



Quarterly Newsletter

| September 2020 | Yellow Brick Road Project HNRNPH2 News

Latest News

The first ever **HNRNPH2 Awareness Week** was held from July 26 to August 1, 2020. It was an astounding success, raising more than **\$50,000** towards research into treatment!

If you missed the amazing Everyday Life series featuring videos of our inspiring patients, you can still find these on the Yellow Brick Road Project Facebook page.

Thank you for helping us spread the word about HNRNPH2 mutations!

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Your support is vital! To donate, please visit our website at www.ybrp.org or our Facebook page at www.facebook.com/yellowbrickroadproject



Featured Family: Meet Maria Miguel

Maria Miguel is 6 years old and she lives in Vila do Conde, Portugal with her parents and her younger sister.



We - the family, her teachers and paediatrician - knew something wasn't right with her neuro-development early in life, but the HNRNPH2 mutation diagnosis only came when she was 3.5 years old.

Before that she had been tested for metabolic and other genetic diseases and for that she had several blood samples, muscle and skin biopsies and an MRI – all normal. It was only when I got pregnant with my second daughter that the hospital allowed the WES (whole exome sequencing) and the worst and longest day of our lives arrived. By that time all the information the clinicians in Portugal had about the mutation was published in one scientific article, describing 6 cases known worldwide. On that day we understood that her specific needs would be forever and that no treatment was known for the mutation (of course); all we could do was to “keep trying to do your best” for her. Fortunately, things have changed a little bit and these days we are all dreaming about a future treatment for these individuals.

Once the shock went way (or more accurately, faded away) we decided to contact the clinicians and publishers of the article and the answers we received were so much better than we expected. Dr. Jennifer Bain wrote us back, introduced us to the HNRNPH2 parents unite group and our lives changed again, but this time for the better. We spent several hours talking to them by Whatsapp and Facebook, learning about the Yellow Brick Road Project, their older kids and their similarities with Maria and one year later we went to the USA to the 2018 Family Meeting. There we met other families and saw children and teenagers that could be our daughter. After years of feeling alone, we could

finally meet adults that truly understood our feelings and fears. That was a unique, priceless and overwhelming experience.

Maria Miguel is a lovely happy girl with beautiful brown eyes and the most wonderful smile in the world. She “earns” everyone’s love with her tenderness and happy demeanour, but also with her kisses and cuddles. She can be pretty stubborn and it’s definitely not easy to make her do something she doesn’t want to. She understands reality much better than some might think and she has us wrapped around her fingers; if she wants to, she can even blackmail you! She loves to sing (and she sings really well) and we usually say she learned most of her vocabulary from songs and movies.

She has moderate to severe global development delay and she is adult-dependent for almost all her daily activities, which we know generates some frustration for her. She can’t walk without support, but she is now learning to use a walker. She speaks and can understand most of our orders. As she is getting older, she is struggling with more



behaviour issues, mainly anxiety. She has speech, physical and occupational (sensory integration) therapies weekly since she was very young and now she also attends hippotherapy (that she adores) and hydrotherapy (waiting for the pandemic to be over to restart). Today is her first day at school so fingers crossed!

Having a child with an ultra-rare disease made us better and more grateful people. We couldn’t love her more.

Spotlight On: Seizures

Just under 50% of patients with HNRNPH2 mutations also experience seizures. They may or not be a sign of epilepsy and they may require medication. But what are seizures and what should you do if the patient you care for has one?

What causes a seizure?

Brain cells are constantly sending messages to each other which control all our thoughts, movements, senses and body functions. The transfer of these messages produces electrical activity. Sometimes there is a sudden, intense burst of electrical activity which causes these messages to get mixed up. When this happens, the result is a seizure.

Types of seizures

Some people have only one type of seizures while others have more than one type. The most common types of seizures are:

1. Focal seizures. These take place in one part of the brain. They may also be called partial seizures. The patient may or may not remain aware of what's happening.
2. Tonic-clonic seizures. Also called grand mal seizures, these are the most recognizable type of seizure. These affect the whole brain. There are two phases: during the 'tonic' phase, the patient loses consciousness and goes stiff. If standing, they will fall to the floor. During the 'clonic' phase, their limbs will jerk. Most tonic-clonic seizures last between one and three minutes. If it lasts longer than five minutes, emergency medical treatment may be needed.
3. Absence seizures. Also called petit mal seizures. These affect the whole brain. Usually the patient loses consciousness, but does not fall. They may appear to be daydreaming or 'spaced out'.
4. Myoclonic seizures. These can affect one side or both sides of the brain. They are sudden, short jerks which can be mild or forceful. They are usually too short to affect consciousness.
5. Tonic seizures. These are similar to the tonic phase of a tonic-clonic seizure. The patient's muscles tighten and their body goes stiff. They usually last less than 60 seconds, but the patient may feel sleepy or confused afterwards.
6. Atonic seizures. Sometimes called drop attacks. All the patient's muscles go limp and their head will drop or they will drop completely to the floor. They usually last just one or two seconds. They regain full muscle control immediately afterwards.

