



| June 2020 | Yellow Brick Road Project HNRNPH2 News

Latest News

The 2020 family meeting will be taking place on July 22, 23 and 24. Individual appointments for families taking part in the natural history study will take place on July 20 and 21.

The meeting will take place entirely online, with presentations by a variety of researchers and clinicians as well as roundtable discussions and opportunities to connect with others around the world.

Full details of how to register for the meeting will be shared in early July.

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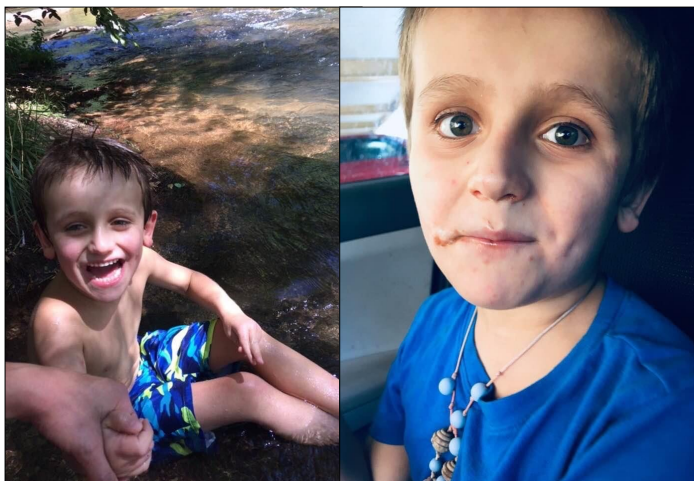
YELLOW BRICK ROAD
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www.facebook.com/yellowbrickroadproject

Featured Family: Meet Kaleb

This is Kaleb and he just turned 8 years old. He lives in Arizona and has his entire life. He is almost always a very happy boy that loves to laugh and be silly.



On the other side of things, Kaleb struggles with behavioral issues that include self injury. He isn't on any medications, so these behavioral hurdles are usually overcome by deep sensory input/diet.

Every weekday he attends public school where he is in a self contained classroom with other kids with special needs. He enjoys seeing familiar faces and having his own routine in the classroom. Therapies play an active role in Kaleb's life. He has had speech, occupational, and physical therapy since he was a year old. These much needed therapies have really helped Kaleb make progress developmentally. He learned to crawl when he was 3, and took his first independent steps at age 5. He can now walk independently and there is no need for assistive equipment. He is cautious when it comes to stairs or changing surfaces, but can usually maneuver them with assistance.

Although Kaleb is non-verbal, he can follow one and two steps instructions and uses visual cues to communicate. He also just started potty training!

Kaleb can hand feed himself but needs help with utensils. Outside of school he enjoys anything to do with water and is learning to swim. Also if you have a ball, you are Kaleb's best friend!

We received our HNRNPH2 diagnosis when he was 4 years old. The only diagnosis we had before this was autism and global developmental delay. Kaleb had several negative genetic tests including Fragile X and Angelman Syndrome. It wasn't until a geneticist at Phoenix children's hospital suggested whole exome sequencing, and that eventually lead to his diagnosis. At the time Kaleb was the only boy diagnosed out of a group of about 20 girls. When we got the diagnosis, it was pretty overwhelming. But now being part of this extraordinary group we are so grateful! Being able to communicate with other families and knowing we aren't alone has definitely made our journey easier.



Spotlight On: Hypotonia

For many neurodevelopmental disorders, including HNRNPH2 mutations, one of the first visible symptoms of the condition is hypotonia. This is the medical term for decreased muscle tone, and it is often the reason that early developmental milestones are missed. It affects all aspects of a child's motor development, including relatively simple things like breathing, swallowing and grasping.

Hypotonia is not the same as muscle weakness, although it is possible for someone to have both low muscle tone and muscle weakness. Low muscle tone is a neurological condition where the signals that travel from the brain to the nerves to tell the muscles to contract are not functioning properly. Healthy muscles are never fully relaxed; they retain a certain amount of tension and stiffness that can be felt as resistance to movement. For example, we all rely on the tone in our back and neck muscles to maintain our position when standing or sitting up. This tension is significantly decreased in someone with low muscle tone.



