News from the Hereditary Disease Foundation

A Scientific Journey Starts with Yeast

For Joan Steffan, Ph.D., Huntington's disease (HD) researcher and member of the Hereditary Disease Foundation Scientific Advisory Board, science is an exciting family tradition. Both of her parents were scientists. She entered graduate school at University of California, San Diego and became a reproductive endocrinologist because she wanted to be like her father – Dr. Charles H. Sawyer, a groundbreaker in the field of neuroendocrinology. She later decided to pursue a different scientific path – as a yeast geneticist. Yes, the same yeast used to bake bread is a great tool to study mammalian cells. "Yeast cells are easy to manipulate and a simple model to study the processes of everyday human cells," she points out. What followed is a brilliant career in which she has become one of the top researchers unlocking the secrets of HD.

"Science is a fun career because everyone gets an opportunity to put a brick in the wall. I'm grateful that HDF gave me the chance to put my brick into the wall of Huntington's research."

In 1998, Joan left yeast genetics and moved into the field of human genetics, joining the University of California, Irvine lab of her longtime friend and pioneering HD researcher Leslie Thompson. Leslie is also a member of the HDF Scientific Advisory Board and was the 2013 recipient of the Leslie Gehry Brenner Prize for Innovation in Science.

"We knew that the abnormal protein was killing brain cells in HD. We wanted to discover how it was doing it. Could we stop it, slow it down or influence its path of death and destruction?" Joan says. In 1998, they submitted their project to the Hereditary Disease Foundation for funding. "Nancy Wexler flew out to the lab at UC, Irvine and wanted to know how soon we could start and how much funding we needed," Joan recalls. "She was immediately wonderful and supportive."

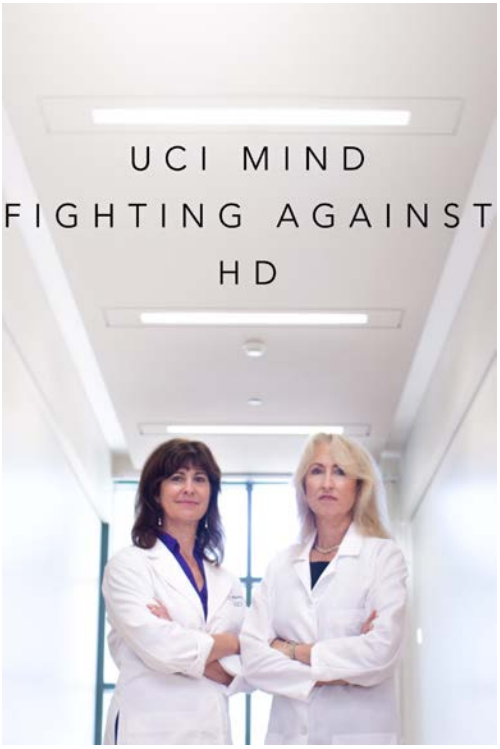
Taking Out the Trash: How a reduction in cellular housekeeping in the brain may contribute to the onset and progression of HD.

Joan discovered that one of the normal Huntingtin protein's functions is in a cellular process called "autophagy" that has been genetically defined in yeast. Autophagy normally enables a cell to take out and recycle its "garbage." When the cell gets too stressed from accumulating trash, for example in aging or disease, it turns on this cleaning process. In HD, brain cells accumulate trash, perhaps because of the reduced function of the abnormal Huntingtin in autophagy. The abnormal version of the Huntingtin protein creates huge sticky aggregates – "clumps" – that gum up the works. It sticks everywhere when autophagy fails, and accumulates with the garbage.

Joan is studying how to turn on and off these trash collection pathways. Joan has discovered several modifications of the normal Huntingtin protein that allow it to clean the cell most effectively. These modifications are like zip codes, directing Huntingtin to activate autophagy and clear cellular waste in the appropriate part of the cell. Huntingtin's normal function of keeping the cell clean reduces cellular stress. When this process is impaired by abnormal Huntingtin, the cell becomes stressed, just like in a city when the cleaning crew goes on strike and trash accumulates on every corner! We can target new therapies and cures when we understand more about Huntingtin's normal function in autophagy, and how those functions are altered in HD.

The Family Is at the Table

Joan's role on the HDF Scientific Advisory Board allows her to work with other distinguished scientists in setting the scientific priorities for the Foundation and ensuring that the most innovative and promising research projects are funded. "HDF funded my research all the way through, and allowed me to contribute my piece to Huntington's disease research. It's a privilege to be able to play a part in continuing the support for HD-scientists in the US and abroad as we work together to understand the complexities of HD and to find treatments and ultimately cures."



Joan Steffan and Leslie Thompson in the Institute for Memory Impairments and Neurological Disorders at the University of California, Irvine (UCI MIND).

Joan places great value on the collaborative spirit the Hereditary Disease Foundation fosters among scientists. "True collaboration is everything," she says. "HDF is really a family. The family is seated around the table and everyone has a chance to contribute to the conversation."

HDF Funding Future Research

Our deadline for receiving Letters of Intent from scientists for funding this year was February 1. We are excited to report that we've received over 100 Letters from countries around the world, including the US, Switzerland, New Zealand, France, Hungary, Spain, India, the United Kingdom, Cyprus, Italy, Argentina, Denmark, Germany, Greece and Portugal. Our Scientific Advisory Board will review and select the most innovative and promising projects to fund. Thanks to all of the scientists who are dedicated to HD research. And thanks to all of you who are making it possible for us to support their vital work. Research is making a difference!

Innovating Research…Discovering Cures

Donate Today

Contact Us:

Web
Twitter
Facebook

Published February 2019