Does having seizures mean you have epilepsy?

Not necessarily. It is possible to have one-off seizures without having epilepsy. Being diagnosed with epilepsy means there is a high chance of additional seizures. It is usually diagnosed after more than one seizure and sometimes following an electroencephalogram (EEG) which measures brain wave activity.

What should I do if my child/patient has a seizure?

Stay as calm as possible. Take a note of how long the seizure lasts and how their body reacts. If they lose consciousness, make sure they are safe and comfortable and cannot injure themselves. If possible, take a video. Tell your doctor about it. They may refer you to a neurologist and/or for an EEG test to monitor electrical activity in the brain.

Status Epilepticus

Status epilepticus is when a seizure or seizures last too long and do not stop on their own. It can happen with any type of seizure, but tonic-clonic status epilepticus is the most dangerous and can sometimes be a cause of death. If your patient has a seizure of any kind that lasts longer than five minutes, you should take them to the emergency room.

Other risks associated with seizures

Besides status epilepticus, there are dangers associated with sleep seizures and with drowning. Medication can help to reduce the risk of sleep seizures. A patient with a history of seizures should never be left unattended in the bath or around water.

Seizure Medications

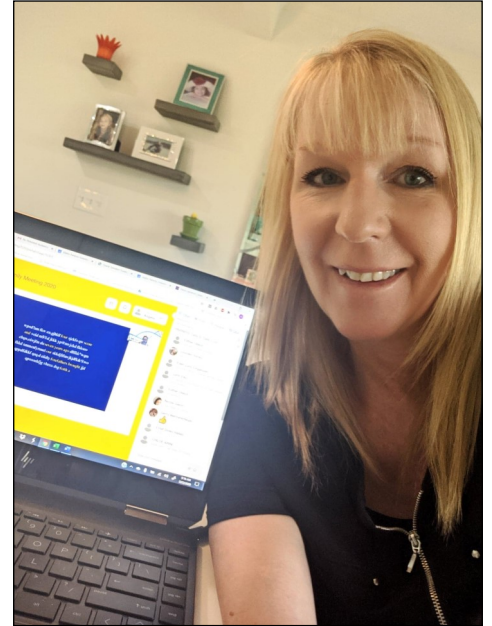
There are many medications available to treat epilepsy. Most HNRNPH2 patients with epilepsy have found that medication helps to control seizures. Along with regular preventative medication, there are emergency medications available to immediately stop seizure activity. You should receive training before using any emergency medications.

2020 Family Meeting

The 2020 HNRNPH2 Family Meeting was held online from July 22 to 24, 2020. The Yellow Brick Road Project was delighted to host many of our patient families as well as the leading experts in HNRNPH2 research and other health professionals.

Highlights of the presentations at the meeting included:

- ◆ From Columbia University Medical Center, Drs. Wendy Chung, Geneticist, Jennifer Bain, Pediatric Neurologist, and Joshua Hyman, Pediatric Orthopedist illuminated what is currently understood about the disorder.
- ◆ Jennifer Tjernagel provided information on Simons Searchlight, the organization that supports rare disease groups like ours in cataloguing, privatizing and safeguarding our rare children's information and making it available for reputable, interested researchers now and into the future.
- ◆ Dr. Yael Gruenbaum-Cohen shared extremely exciting news of the creation of the private company, Andlit Therapeutics, the recipient of the first research grant awarded by the YBRP.
- ◆ Dr. James Eubanks from the Krembil Institute in Canada discussed his preliminary mouse model research findings.
- ◆ Dr. Melissa Carter discussed research she is beginning to work to sort out the overlapping features and connection found between HNRNPH2 and Rett Syndrome.
- ◆ Dr. J. Paul Taylor from St. Jude Children's Research Hospital provided detailed results on the extensive studies he and his team have been conducting since 2016. The news gave direction to potential treatments that will be further validated to intervene on HNRNPH2 mutations.
- ◆ From the orphan drug company Cydan, CEO Chris Adams gave insights into the process of drug development for rare disease and gave guidance based on his 20+ years' experience in the field on how to continue to press forward in our quest for a cure.
- ◆ Dr. Christine Roman spoke on Cortical Visual Impairment, a diagnosis we see being more and more commonly detected among our patients.
- ◆ Donna Appell, Executive Director of the Hermansky-Pudlak Syndrome Network gave an interview to share her thoughts on the topic of the Power of Family Involvement and its importance.
- ◆ YBRP representatives spoke about the mission, summarized activities and funds raised to date, and a look at all that's happened behind the scenes since the last family meeting. Partnerships that have been developed, new committees that have been formed, awareness, data initiatives and fundraising activities were all given special attention.



