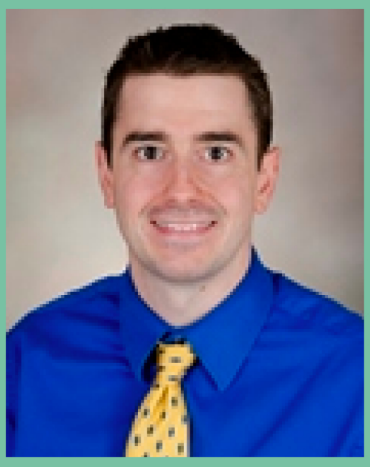
NBIAcure NEWSLETTER
- AUGUST 2018 -

Team Member Spotlight



Dr. Caleb Rogers is a Pediatric Geneticist who joined our team in 2014. In clinic, Caleb works with kids and their families to diagnose and treat genetic disorders.

He started working with the NBIAcure team on two different research projects. His first project involved examining the MRIs of patients with NBIA disorders in order to see if the density of iron accumulation could indicate a specific subtype of NBIA (PKAN, BPAN, MPAN, etc). Caleb explained that this can be important in a clinical setting, because insurance companies may cover testing on only some genes. If studying a patient's MRI helps indicate which gene to test for, then this can help families get a diagnosis faster and at a lower cost.

Caleb also works on Whole Exome Sequencing (WES) for undiagnosed NBIA patients. For this project, Caleb has helped analyze genetic data for 54 families and found diagnoses for 20 of them. While 54 families may not seem like a large number for four years of work, each family's genetic data is vast. In total, Caleb has sifted through more than 200,000 genetic variants, trying to find which may be causing disease. He continues combing through the genetic information as we learn about more genes, all while working full time as a clinician!

To learn more about the WES project, please see page 2

Goals for BPAN Research

A family whose child has BPAN recently asked us to "give them a goal" for fundraising. This got us thinking about what, in a perfect world, our team would need to accelerate BPAN research. We realized that what we really need is a BPAN focused Post-Doc!

For PKAN we have a wealth of data both from the PKANready Natural History Study, as well as from lab experiments and our mice models. Here at OHSU, Assistant Professor, Dr. Suh Young Jeong works hard on all NBIA disorders but currently is focused on PKAN experiments as we get closer to a clinical trial. (Tune in to the October Newsletter to read more about Suh).

The BPAN Natural History Study just recently launched, and thanks to over 40 families who have already enrolled, information on BPAN is starting to build up. In addition to continued enrollment and participation in BPANready, the piece we need to make BPAN treatment a reality is more robust lab research. In order to better understand the WDR45 gene, the pathways in the body it affects, and targets for possible therapeutics, we would need another postdoctoral researcher to join our lab. While our team has brainstormed, hypothesized and done experiments for many of the NBIA disorders, what we really want and need is for someone to join our team who can focus solely on BPAN. We would be looking for someone with strong experience in autophagy, one of the main functions that is disrupted in BPAN, as well as a deep desire to work in the rare diseases field.

Apart from finding this Post-Doc researcher with autophagy experience and an interest in BPAN, we would also need to guarantee funds for them for at least three years. Including salary, benefits, research supplies and lab space, we would need a sum of $150,000 per year - a total of $450,000. While that may seem like a hefty goal, we believe the advances in BPAN research that would be made would be well worth it. If you would like to contribute to the goal of an OHSU BPAN Post Doc, please click on the link to the left to access the BPAN-specific Research OHSU Foundation Page.

OHSU FOUNDATION DONATION PAGE

Searching for a Diagnosis using WES

In 2014 the Hayflick lab started a project with the University of Washington to sequence DNA for our patients who did not yet have a genetic diagnosis. These 54 subjects had symptoms similar to those of NBIA, but they did not have variants in any of the known NBIA genes. These samples were tested at the University of Washington using Whole Exome Sequencing (WES). The team at UW sent us back all the genetic variants they had found. These included genetic changes that were benign (not disease causing), changes that are pathogenic (disease causing), and changes with unknown effects.

Dr. Caleb Rogers started his search narrow, and looked for any variants in known NBIA genes. He then progressively broadened his scope, including genes that are associated with ataxia, dystonia and other neurological diseases. For patients who still did not have a diagnosis, he looked at genes that were known to have a strong, negative impact on the body if they are not functioning correctly. Once a potential variant is found in a gene, lab scientists like Dr. Suh Young Jeong look at the function of that gene to see if it is related to iron accumulation, CoA, autophagy, or anything else we have seen in NBIA. Dr. Hayflick and Dr. Hogarth also weigh in, and determine whether losing function in this gene would match the symptoms of the patient. If all this lines up, then a tentative diagnosis is given to the patient, and the search to find more patients with this diagnosis begins. A great example of this project in action is on the NBIA website, and follows Mike Cohn's road to a diagnosis of MePAN.

Even with our team searching through WES data with a fine toothed comb, 63% of the families still have not received a diagnosis. This is the case for many reasons, such as sequencing mistakes, variants that are not in the part of DNA that WES sequences, and the fact that we do not yet know what all of the genes in our DNA do. However, the search continues. Each time we learn about a new gene, we go through our data again, searching for another diagnosis.

WES Statistics

20 Genetic diagnoses made

200,00+ Genetic variants analysed

600 Gigabytes of data stored

Familiar Faces!

Right to Left: Leila Schwanemann (our previous study coordinator) visited Brent Bonfiglio and his parents Veronica and Gaetano in Fremont, California. On a recent trip to Northern California from her new home in Southern California, Leila met up with Brent and his family. They all had a chance to catch up and eat gelato at the Bonfiglio's family owned gelato shop!