IN BRIEF

NEURODEGENERATIVE DISEASE

Toll-like receptor 4 agonist shows benefit in AD

Compounds that stimulate the immune system to clear amyloid- β (A β) 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 A β 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)