The child on the left has hypotonia. Her neck and limbs appear limp and floppy, as if they are pulled to the ground. The child on the right has greater natural muscle tension, making it easier to raise her arms and legs off the ground.

Hypotonia is often noticeable by the time a child is six months old, if not before. Newborn babies and young children with severe hypotonia are often described as being "floppy".

Signs of hypotonia in a child include:

- ♦ having little or no control of their neck muscles, so their head tends to flop
- ♦ feeling limp when held, as though they could easily slip through your hands
- ♦ being unable to place any weight on their leg or shoulder muscles
- ♦ their arms and legs hang straight down from their sides, rather than bending at their elbows, hips and knees
- ♦ finding sucking and swallowing difficult
- ♦ a weak cry or quiet voice
- ♦ fatigue when performing gross motor skills

A child with hypotonia often takes longer to reach motor developmental milestones, such as sitting up, crawling, walking, talking, and feeding themselves.

There is no cure for hypotonia as muscle tone does not change. However, a child's motor development may steadily improve over time. Treatment such as physiotherapy, occupational therapy and speech and language therapy can help to improve motor functions. The main objectives of physiotherapy treatment for hypotonia are to improve posture and co-ordination to compensate for low muscle tone and to strengthen the muscles around the joints of the arms and legs so they provide more support and stability. Equipment to help the child move more easily may also be recommended, such as ankle or foot supports. Speech and language therapists can assist with feeding support and identifying swallowing problems that can sometimes be associated with hypotonia.

2020 Family Meeting

The 2020 HNRNPH2 Family Meeting will be taking place the week of **July 20 - 24, 2020**. The event will be held entirely online this year because of the ongoing COVID-19 pandemic.

The meeting will be made up of two primary components:

1. PRESENTATIONS AND ROUNDTABLE DISCUSSIONS

The Yellow Brick Road Project will be hosting a series of presentations, Q&A sessions and roundtable discussions on areas of interest to our families. These will take place over the meeting days of July 22, 23 and 24 and will be recorded where possible for those who cannot attend live. Families will need to register for the meeting platform – further details will be provided closer to the day!

Presenters will include scientists such as Dr Wendy Chung and the St. Jude Children's Research Hospital team, clinicians and others studying or having interest in HNRNPH2 mutations. Dr Jennifer Bain will provide an update on the Natural History Study and upcoming publications.

Roundtable discussions will be led by a subject matter expert and will provide a great opportunity for parents/caregivers to ask questions and share experiences on many different aspects of living with an HNRNPH2 mutation.

Everyone is welcome to attend all of these sessions!

2. EVALUATIONS FOR THE NATURAL HISTORY STUDY

A key part of the family meeting for the past two years has been the gathering of data for the Natural History Study being conducted by Dr Jennifer Bain. Dr Bain is eager to ensure that this information can still be collected this year as part of our virtual meeting. This will be done in two ways:

- a) Families will be asked to film their child completing some tasks for the team to evaluate prior to the start of the family meeting
- b) Families will be invited to a 1-on-1 session with Dr Bain and her team, likely to be held during the days of Monday, July 20 and Tuesday, July 21

Dr Bain and her team will be in touch with each family that is registered in the Natural History Study to provide further details and to schedule the 1-on-1 sessions at a time that is mutually convenient. If you would like to take part in these evaluation sessions, you **MUST** be fully enrolled in the Natural History Study and have signed the study consent form. If you are not yet registered, please contact Dr Bain at jb3634@cumc.columbia.edu



The poster for the 2020 HNRNPH2 Family Meeting features a collage of images: a family with children in a park, a group of people in a meeting, and a DNA double helix. The text on the poster includes the title '2020 HNRNPH2 Family Meeting' and dates 'July 22, 23 and 24'. It also mentions 'with individual evaluation sessions for participants in the Natural History Study July 20 & 21'. A central message reads 'Families, researchers and clinicians gathering online to change the lives of those affected by this rare X-linked genetic mutation'. A yellow circle on the right says '3rd annual meeting'. At the bottom, logos for Columbia University Medical Center, Yellow Brick Road Project, St. Jude Children's Research Hospital, and Simons Searchlight are displayed.

