Step by step, HD treatments closer to human clinical trials
Gene silencing heads promising updates at HDSA National Convention

“There’s never a good time to have HD, but this is the best time so far in history.”

That is the sentiment of a Huntington disease patient quoted in a newspaper article. And it’s a sentiment that Dr. Jeff Carroll and Dr. Ed Wild told the audience at the 2013 HDSA National Convention in Jacksonville, Fla., they wholeheartedly agree with. The co-creators of HDBuzz and other speakers at the convention gave the 860 people in attendance reasonable hope that multiple promising therapies for HD are moving toward trials in humans.

“The day we can treat Huntington’s disease is getting closer every day,” said Wild, a clinical lecturer in neurology at UCL in London.

During their presentation titled “The Drugs are Coming,” Carroll and Wild said the journey toward effective therapies for HD is made up of many small steps, but those steps are being taken by scientists each day.

One promising therapy highlighted by Carroll, Wild and several other presenters at the convention is often referred to as “gene silencing.” When an individual has the HD mutation in his or her DNA, cells that make the Huntingtin protein receive the harmful mutation from the messenger RNA, causing the protein to change shape, which “messes up all the smooth running processes that enable yourselves to stay healthy,” Wild said. But if a chemical were used to stop RNA from delivering the harmful HD mutation, the Huntingtin protein would function properly and stop causing all the symptoms associated with HD.

There are a number of prominent research labs exploring different methods to achieve the goal of stopping the harmful RNA messaging, including Dr. Beverly Davidson at the UI, whose method would involve injecting the drug treatment directly into the brain.

“If we can get rid of the mutant gene, we all hope we can affect the course of disease,” said Carroll, an assistant professor of psychology at Western Washington University. “We think trials in HD patients are likely to start very soon.”

In the meantime, well-known HD researcher Dr. Michael Hayden from the University of British Columbia said during his presentation at the convention that HD family members and researchers need to continue to be present and make their voices heard, whether it be heard by drug regulatory agencies or in the corridors of Congress.

“We’re just before the emergence of much of this,” he said. “We’ve got to keep stepping up in ways we haven’t done before. We have a real opportunity to change lives.”

Dr. Ed Wild, co-founder of HDBuzz, told convention attendees “the drugs are coming, but if you want to make them happen more quickly, HD research needs you [to participate]” in observational studies like PREDICT-HD.

On the Web
Click here for select videos from the convention from www.hdsa.org.

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photo courtesy HDSA

UI Senior Jolene Luther had a special bond with her grandfather. When he died from HD in 2011, she decided to get involved and help those with HD and their families, and spent the summer conducting HD research. Read her story on Page 3.

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Walk for HD hope in Ankeny, Iowa City

By Sarah Petitt
UI HDSA COE Public Relations Assistant

Walking is good for the mind, body, soul and, as it turns out, Huntington disease research. The HDSA Iowa Chapter will be raising money this fall with a Team Hope Walk in Ankeny on Sept. 28 and a new walk in Iowa City on Oct. 19.

The Ankeny walk will take place at the Des Moines Area Community College campus at Building 7. Same-day registration is at 8 a.m., followed by a 5K run and one-mile fun run at 8:30 a.m., and the walk at 9:30 a.m.

The Iowa City Team Hope Walk will begin at Hubbard Park on the UI campus. Same day registration and a 1.75-mile walk along the Iowa River and through the UI campus will commence at 8 a.m.

Early registration for adults in the Ankeny walk is $25 and $30 for same-day registration. Kids are $15 in advance or $20 on the day of the walk. Registration for the Iowa City walk will be $15 for adults and $10 for kids.

In addition to the walk/run, HDSA Iowa Chapter President Lori Wesack said the Ankeny event will also include a bouncy house for kids. HDSA advocate Brandon Rogers said the Iowa City walk will include face painting and a punt, pass and kick competition for kids. Participants will also be eligible for a drawing with prizes such as movie tickets and a family pass to the Iowa Children’s Museum.

For more information on both events, email hdsaiowachapter@gmail.com.

Intern connects with HD community

I’ve worked in claustrophobic cubicles before, surrounded by infinite piles of administrative paperwork, research assignments and press releases. While working for the UI HDSA COE, I completed similar work with intrinsic dedication — something I never experienced before.

I’ve learned just how imperative communications can be to help with the HD fight. Failed or proven hypotheses are a positive discovery that builds HD’s rainbow of hope, and I was honored to read complex studies, write about them for the general public and work on social media to spread HD awareness.

