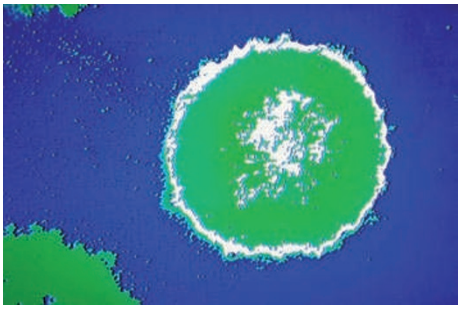
IN BRIEF



HIV

HIV enters cells via endocytosis and dynamin-dependent fusion with endosomes

Miyauchi, K. *et al. Cell* **137**, 433–444 (2009)

It has been assumed that HIV-1 fuses directly with the plasma membrane to initiate entry into host cells. However, using time-resolved imaging of single viruses, this paper revealed that HIV-1 uses the endocytic machinery to enter into and fuse with target cells. HIV-1 underwent receptor-mediated internalization long before endosomal fusion, thus minimizing the surface exposure of conserved viral epitopes during fusion and reducing the efficacy of inhibitors that targeted these epitopes. So, to efficiently block intracellular fusion events, new HIV entry inhibitors need to be able to permeate the cell membrane.

CANCER

RNAi screen for rapid therapeutic target identification in leukemia patients

Jeffrey, W. *et al. Proc. Natl Acad. Sci. USA* **106**, 8695–8700 (2009)

Jeffrey and colleagues developed an RNA interference (RNAi)-assisted protein target identification (RAPID) screen to identify specific tyrosine kinases that are required for the survival of malignant cells. When applied to primary leukaemia cells from 30 patients, the screen identified known, activating mutations in janus kinase 2 and KRAS, patient-specific sensitivity to inhibition of a collection of kinases, and a previously unknown activating mutation in the thrombopoietin receptor. Application of the RAPID screen could aid personalized diagnosis of molecular cancer targets.

NEUROLOGICAL DISEASE

Endothelial basement membrane laminin α5 selectively inhibits T lymphocyte extravasation into the brain

Wu, C. *et al. Nature Med.* **15**, 519–527 (2009)

This study showed that disrupting the interaction between lymphocytes and laminins on the endothelial basement membrane can reduce multiple sclerosis without compromising innate immune responses. When integrin α6β1, the major laminin α4 receptor on encephalitogenic T lymphocytes, was genetically eliminated or blocked with antibodies, mouse models of multiple sclerosis had reduced disease susceptibility and severity, owing to a reduction in T lymphocyte infiltration into the brain. So, the distinct mechanisms used by T lymphocytes to penetrate the endothelial basement membrane barrier permit specific targeting of this cell population.

ALLERGIC DISEASES

A sensory neuronal ion channel essential for airway inflammation and hyperreactivity in asthma

Caceres, A. L. *et al. Proc. Natl Acad. Sci. USA* **106**, 9099–9104 (2009)

The limited efficacies of immune-directed therapies in asthma suggest additional mechanisms in airway inflammation. In mouse models of allergic asthma, Caceres and colleagues showed that genetic ablation or antagonist blockade of transient receptor potential cation channel A1 (TRPA1) — an irritant-sensing ion channel expressed in airway chemosensory nerves — inhibited allergen-induced leukocyte infiltration in the airways, reduced cytokine and mucus production, and almost abolished airway hyperreactivity.