2020 HNRNPH2 Family Meeting
July 22, 23 and 24

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3rd annual meeting

COLUMBIA UNIVERSITY
MEDICAL CENTER

YELLOW BRICK ROAD
PROJECT

St. Jude Children's
Research Hospital

andlit

NewYork-Presbyterian

SIMONS
SEARCHLIGHT

HNRNPH2 Awareness Week: July 26—August 1, 2020



This summer we will be holding our first-ever **HNRNPH2 Awareness Week!** It will follow on directly from the family meeting, taking place over the week of July 26 to August 1.

Since the initial study in 2016 which described 6 girls, we have grown to a community of more than 80 diagnosed patients around the world, boys and girls. And we want the world to know about us!

The highlight for this year will be a series of Everyday Life videos made up of clips submitted by our families which will highlight different aspects of life with an HNRNPH2 mutation. There are lots of challenges for our patients but also a lot of successes and we want to share the highs and lows with all of our supporters.

In future years, we hope to expand this week to include a global fundraising event as well as awareness-raising activities online and out in the real world. Please be sure to follow us on Facebook, Instagram and Twitter for all the updates and share with all your friends!

NORD Membership

The Yellow Brick Road Project is now an official member of NORD, the National Organization for Rare Disorders. NORD is a patient advocacy organization dedicated to individuals with rare diseases and the organizations that serve them.

NORD, along with its more than 300 patient organization members, is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient services. By partnering with them, we can raise awareness of our condition, combine resources with other groups with similar conditions and learn from organizations who are farther along the advocacy journey than we are. The benefits of NORD are summed up in their slogan:

Alone we are rare. Together we are strong.

Visit the NORD website to learn more:

<https://rarediseases.org/>



Natural History Study Update

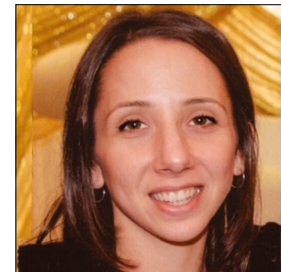
The newsletter will contain a regular update from the research team conducting the HNRNPH2 Natural History Study. Dr Jennifer Bain is the principal investigator and Olivia Thornburg is her Research Assistant. They are based at Columbia University in New York City, USA.



Dr Jennifer Bain

What is a natural history study?

A natural history study follows a group of people over time who have a specific medical condition or disease. The study collects health information in order to understand how the condition develops and how to treat it. It can be used as a baseline to determine if proposed treatments are effective.



Olivia Thornburg

In 2016, we identified 6 girls with variants in the *HNRNPH2* gene. Each individual had developmental delay or intellectual disability, as well as atypical muscle tone. Many of the girls also experienced seizures and comorbid psychiatric and behavioral conditions, such as anxiety and autism spectrum disorder (ASD). We discovered variants in *HNRNPH2* also seemed to affect other organ systems in the body aside from the brain. For instance, patients with variants in *HNRNPH2* also had problems with growth, gastroesophageal reflux disorder, scoliosis and other skeletal problems, heart problems, and atypical facial features.

Since the initial 6 individuals were identified, we have discovered 36 additional cases of individuals with variants in *HNRNPH2*. The majority of individuals affected are girls, although we have confirmed variants in 5 boys. Our research has employed the use of a prospective testing battery where we administer assessments remotely to test for various neurologic, behavioral, psychiatric, developmental, and social factors in this genetic group. We have also gathered information from former genetic reports and medical records. Additionally, we conducted motor assessments as well as electroencephalography at our *HNRNPH2* family meeting in July of 2018 and 2019. These testing measures revealed similar clinical symptoms to that of the original cohort, including atypical facial features, neurologic abnormalities, atypical gait, and abnormal muscle tone. The expanded cohort reported fewer seizures than the original group. We also discovered a predominance of comorbid anxiety in the expanded group.