Everyone at the UI HDSA COE is motivated to help people, young and old, affected by HD. In fact, Stephen Cross, one of our research assistants, said that long ago he caught the “HD bug” and feels forever connected to people in the HD community. As I complete my last day, I feel that I, too, have caught the bug; an inexplicable connection to people affected by the disease, a disease that only a few months ago for me was just another term.

Maybe my supervisor’s goal from the beginning was to hire an ill-informed graduate and turn her into a dedicated HD advocate. I’m here to say he succeeded.

HD Support Groups:

Des Moines
Valley View Village Conference Room
2571 Guthrie Avenue
Third Sunday at 1:30 p.m.
Mark Hillenbrand
(515) 208-3511

Omaha, Nebraska
Perkins Restaurant
108 L. Street
Second Monday at 6 p.m.
Cathy McNeill
(402) 537-0739

Iowa City
University of Iowa Hospitals and Clinics
Della Ruppert Conference Room
Sunday, Oct. 20, 1 p.m.
Shawna Feely
(319) 353-4307

At-risk/presymptomatic
Every other month
Brandon Rogers
(319) 333-2211

HD awareness on the UI campus

In recognition of HD Awareness Month in May, the UI HDSA COE designed custom shirts (seen in this group photo) to raise awareness and show support for the HD community. Other awareness month activities included an HD info table at the UI Hospitals and Clinics.
Making a difference

Juvenile HD advocates meet at the UI HDSA COE for research

They've each made contributions to raising awareness of Juvenile Huntington disease and raising funds for research in their communities and beyond, and in early August, five JHD advocates joined forces to make a substantial contribution to research as participants.

The idea for the joint research visit came from Jacey Mukka, founder of the website www.jhdkids.com, which tells the stories of kids with JHD from around the world, while providing support and fundraising for JHD research at the UI HDSA COE. Mukka said the group could meet in Iowa City, each do a research visit for the JHD Natural History Study, and enjoy each other's company while trading stories of JHD advocacy. They also attended a JHD support group gathering at UI HDSA COE Co-director Jane Paulsen's rural home, where they rode horses and completed a craft project.

“Each of them have been incredibly brave in stepping forward in their communities and online, sharing their personal JHD stories and doing so much for awareness,” Paulsen said. “We can't thank them enough for all they do and for coming here for this joint research visit.”

Aidan Smith, 8, says hello to a horse at Jane Paulsen's farm. Smith and his mother, Denise Hudgell, have been active JHD advocates in the Council Bluffs area, holding fundraisers and giving presentations about the disease to raise awareness.

Virginia Buck said riding a horse was on her “bucket list.” She accomplished that goal on Aug. 7 at Jane Paulsen's farm. Buck, 10, collects pennies in her community and online for JHD research and raised nearly $2,400 at a single fundraiser she organized in 2012.

Virginia Buck, Jacey and Erica Mukka of Michigan, Cathy Harrell of Texas, Libby Buck and UI HDSA COE Research Assistant Courtney Shadrick work on crafts.
Driven from her heart to HD fellowship
Special bond with grandfather leads UI student to conduct HD research

By Sean Thompson
HIND-Sight Editor

University of Iowa senior Jolene Luther’s face lights up as she keenly talks about her grandfather and his major influence on her life.

Though William Holcomb died from Huntington disease in the fall of 2011, his impact continues to live on through Luther and the research she did this summer at the UI as a 2013 HDSA Donald A. King Summer Research Fellow.

The Belgium, Wis., native was one of two fellows selected by the HDSA for this research initiative. The fellowships are intended to advance HD research while welcoming bright young researchers into the fight against HD.

For 10 weeks this summer, Luther looked at MRI scans of Huntington disease research participants to identify whether or not there are increased levels of iron in the brain, a possible indication of disease progression. She was mentored by UI HDSA COE Co-director Jane Paulsen, Ph.D., and Hans Johnson Ph.D., assistant professor of psychiatry.

The relationship that defined a future fellow

A pre-med Spanish major, Luther has a love for medicine and science. But it’s the special bond with her grandfather that Luther’s mother Stephanie Bernander says led Luther to get involved in the Huntington disease research field.

“It’s from her heart that she’s driven to do this,” Bernander said.

Luther says she and her grandfather were close from the start. They would go on many camping trips in Wyoming where Holcomb lived.

As his family had feared, Holcomb tested positive for HD when Luther was 11 years old. As described in an article she wrote for the Huntington’s Disease Youth Organization, Luther watched as “the mountain climbing, long-distance biking, bread making, swim coaching man that everyone loved changed before our eyes and there was nothing we could do about it.” Her family had great difficulty finding specialists and resources needed to properly care for their loved one.

