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IN BRIEF

NEURODEGENERATIVE DISORDERS

New Huntington disease target identified

Huntington disease (HD) is caused by the expansion of a CAG repeat tract in the gene encoding huntingtin (HTT), resulting in aggregation of a toxic mutant HTT protein (mHTT). Using an siRNA-based screen in human cultured cells, followed by hit validation in *Drosophila melanogaster*, Jiminez-Sanchez *et al.* have identified glutaminyl cyclase (QPCT) as a potent suppressor of HTT-induced toxicity and aggregation. Design and *in vitro* screening of a series of small-molecule modulators of QPCT activity revealed three compounds that reduced mHTT aggregation and suppressed associated apoptosis in cells, resulting in rescue of HD-related phenotypes in *D. melanogaster* and zebrafish HD models.

ORIGINAL RESEARCH PAPER Jimenez-Sanchez, M. *et al.* siRNA screen identifies QPCT as a druggable target for Huntington's disease *Nature Chem. Biol.* **11**, 347–354 (2015)

CANCER

Towards a personalized cancer vaccine

Systematic targeting of tumour-specific mutations using vaccine approaches represents a promising anticancer strategy. However, the development of such vaccines is challenging as they need to be individually tailored according to each patient's specific mutations. Here, Kreiter *et al.* show in mouse tumour models that cancer-associated mutations are frequently immunogenic and are predominantly recognized by $CD4^+$ T cells. Vaccination of mouse cancer models with engineered RNAs coding for mutant MHC class II epitopes that had elicited strong $CD4^+$ T cell responses — 'mutanome engineered RNA immunotherapy' (MERIT) — reduced tumour growth and increased survival. The authors develop an algorithm, which identifies abundant mutations that are predicted to bind to MHC class II, to aid rapid personalized vaccine development.

ORIGINAL RESEARCH PAPER Kreiter, S. *et al.* Mutant MHC class II epitopes drive therapeutic immune responses to cancer *Nature* **520**, 692–696 (2015)

HEART DISEASE

Stimulating cardiomyocyte regeneration after heart failure

The epidermal growth factor family member neuregulin 1 (NRG1) is required for cardiac development, and administration of recombinant NRG1 (rNRG1) has been proposed as a strategy to promote cardiac regeneration following heart failure. Now, two new papers provide insight into the mechanisms of action of NRG1 and its potential to be therapeutically exploited. D'Uva *et al.* focused their studies on the NRG1 co-receptor ERBB2, which they show is necessary for NRG1-induced cardiomyocyte (CM) proliferation in neonatal mice and which becomes limited as CMs cease division 1 week after birth. Induction of a constitutively active ERBB2 (caERBB2) in neonatal, juvenile and adult CMs generated pronounced cardiomegaly, whereas transient caERBB2 induction in juvenile or adult mice stimulated CM proliferation and allowed heart regeneration after ischaemic injury. Polizzotti *et al.* investigated the potential of rNRG1 to treat paediatric heart failure. Thirty-four days of rNRG1 administration to newborn mice subjected to cryoinjury improved myocardial function and reduced transmural scarring through CM protection and proliferation. Moreover, rNRG1 induced CM proliferation in intact cultured myocardium from infants with heart disease who were less than 6 months old.

ORIGINAL RESEARCH PAPERS D'Uva, G. *et al.* ERBB2 triggers mammalian heart regeneration by promoting cardiomyocyte dedifferentiation and proliferation. *Nature Cell Bio.* **17**, 627–638 (2015) | Polizzotti, B. *et al.* Neuregulin stimulation of cardiomyocyte regeneration in mice and human myocardium reveals a therapeutic window. *Sci. Transl Med.* **7**, 281ra45 (2015)

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