IN BRIEF

NEURODEGENERATIVE DISEASE

Toll-like receptor 4 agonist shows benefit in AD

Compounds that stimulate the immune system to clear amyloid-β (Aβ) could have therapeutic potential in Alzheimer's disease (AD). Michaud *et al.* showed that systemic injections of monophosphoryl lipid A (MPLA) — a Toll-like receptor 4 agonist that has immunomodulatory properties — reduced Aβ load in the brain and enhanced cognitive function in a mouse model. At a cellular level, MPLA induced a strong phagocytic response by microglia (but only triggered a low inflammatory response).

ORIGINAL RESEARCH PAPER Michaud, J-. P. *et al.* Toll-like receptor 4 stimulation with the detoxified ligand monophosphoryl lipid A improves Alzheimer's disease-related pathology *Proc. Natl Acad. Sci. USA* **110**, 1941–1946 (2013)

CANCER

A target for drug resistance

This study used gene expression profiling of multiple myeloma samples to identify genes involved in drug resistance. Expression of *NEK2*, a chromosomal instability gene that encodes a protein kinase, was correlated with drug resistance (through the activation of efflux pumps), rapid relapse and poor outcome in multiple myeloma and other cancers. RNA-mediated knockdown of NEK2 overcame drug resistance and induced apoptosis in a xenograft mouse model of multiple myeloma, suggesting that NEK2 could act as a marker of drug resistance and poor prognosis as well as a new target for therapy.

ORIGINAL RESEARCH PAPER Zhou, W. *et al. NEK2* induces drug resistance mainly through activation of efflux drug pumps and is associated with poor prognosis in myeloma and other cancers. *Cancer Cell* **23**, 48–62 (2013)

ANTIBIOTICS

Boosting antibiotic activity via ROS

This study showed that inducing microbial reactive oxygen species (ROS) can potentiate antibiotic activity. The authors used a systems biology approach to identify ROS-generating reactions in *Escherichia coli* metabolism, then experimentally tested deletions of genes that encode these metabolic enzymes. Deletion of either of four target genes (*cyoA*, *nuoG*, *sdhC* or *pta*) increased the sensitivity to β-lactam and/or fluoroquinolone antibiotics. Moreover, chemical inhibition of one target — succinate dehydrogenase — increased the sensitivity to oxidant and ampicillin treatment.

ORIGINAL RESEARCH PAPER Brynildsen, M. P. *et al.* Potentiating antibacterial activity by predictably enhancing endogenous microbial ROS production. *Nature Biotech.* **31**, 160–165 (2013)

OCULAR DISORDERS

A new target in age-related macular degeneration

In age-related macular degeneration (AMD), exudation of choroidal neovascularization (CNV) results in severe vision loss. This study investigated the role of JUN kinase (JNK) in the development of CNV. In a model of wet AMD, mice lacking JNK1 had reduced inflammation, reduced CNV and lower levels of choroidal vascular endothelial growth factor (VEGF). Intravitreal injection of a specific peptidic JNK inhibitor decreased choroidal VEGF expression and reduced pathological CNV. These results suggest that JNK inhibition could complement existing VEGF-targeted therapies in AMD.

ORIGINAL RESEARCH PAPER Du, H. *et al.* JNK inhibition reduces apoptosis and neovascularization in a murine model of age-related macular degeneration. *Proc. Natl Acad. Sci. USA* **110**, 2377–2382 (2013)