IN BRIEF

NEURODEGENERATION

Search and rescue

Phenotypic cell-based models of neurodegenerative disease can be useful for drug screening, but progress has been hampered by the difficulty of establishing robust neuronal phenotypes. Accumulation of α-synuclein (α-syn) is associated with Parkinson's disease; two studies now take advantage of cellular responses to overexpression of α-syn that are conserved from yeast to humans to identify a neuroprotective compound and to determine its mechanism of action. Tardiff *et al.* showed that, in yeast, α-syn expression disrupts endosomal transport and alters mitochondrial function (hallmarks of α-synucleinopathies such as Parkinson's disease). A drug screen revealed that these phenotypes were rescued by *N*-aryl benzimidazole (NAB) treatment. NAB was shown to be neuroprotective against α-syn toxicity in human neurons by activating the E3 ubiquitin ligase NEDD4 pathway. Similarly, Chung *et al.* found that both yeast overexpressing α-syn and neurons derived from a patient carrying a highly penetrant form of α-syn exhibited endoplasmic reticulum and nitrosative stress, and that these effects were rescued by NAB or its target, NEDD4 or Rsp5 (the yeast NEDD4 homologue). These papers demonstrate the utility of yeast-based screens in helping to identify novel compounds that might have neuroprotective benefits in Parkinson's disease.

ORIGINAL RESEARCH PAPERS Tardiff, D. F. *et al.* Yeast reveal a "druggable" Rsp5/Nedd4 network that ameliorates α-synuclein toxicity in neurons. *Science* http://dx.doi.org/10.1126/science.1245321 (2013) | Chung, C. Y. *et al.* Identification and rescue of α-synuclein toxicity in Parkinson patient-derived neurons. *Science* http://dx.doi.org/10.1126/science.1245296 (2013)

NEUROGENETICS

Expression restrictions

Amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) can be caused by an expanded non-coding hexanucleotide repeat in chromosome 9 open reading frame 72 (*C9ORF72*), but the underlying mechanism is not known. Suzuki *et al.* identified the mouse orthologue of *C9ORF72* and found that its expression was localized mainly in neurons that, in humans, are known to degenerate in ALS and FTD. These findings suggest that the high expression of *C9ORF72* may be responsible for the selective vulnerability of certain neuronal types in ALS and FTD.

ORIGINAL RESEARCH PAPER Suzuki, N. *et al.* The mouse *C9ORF72* ortholog is enriched in neurons known to degenerate in ALS and FTD. *Nature Neurosci.* http://dx.doi.org/10.1038/nn.3566 (2013)

NEUROIMAGING

More precise MRI

Quantitative MRI has the potential to be tremendously useful in clinical research, but its use has so far been hampered by problems such as low signal-to-noise ratio and low accuracy. In this paper, Mezer *et al.* show how quantitative MRI can be combined with other imaging techniques to enhance the measurement of the macromolecular tissue volume (MTV) and the quantification of tissue reorganization. They also show that MTV can be used to monitor white matter volume changes in patients with multiple sclerosis — with potential for monitoring neuroanatomical changes in other clinical disorders.

ORIGINAL RESEARCH PAPER Mezer, A. *et al.* Quantifying the local tissue volume and composition in individual brains with magnetic resonance imaging. *Nature Med.* http://dx.doi.org/10.1038/nm.3390 (2013)