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New discovery in fight against Huntington's disease

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Researchers at National University of Ireland Galway have made a significant scientific discovery in the fight against Huntington's disease. The novel findings are published 21 February in the online, open access journal *PLoS Biology*.

Huntington's disease is an incurable, inherited, neurodegenerative disorder that causes uncontrolled movements, emotional disturbances, and severe mental deterioration. It affects over 100,000 people worldwide, with another 300,000 likely to develop symptoms in their lifetime. There is currently no way to halt progression of the disease, and available treatments are designed only to manage the symptoms.

The new research identifies specific enzymes called HDACs, or histone deacetylase complexes, as positive agents for the mutation that underlies Huntington's disease. When HDACs are active, they exacerbate the disease-causing mutation in cells, possibly contributing to the severity of the disorder. The new research found that blocking these HDACs with experimental drugs greatly reduced the risk of further mutation.

"Ongoing mutations in the brain of Huntington's patients are thought to drive progression of the disease," said Professor Robert Lahue of National University of Ireland Galway's Centre for Chromosome Biology, and lead author on the new research paper. "Our discovery suggests that inhibiting HDAC function slows down the mutation process, and thereby could slow disease progression. A key finding of the research was to pinpoint specific HDACs for selective inhibition."

Several laboratories in the United States of America are currently testing new HDAC inhibitors for efficacy and safety in laboratory models of Huntington's and other diseases. Professor Lahue and his research group hope to work with these labs to evaluate the effect of HDAC inhibitors on the mutational process.

"Huntington's is a particularly cruel disease, as it is passed from parent to child, often with increased severity or earlier onset," Professor Lahue adds. "With modern genetic testing, people can now establish whether they received the mutant gene from their parent, but then they live a waiting game for the onset of symptoms, which usually appear around the age of 40."

Professor Lahue emphasised that the HDAC inhibitors are still experimental, and that their development to potential drugs is still some way off. "It is very exciting that basic research at National University of Ireland Galway, funded by Science Foundation Ireland, has created a new possibility for helping Huntington's patients and their families."

The findings may also have implications for research into certain other neurological disorders, such as myotonic dystrophy type I, a type of muscular dystrophy caused by the same sort of mutation as seen in Huntington's.

More information: Debacker K, Frizzell A, Gleeson O, Kirkham-McCarthy L, Mertz T, et al. (2012) Histone Deacetylase Complexes Promote Trinucleotide Repeat Expansions. *PLoS Biol* 10(2): e1001257. doi:10.1371/journal.pbio.1001257

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