NBIAcure NEWSLETTER

- OCTOBER 2018 -

Team Member Spotlight

Dr. Suh Young Jeong has been a part of the Hayflick lab since 2014. Originally from South Korea, Suh moved to Canada for her graduate education at McGill University. She has been involved in NBIA research since her PhD research also at McGill University. There she studied ceruloplasmin protein, a protein that is deficient in people with an NBIA disorder, Aceruloplasminemia. At the time, PKAN was the only other, known NBIA disorder. So, while Suh was studying the ceruloplasmin protein, she admits to also having PKAN in the back of her mind.

Fast forward to 2010. Suh was continuing to study iron in brain at the National Institute of Health in Bethesda, Maryland. That same year, the NBIA Disorders Association had their scientific meeting right next door. Suh presented some of her work at the meeting, and was able to meet Dr. Hayflick.

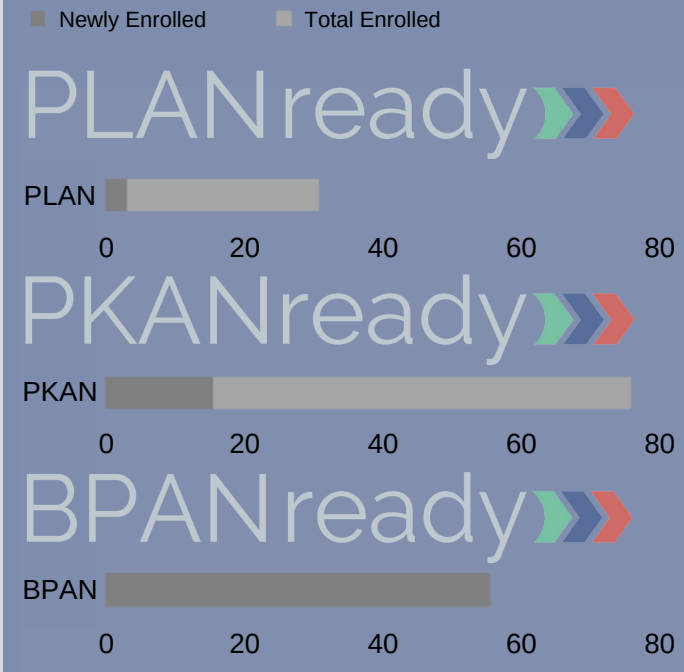
A few years after this meeting, Suh started to look for another position and she had a specific criteria in mind. While she enjoyed her past jobs, she felt that she was missing a human component. She wanted to be where her work would not only be academic, but would also have a practical impact on peoples' lives. Suh's first choice was to work for Dr. Hayflick because not only does she combine clinical care with research, but it is her investment in her patients that drives Dr. Hayflick to do research in the first place.

Suh, with her specific background and expertise, has been instrumental in driving PKAN research. When Suh arrived, our team had a PKAN mouse, but the mouse did not show any outward signs of PKAN. In fact, it did not look any different at all! Suh set to work trying to find a difference. Her work eventually led to the discovery of the first biomarker that we can use as a kind of "measuring stick" for the effectiveness of possible PKAN therapeutics in mice. Without this measuring stick, CoA-Z could never have been tested in the mouse model, let alone potentially transferred to humans.

Suh's success illustrates that because NBIA disorders have various origins of disease (e.g. energy metabolism vs. autophagy) we need experts with the right background to research each disease. This is why we believe the next step to accelerate BPAN research is to have a dedicated postdoctoral researcher with a background in autophagy.

NBIAready Updates

Enrollment progress since February 2018



Skin Biopsy Updates

You may recall "The Life of a Skin Biopsy" from our June Newsletter, well the saga continues. We are not only asking patients for samples, but are now getting healthy control samples too! When our lab runs experiments using NBIA patient skin biopsies, it is important that they have healthy skin samples to compare the results with. These samples ideally should be from children around the same age, without an NBIA disorder. As you can imagine, young, healthy children are not lining up at the door to receive a skin biopsy! Recently our team partnered with the surgical unit at OHSU. Now when a child is getting a surgery we are able to obtain a small piece of skin, with their parents consent. They won't miss it, and we can use it in NBIA research for years to come.

Suh's Favorite Experiments

"I actually have two favorite experiments. The first one was testing the psychological behavior of PKAN mice. It was really interesting to learn about behavioral characteristics in mice that can reflect PKAN patients, even if we did not get the results we were hoping for."

"My other favorite experiment was seeing how physiologically effective CoA-Z was. As we feed the drug to mice and cells, our biomarkers responded according to dosage, treatment period and the withdrawal time. This data indicated that CoA-Z can be effective yet safe in human.."

MEPAN Website

Our website has recently been updated to include a section with information about Mitochondrial Enoyl CoA Reductase Protein-Associated Neurodegeneration (MEPAN). To learn more about MEPAN, click on the link below.

http://nbiacure.org/learn/nbia-disorders/mepan/

Timeline

For many of you (and for us too!) it might feel as if you have waited forever for a clinical trial. We wanted to give you an idea of all that has been accomplished, with your help, since the discovery of the *PANK2* gene, as well as our next steps. We hope that other NBIA disorders will follow a similar or faster trajectory towards therapeutic development and we are especially encouraged by the enormous progress that has been made in the last 3.5 years years alone.

1922

PKAN is first described and originally called "Hallervorden-Spatz syndrome"

1996

Genetic cause of PKAN narrowed down to chromosome 20

2001

Mutations in the *PANK2* gene are discovered to be the cause of PKAN

2005

First mice with the *PANK2* gene "turned off" are created in collaboration with UCSF

2010

Fruit flies with *pank2* mutations are created by Dr. Sibon's team to better understand PKAN

Pantethine is discovered to rescue fruit flies with PKAN but can't cross the human blood-brain barrier

2015

The PKANready natural history study is launched

Dr. Sibon's team was able to find a compound that crosses the blood-brain barrier (now called CoA-Z)

New mice with different *pank2* mutations are created using funding by the NBIA disorders Association

2016

Mice with PKAN are fed CoA-Z and it normalizes all chemical signs of the disease in the brain

2017

A blood biomarker is discovered by Dr. Jeong that allows us to measure disease and response to treatments

Dr. Hayflick and Dr. Hogarth meet with the FDA , who are enthusiastic about the project and support a fast route to developing CoA-Z

A nonprofit organization called the Spoonbill Foundation is created to facilitate the developing of CoA-Z and to keep the price as low as possible

2018 and Beyond

Step 1 A manufacturing company is identified to find the best method of producing large batches of highly pure CoA-Z

Step 2 Our collaborators develop a version of CoA-Z that can be dispensed through a g-tube or taken by mouth

Step 3 Drs. Hayflick and Hogarth meet again with the FDA, who are supportive of our idea for a remote clinical trial

Step 4 Our team begins preliminary packaging and formulation studies to narrow down the options

Step 5 In August 2018, the manufacturing company discovers a process to make highly pure CoA-Z and begins production of the first large batch

Pending Complete formal shelf-life studies for CoA-Z to determine the ideal packaging and storage methods

Pending Receive final approval from the FDA for our clinical trial design

Pending Formulate and package CoA-Z for distribution to clinical trial participants

Pending Work with regulatory authorities in other countries to allow CoA-Z to be tested worldwide