

IN BRIEF

PULMONARY DISORDERS

Dynamic regulation of cardiolipin by the lipid pump *Atp8b1* determines the severity of lung injury in experimental pneumonia

Ray, N. B. *et al. Nature Med.* **16**, 1120–1127 (2010)

Ray and colleagues show that mice and humans with bacterial pneumonia have elevated amounts of cardiolipin, a mitochondrion-specific phospholipid that disrupts surfactant function. They also identified a unique cardiolipin transporter, *Atp8b1*, which has insufficient capacity to remove cardiolipin from lung fluid during inflammation or when *Atp8b1* is defective. Administration to mice of a peptide that encompassed the cardiolipin-binding motif attenuated bacteria-induced lung injury and improved survival.

ANTICANCER DRUGS

HSP90 is a therapeutic target in JAK2 dependent myeloproliferative neoplasms in mice and humans

Marubayashi, S. *et al. J. Clin. Invest.* **120**, 3578–3593 (2010)

Activating mutations in JAK2 kinase occur in patients with myeloproliferative neoplasms (MPNs), but JAK2 inhibitors have shown limited efficacy in clinical trials. This paper shows that JAK2 is a substrate of the chaperone protein HSP90 and that a HSP90 inhibitor — PU-H71 — causes degradation of JAK2. In mouse models of MPN, PU-H71 normalized peripheral blood counts and improved survival at doses that did not degrade JAK2 in normal tissues. Importantly, it also reduced the mutant allele burden in mice, suggesting that HSP90 inhibition could be useful in treating JAK2-dependent MPN.

BIOTECHNOLOGY

An antibody as a surrogate receptor reveals determinants of activity of an innate immune peptide antibiotic

Lomash, S., Nagpal, S. & Salunke, D. M. *J. Biol. Chem.* 13 Sep 2010 (doi:10.1074/jbc.M110.150516)

Lack of knowledge about target receptors can hinder the discovery of new ligands. This paper shows that monoclonal antibodies (mAbs) can act as surrogate receptors for innate immune peptide antibiotics. A mAb was raised against indolicidin, a broad-spectrum antimicrobial peptide of innate immune origin. Studies of the interactions between the peptide and the mAb identified an antibiotic motif in indolicidin, and additional independent bactericidal sequences were identified from a random peptide library. Such bactericidal motifs may be used as a template for the design of future antibiotics.

NEURODEGENERATIVE DISEASE

Acetylation of tau inhibits its degradation and contributes to tauopathy

Min, S.-W. *et al. Neuron* **67**, 953–966 (2010)

Hyperphosphorylation of tau is a hallmark of several neurodegenerative disorders, but the mechanisms that regulate the turnover of phosphorylated tau are unknown. Min and colleagues show that tau is acetylated by histone acetyltransferase p300 and that acetylation prevents the degradation of phosphorylated tau. Moreover, tau acetylation was elevated in patients with tauopathy. In a neuronal model of tauopathy, a small-molecule inhibitor of p300 eliminated phosphorylated tau, suggesting that modulating tau acetylation could reduce tau-mediated neurodegeneration.