“From there, I knew that I wanted to be that person that could help out a family who was struggling and didn’t have the help that they needed,” Luther said.

Memorializing through HD involvement

Luther felt empty the spring following her grandfather’s passing in the fall of 2011 and wanted to do something to honor him. She reached out to the UI HDSA COE and spent the summer working on writing projects. But she didn’t want to stop there.

Luther’s combination of high academic achievement and passion to do something special for the HD community personifies the “ideal student” HDSA Director of Medical and Scientific Affairs George Yohrling had envisioned for the fellowship.

Her fellowship research involves looking for increased iron levels in MRI scans of brains of people in the PREDICT-HD study who have tested positive for the HD gene but are not yet diagnosed with symptoms of HD (known as the prodromal stage of HD). These iron deposits are detectable on the scans by identifying dark, lower-intensity spots on the images known as hypointesities. Increased iron levels are higher overall than control participants and also in a smaller study of prodromal HD (known as the prodromal stage of HD). These iron deposits may be a biomarker or measure of disease progression for HD.

If the levels in prodromal individuals are higher overall than control participants and higher as a person progresses closer to estimated diagnosis, Luther says the iron deposits may be a biomarker or measure of disease progression for HD.

If this turns out to be the case, Yohrling says Luther and her mentors will have made an “incredibly significant” finding.

An everlasting connection

Bernander feels overwhelmed when she thinks about her daughter’s pursuits in HD research and succumbs to tears when talking about it.

“To have Jolene be so committed, knowing that she likely won’t have to face it in her personal life again, yet wanting to give back to all the other people that will experience what we did, it’s beyond description just how proud I am of her.

In a small but significant way, Luther says her contributions to HD research help make up for the fact that her grandfather is no longer with her.

“I was so young when his disease was progressing,” she said. “He didn’t really get to know me in my adult life. This is kind of my way of getting to contribute something to him, even though he’s not here to see it. I think he’d be really proud of me.”

HD studies currently enrolling at the UI

- PREDICT-HD: An observational study for pre-symptomatic, gene-positive individuals. Contact Stephen Cross, predict-hd@uiowa.edu, 319-384-1008
- HDQLIFE: An observational study for adults diagnosed with HD or PREDICT-HD participants who are gene positive. Contact Courtney Shadrick, courtney-shadrick@uiowa.edu, 319-353-5443
- CREST-E: A clinical drug trial for symptomatic, diagnosed individuals. Contact Jacky Walker, jacky-walker@uiowa.edu, 319-353-4357
- Enroll-HD: An observational study for anyone in the HD community. Contact Greg Roskos, gregory-roskos@uiowa.edu, 319-335-6640.
Amanda Miller  
1-308 MEB  
Iowa City, Iowa 52242  
(319) 335-6640  
hdcenter@uiowa.edu


Chronic stress can lead to depression and anxiety in humans. Scientists recently discovered a very similar link in fish.

Normally, the stress hormone cortisol helps fish, as in humans, to regulate stress. Fish that lack the receptor for cortisol as a result of a genetic mutation exhibited a consistently high level of stress. These findings demonstrate a direct causal link between chronic stress and behavioral changes which resemble depression.

An international team led by Herwig Baier from the Max Planck Institute of Neurobiology in Martinsried, Germany, and the University of California in San Francisco observed that zebrafish suffering from chronic stress as a result of a genetic mutation showed signs of depression in behavioral tests. The zebrafish is a popular model organism for medical research.

All animals experience stress upon moving to an unfamiliar environment. Zebrafish initially act withdrawn in this situation and swim around very hesitantly in the first few minutes. But ultimately, curiosity prevails, and they begin to investigate their new tank. However, the fish with the mutation had a particularly strong reaction to the isolation: they sank to the bottom of the tank and stayed completely still. They took an exceptionally long time to get used to the new environment.

“We therefore postulated that these fish were suffering from chronic stress and were exhibiting certain aspects of depressive or perhaps hyper-anxious behavior,” says Baier. To put this assumption to the test, the scientists added the antidepressant fluoxetine (Prozac) to the water. Shortly afterwards, the fish’s behavior returned to normal.

The scientists uncovered a mutation in the glucocorticoid receptor, which is present in almost all of the body’s cells and which binds the hormone cortisol. Normally, when cortisol is bound to this receptor it restricts the release of the stress hormones CRH and ACTH. It is this regulating mechanism that enables humans and many animal species to cope with stress. In the type of fish the scientists examined, however, the glucocorticoid receptor was unable to function, and so the level of stress hormones remained high.

Understanding the molecular and neurobiological relationships between stress regulation and affective disorders is important in the search for new treatments and drugs.