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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GENE VERITAS

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TUESDAY, MARCH 20, 2012

A new, more holistic view of Huntington's disease: the systems/P4 approach

When I learned in late 1995 that my mother suffered from Huntington's disease, a disorder unknown to my family, my reaction went from perplexity to utter shock as I listened to the details: HD caused shaking and severe dementia, was fatal, and *had no treatment or cure*.

Over the next decade, as my mother lost the ability to walk, talk, eat, and care for herself, her doctors could do little to help.

With a 50-50 chance of inheriting HD, I felt desperate as I waited in limbo. In 1999, my positive test for HD multiplied my fears.

When my mother died in 2006, a treatment didn't even appear remote.

Even today, the medicines prescribed for HD patients treat only symptoms, sometimes with serious side effects. They do not arrest the disease in any way.

The lack of therapies (a medically more appropriate word than "treatments") devastates affected families, perhaps more than any other of the cruel realities of HD.

However, as I described in my previous two articles, leading HD researchers are planning for eight new clinical trials in just the next two years (click here and here to read more).

The vastly increased knowledge of HD's causes and the very real possibility of effective therapies behoove us to think about HD in a radically new way. Instead of reacting with the traditional (and quite understandable) fear and pessimism, I believe we must now embrace hope and optimism.

Rather than anticipating the worst, we must expect the best, even if we cannot predict the timetable.

Shifting from 'incurable' to 'treatable'

To turn the emotional tide and spur greater patient and family involvement in crucial research and clinical trials, the HD community must replace the phrase "HD is incurable" with "HD is treatable" or, perhaps more precisely, "HD will be effectively treatable."

"For so long we've talked about HD as an incurable disease," I told an audience of some 100 people at the southern California Huntington's Disease Regional Education Day at the University of California, Irvine, on March 10, sponsored by the Huntington's Disease Society of America (HDSA), Lundbeck, and Remind. "That keeps people behind the mask, keeps them in the closet, keeps them in denial. But the fact that you have the trials coming on line means that this statement is no longer accurate. It's no longer an incurable disease. I believe it's a disease that's going to be

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
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Chris Furbee: Huntingtons Dance
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treated, and going to be treated successfully sometime in the next five to ten years.

"So going back to the old HDSA phrase of some years ago: *let's make this the last generation with HD*. I believe it's going to be the last generation with HD, or that has HD in the way we've known HD, because I think we're going to be controlling and managing HD."

You can see the entirety of my speech in the video below.

Solid reasons for hope

People have occasionally cautioned me against raising false hopes, warning that if a potential drug fails, some in the HD community might withdraw from involvement in research and clinical trials. Many remember how in the early 2000s some people placed great hope in LAX-101 (also known as Miraxion or ethyl-EPA), a fish-oil extract, only to experience a letdown after mainly ineffective clinical trial results.

The cold, hard fact is that 90 percent of all clinical trials do not produce an actual drug. It takes *time* for scientists and drug companies to develop, test, and fine-tune drugs.

Furthermore, scientists do not view those 90 percent as unsuccessful or "failures." Rather, a trial that ends without a successful therapy simply indicates that researchers should make a correction in the path or choose a different one.

Therefore, we must *not give up* if a trial or therapy does not fulfill our personal expectations. Drug discovery requires the participation of the entire HD community. Only by working together can we assemble all of the pieces of the therapy puzzle.

I also think that we have solid reasons for hope.

Having followed HD research the past 15 years, I believe the current lineup of planned trials stands out as qualitatively far different from LAX-101 and other supplement-like substances in other trials or drugs originally designed for other conditions that didn't prove effective in HD.

The new generation of potential drugs benefits from new biological discoveries (such as RNA interference), new drug-discovery technologies (such as high-throughput screening), and a much greater (though still far from complete) understanding of how HD damages the brain.

In addition, in the words of Dr. Robert Pacifici, the chief scientific officer of CHDI Management, Inc., the multi-million-dollar HD therapy initiative, the new HD drug candidates are "custom-crafted" for HD.

A visionary turns to HD research

The annual CHDI HD Therapeutics Conferences provide a panorama of the progress in HD research. I am preparing a report on the scientific findings of the seventh conference, held February 27-March 1 in Palm Springs, CA.

Here I want to reflect on one speaker, Dr. Lee Hood, whose scientific vision is beginning to influence the search for HD therapies.

An M.D., Ph.D., Dr. Hood worked with colleagues to invent four instruments important for the success of the Genome Project (as well as other research): the DNA sequencer and synthesizer and the protein sequencer and synthesizer. Dr. Hood helped to found 14 biotech companies, holds 30 patents, and stands among only ten people in the world to belong to all of three major American scientific organizations, the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. In 1987 he won the Lasker Basic Medical Research Award (the American equivalent of the Nobel Prize).

