HNRNPH2 FAMILY MEETING

JULY 26-27, 2018

NYP - CENTER FOR AUTISM AND THE DEVELOPING BRAIN, NEW YORK

WRAP UP

YELLOW BRICK ROAD PROJECT (YBRP)

JENNIFER M. BAIN, COLUMBIA UNIVERSITY MEDICAL CENTER

SIMONS VIP

SUMMARY OF SPEAKERS

- **Dr. Wendy Chung (Columbia, Simons VIP)**
  - Genetics 101
  - This is NO ONE'S "fault"
- **Dr. Hong Joo Kim (St. Jude's Children's Hospital)**
  - Using cell lines and induced pluripotent stem cells (iPSCs) and mini brain organoids to study HRNPH2 function both in normal development or variants (mutants)
  - They have found differences in the behavior of the different variants in cell lines
- **Dr. Ane Korff (St. Jude's Children's Hospital)**
  - Using animal models (mouse lines) to study HRNPH2 function both in variants (mutants)
  - They have found differences in the behavior of the different variants in mice

- **Amy Lerner, Occupational therapist**
  - Many of the individuals have sensory issues
  - She has MANY resources and recommendations you can check out to help.
- **Andreia Boutard-Zanelato, Physical therapist**
  - PT is necessary for muscle development and should be started as early as possible, even BEFORE a diagnosis is made
  - "Do not set limits we do not know." We must DEFINE the limits!
- **YBRP**
  - Try to reach out and find more HNRNPH2 cases
  - Try to help with fundraising and bring awareness locally
  - Share your skills with our team so you can help too

- **Stephanie Bellatoni, Outreach Coordinator**
  - Navigating and advocating in the educational maze
  - Know your limits but be an important member of the discussion
- **Dr. Arezou Heshmati**
  - Discussed better sleep hygiene, aka “behavioral strategies”
  - Reviewed some of the sleep questionnaire feedback & explained the difference between sleep studies and overnight EEG
- **Nicole Jablon, LMSW**
  - Caring for the caregiver session

1 paper
6 girls

First Family Meeting
4 parents
Bain & Chung
CUMC, NYC

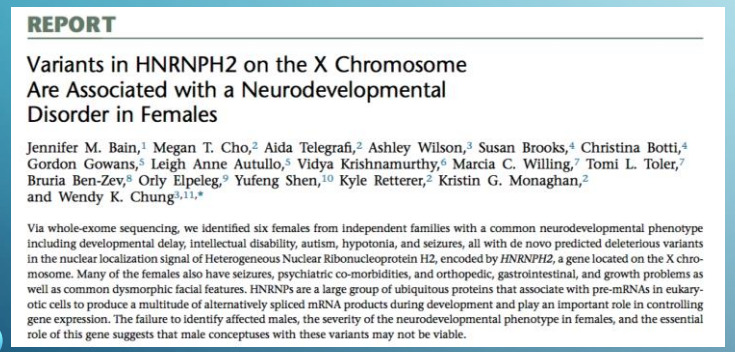
Simons VIP
10 girls

CUMC Registry
> 20 girls

September 2016

January 2017

January 2017



REPORT

Variants in HNRNPH2 on the X Chromosome Are Associated with a Neurodevelopmental Disorder in Females

Jennifer M. Bain,[1] Megan T. Cho,[2] Aida Telegrafi,[2] Ashley Wilson,[3] Susan Brooks,[4] Christina Botti,[4] Gordon Gowans,[5] Leigh Anne Autullo,[5] Vidya Krishnamurthy,[6] Marcia C. Willing,[7] Tomi L. Toler,[7] Bruria Ben-Zev,[8] Orly Elpeleg,[9] Yufeng Shen,[10] Kyle Retterer,[2] Kristin G. Monaghan,[2] and Wendy K. Chung[3,11,*]

Via whole-exome sequencing, we identified six females from independent families with a common neurodevelopmental phenotype including developmental delay, intellectual disability, autism, hypotonia, and seizures, all with de novo predicted deleterious variants in the nuclear localization signal of Heterogeneous Nuclear Ribonucleoprotein H2, encoded by *HNRNPH2*, a gene located on the X chromosome. Many of the females also have seizures, psychiatric co-morbidities, and orthopedic, gastrointestinal, and growth problems as well as common dysmorphic facial features. HNRNPs are a large group of ubiquitous proteins that associate with pre-mRNAs in eukaryotic cells to produce a multitude of alternatively spliced mRNA products during development and play an important role in controlling gene expression. The failure to identify affected males, the severity of the neurodevelopmental phenotype in females, and the essential role of this gene suggests that male conceptuses with these variants may not be viable.

