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The search for Huntington's disease treatments is indeed 'rocket science' – and we can all help build the rocket

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At Risk for Huntington's Disease

HD is a genetically caused brain disorder that causes uncontrollable bodily movements and robs people's ability to walk, talk, eat, and think. The final result is a slow, ugly death. Children of parents with HD have a 50-50 chance of inheriting the disease. There is no cure or treatment.

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WEDNESDAY, MAY 20, 2015

The search for Huntington's disease treatments is indeed 'rocket science' – and we can all help build the rocket

For people facing Huntington's disease and other devastating, untreatable conditions, the powerful wish for a cure can conjure up the image of an elated scientist bursting from a laboratory and declaring "Eureka!"

However, it is unlikely a treatment for HD will emerge in this way.

We often misunderstand scientific progress, as explained in an essay in the May 16, 2015, edition of *The New York Times* by prominent physicist Leonard Mlodinow, Ph.D.

"Why do we reduce great discoveries to epiphany myths?" asked the sub-headline for Dr. Mlodinow's online article, which was titled "It Is, in Fact, Rocket Science."

"The mythical stories we tell about our heroes are always more romantic and often more palatable than the truth," Dr. Mlodinow writes. "But in science, at least, they are destructive, in that they promote false conceptions of the evolution of scientific thought."

From Isaac Newton to Charles Darwin to Stephen Hawking, we have oversimplified the process of discovery, Dr. Mlodinow explains. Rather than the eureka moments popularized in books and the media – like the apple falling on Newton's head – these scientists' discoveries involved years of hard work and questioning of assumptions, including their own.

Thus, Dr. Mlodinow reminds us that breakthroughs result from the cumulative build-up of *many* moments of discovery by scientists past and present.

He thus underscores a crucial point for the Huntington's disease community: finding treatments will necessarily involve a *collective* effort by scientists and volunteers in research studies and clinical trials.

"Even if we are not scientists, every day we are challenged to make judgments and decisions about technical matters like vaccinations, financial investments, diet supplements and, of course, global warming," Dr. Mlodinow points out. "The myths can seduce one into believing there is an easier path, one that doesn't require such hard work."

We in the HD community must all play our part in the quest for treatments.

A eureka moment deflated

As a carrier of the deadly HD mutation who watched his mother succumb to the disease, I have sometimes fallen prey to the seductive scenario described by Dr. Mlodinow, and even done so in this blog.

HD Links

Huntington's Disease Society of America
International Huntington Association
Huntington's Disease Drug Works
Huntington's Disease Lighthouse
Hereditary Disease Foundation
Huntington's Disease Advocacy Center
Thomas Cellini Huntington's Foundation
HDSA Orange County (CA) Affiliate
HD Free with PGD!
Stanford HOPES
Earth Source CoQ10, Inc.

HD Blogs and Individuals

Chris Furbee: Huntingtons Dance
Angela F.: Surviving Huntington's?
Heather's Huntington's Disease Page

Four years ago this month, I was so excited about Alnylam Pharmaceuticals' progress towards a remedy that I posted a picture of myself holding an Alnylam compound designed to attack HD at its genetic roots. I wrote that the compound, "the potential cure in my hand," seemed magical.

I later made the image my Facebook profile photo.

(See the photo below and click here to read more.)

Gene Veritas holding the Alnylam compound in 2011 (photo by Dr. Matthias Kretschmer, Alnylam)

I had perhaps become overconfident about the Alnylam project.

In collaboration with its partners Medtronic and CHDI Foundation, Inc., the nonprofit virtual biotech focused on HD treatments, Alnylam was planning to apply in 2012 for permission to start a clinical trial.

In early 2012, however, Alnylam cut a third of its work force in order to reduce costs. In May of that year, less than a year after my 2011 visit, the company shifted its business strategy. It downgraded the HD project and fired the scientific director in charge

Alnylam chose instead to concentrate on less complex – and perhaps more profitable – projects to find drugs for other conditions. Alnylam passed on the responsibility for testing the compound in a human clinical trial to Medtronic.

To date, Medtronic has announced no plans for a human clinical trial of the Alnylam compound.

"Medtronic believes the siRNA [gene-silencing] drug-device program continues to represent an exciting opportunity to combine an innovative therapeutic strategy with state-of-the-art drug device delivery technology for Huntington's disease," Jack Lemmon, Ph.D., a Medtronic program

manager, responded in an e-mail to my request for an update on the project. "Pre-clinical work has generated promising results; however the therapy research program has been paused since 2013 until partnerships can be established allowing us to sustain the research. At this time, it is premature to discuss timeframes, but we hope to continue work to find a treatment for this devastating neurodegenerative disease."

Shots on goal

I am concerned that the project runs the risk of entering a not uncommon limbo, which one former director of the National Institutes of Health calls the "valley of death," the increasingly difficult transition between laboratories and clinical trials.

Devising the Alnylam compound involved a significant investment of time, money, and expertise. In my extensive interviews with Alnylam scientists in 2011, and even in a conference call with some of those same researchers after the announcement of the 2012 cutback, they expressed enthusiasm about the promise of the compound.

The Alnylam compound may – or may not – ultimately play a role in the search for treatments.

Without the Alnylam compound, the HD community would have one less shot on goal in the critical gene-silencing field.

