IN BRIEF

IMMUNOTHERAPY

Identification of class I MHC-associated phosphopeptides as targets for cancer immunotherapy.

Zarling, A. L. *et al. Proc. Natl Acad. Sci. USA* **103**, 14889–14894 (2006)

Infection or cellular transformation can be accompanied by changes in protein expression and/or metabolism that alter the peptides displayed on MHC class I molecules and recognized by $CD8^+$ T cells. Indeed, one of the hallmarks of malignant transformation is alterations in the phosphorylation of cellular proteins. Zarling *et al*. proposed that, when these phosphoproteins are degraded by the proteasome, cancer-specific phosphopeptides could be generated, and these could be presented by MHC class I molecules on malignant cells. A comparative analysis of phosphopeptides presented at the surface of various cancer cells showed that these endogenously expressed MHC-class-I-associated phosphopeptides were recognized by specific $CD8^+$ T cells. This recognition is a result of both the level of expression and the phosphorylation of the underlying source proteins. These phosphopeptides are therefore potential targets for cancer immunotherapy.

VIRAL IMMUNITY

Virus-induced type I IFN stimulates generation of immunoproteasomes at the site of infection.

Shin, E.-C. *et al. J. Clin. Invest.* 12 Oct 2006 (doi:10.1172/JCI29832)

Type II interferon (IFN) is known to be the initial and main inducer of the 26S proteasome (also known as the immunoproteasome; an important cytosolic antigen-processing complex) during viral infections. A type I IFN response, however, is induced by many viruses much earlier than a type II IFN response, so in this study the role of type I IFNs in the induction of immunoproteasomes was investigated. *In vitro*, type I IFNs triggered the induction, assembly and proteolytic activity of immunoproteasomes in human liver cells. *In vivo*, in contrast to the currently held view, the intrahepatic induction of functional immunoproteasomes in response to infection of chimpanzees with hepatitis C virus occurred earlier than the intrahepatic expression of type II IFN. The authors propose that this might be one explanation for the effectiveness of type-I-IFN-based therapies when administered early during infection with hepatitis C virus.

AUTOIMMUNITY

Persistent expression of autoantibodies in SLE patients in remission.

Yurasov, S. *et al. J. Exp. Med.* **203**, 2255–2261 (2006)

Untreated systemic lupus erythematosus (SLE) is characterized by defective early B-cell-tolerance checkpoints, so autoreactive and polyreactive antibodies accumulate in the circulating mature naive (resting) B-cell compartment. Current treatment protocols can induce long-term remission but frequently fail to prevent relapses. This report investigated the status of early B-cell tolerance in patients with SLE who are in clinical remission. Increased amounts of autoreactive and polyreactive antibodies continued to be produced in these patients, although they had fewer B cells that express these antibodies than did patients with active disease. The persistence of autoreactive mature naive B cells in patients with SLE who are in clinical remission indicates that abnormalities in early B-cell-tolerance checkpoints are an integral feature of SLE.