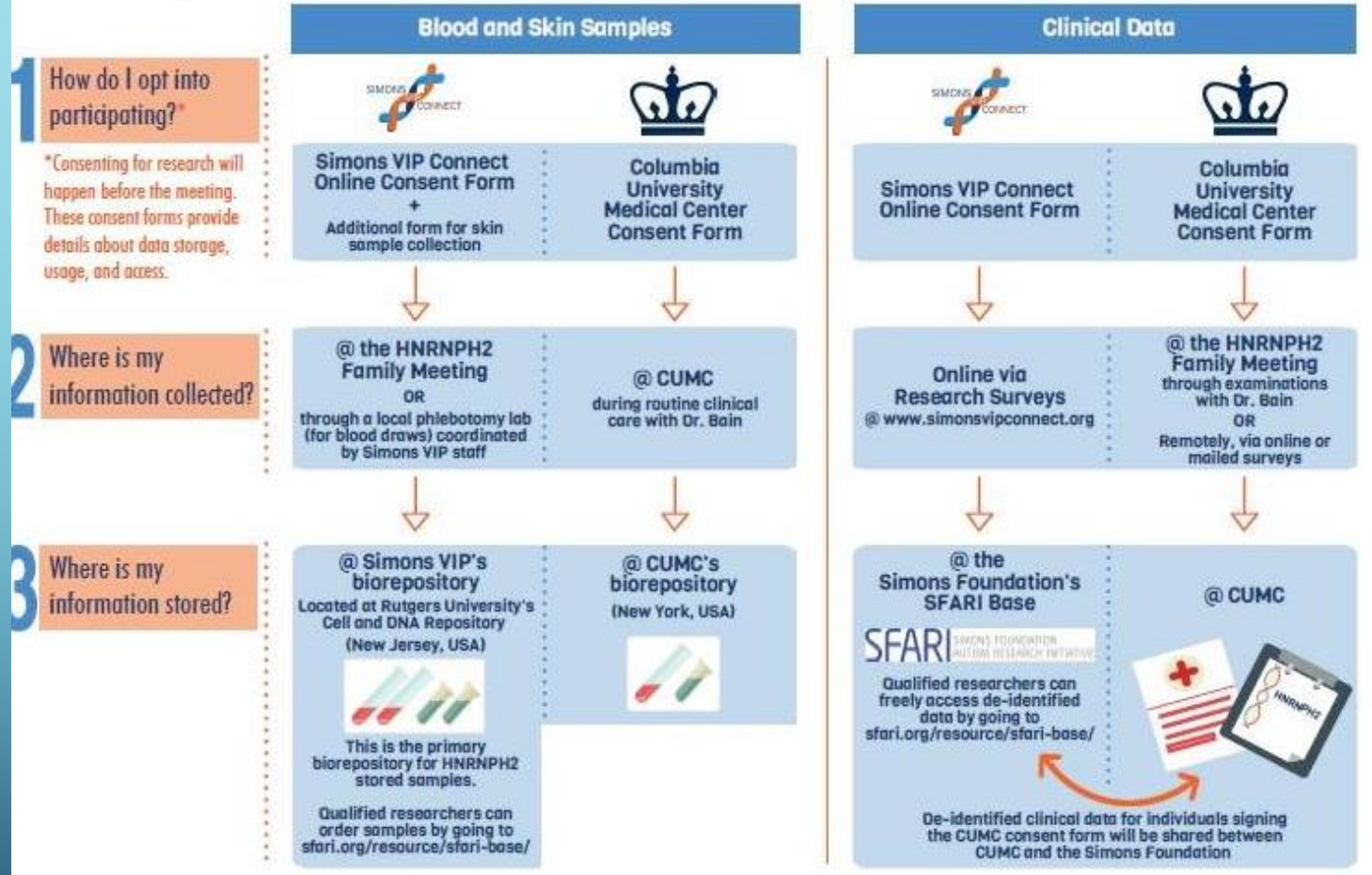
p.Arg206Trp (15)
p.Arg206Gln (4)
p.Arg206Gly (1)
p.Pro209Leu
p.Tyr210Cys (2)
p.Arg212Thr (1)
p.Asp340Val (1) *

p.A371Cfs (1) *

Still unknown variant (5)

Research at the HNRNPH2 Family Meeting

Dr. Jennifer Bain from Columbia University Medical Center (CUMC) and Simons VIP Connect are collaborating to collect samples and research data from families at the upcoming family meeting. Any information your family opts into providing may be accessed by researchers interested in learning more about HNRNPH2 genetic changes. As part of the meeting's research activities, the Simons VIP team will be offering blood draws/skin biopsies for eligible families and Dr. Bain will be completing various clinical evaluations. Below is a breakdown of how you can consent to being involved in research, where the data may be collected, and how it is stored and accessed by researchers:



If you have any questions about consenting for sample/data collection or the research process, please reach out to the Simons VIP Connect coordinators:

EMAIL: coordinator@simonsvipconnect.org PHONE: 1-855-329-5638

HNRNPH2 FAMILY MEETING 2018

- **Day 1**
  - Simons VIP —> Blood draw
  - Basic check up: height, weight, head circumference —> ALL 10 GIRLS
  - History & Physical examination (Jen Bain) —> ALL 10 GIRLS
  - Physical therapy assessment (Rachel, Nicole, Sara) —> ALL 10 GIRLS
  - EEG assessment (Dr. Goldman, Natasha, Arielle & Christina) —> ALL 10 GIRLS
- **Day 2**
  - Gait assessment (Dr. Goldman's team)
  - Foot and Face Portraits (Physical therapy team)

SUCCESSFUL FIRST HNRNPH2 MEETING!

- 10 girls
- 14 families
- 10 neurological exams
- 10 physical therapy assessments
- 10 EEGs
- 3 skin biopsies
- 5 blood collections
- 6 gait assessments
- 9 face portraits
- 9 feet portraits

THANK YOU

- YBRP
- Olivia Thornburg
- Neuromuscular/PT Team: Rachel Salazar, Sara Beenders, Nicola Holuba
- Sylvie Goldmans Team
  - Christina Layton
  - Cheryl Pan
  - Sophia Wyne
  - Natasha Yamane
  - Damiano Zanotto & Team

Keep in Touch — and please watch your emails for more research emails!

THANK YOU!!

SEE YOU SOON!