IN BRIEF

ANALGESIA

Distinct roles of matrix metalloproteases in the early- and late-phase development of neuropathic pain.

Kawasaki, Y. *et al. Nature Med.* 10 Feb 2008 (doi:10.1038/nm1723)

The mechanisms that underlie neuropathic pain are poorly understood. Kawasaki and colleagues report that early- and late-phase neuropathic pain development requires different matrix metalloproteinases (MMPs). MMP9 serves as a trigger for early-phase pain development through interleukin (IL) 1 cleavage and p38 activation, whereas MMP2 produces late-phase pain through IL1 cleavage and ERK activation. Endogenous inhibitors of MMPs suppressed pain, suggesting that MMP inhibition might provide a new approach to neuropathic pain treatment at different phases.

CHEMICAL BIOLOGY

Large-scale chemical dissection of mitochondrial function.

Wagner, B. K. *et al. Nature Biotechnol.* 24 Feb 2008 (doi:10.1038/nbt1387)

To investigate how mitochondrial oxidative phosphorylation (OXPHOS) — a process central to energy homeostasis — is integrated in cells, Wagner and colleagues combined four cell-based assays of OXPHOS physiology with multiplexed measurements of nuclear and mitochondrial gene expression across 2,490 small-molecule perturbations in cultured muscle. The study provided a screening compendium that can be used as a discovery tool both for understanding mitochondrial biology and toxicity and for identifying novel therapeutics.

ANTI-PARASITIC DRUGS

Discovery of potent pteridine reductase inhibitors to guide antiparasite drug development.

Cavazzuti, A. *et al. Proc. Natl Acad. Sci. USA* **105**, 1448–1453 (2008)

Inhibition of pteridine reductase (PTR1) — an enzyme essential for parasitic trypanosomatid survival — might represent a therapeutic approach for African sleeping sickness. Cavazzuti and colleagues combined a rapid-screening strategy using a folate-based library with structure-based design to identify PTR1 inhibitors with biological activity. An additive profile was observed when PTR1 inhibitors were used in combination with known dihydrofolate reductase inhibitors, indicating the potential of targeting two enzymes for the development of previously undescribed antiparasitic drugs.

ANTICANCER DRUGS

Correlation of tumor growth suppression and methionine aminopetidase-2 activity blockade using an orally active inhibitor.

Garlich, J. R. *et al. Proc. Natl Acad. Sci. USA* **105**, 1838–1843 (2008)

Garlich and colleagues have discovered a class of orally active sulfonamide methionine aminopeptidase 2 (MetAP2) inhibitors, exemplified by A-800141, a bioavailable inhibitor that they found to have anticancer activity in a variety of tumour xenografts. A glyceraldehyde-3-phosphate dehydrogenase biomarker assay was developed to evaluate *in vivo* MetAP2 inhibition in circulating mononuclear cells and in tumours; together with the MetAP2 inhibitors, this assay might be developed for cancer treatment.