IN BRIEF

LUNG DISEASE

Blocking TGFβ improves emphysema

Signalling mediated by transforming growth factor-β (TGFβ) is dysregulated in lung disorders such as emphysema. This study showed that blockade of TGFβ improved disease symptoms in a mouse model of cigarette smoke-induced emphysema. Administration of a TGFβ-specific neutralizing antibody prevented alveolar cell death, and improved lung architecture and lung mechanics. The clinically used angiotensin receptor type 1 antagonist losartan — which blocks TGFβ signalling — additionally normalized oxidative stress, inflammation, metalloproteinase activation and elastin remodelling, suggesting that TGFβ-targeted therapies could have potential in lung disease.

ORIGINAL RESEARCH PAPER Podowski, M. *et al.* Angiotensin receptor blockade attenuates cigarette smoke-induced lung injury and rescues lung architecture in mice. *J. Clin. Invest.* **122**, 229–240 (2012)

DRUG SAFETY

Predicting adverse drug reactions

Cami *et al.* describe a computational network-based method for predicting adverse drug reactions (ADRs). They collected drug safety data from 2005 and used it to construct a network of known drug–ADR associations. This was used to train a logistic regression model to predict unknown side effects of drugs in the network. The performance of the model was evaluated by comparing these predictions with the new drug–ADR associations that were reported between 2006 and 2010. The model was able to predict seven out of eight drugs that were deemed to be associated with ADRs, highlighting that predictive network methods can be used to predict ADRs.

ORIGINAL RESEARCH PAPER Cami, A. *et al.* Predicting adverse drug events using pharmacological network models. *Sci. Transl. Med.* **3**, 114ra127 (2011)

NEURODEGENERATIVE DISORDERS

A neuroprotective role for sirtuin 1

Cellular metabolism has a key role in the pathogenesis of Huntington's disease (HD), which is caused by the accumulation of mutant huntingtin protein (HTT). These two studies show that sirtuin 1 (SIRT1), an NAD-dependent protein deacetylase involved in the control of cellular metabolism, has neuroprotective effects in mouse models of HD. Jiang *et al.* showed that overexpression of SIRT1 in mice with HD (N171-82Q mice) improved motor function, decreased brain atrophy, and attenuated the metabolic abnormalities and decline in brain-derived neurotrophic factor (BDNF) concentration induced by mutant HTT. Furthermore, they showed that mutant HTT interacts with SIRT1 to inhibit its deacetylase activity, which prevents its pro-survival function. In agreement with these findings, Jeong *et al.* showed that brain-specific SIRT1 overexpression improved the survival, neuropathology and expression of BDNF in another mouse model of HD (R6/2 mice), and that the deacetylase activity of the enzyme is required for its neuroprotective effects. They also showed that mutant HTT disrupts the interaction between cAMP-responsive element binding protein (CREB) and CREB-regulated transcription co-activator 1 (TORC1; indentified as a new SIRT1 substrate), which suppresses the transcription of BDNF; overexpression of SIRT1 restores this interaction by deacetylating and activating TORC1. Together, these findings suggest that modulation of SIRT1 could be beneficial in HD.

ORIGINAL RESEARCH PAPERS Jiang, M. *et al.* Neuroprotective role of Sirt1 in mammalian models of Huntington's disease through activation of multiple Sirt1 targets. *Nature Med.* 18 Dec 2011 (doi:10.1038/nm.2558) | Jeong, H. *et al.* Sirt1 mediates neuroprotection from mutant huntingtin by activation of the TORC1 and CREB transcriptional pathway. *Nature Med.* 18 Dec 2011 (doi:10.1038/nm.2559)