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Huntington's disease study shows animal models on target

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An international team of researchers has published a benchmark study showing that gene expression in several animal models of Huntington's Disease (HD) closely resembles that of human HD patients.

The results, published August 1, 2007, in the journal *Human Molecular Genetics*, validate the applicability of using animal models to study human disease and will have important consequences for the pertinence of these models in preclinical drug testing.

Huntington's disease is an incurable and fatal hereditary neurodegenerative disorder caused by a mutation in the gene that encodes the huntingtin protein. Neurons in certain regions of the brain succumb to the effects of the altered protein, leading to severe motor, psychiatric, and cognitive decline. Several recent studies have shown that the mutant huntingtin protein modifies the transcriptional activity of genes in affected neurons. This disease mechanism is a promising new avenue for research into the causes of neuronal death and a novel potential approach for treatment.

Led by EPFL professor Ruth Luthi-Carter, and involving collaborators from six countries, the current study found a marked resemblance between the molecular etiology of neurons in animal models and neurons in patients with HD. This implies that animal models are relevant for studying human HD and testing potential treatments.

To come to this conclusion, the scientists measured the gene expression

profile of seven different transgenic mouse models of HD, representing different conditions and disease stages. These profiles clarified the role of different forms and dosages of the protein hungtintin in the transcriptional activity of neurons. They then designed and implemented novel computational methods for quantifying similarities between RNA profiles that would allow for comparisons between the gene expression in mice and in human patients. “Interestingly, results of different testing strategies converged to show that several available models accurately recapitulate the molecular changes observed in human HD,” explains Luthi-Carter. “It underlines the suitability of these animal models for preclinical testing of drugs that affect gene transcription in Huntington’s Disease.”

Source: Ecole Polytechnique Fédérale de Lausanne