



HD Therapeutics Conference 2012 Updates: Day 2

Day 2 of our coverage of the Huntington's Disease Therapeutics Conference



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Our second daily report from the annual Huntington's Disease Therapeutics Conference in Palm Springs, California. The second day's sessions focused on gene silencing. You can tweet @HDBuzzFeed or email palm springs@hdbuzz.net with your questions, comments and queries.

Wednesday, February 29, 2012

9:03 - HD Therapeutics Conference Update: This morning is focused on gene silencing - a very exciting potential therapy. Stand by!



The Huntington's Disease Therapeutics Conference takes place in Palm Springs, California

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9:35 - **Beverly Davidson** (University of Iowa): silencing the mutant HD gene in mice has clear benefits, but we need to consider any unintended toxic effects

9:45 - **Davidson** is behind one of three recent papers showing huntingtin gene silencing safe in primates - a key step to human trials

9:49 - **Davidson's** team is now working on new gene silencing drugs that silence the mutant copy of the gene more than the 'healthy' copy.

9:50 - Targeting the mutant gene selectively might be safer but is more challenging. Both approaches are being worked on.

10:06 - **Frank Bennett** (Isis Pharmaceuticals) uses slightly different DNA-like molecules called ASOs to silence the Huntingtin gene

10:07 - **Bennett:** Huntingtin seems to be relatively easy to silence compared to other genes - lucky break!

10:00 - **Bennett's** ASO drugs are absorbed into cells better than RNAi drugs. Might make it easier to get to patients - no brain surgery?

10:13 - **Bennett's** company Isis pharmaceuticals is experienced in gene silencing - 2,000+ patients with other diseases have received their drugs

10:17 - **Bennett:** when tested in 2 different HD mouse models, ASO gene silencing drugs produced improvements in coordination and cognition

10:19 - **Bennett:** infusion of ASO into the fluid at the base of the spine in primates is enough to get the drug to large areas of the brain

10:22 - **Bennett:** even one-off injections of the gene silencing ASO may be enough to treat the brain. But deep brain regions harder to reach

10:25 - **Bennett:** many people have small spelling differences, apart from the expanded CAG, between the 2 copies of Huntingtin gene. These differences can be targeted, to design drugs that silence only the mutant gene.

11:04 - **Steve Zhang** (Sangamo BioSciences): 'zinc finger proteins' can bind to specific DNA sequences, raising the possibility of 'editing' our genes

11:07 - For anyone wanting more detail, video of the talks will be available online soon, and we're writing a summary article too

11:00 - **Zhang:** other uses of zinc finger proteins include designing stem cells to study generic diseases in human cells

“Many people have small spelling differences, apart from the expanded CAG, between the 2 copies of Huntingtin gene. These differences can be targeted, to design drugs that silence only the mutant gene.”

11:18 - **Zhang's** company Sangamo has successfully treated hemophilia in a mouse model using 'genome editing'

11:19 - **Zhang:** Zinc fingers can also be used to switch genes on and off, another possible approach to gene silencing

11:20 - **Zhang:** we could also try to switch on helpful genes, so that the brain produces more protective chemicals

11:25 - **Zhang:** zinc finger drug that makes the brain produce the protective chemical GDNF is about to start a trial in Parkinson's disease

11:26 - Sangamo is now involved in Huntington's disease research.

11:29 - **Zhang:** Sangamo's current strategy is to try to reduce Huntingtin production with a tailor-made zinc finger drug

11:36 - **Zhang:** they're also working on a zinc finger silencing drug that only works on huntingtin genes with expanded CAG repeats

11:53 - **Bill Kaemmerer** (Medtronic): To make new silencing trials happen we need 'biomarkers'- tests of safety & measurements to tell us if it's working

12:02 - **Kaemmerer:** A combination of MR imaging, CSF chemicals and clinical measures will be used for early RNAi gene silencing trials

12:07 - **Kaemmerer** is part of the team behind another recent primate safety trial of huntingtin gene silencing

12:37 - **Neil Aronin** (University of Massachusetts School of Medicine) and his team are trying to understand how one gene silencing approach, RNAi, works in great detail to design good drugs

12:46 - **Aronin** and his team are using sheep to practice the neurosurgical techniques needed for gene silencing trials in humans

Sunset conclusions

Several different strategies are being developed in parallel to 'silence' the huntingtin gene that's the ultimate cause of all problems in HD. There are a few wrinkles to iron out, but basically so far each approach has cleared every hurdle it's encountered. Several clinical trials involving HD patients are being planned, all aiming for a rapid start - within months rather than years. The stakes are high, but it's a genuinely exciting time.

Dr Wild and Dr Carroll's registration fee for the Therapeutics Conference has kindly been waived by CHDI Foundation, Inc., sponsors of the Conference, but their attendance is supported by HDBuzz and the European HD Network, from funds independent of CHDI.

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GLOSSARY

Parkinson's Disease A neurodegenerative disease that, like HD, involves motor coordination problems

gene silencing An approach to treating HD that uses targeted molecules to tell cells not to produce the harmful huntingtin protein

Genome Editing The use of zinc-finger nucleases to make changes in DNA. 'Genome' is a word for all the DNA we each have.

therapeutics treatments

stem cells Cells that can divide into cells of different types

primate a group of mammal species including monkeys, apes and humans

GDNF glial cell-derived neurotrophic factor: a growth factor that protects neurons in Parkinson's Disease, and maybe HD

RNA interference A type of gene silencing treatment in which specially designed RNA molecules are used to switch off a gene

ASOs A type of gene silencing treatment in which specially designed DNA molecules are used to switch off a gene

CSF A clear fluid produced by the brain, which surrounds and supports the brain and spinal cord.

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