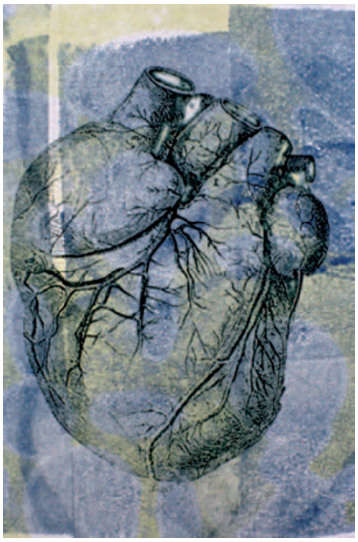
IN BRIEF



CARDIOVASCULAR DISEASE

Histone deacetylase (HDAC) inhibitors attenuate cardiac hypertrophy by suppressing autophagy

Cao, D. J. *et al. Proc. Natl Acad. Sci. USA* **108**, 4123–4128 (2011)

Histone deacetylases (HDACs) regulate cardiac plasticity but their molecular target (or targets) are not known. This paper showed that autophagy mediated by HDAC1 and HDAC2 contributes to pathological cardiac remodelling. In cultured cardiomyocytes, hypertrophy and autophagy were blocked by any of three structurally distinct HDAC inhibitors, and in mice with pre-existing hypertrophy, treatment with the HDAC inhibitor trichostatin A caused ventricular mass to revert to near-normal levels and completely normalized ventricular function.

PROTEIN BIOCHEMISTRY

Protein native-state stabilization by placing aromatic side chains in N-glycosylated reverse turns

Culyba, E. K. *et al. Science* **331**, 571–575 (2011)

Aspargine glycosylation of protein therapeutics at sites that are normally not glycosylated could increase their stability. This study showed that inserting a structural module in which a phenylalanine residue is placed two or three positions before a glycosylated asparagine in distinct reverse turns — which are tertiary structural features in which a polypeptide chain turns back on itself — facilitates stabilizing interactions between the aromatic side chain of the phenylalanine residue and the glycan. Introducing this structural module into three different proteins stabilized their native states and increased the efficiency of cellular glycosylation.

NATURAL PRODUCTS

XPB, a subunit of TFIIH, is a target of the natural product triptolide

Titov, D. V. *et al. Nature Chem. Biol.* **7**, 182–188 (2011)

This study identified the molecular target of triptolide; triptolide is a natural product that is isolated from a Chinese medicinal plant and has anti-inflammatory, immunosuppressive and antitumour activities. The authors showed that triptolide covalently binds to human XPB — which is a subunit of the transcription factor TFIIH — and inhibits its DNA-dependent ATPase activity, which leads to the inhibition of RNA polymerase II-mediated transcription. This mechanism accounts for most of the known actions of triptolide, and suggests a new target (that is, TFIIH) for an anticancer agent.

CANCER

Sensitivity to antitubulin chemotherapeutics is regulated by MCL1 and FBW7

Wertz, I. E. *et al. Nature* **471**, 110–114 (2011)

The mechanism of action of, and resistance to, anticancer agents that target microtubules — such as paclitaxal — is not completely understood. Wertz and colleagues showed that in antitubulin agent-treated cells the pro-survival protein MCL1 first interacts with the tumour suppressor protein FBW7 and is then targeted for degradation. The decline in MCL1 protein levels potentiates cell death. In patient-derived tumour cells that lacked FBW7, MCL1 degradation was blocked, which conferred resistance to antitubulin agents. These findings suggest that profiling for FBW7 and MCL1 in tumours could be used to predict responses to antitubulin agents.