In 2000, Dr. Hood founded the Institute for Systems Biology (ISB). Located in Seattle, the non-profit ISB teams scientists and technologists from many disciplines to pioneer the future of research in biology, biotechnology, medicine, environmental science, and science education. Dr. Hood is the ISB president.

Dr. Lee Hood at the 7th Annual CHDI HD Therapeutics Conference (photo by Gene Veritas)

When he turned 70 in 2008, Dr. Hood stated that he aimed to achieve the "most ambitious things ... in my career," including the advancement of systems biology and advocating for the widespread adoption of "proactive P4 medicine" (predictive, preventive, personalized, and participatory).

Among other cutting-edge collaborative projects, ISB has pioneered proteomics, the study of the more than 23,000 proteins in the human body.

"What we've done is to democratize proteins – that is, make them accessible to all biologists – just as the Human Genome Project democratized genes and made them available to all biologists," Dr. Hood told the audience at the HD Therapeutics Conference.

A new, even more exciting project aims to develop "global proteomic analysis" by digitizing all of the human peptides (the chemical building blocks of proteins), Dr. Hood added. Just as people can hone in on a geographic location using Google Earth, scientists will soon compare peptides in a digital catalogue, he said.

The next stage will involve studying proteomics and genomics together, he said.

The importance of systems biology

In his HD Therapeutics Conference presentation, "Systems Approaches to Neurodegenerative Diseases and the Emergence of Transforming Technologies," Dr. Hood explained systems biology (SB) and how it can impact the search for HD therapies.

SB emerged because of two revolutions: Darwin's work on evolution, which revealed the enormous complexity of biology and disease, and the late-20th-century explosion in digitized biological information.

"We need this thing called systems biology to de-convolute that complexity," Dr. Hood stated.

In a nutshell, SB offers a holistic view of disease. In Dr. Hood's words, the body is a hierarchical "network of networks" that interact – beginning with genes, extending to molecules, reaching the organs, rising up to the individual human, and ultimately including society and the physical environment.

In my own shorthand, I think of SB as the "big picture of disease."

SB uses the power of computing to mine, integrate, and visualize very large and complex sets of biological information, Dr. Hood added.

He described the SB approach to disease as providing an "informational view of science" that seeks to "capture the dynamics of disease."

In this approach, biology drives technology, which in turn drives analytical tools (computation).

"It's this holy trinity of biology driving technology driving computation that's really at the heart of systems biology," Dr. Hood explained. "I realized this first in the context of developing the automated DNA sequencer."

SB scientists seek to tackle a complex system like HD, build a model of the disease, test that model, and then "perturb" its system repeatedly to see the disease mechanism at work. From this experimentation, they draw conclusions about the disease and how to treat it.

Hunting for HD modifier genes

In collaboration with leading HD specialists, ISB has set out to identify modifier genes for HD. HD results from a mutated form of the huntingtin gene, but one or more modifier genes may affect the onset of the disease. This would help explain why onset occurs at different times in people with the exact same degree of mutation.

To conduct this research, ISB has resorted to the SB approach of gathering large amounts of genetic information.

"We've now analyzed more than 60 human genomes from families that have Huntington's disease," Dr. Hood told the HD Therapeutics Conference audience. "What we've found is these families place enormously interesting constraints on areas where you may find modifiers, but we don't have sufficient data at this point to really identify candidates. What we're excited about is integrating these data together with the GWAS (genome-wide association study) data that will be coming later in the year."

SB and a better understanding of HD

Dr. Hood concluded that SB can assist a search for HD therapies in four other ways. First, it can bring "new insights" into how HD works.

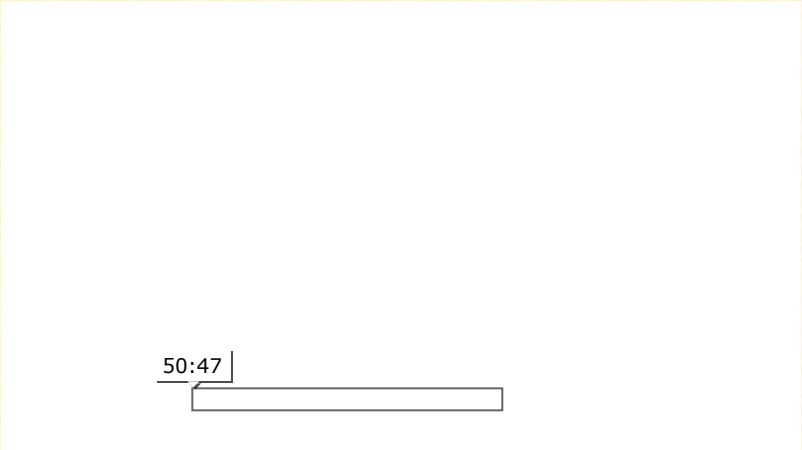
Secondly, "we can make blood into a window for health and disease" by discovering and measuring markers of "drug toxicity as well as disease diagnostics."

