IN BRIEF

ALZHEIMER'S DISEASE

Amyloid-β dynamics are regulated by orexin and the sleep-wake cycle

Kang, J-. E. *et al. Science* 24 Sep 2009 (doi:10.1126/science.1180962)

The accumulation of amyloid-β in the brain is a crucial event in the pathogenesis of Alzheimer's disease. The authors found that amyloid-β levels in brain interstitial fluid correlated with wakefulness in mice and in healthy human volunteers. In transgenic mice that express a mutated form of human amyloid precursor protein, amyloid-β levels increased during sleep deprivation and during infusion of orexin — a hormone that regulates wakefulness — but decreased with infusion of an orexin receptor antagonist. Thus, the sleep-wake cycle and orexin could modulate the pathogenesis of Alzheimer's disease.

CANCER

Evidence that mitotic exit is a better cancer therapeutic target than spindle assembly

Huang, H-.C. *et al. Cancer Cell* **16**, 347–358 (2009)

Cancer cells can resist drugs that target spindle proteins and activate the spindle assembly checkpoint by undergoing premature mitotic exit. Huang and colleagues reasoned that blocking mitotic exit downstream of the checkpoint might overcome drug resistance. RNA interference-mediated knockdown of the cell cycle regulatory protein Cdc20 blocked mitotic exit independently of the spindle assembly checkpoint and slowed cyclin B1 proteolysis, allowing more time for cell death initiation. This study aids the understanding of how mitotic arrest triggers cell death and suggests that targeting Cdc20 may be an effective therapeutic strategy.

HIGH-THROUGHPUT SCREENING

High-throughput *in vivo* screening of targeted molecular imaging agents

Gagnon, M. K. *et al. Proc. Natl Acad. Sci. USA* **106**, 17904–17909 (2009)

The development of targeted molecular imaging agents is currently a slow process. This paper used combinatorial chemistry, site-specific solid-phase radiolabelling and ***in vivo*** imaging to rapidly screen molecular imaging agents. Evaluation of a one-bead–one-compound library led to the identification of 42 lead peptides that targeted the $\alpha_v\beta_6$ integrin. These peptides were radiolabelled and then evaluated ***in vivo*** using micro-positron emission topography. As a result, four promising new molecular imaging agents were identified that otherwise would not have been selected based solely on ***in vitro*** data.

ANTICANCER DRUGS

A small molecule inhibitor of inducible heat shock protein 70

Leu, J. I. -J. *et al. Mol. Cell.* **36**, 15–27 (2009)

Heat shock protein 70 (HSP70) expression contributes to resistance to cancer therapy. Leu and colleagues showed that the small molecule 2-phenylethynesulfonamide (PES) interacts with HSP70 and leads to a disruption of the association between HSP70 and several of its co-chaperones and substrate proteins. Treatment of tumour cells with PES promoted cell death and was associated with impaired autophagy and inhibition of lysosomal function. In a mouse model of Myc-induced lymphomagenesis, PES suppressed tumour development and enhanced survival.