molecular interventions
pharmacological perspectives from biology, chemistry and genomics

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DEPARTMENTS

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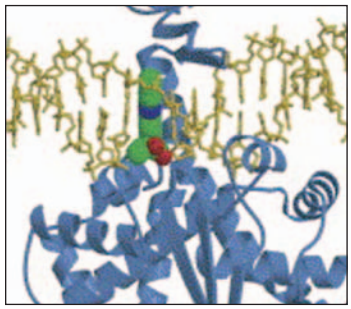


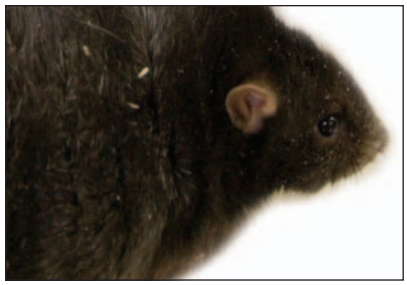
page 245
Untangling the web of death smallpox weaves

VIEWPOINTS

Smallpox is a serious and highly contagious disease that is caused by the variola virus. It is one of the most severe infectious human diseases known, with mortality rates as high as 30%. A successful worldwide vaccination program led to the eradication of smallpox in 1980. However, the high transmission rate of variola virus, coupled with the deadly nature of smallpox, makes this virus a potentially devastating weapon for bioterrorism. Currently, there is no specific treatment for smallpox. However, a recent article on the structure of a variola topoisomerase IB–DNA complex provides an intriguing starting point for the rational design of drugs with potential activity against smallpox.

Neil Osheroff

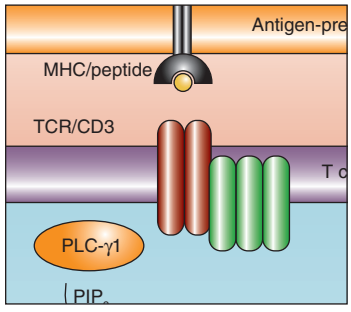
In the battle to treat the pandemic of obesity, one therapeutic strategy is to block endogenous signals that stimulate appetite and control body weight. One such molecule is ghrelin, a gut peptide that is the only known orexigenic hormone and is a likely contributor to mealtime hunger. The relative importance of ghrelin in long-term body-weight regulation (and thus its promise as an anti-obesity target) is uncertain, however, because genetic and pharmacologic blockade of ghrelin signaling have yielded variable results to date. Using a novel approach of vaccinating rats against their own ghrelin, Zorilla et al. report that animals with high ghrelin-specific antibody titers displayed restricted body weight, without evidence of non-specific inflammation following the vaccine. These results favor a meaningful role for ghrelin in energy homeostasis, hinting at a possible new anti-obesity approach. More broadly, the work of Zorilla et al. supports the feasibility of vaccinations directed against specific autologous targets—immunopharmacotherapy that could potentially be developed to target a wide array of medical conditions.



page 249
First steps toward a vaccine

Molly J. Carlson and David E. Cummings

Severe Combined Immunodeficiency (SCID) is a rare primary immunodeficiency disease often characterized by a block in T cell development, which may also affect the normal development of B cells and NK cells. Several different mutations are known to give rise to SCID, and multiple genes are involved. Consequently, there are several different forms of SCID, which can be classified according to the metabolic and cellular defects that impede normal lymphocyte function. The two most prevalent forms of SCID are X-linked SCID and adenosine deaminase (ADA) deficiency SCID, together accounting for approximately 70–80% of disease cases. Other genetic abnormalities associated with this syndrome range from defective T cell receptor rearrangement to non-functional signaling molecules. Recently, a new genetic defect has been described in which mutations in a key component of Ca^{2+} release activated–channels (CRAC) result in T lymphocyte malfunction.



page 253
CRAC'ing open the regulation of T cell activation

Helen P. Carroll, Benjamin B.A. McNaull, and Massimo Gadina

REVIEWS