While we have learned a lot more about *HNRNPH2*, we still have a lot to learn. We are actively recruiting *HNRNPH2* patients in our study, and hope to continue to employ various testing measures to understand clinical features of individuals with these gene variants. Please see our posting on clinicaltrials.gov for more information on our study: <https://clinicaltrials.gov/ct2/show/NCT03492060?cond=hnrnp&rank=1>.

We invite families with *HNRNPH2* variants to help us improve our understanding by contacting us and partnering. We need to better understand why changes in *HNRNPH2* causes problems with brain function so we can develop new treatments.

Patient Data - An Important Resource

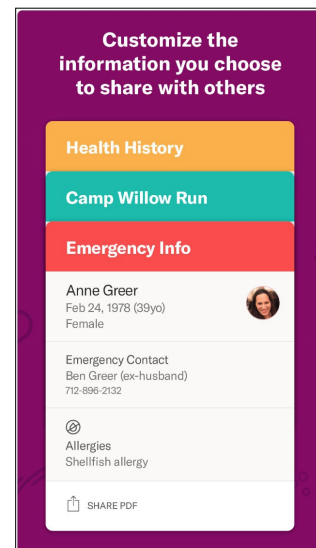
How many people in the world have HNRNPH2 mutations? How old are they and where do they live? What symptoms do they have and how severe are they? These are straightforward questions, and the answers can be incredibly important when considering research opportunities, potential treatments and clinical trials, to name just a few examples. But at the moment we do not have enough information to answer them accurately.

To help us collect this important information, we are launching two new data initiatives.

BACKPACK: A PATIENT REGISTRY

A patient registry is a database or a collection of records of people with a particular condition. It includes personal information (ie age and sex) and clinical information (ie gene variant and severity of symptoms). The Yellow Brick Road Project has chosen a company called **Backpack** to create our patient registry.

Backpack can be used through an app or a website, available on iOS, Android and the web. It is free to use. It can be accessed in English, Spanish, French, Portuguese, German and Italian. Parents or carers of HNRNPH2 patients will create an account and complete the patient information, and then choose to share the **relevant de-identified** data with the Yellow Brick Road Project. This means that YBRP will not have access to names or contact information in the family accounts, but we will have the important demographic and clinical data that will help us to better understand our patients and how we can help them.



There will be a presentation during the family meeting to help families get started and explain how to share information with us. It will be available to view later for those not able to attend on the day.

TREND: HARNESSING OUR COMMUNITY'S EXPERTISE

Another important source of data for our group is found within the conversations that take place in our parents-only Facebook group. When identifying research opportunities, the Yellow Brick Road Project is often asked: What are the symptoms that matter the most to the patient? and What are the daily challenges that patients most need help with? Our Facebook group has had many valuable conversations that, if analyzed, may be very useful in answering these questions.

The technology company, **TREND Community** has offered to do such an analysis for us free of charge. They can create reports on the trending topics discussed in our group. Again, this information is **de-identified**, so conversations are extracted by TREND without access to usernames or profile information. The report we receive will be shared back with the parent group to help us all better understand the things that are most important to our group.

Jennifer M. Bain, MD, PhD

Assistant Professor of Neurology and Pediatrics

*Department of Neurology
Division of Child Neurology*



*Attending Physician
New York Presbyterian
Columbia University Irving Medical Center
Morgan Stanley Children's Hospital of New York*

June 21, 2020

Dear Families affected by *HNRNPH2*,

My name is Jennifer Bain and I am a child neurologist at Columbia University in New York City. I am a physician scientist which means I am primarily a researcher on human disease and also see patients in clinical practice with neurodevelopmental disorders including rare genetic disorders, autism and developmental delay. I worked with Dr. Wendy Chung and described the first [6 girls](#) with [HNRNPH2-related disorder in 2016](#). Since that time, I have had the privilege to meet many more families affected by this gene from around the world.

