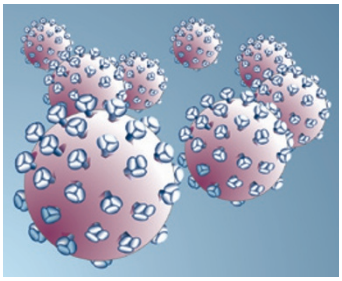
IN BRIEF



HIV

Identification of host proteins required for HIV infection through a functional genomic screen.

Brass, A. L. *et al. Science* 10 Jan 2008 (doi 10.1126/science.1152725)

Brass and colleagues performed a large-scale small interfering RNA screen to identify over 250 HIV-dependency factors required for HIV-1 infection. These factors participate in a broad range of cellular functions and implicate new pathways in the viral life cycle, and so may be potential targets for therapy. Transcriptional analysis revealed that HIV-dependency factor genes were enriched for high expression in immune cells, suggesting that viruses evolve in host cells that optimally perform the functions required for their life cycle.

AIRWAY DISEASES

Mast cell renin and a local renin–angiotensin system in the airway: role in bronchoconstriction.

Veerappan, A. *et al. Proc. Natl Acad. Sci.* USA **105**, 1315–1320 (2008)

Veerappan and colleagues demonstrated the existence of an airway renin–angiotensin system that is triggered by the release of mast-cell renin. In a guinea pig model of immediate-type hypersensitivity, anaphylactic mast-cell degranulation resulted in angiotensin II-mediated bronchoconstriction, which was inhibited by a renin inhibitor, an angiotensin type 1 receptor antagonist, and a mast-cell stabilizer. These results show that locally produced angiotensin II is a critical factor governing bronchoconstriction, opening the possibility for novel therapeutic targets in the management of airway disease.

ANTIBACTERIAL DRUGS

Domain requirement of moenomycin binding to bifunctional transglycosylases and development of high-throughput discovery of antibiotics.

Cheng, T. J. *et al. Proc. Natl Acad. Sci. USA* **105**, 431–436 (2008)

Multidrug-resistant bacterial pathogens create the urgent need for new antibiotics. Cheng and colleagues compared the binding affinities of moenomycin A with various penicillin-binding proteins (PBPs) — key enzymes in bacterial cell wall synthesis — and found that the transmembrane domain is important for moenomycin binding. They devised a general method for expressing and purifying class A PBPs and developed a high-throughput assay that enabled the identification of transglycosylase inhibitors.

ANTICANCER DRUGS

A vascular targeted pan phosphoinositide 3-kinase inhibitor prodrug, SF1126, with antitumor and antiangiogenic activity.

Garlich, J. R. *et al. Cancer Res.* **68**, 206–215 (2008)

The pan phosphoinositide 3-kinase (PI3K) inhibitor LY294002 exerts control over tumour growth, but is not a viable drug candidate. Garlich and colleagues describe a novel LY294002 prodrug — termed SF1126 — that has increased solubility and binds to specific integrins within the tumour compartment, resulting in enhanced delivery to the tumour vasculature and tumour. These results support the application of pan-PI3K inhibitory prodrugs for the treatment of cancer, and provided the rationale for the recent initiation of Phase I clinical trials of SF1126.