

PRESS RELEASE

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VIRUS HOPE FOR TREATMENT OF HUNTINGTON'S DISEASE

New gene therapy techniques being studied in France are showing potential for treating and even curing Huntington's disease, a genetic disorder that causes problems with movement and cognition. The research, announced today (Tuesday 15 July) at FENS 2008, involves two different techniques – in one, viruses are used to introduce new genes into the brain that allow it to protect itself against degeneration, and in the other the faulty gene that causes Huntington's disease is deactivated using viruses that allow brain cells to produce special strands of RNA, a molecule similar to DNA.

Huntington's disease (HD) is caused by a faulty gene on chromosome 4. This abnormal gene produces the protein huntingtin, and it's thought this protein may cause HD by preventing brain cells from being able to protect themselves from toxic chemicals. Currently there is no cure for HD, and no treatment to prevent the neurodegeneration that the disease causes. But Dr Nicole Déglon, one of the members of the team at CEA, Institute of Biomedical Imaging and Molecular Imaging Research Center in Orsay, France, is optimistic that gene therapy using viruses could offer an effective way to treat the disease.

The first technique she and the team are testing is based on the idea that increasing the amount of a "neuroprotective" molecule in the brain will help it to defend itself against the degenerative effects of HD. The molecule the team are using is called ciliary neurotrophic factor, or CNTF. "When the brain has a problem or a lesion then the synthesis of CNTF is increased, and this factor is secreted and is somehow helping the neurons to respond to this injured environment and better survive," says Dr Déglon. The team's previous work had used special cells engineered to produce CNTF, encapsulated in polymer rods that were implanted in the brain. "The conclusion was that the CNTF is fine but the delivery we have used was not good enough for long-term application," says Dr Déglon. "We decided to

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continue the work and try to find a better delivery system, and we switched to viral vectors.”

They're now testing this new technique in primates. A genetically modified virus is used to deliver a gene into the brain cells that will allow continuous and long-term delivery of CNTF. The specially engineered viruses are injected into the region of the brain that degenerates in HD, the striatum, where they infect brain cells and insert the gene that allows the production of CNTF. “With CNTF the added value is that it's a secreted molecule, so [even] if you don't infect all the cells with the virus, the protein will diffuse and have a large effect,” says Dr Déglon. The results show that the technique does protect brain cells in the striatum in rats and primates, and the team is now moving towards a clinical trial for this promising treatment. “Our hope is that the patient will benefit for several years, but the answer will be the clinical data,” says Dr Déglon.

The second and more experimental treatment uses RNA, a molecule similar to DNA. RNA acts as a messenger molecule, controlling which proteins cells make, and is produced from the DNA in the nucleus of each cell. “The idea is, why not destroy the messenger RNA expressing the mutant huntingtin which is causing Huntington's disease, and therefore totally prevent the synthesis of the protein and all the symptoms?” explains Dr Déglon. Again the researchers hope to accomplish this feat using specially engineered viruses that will infect the brain cells, inserting a gene that allows the cell to produce special RNA that will deactivate the mutant RNA produced naturally by the cell. However this time the challenges facing the team are slightly different. “If you want to cure a cell you need to infect the cell – the neighbouring ones will not be affected. So in terms of delivery it's certainly much more challenging,” says Dr Déglon. The next step for this exciting technique will be preclinical studies in large animals such as primates. This will allow the team to test whether the treatment will affect both the motor *and* cognitive deficits HD produces.

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Notes to Editors

FENS 2008 is hosted by the Swiss Society for Neuroscience and will attract over 5,000 international delegates. The Federation of European Neuroscience Societies, founded in 1998, aims to advance research and education in neuroscience, representing neuroscience research in the European Commission and other granting bodies. FENS is the European partner of the American Society for Neuroscience. FENS represents a large number of national European neuroscience societies and has around 16000 members. <http://fens2008.neurosciences.asso.fr/>