I wanted to thank each of you for your participation in the [natural history study](#) and participation in our first 2 family meetings in 2018 and 2019 in New York City. We are excited to host a virtual meeting this summer 2020 (more details to come from the I wanted to update those who have participated in our study and also reach out to those who have not yet joined in these research efforts.

We are nearing completion of our 2nd manuscript describing 33 individuals with this genetic disorder! We could not have done this without each of you! THANK YOU! We hope this manuscript will increase awareness of this disorder, encourage more families to join in our efforts and provide us more information for future research and potential interventions. Please contact me if you are willing to join in our efforts and have not signed up for our study yet. I am here to answer questions or concerns you may have about participation.

I also wanted to take this opportunity to send warm wishes to each of your families during this absolutely "crazy" time in the pandemic. As a parent of 3 young children, I personally struggle with managing my personal life and a full-time job while providing support to my patients! You are not alone! Moreover, the young brain needs to be supported with early interventions and therapies, and I imagine that many worry about potential loss of skills or regression during these times. Others may worry about how this pandemic may affect their child with *HNRNPH2*-related disorder. My best recommendations as a physician scientist studying *HNRNPH2* and caring for children in child neurology:

- **Keep Calm.** We will get through this and transition to a "new normal."
- **Be informed** by appropriate sources such as the [CDC](#) and [WHO](#). Watch out for ill-informed news reports that may cause fear or anxiety about issues instead of well-founded scientific updates!
- **[You are not alone!](#)** Many people are struggling at this time with rare diseases, so reach out to your network - clinical providers, educators and social network.

Jennifer M. Bain, MD, PhD

Assistant Professor of Neurology and Pediatrics

*Department of Neurology
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*Attending Physician
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- **Your primary role is to be a loving, supportive advocate and PARENT to your child during this time.** You do not need to be their educator and therapist at all times! If you can, great...but if you cannot fit EVERYTHING into your busy life right now, that is OKAY! As a parent or caregiver for a child with special needs, you know that you need to take care for your child! I am sure you have heard this before, but this is particularly important at this time! Please keep checking in on your *own* mental health during this time. Here are some free digital [NYC resources](#) I have been referring my patients to use in their own "free time."
- You still have [educational rights](#) to receive some services and support during this time of distant learning. Reach out to others in your local community (school contacts, advocate organizations such as [Parent to Parent](#), etc) to discuss what have/have not been receiving with regards to your child's services. It will vary between districts but you do have rights to be aware of.
- **Some basic tips that may help you and your family: Provide a daily schedule, get daily exercise, maintain good sleep habits and limit electronics (as a parent of 3, I "get it" that we need a break sometimes, but as best as possible!!!!)**

If you are interested in participating in other research about how COVID19 has impacted your family affected by a rare disease, the [Rare Disease Clinical Network](#) has the following survey available: For more information on the RDCRN COVID-19 survey, visit <https://www.rarediseasesnetwork.org/COVIDsurvey>.

Here some other helpful websites that may provide some support for you and your family during this time and as always, feel free to email me or call for anything and I will try to help.

<https://rarediseases.org/covid-19/>
<https://rarediseases.org/in-support-of-rare-disease-patients-impacted-by-covid-19-nord-launches-premium-and-limited-medical-relief-program/>
<https://globalgenes.org/coronavirus-covid-19-resources/>
<https://everylifefoundation.org/covid19/>

Wishing you all a wonderful weekend, and a recent Happy Mother's and Father's Day to all the wonderful parents and caregivers out there!

All my love to you and your families!

Jen

jb3634@cumc.columbia.edu

Cell 908-230-5780

180 Fort Washington Avenue, 5th Floor, Office 519
New York, NY 10032
jb3634@cumc.columbia.edu