IN BRIEF

THERAPEUTIC ANTIBODIES

Anti-phospholipid human monoclonal antibodies inhibit CCR5-tropic HIV-1 and induce β-chemokines

Moody, M. A. *et al. J. Exp. Med.* **207**, 763–776 (2010)

HIV-1 vaccine development is focused mainly on the induction of antibodies specific for the HIV-1 envelope glycoproteins gp41 and gp120, but no immunogen has so far been able to induce broadly neutralizing antibodies against these targets; so other antibody specificities are also being investigated. This study describes four human monoclonal antibodies specific for phospholipids that can potently neutralize the infectivity of a range of primary and transmitted HIV-1 isolates that use CC-chemokine receptor 5 (CCR5) as a co-receptor, but not isolates that use CXC-chemokine receptor 4 (CXCR4), in peripheral blood mononuclear cells. The phospholipid-specific antibodies do not bind HIV-1 virions but instead mediate neutralization by triggering production of the CCR5 ligands CCL3 and CCL4 by monocytes.

THERAPEUTIC ANTIBODIES

From transcriptome analysis to therapeutic anti-CD40L treatment in the SOD1 model of amyotrophic lateral sclerosis

Lincecum, J. M. *et al. Nature Genet.* 28 Mar 2010 (doi:10.1038/ng.557)

This study provides an example of how genome-wide transcriptional profiling can be used to identify new targets for therapeutic antibodies in a disease model. In a mouse model of amyotrophic lateral sclerosis (ALS) — which involves fatal degeneration of motor neurons — the authors observed an increase in expression of genes involved in co-stimulatory interactions between T cells and antigen-presenting cells in skeletal muscle, spinal cord and sciatic nerve. This was associated with the accumulation of macrophages in the peripheral nerves during disease onset and progression. When the mice were treated with a CD40 ligand-blocking monoclonal antibody to inhibit co-stimulation before disease onset, body-weight decline and the onset of paralysis were delayed and survival time was increased. CD40 ligand-specific antibody treatment reduced macrophage infiltration in the peripheral nerves and decreased the expression of genes in the co-stimulatory pathway.

THERAPEUTIC ANTIBODIES

Antigenic modulation limits the efficacy of anti-CD20 antibodies: implications for antibody selection

Beers, S. A. *et al. Blood* 11 Mar 2010 (doi:10.1182/blood-2010-01-263533)

Differential modulation of cell-surface expression levels of CD20 might explain the variable potencies of different CD20-specific antibodies in different types of lymphoma. Type I (rituximab-like) antibodies decreased the cell-surface level of CD20 by 80–90% in CD20-transgenic B cells through antibody-mediated internalization, whereas type II (tositumomab-like) antibodies had no effect on CD20 expression levels. The decrease in CD20 cell-surface expression level mediated by type I antibodies correlated with a decreased antibody half-life and resulted in decreased phagocytosis by macrophages and faster B cell repopulation. The rate of internalization of type I CD20-specific antibodies varied between different types of primary B cell lymphoma, which might explain why they have different therapeutic responses. Blocking CD20 internalization might increase the efficacy of type I antibodies, which are used more often than type II antibodies in the clinic.