous laboratory that discovered the cystic fibrosis gene.

He knew little about autism. However, as the Centre launched, two mothers of autistic children contacted him. Both children had genetic alterations in the same region of chromosome 7 near where the gene involved in cystic fibrosis had been discovered.

He became intrigued and read an Oxford University paper that was one of the first to map genetic variations in several autistic children to the same region of chromosome 7. He met with autism experts at the hospital, one of whom was already collecting DNA samples of autistic children. Shortly after, he became the Canadian co-lead of the newly launched international Autism Genome Project.

Dr. Scherer says the "real game changer" came in the early 2000s when his lab decided to study the structure of chromosomes and started developing technologies to scan the entire genome in one experiment. He and his team selected DNA samples from families with autism. They found that 7% of children with an autism diagnosis had spontaneous (not found in either parent) genetic variants, called copy number variants, versus fewer than 1% of people without autism.

Another US-based study came up with the same results at the same time, scientifically replicating the results. In science, replication is important.

Role of sex chromosomes in autism

Many studies were also concluding that boys are four times more likely to be diagnosed with autism than girls. For technical reasons, however, most studies had excluded the X chromosome from analysis.

Since females have two X chromosomes while males only have one X chromosome (along with one Y chromosome), Dr. Scherer suspected that genetic variants on the X chromosome were an important determinant of autism. He decided to study whether females' second X chromosome acts as "back-up" DNA that provides them with greater protection against signs of autism.

In 2012, the international team he co-led collected information on the X chromosome from over 4,000 Canadian families, which confirmed this "female protective effect." Another US-based team also replicated this study.

This led Dr. Scherer to investigate the role sex chromosomes play in autism further. In 2022, he and his team completed whole genome sequencing on 11,000 autistic and non-autistic individuals and found 134 genes linked with autism, as well as a range of genetic variants.

Most recently, the exciting results of two additional studies have just been published, in December 2024 and January 2025, respectively:

- In one study, he and his team at SickKids and Dr. Marcello Scala at Italy's Istituto Giannina Gaslini analyzed over 15,000 X chromosomes. They identified 36 families bearing autism-linked variants in DDX53, a gene that plays an important role in brain development but had never been linked to autism before. Of this total pool of 36 individuals, 31 were male.

- In the second study, Dr. Scherer and SickKids' Research Fellow Marla Mendes conducted an X-chromosome-wide association study using whole genome sequencing data from over 6,800 autistic and almost 9,000 non-autistic individuals. They identified 59 genetic variants in 14 genes on the X chromosome that are significantly associated with autism.

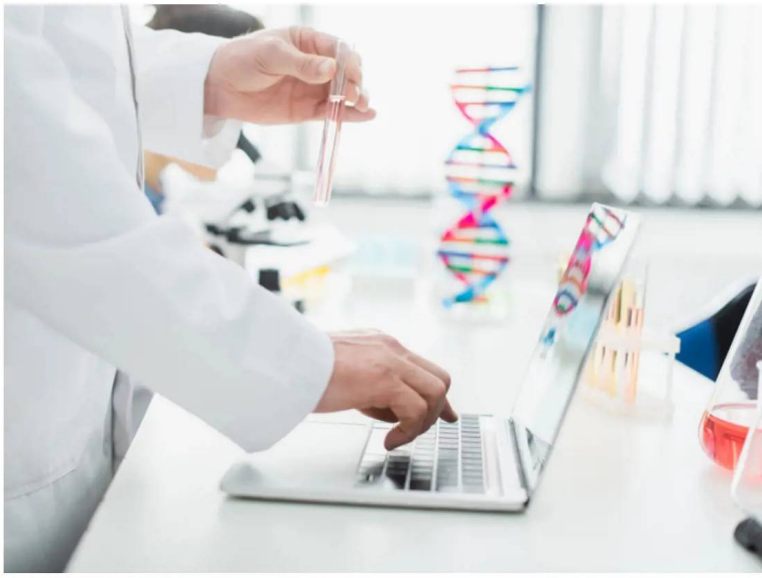
Ongoing studies from Dr. Scherer's lab are continuing to explore the role of certain genes found on the X chromosome in the genetic underpinnings of the condition, with more findings anticipated to be published this year.

What the future holds

Dr. Scherer notes that these genetic variants currently account for approximately 20% of autism. He believes that with further research, genetic variants will be found to account for 50% or more, although, in our interview, he laughed, "I am not a betting man, so let's see!"

The other 50% may be due to non-genetic factors, although Dr. Scherer says we don't know how much of a role environmental factors play. Research has pointed to several risk factors, including:

- premature births
- paternal age
- pregnancies less than one year apart
- low birth weight
- congenital heart disease
- severe infections
- high blood pressure and diabetes during pregnancy
- already having one biological child with autism or another neurodevelopmental condition.



Dr. Scherer's data underscore the multi-faceted complexity of autism and validate the important contribution of genetics, including male prevalence. His work is identifying genetic pathways that will lead to more informed decision-making for autistic individuals and their families, as well as for clinicians and researchers.

It will play a critical role in helping to improve testing, obtain diagnoses as early as possible to benefit from early autism intervention, and develop targeted medications, supports, and therapies to improve care and outcomes.

Above all, Dr. Scherer is grateful to the families who participate in these studies. Their participation drives research advances and optimizes a better understanding of autism to enhance the lives of autistic individuals and their loved ones.

While we are only beginning to understand the important role that sex chromosomes play, he believes these discoveries will help end "the odyssey of diagnosis" that many parents endure and provide answers to the questions:

- Why?
- What can we do next?
- How can we help other families?

Thanks to Dr. Scherer and his team, we are on the cusp of unlocking autism's genetic mysteries.

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Jan Stewart is a highly regarded autism and neurodiversity advocate, author, and recipient of the prestigious Mom's Choice Award®. Her best-selling memoir Hold on Tight: A Parent's Journey Raising Children with Mental Illness describes her emotional roller coaster story of parenting two children with multiple mental health and neurodevelopmental disorders, including autism. Her mission is to inspire and empower parents to persevere, have hope, know they are not alone, and better educate their families, friends, healthcare professionals, educators, and employers. Jan chairs the Board of Directors at Kerry's Place Autism Services, Canada's largest autism services provider, is a Today's Parent columnist on autism, has written for Autism Parenting Magazine, and was previously Vice Chair at the Centre for Addiction and Mental Health. She spent most of her career as a senior Partner with the global executive search firm Egon Zehnder. Jan is a Diamond Life Master in Bridge and enjoys fitness, genealogy, and dance.