

FOXP1 Syndrome

What is the *FOXP1* gene and what does it do?

FOXP1 is a gene located on chromosome 3 and includes the instructions for making the Forkhead Box P1 protein, which is a member of a family of transcription factors. Transcription factors are proteins that regulate the expression of other genes. In particular, *FOXP1* controls when and how other genes important for the development and correct functioning of the nervous and other systems, are expressed. When a transcription factor such as *FOXP1* doesn't function correctly, the expression of other genes can be disturbed, possibly leading to a range of developmental and medical issues.

What causes FOXP1 syndrome?

Chromosomes are the structures that carry an individual's genetic information. This information is encoded by units called genes, which can be thought of as long words made up of strings of 4 different "letters" (A, G, T, and C). Genes are arranged along the chromosome like words in a sentence. In humans, each cell normally contains 23 pairs of chromosomes, for a total of 46 chromosomes. Twenty-two of these pairs (autosomes) look the same in males and females. The 23rd pair (sex chromosomes) differs between sexes. Humans usually have two copies of every gene on the autosomes, including *FOXP1*.

FOXP1 syndrome is caused by genetic lesions (mutations) of the *FOXP1* gene. These include a swap of a single letter or loss or gain of a few letters on one copy of the gene, as well partial or total deletions of one copy of the gene. The disorder is referred to as "autosomal dominant" because mutations of a single copy of *FOXP1* are enough for a person to be affected. *FOXP1* mutations typically arise spontaneously in affected individuals (that is, not inherited), and are therefore referred to as "de novo" mutations. Because the parents would typically have two normal copies of the *FOXP1* gene, there is a very small chance to have a second child with FOXP1 syndrome.

What are the features of FOXP1 Syndrome?

The features associated with FOXP1 syndrome result from mutations in one of the two copies of the *FOXP1* gene. The most noticeable effects of these mutations are neurodevelopmental and behavioral in nature, and can include:

- Global developmental delay (speech, language, cognition)
- Intellectual disability (low IQ)
- Poor fine and gross motor skills; low muscle tone
- Autism or autistic-like features
- Anxiety
- Attention deficit
- Hyperactivity
- Obsessive-compulsive traits
- Sensory reactivity symptoms
- Other behavior problems

Some individuals share certain facial features, including macrocephaly (large head), prominent forehead, and short nose. Epilepsy and immune system alterations have also been diagnosed in some individuals. Careful cardiac examinations are recommended, as well as brain imaging studies, especially for those with macrocephaly.

How common are *FOXP1* gene mutations?

FOXP1 mutations are rare, but more and more cases are being identified as genetic testing becomes more widespread. There are online parent groups with a few dozen families represented. There are likely many more people carrying mutations in the gene who have not yet been diagnosed.

What can we expect for our child, and how can we best help?

Infants

Infants and children with FOXP1 syndrome should be followed by a clinician with expertise in working with children with neurodevelopmental disorders (for example, developmental pediatricians, child and adolescent psychiatrists, and neurologists). A primary clinician can follow the child as they develop and recommend follow-up with other physicians, psychologists, or other therapists as needed.

Early intervention is important to help infants identified early with FOXP1 syndrome to maximize their potential. As many infants with FOXP1 syndrome have low muscle tone, physical therapy can help with meeting motor milestones like sitting, crawling and walking. Occupational therapy can also help infants learn to develop fine motor skills, which are often delayed, such as learning to pick up pieces of food for feeding. Some children with FOXP1 syndrome will require an occupational therapist with expertise in feeding difficulties. Since FOXP1 syndrome is associated with language delays, children should begin speech therapy with a certified speech and language pathologist (SLP) by 12 months of age. If a child is not making sounds of pleasure (coos, laughs) and vowel sounds by 6 months of age, a consultation with a an SLP is warranted.

Because most individuals with FOXP1 syndrome have intellectual disability and behavioral challenges, applied behavior analysis (ABA) may be recommended. It is also important to access special education services in the school system as the children approach school age.

Children

Children may benefit from a variety of therapies to target language, motor, and cognitive development. Speech therapy should focus on functional communication (e.g., ability to express basic wants/desires). As a child's functional language develops, speech therapy should focus on pragmatic language, or the social use of language. Pragmatic language interventions may focus on initiating, maintaining, and terminating back and forth exchanges. Occupational therapy should focus on fine motor skills, activities of daily living (e.g., feeding, dressing, toileting) and sensory reactivity. "Sensory diets" may be helpful for children who are sensory-seeking or sensory-averse to specific stimuli. Sensory diets can range from fine-motor manipulatives and activities for tactile stimulation to gross-motor activities such as jumping on a trampoline. Physical therapy may also be necessary when gross motor delays are present.

Behavioral issues may start to become more prominent during childhood. Some common behavioral issues reported are hyperactivity, impulsivity, anxiety, autism or autistic-like behaviors, and obsessive-compulsive traits. These include narrow interests, intense preoccupations or obsessions, repetitive behaviors and difficulty dealing with changes in routine or environment. Some parents have found that interventions helpful for children with autism also help their children with FOXP1 syndrome, including:

- Applied behavior analysis (ABA)
- Visual supports such as picture schedules and social stories
- Behavior and reward charts
- Sensory tools

As the child grows, psychologists can provide valuable behavior-enhancement and management advice. Especially for teachers unfamiliar with neurodevelopmental disorders, it will be important to share general information about the issues faced by children with FOXP1 syndrome, as well as specific adaptations and behavior management practices that have been found to help your child.

Academic curricula should focus on academic fundamentals (reading, writing and

basic math) and activities of daily living in order to teach students with FOXP1 syndrome the skills necessary to achieve maximum independence.

Teenagers

A few FOXP1 syndrome families have reported issues with worsening behavior issues after puberty, especially aggressive behaviors. An important area for future research is to understand how prevalent these issues are, and what behavior management practices can help FOXP1 syndrome teenagers and their families deal with these behavior issues.

Families may benefit from working with a Board Certified Behavior Analyst (BCBA) to address challenging behavior. A Functional Behavioral Assessment (FBA) can be performed in the home or at school to develop appropriate treatment plans. Some adolescents may benefit from cognitive behavioral therapy (CBT) with a licensed psychologist to target internalizing symptoms such as anxiety. A child and adolescent psychiatrist with expertise in treating individuals with neurodevelopmental disorders will be critical in addressing clinically significant externalizing (i.e., hyperactivity, aggression) and internalizing (i.e., anxiety, depression) symptoms.

Academic curricula should continue to focus on functional academics and activities of daily living. Vocational training may begin during this time, as well as plans for transition to adulthood.

Adults

To date, there is little known about adults with FOXP1 syndrome and future studies will be dedicated to learning more about the natural history of the syndrome. Families should be prepared to explore assisted living and other residential or day-habilitation programs.

Final note

This summary document was prepared by a group of parents of FOXP1 individuals, with assistance and review by investigators at the Seaver Autism Center for Research and Treatment at the Icahn School of Medicine at Mount Sinai in New York and the INSERM in Paris.

For further information regarding the [Seaver Center's](#) research into FOXP1, please contact the research coordinator Allison Durkin (Allison.durkin@mssm.edu); phone: 212-241-2993) or theseavercenter@mssm.edu; phone: 212-241-0961