HNRNPH2 mom Angela Lindig attending the 2020 Family Meeting

Parents of HNRNPH2 patients also had a chance to attend roundtable discussions on areas of interest and contribute to the Natural History Study research.

The YBRP greatly appreciates the time and commitment of all of the presenters and subject matter experts who shared information, answered questions and helped to lead conversations.

Andlit Research Project

The Yellow Brick Road Project is very excited to be partnering on a new research project with **Andlit Therapeutics**.



Andlit Therapeutics is a biotech venture from Medison, one of the world's largest commercial partners of leading global biotech companies. Andlit has been formed specifically to develop therapeutic treatment for HNRNPH2 mutations.

The current project will consist of two main parts:

- 1) researching the expression of the disorder at the cellular level; and
- 2) exploring possible avenues for treatment, targeting therapies based on the results of the stage 1 analysis

Andlit's CEO, Dr Yael Gruenbaum-Cohen, attended and presented at the 2019 and 2020 HNRNPH2 family meetings. She has assembled an exceptional team of researchers and scientific advisors which will be overseen by Andlit's CTO, Dr Rotem Karni. Dr Karni works in the Faculty of Medicine at the Hebrew University of Jerusalem where his lab is involved in genetic research.



Dr Gruenbaum-Cohen

Dr Karni

Please visit the Andlit website for more information at <http://www.andlit.com>

The Disorder Channel

Like most events this year, the Disorder Rare Disease Film Festival was postponed due to COVID-19. However, the coalition behind the festival has now launched The Disorder Channel as a new platform to provide another showcase for rare disease films. It features many previously unseen rare films and original videos. The channel also includes some films intended for this year's festival as well as favourites from previous years. The aim is to raise awareness, find a cure and spread hope for those affected with a rare disease or a genetic disorder.



YBRP's **Quest for a Cure** is one of the featured films. The Disorder Channel is available through Roku or Amazon Fire TV. Please see their website for more details: <https://www.thedisordercollection.com/>

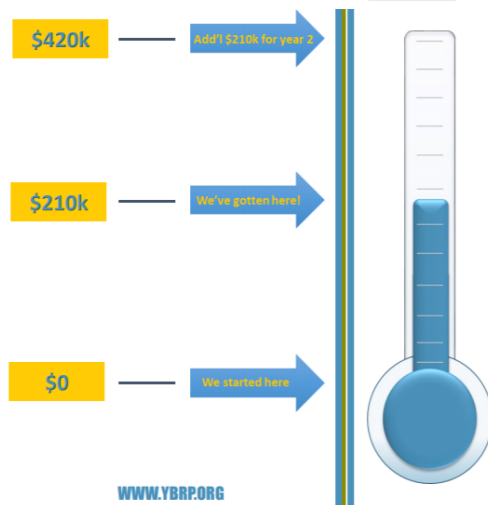
Fundraising Update

The grant that the Yellow Brick Road Project has awarded to Andlit Therapeutics is to provide \$420,000 for research into HNRNPH2 mutations and potential treatments.

In July 2020, the first payment of \$150,000 was issued from funds that were raised in previous years. Since then, through the efforts of our wonderful parents and partners, we have succeeded in raising an additional \$60,000.

We still need to raise an additional \$210,000 by July 2021 in order to continue funding this important work.

There are many ways to get involved and contribute to our fundraising efforts. Please visit our website at www.ybrp.org for all the details or read on to learn more about two of these efforts.



Fundraising: Maria's Family's Story

We wanted to help the YBRP since we first met other families like ours at the 2018 family meeting, but when the foundation signed the agreement with Andlit to fund research into HNRNPH2 mutations we decided to go much further. Maria is getting older and there are no specific treatments available for this rare syndrome so time is running out and the time is NOW.

Sharing our daughter's life with the world - her struggles, disabilities and achievements - was not an easy decision. We are obviously submitting her to a lot of exposure, but the goal is so big that we can not give up. We need help... we need to get more people to know us, we need to keep searching for more individuals, we need clinicians and scientists to get curious and continue with the great job they're doing - studying the gene, its mutations and their consequences. So we need to share.

Earlier this year I went to our national TV to speak about "Caregiver Burnout", because raising a child with a rare disease can be hard and sometimes we get lost and feel like throwing in the towel. Later we realized we needed to have a greater way to share our lives and news about Maria; the YBRP website and Facebook page are great, but they share general information about all the individuals and, of course, always in English. So Maria's Facebook page - [O Sorriso da Mariocas \(Marioca's Smile\)](#) - was created and since then we try to keep it updated and share with as many people as we can. Also, we were invited to talk about this little project on the TV, which was pretty nerve-racking but also amazing; since that moment our page has grown a lot and we've received messages from people all over the world.



