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IN BRIEF

NEURODEGENERATIVE DISEASE

Lethal sequestration by mutant HTT

Huntington's disease is associated with NMDA receptor dysfunction, but how the expanded polyglutamine repeat in the huntingtin (HTT) protein contributes to its dysfunction is unclear. The authors of a new study show that mutant HTT protein aggregates disrupt the localization of NMDA receptors containing GluN3A subunits. By sequestering the endocytic adaptor protein PACSIN1, mutant HTT allows GluN3A-containing receptors to reach the surface of neurons and enhance NMDA receptor currents that have been linked to cell death.

ORIGINAL RESEARCH PAPER Marco, S. *et al.* Suppressing aberrant GluN3A expression rescues synaptic and behavioral impairments in Huntington's disease models. *Nature Med.* http://dx.doi.org/10.1038/nm.3246 (2013)

NEUROLOGICAL DISORDERS

Counterproductive bias

A meta-analysis of animal studies across neurological disorders suggests that the number of studies that report statistical significance is too large to be true. The authors assessed 4,445 datasets and compared the number of studies that reported statistically significant results with the expected number, which was based on the statistical power of each study under different assumptions for the plausible effect size. Only 919 nominally significant results were expected, but 1,719 had been reported. This highlights a strong bias in the reporting of results and may help to explain why so many biomedical experiments in animals fail to translate into human clinical trials.

ORIGINAL RESEARCH PAPER Tsilidis, K. K. *et al.* Evaluation of excess significance bias in animal studies of neurological diseases. *PLoS Biol.* **11**, e1001609 (2013)

GENETICS

First step towards chromosome therapy

Down's syndrome is a common genetic disorder and is caused by the presence of three copies of chromosome 21. The authors of this study attempted to correct the gene over-dose across a whole chromosome by manipulating a single gene. An inducible version of *XIST* (the X-inactivation gene) was inserted into one copy of chromosome 21 in Down's syndrome pluripotent stem cells. The edited chromosome was enriched in repressive histone marks and chromosome-wide transcriptional silencing was achieved 5 days after *XIST* induction. The reversal of deficits in cell proliferation and neurogenesis that were observed suggests that this approach could eventually lead to gene therapies that reduce the symptoms of Down's syndrome.

ORIGINAL RESEARCH PAPER Jiang, J. *et al.* Translating dosage compensation to trisomy 21. *Nature* http://dx.doi.org/10.1038/nature12394 (2013)

ADDICTION

Smoking and craving a drink?

A new study in rats sheds light on the neural mechanisms through which smoking increases the risk of alcohol abuse. Pre-exposure to nicotine blunted the dopamine response to alcohol and increased alcohol self-administration. The decreased dopamine responses to alcohol arose via activation of stress hormone receptors in the ventral tegmental area and a subsequent increase in alcohol-induced inhibitory neurotransmission.

ORIGINAL RESEARCH PAPER Doyon, W. M. *et al.* Nicotine decreases ethanol-induced dopamine signaling and increases self-administration via stress hormones. *Neuron* http://dx.doi.org/10.1016/j.neuron.2013.06.006 (2013)