SYNGAP1

Resource Guide

Bridge the Gap
SYNGAP
Education & Research Foundation

Connect Local

Collaborate Global

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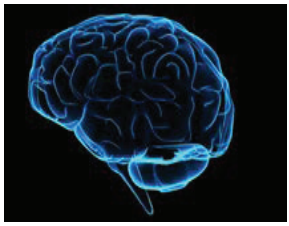
SYNGAP1 – Normal Function



• The SynGAP gene provides instructions for making a protein, called SYNGAP1 that plays an important role in nerve cells in the brain.

• SynGAP is found at the junctions between nerve cells (synapses) where cell-to-cell communication takes place.

• Connected nerve cells compose the “wiring” in the circuitry of the brain.

• Synapses are able to change and adapt over time, rewiring brain circuits, which is critical for learning and memory.

• SynGAP helps regulate synapse adaptations and promotes proper brain wiring.

• The protein’s function is particularly important during a critical period of early brain development that affects future cognitive ability.

Uniqueness' in SYNGAP1

What Makes SYNGAP1 Different?

- Some of the symptoms are shared with other disorders but the underlying cause of the symptoms differ.
- The severity and onset of the symptoms can vary from patient to patient; it is considered a spectrum disorder.
- It has a genetic basis meaning that the gene that causes the disorder has been identified; a mutation on the SynGAP1 gene will present with symptoms.
- It has an emerging collection of symptoms, but there may be insufficient unique clinical characteristics to enable an early clinical diagnosis.
- There is a long journey of research and analysis ahead to further inform on SYNGAP1, and the points made here are reflective of that journey.

What SYNGAP1 has in Common with Other Rare Diseases?

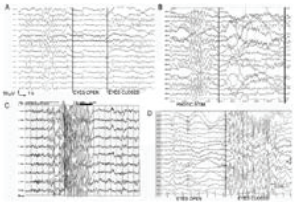
- There is presently no cure or approved treatments.
- The SYNGAP1 patient has placed their life in our hands, they will remain DEPENDENT on other parties for their basic survival, and for all their needs throughout their lives:
- Social
- Cognitive
- Physical
- Emotional

Common Symptoms of SYNAGP1 Mutations…

Not all of these symptoms will be present in every affected person. However, to date the most commonly described symptoms are:

Our Goal is to improve the Quality of Life, While Searching for Effective Treatments

- Intellectual Disability – can vary across the range, mild to severe
- Global Developmental Delay – onset infancy
- Hypotonia (low muscle tone)
- Spectrum of Epilepsies – usually difficult to achieve seizure control
- Speech Delay – both receptive and expressive, can remain nonverbal
- Delayed development of motor skills
- Language Disorder – Apraxia
- Autism Spectrum Disorders
- Sensory Perception Disorders
- Sleep Disturbances
- Constipation
- Joint, Spine and Gait issues – likely linked to low muscle tone



SYNGAP1 Mouse Biomarker for Epilepsy

Effect of SYNGAP1 Mutations

SYNGAP1 AS A SYNDROME

- De novo mutations in the SYNGAP1 gene have been found to cause SYNGAP1-related intellectual disability; with Epilepsy, Hypotonia, and Speech Impairment in combination, being significant other symptoms.
- It is also a Genetic disorder as the genetic change which causes the disorder is known. This is only identified since 2009.
- SYNGAP1 is considered both a Rare Disorder and a Rare Disease; these titles can be used interchangeably for the purposes of understanding this document.
- There is currently no cure or treatment to reverse or contain/improve the disorder as researchers and clinicians are still trying to understand its underlying intricate biology.

We are entering an era of rapid scientific discovery. We can succeed in harnessing the great power of these advances by working together. By forging connections between the children and their families, the physicians who care for them and a growing community of scientists, we are able make the fastest possible progress in our understanding of this condition to improve the outcome." ***Dr. Jacques Michaud Researcher & Head Department of Medical Genetics, CHU Sainte-Justine Research Centre***

How We Got Here…

Chronology of SYNGAP1

- **1998 - Discovery of Syngap1 gene (Huganir Lab; Kennedy Lab)**
- **2002 - First Mouse Model Created (Grant Lab)**
- **2009 - First SYNGAP1 patients identified (Michaud Lab)**
- **2012 - First studies addressing disease mechanisms (Rumbaugh Lab)**
- **2014 - First International Patient Organization founded focusing on SYNGAP1**
- **(*Bridge the Gap – SYNGAP1 Education and Research Foundation, USA)***
- **2016 - First SYNGAP1 International Conference**
- **First SYNGAP1 (MRD5) Registry and Natural History Study Launched**
- **2017 - First SYNGAP1 Drug Discovery Project began (Rumbaugh Lab)**

ABOUT US

Mission Statement:

To serve, educate and fund research for families coping with the effects of SYNGAP mutations.

Our Desired Impact:

Our aim is to empower patient families, clinicians, and researchers with information necessary to move forward to treatment. We will clear a path on our way to finding a cure to help patients with SYNGAP1 mutations

- **Raise awareness of SYNGAP1 and unite SYNGAP1 patient families**
- **Educate researchers/medical professionals to improve time to early diagnosis and identification of potential treatments that will help our children now**
- **Create a behavior/medical profile using the SYNGAP1 individuals using data provided by the SYNGAP1 (MRD5) Patient Registry**
- **Educate families and clinicians to create customized treatment plans that can result in the best outcomes for progress made by each individual**

SYNGAP1 Centers of Excellence and Participating Research Institutions

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