Right now, our major goal is to help raise money to fund the research that is being done. The first big fundraiser we created was overwhelming and we raised the incredible amount of 13,631€ (~\$15,800); but we want to contribute with much more than this and another fundraiser was created after that. We believe the key to success was to share videos and photos of Maria to illustrate our stories that helped people understand better why we need this research to proceed.

With some friends' help, we've designed masks that we can all use with our YBRP logo and the profit will go directly to the fundraiser. It's our daughter's and many other kiddos' quality of life we're talking about so we will not leave it to chance. Join our cause and help us all.

The Bricklayer Program

The YBRP's new Bricklayer Corporate Sponsorship Program is a program that enables companies and organizations to be a part of something ground-breaking. A pathway to treatment for HNRNPH2 patients has been identified using cutting edge medical technology and we are inviting businesses and organisations to be a part of our journey. The Bricklayer Program is a sponsorship program where companies can sponsor a local HNRNPH2 patient with an annual sponsorship and help drive important research towards treatment and a cure, in exchange for some great benefits from YBRP. Help us lay the bricks that will build the road to a cure for these amazing individuals!



ABOUT THE PROGRAM

Sponsors will receive a letter in which they will learn about one of our patients, each of whom has their own unique story. Each sponsor will receive regular updates on their sponsored child, as well as updates on HNRNPH2 research underway to improve the lives of all HNRNPH2 patients.

With this annual commitment, the YBRP can continue to fund this critical research as we work toward our goal of funding our first two-year research project into therapeutics for HNRNPH2 mutations.

If you know a business or organisation that would like to take part, please contact projectybr@gmail.com

SPONSORSHIP LEVELS

	Annual sponsorship amount	Sponsor benefits
RUBY	<ul style="list-style-type: none"> • \$1500 US/Cdn/Aus • or £1000 GBP • or 1000€ Euro 	<ul style="list-style-type: none"> • Logo on YBRP website • Update Letter
ROYAL	<ul style="list-style-type: none"> • \$2500 US/Cdn/Aus • or £2500 GBP • or 2500€ Euro 	<ul style="list-style-type: none"> • Logo on YBRP website • Update Letter • Social Media Post
GOLD	<ul style="list-style-type: none"> • \$5000 US/Cdn/Aus • or £5000 GBP • or 5000€ Euro 	<ul style="list-style-type: none"> • Logo on YBRP website • Update Letter • Social Media Post • Mention in Meeting Program
EMERALD	<ul style="list-style-type: none"> • \$10,000 US/Cdn/Aus • or £7500 GBP • or 7500€ Euro 	<ul style="list-style-type: none"> • Logo on YBRP website • Update Letter • Social Media Post • Mention in Meeting Program • Signage at Meeting

Natural History Study Update

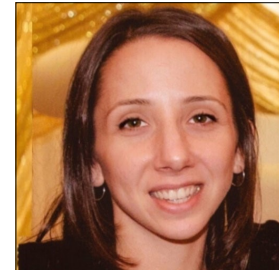
The newsletter will contain a regular update from the research team conducting the HNRNPH2 Natural History Study. Dr Jennifer Bain is the principal investigator and Olivia Thornburg is her Research Assistant. They are based at Columbia University in New York City, USA.



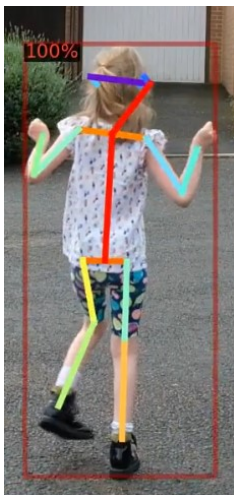
Dr Jennifer Bain

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



Annotated version of gait video analysis

The Bain Research team is thrilled to continue the HNRNPH2 Natural History Study this year using a virtual platform. They are extremely grateful to the families who continue to return every year and provide updates and excited to meet the new families affected by HNRNPH2. The research team has submitted 2 manuscripts for publication and hope to share them with you soon. This year, the team continued to focus on physical motor outcomes but also expanded on the gait assessment using new video technology. They also expanded on the occupational therapy evaluation to include more standardized data collection that will also be shared back with families to use with their our therapy teams. Altogether, the Bain Research team completed 162 assessments from 41 families spanning 19 countries.

	2016	2017	2018	2019	2020
# Countries Represented					
# Total Families Participating		4	14	21	41
# Assessments		0	48	88	162