IN BRIEF

TARGET IDENTIFICATION

A new target for treating progeria

Progeria syndromes, which are caused in part by methylation of prelamin A, result in a premature ageing phenotype. This study showed that a mouse model of progeria that had reduced genetic expression of isoprenylcysteine carboxyl-methyltransferase (ICMT) had increased body weight, fewer bone fractures and a lower death rate. Moreover, the premature senescence of fibroblasts from these mice was abolished. Inhibition of ICMT by a short hairpin RNA delayed senescence in human progeria fibroblasts, which suggests that inhibiting ICMT might be beneficial for treating progeroid disorders.

ORIGINAL RESEARCH PAPER Ibrahim, M. X. *et al.* Targeting isoprenylcysteine methylation ameliorates disease in a mouse model of progeria. *Science* 16 May 2013 (doi:10.1126/science.1238880)

CLINICAL TRIALS

Exenatide provides benefit in Parkinson's disease

Previous *in vitro* studies have suggested that the diabetes drug exenatide — a glucagon-like peptide 1 receptor agonist — has neurotrophic and neuroprotective effects. This clinical study investigated the efficacy of exenatide in 45 patients with moderate Parkinson's disease. Exanatide given for 12 months improved motor symptoms ($P = 0.037$) and some cognitive measures, although weight loss was commonly observed. These data support larger double-blind trials of exenatide as a potential disease-modifying drug in Parkinson's disease.

ORIGINAL RESEARCH PAPER Aviles-Olmos, I. *et al.* Exenatide and the treatment of patients with Parkinson's disease. *J. Clin. Invest.* **123**, 2730–2736 (2013)

NEUROLOGICAL DISORDERS

Identifying pathogenic pathways

Several neurological disorders, including spinocerebellar ataxia type 1 (SCA1), are caused by a toxic build-up of mutant proteins. To identify targets for SCA1, this study used parallel human cell-based and fruitfly genetic screens to show that downregulation of components of the RAS–MAPK (mitogen-activated protein kinase)–MSK1 (nuclear mitogen- and stress-activated protein kinase 1) pathway decreased mutant ataxin 1 levels and suppressed neurodegeneration in fruitflies and mice. Pharmacological inhibition of the pathway also decreased ataxin 1 levels, which suggests that it is a new target in SCA1. These methods could be used to identify targets for other neurodegenerative disorders with similar pathogenic mechanisms.

ORIGINAL RESEARCH PAPER Park, J. *et al.* RAS–MAPK–MSK1 pathway modulates ataxin 1 protein levels and toxicity in SCA1. *Nature* 29 May 2013 (doi:10.1038/nature12204)

CANCER

Preserving fertility during chemotherapy

Chemotherapy can cause premature ovarian failure and infertility. This study showed that the anticancer drug cyclophosphamide induces follicle loss in mice by triggering the growth of dormant primordial follicles (which represent the non-renewable 'ovarian reserve') through activation of the PI3K (phosphoinositide 3-kinase)–PTEN (phosphatase and tensin homolog)–AKT pathway. Administration of AS101, which modulates the PI3K–PTEN–AKT pathway, increased the follicle reserve and rescued fertility after cyclophosphamide treatment. So AS101, which is currently in clinical trials, could be used to preserve fertility in female patients with cancer.

ORIGINAL RESEARCH PAPER Kalich-Philosoph, L. *et al.* Cyclophosphamide triggers follicle activation and "burnout"; AS101 prevents follicle loss and preserves fertility. *Sci. Transl. Med.* **5**, 185ra62 (2013)