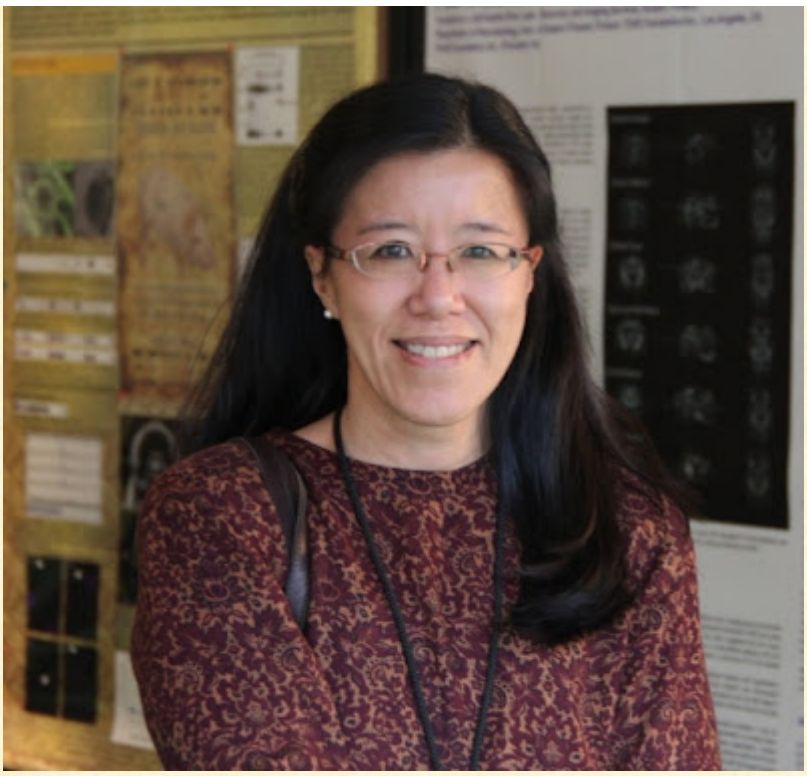
I am disappointed at the lack of action – much less progress – regarding the Alnylam compound.

Fortunately for the HD community, one of those shots is scheduled to take place this year: Isis Pharmaceuticals, Inc., and Roche will start a historic gene-silencing clinical trial using a different type of drug technology. Other companies and labs are also focusing on the development of gene-silencing approaches for HD.

The Alnylam project didn't meet the expectations of many in the community. However, it has still provided valuable data from which other researchers can benefit. I am grateful for Alnylam's contributions to the quest for treatments, and I'm crossing my fingers that Medtronic can resume the project.

I indeed recognize that the path to treatments is not easy. Nor is it straight.

One example of a potentially fortuitous outcome of the Alnylam decision: the dismissed HD project director, Dinah Sah, Ph.D., now works as the senior vice president of neuroscience for Voyager Therapeutics, one of the new companies exploring gene-silencing for HD.



Dinah Sah, Ph.D., of Voyager Therapeutics (photo by Gene Veritas)

A road paved with cooperation

Enthusiasm is essential, but it must be tempered with the recognition that scientists need time – and money – to test hypotheses.

It took some two decades to discover the huntingtin gene. At the time of this breakthrough in 1993, people in the HD community celebrated.

Rightfully so, hope for treatments increased significantly.

Since then, hundreds of researchers from around the globe have published thousands of scientific papers on HD. Along the way they have identified hundreds of potential HD drug targets (biological pathways).

From the 1970s until today, thousands of individuals from HD-affected families have participated in research studies and, more recently, a growing number of clinical trials.

While many of us are disappointed that successful treatments have not emerged, we must recognize that the enormous amount of scientific work regarding HD should contribute – perhaps in ways no one yet knows – to future progress.

The road to treatments is paved with cooperation, and with the recognition that multiple drugs may be needed to manage this complex genetic disorder. (Thus, scientists don't say "cure" when referring to HD.)

Cooperation: the HD community out in force at an HDSA Team Hope Walk (photo by Gene Veritas)

Something larger than ourselves

Our society worships individual "heroes."

However, in the fight to defeat HD, each participant contributes with his or her talents and resources: financial donations, scientific expertise, caregiving, and daily dedication to the cause.

In this long-term commitment, we strive for the well-being of those beyond ourselves: the children who have yet to develop symptoms, the future generations of HD families, and other disease communities such as Alzheimer's, Parkinson's, and many conditions even rarer than HD like dentatorubral-pallidoluysian atrophy, known as DRPLA.

For now, I'll keep my Facebook profile photo as a symbol of hope governed by caution.

Yes, defeating HD is rocket science. When, collectively, we have completed that rocket, we can all ride it together.

(Please remember during HD Awareness Month to donate generously to the Huntington's Disease Society of America or the HD cause of your choice!)

Posted by Gene Veritas at 4:42 PM

Labels: Alnylam , clinical trials , cooperation , cure , gene silencing , heroes , Huntington's disease , Isis , Leonard Mlodinow , Medtronic , research studies , Roche , science , scientists , treatments , valley of death , volunteers

1 comment:

Sharon said...

Gene, I hope you'll add Help 4 HD International to the list of HD links on your blog site!

11:08 PM, May 20, 2015

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