Third, in line with its holistic outlook, SB provides "new approaches to analyzing multi-organ responses." So far, most HD research has focused on the brain. However, scientists know that the huntingtin gene is expressed in every cell in the body and affects muscle and fat.

Fourth, SB presents "new approaches to drug target discovery" that could speed the arrival of therapies.

Finally, Dr. Hood added, "the digitization of information is going to be absolutely fascinating," allowing scientists ever greater access to what happens in HD patients and helping them to plan treatments.

You can watch the entirety of Dr. Hood's presentation in the video below.



P4: predictive, preventive, personalized, participatory

SB is laying the basis for P4 medicine, which holds great relevance not just for HD, but all diseases and the promotion of wellness in a future global system of health.

"P4 medicine, the clinical face of systems medicine, has two major objectives: to quantize wellness and to demystify disease," Dr. Hood and a co-author write in an article in the March 2012 issue of the journal *New Biotechnology* that he sent me shortly after the HD Therapeutics Conference. "Patients and consumers will be a major driver in the realization of P4 medicine through their participation in medically oriented social networks directed at improving their own healthcare."

Several organizations have partnered with ISB to pioneer programs in P4. If it is implemented on a wide scale, Dr. Hood predicts that it will

revolutionize our healthcare system. Costs will plummet, everybody will carry a health monitoring device, and diseases will be predicted and prevented long before onset as the result of tiny blood samples taken from a pin prick, the article states.

"P4 medicine will not be confined to clinics and hospitals," the article continues. "It will be practiced in the home, as activated and networked consumers use new information, tools and resources such as wellness and navigation coaches and digital health information devices and systems to better manage their health."

Care will be "tailored to the circumstances of each individual."

An amazing transition

Systems biology and P4 medicine provide a vastly different picture of Huntington's disease from the largely hopeless one painted for me and my family after my mother's diagnosis in 1995.

And we felt so alone in the impersonal world of traditional medicine.

The fresh, fundamental SB/P4 approach has led to a deeper understanding of the work that lies ahead in the search for HD therapies.

CHDI has adopted the SB approach by hiring one of its key practitioners, Dr. Keith Elliston, to serve as its vice president of systems biology. Dr. Elliston also spoke at the HD Therapeutics Conference.

Dr. Keith Elliston (in cap) confers with scientists at the HD Therapeutics Conference (photo by Gene Veritas).

"I'm also very excited that CHDI has chosen to embrace systems biology and to make that a key tenet of its drug-discovery process," Dr. Nathan Goodman, an ISB researcher and member of an HD-affected family, told the audience. "In essence, this makes CHDI the first systems-biology-driven therapeutics company, yet another in the long line of firsts that CHDI has accomplished. This is a very big step not just for the Huntington's disease field, but for all of biology, all of life sciences, the entire industry of therapeutics. This is an amazing transition by CHDI."

As SB and P4 could very likely represent the future of medicine, I'm betting they will also play a major role in removing HD as a threat to me, my family, and the tens of thousands of families around the world impacted by HD.

We in the HD community have fulfilled the first P: genetic testing allows us to predict our future.

We now must focus on the other Ps: preventing HD; receiving personalized diagnosis and treatment that will optimize our health; and attaining wellness and a long life as a result of having helped find effective treatments through proactive participation in HD research and clinical trials and the contribution of our biological information to a global data bank.

Posted by Gene Veritas at 8:48 PM

Labels: brain , CHDI , clinical trial , cure , dementia , denial , genome , Huntington's , incurable , P4 medicine , RNA interference , Robert Pacifici , scientist , supplement , systems biology , treatable , treatment

3 comments:

Anonymous said...

Hi! Thank you for this informative article. It really lifted my spirits. My husband and I recently found out that he is at risk. His father has HD. We are both in our mid-30's and were married less than a year ago. The thought that he may carry the HD gene is not only incredibly frightening, but also puts our hope to starting a family on hold. My husband definitely wants to get tested. For us, not knowing is almost as difficult as testing positive. Would you have any recommendations on getting tested anonymously? We are concerned that a positive result may affect his career as an attorney. We are in the San Francisco Bay area. Thank you for all you do!

10:50 AM, March 29, 2012

Gene Veritas said...

Dear Anonymous of 3/29/2012 and to Everybody Else: I can be reached at curehdnow at earthlink dot net or on Facebook.
Yours, Gene

9:52 PM, April 01, 2012

Lisa Jones said...

The information and the aspect were just wonderful. I think that your viewpoint is deep, it's just well thought out and truly incredible to see someone who knows how to put these thoughts so well.
Renton Acupuncture

3:04 AM, March 16, 2015

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