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In This Issue

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A bioactive peptide shared by an MHC molecule and a lipid kinase. (See article on pages 1447–1453.) Boytim and colleagues previously reported that a short peptide derived from the class II major histocompati-bility complex (MHC) molecule strongly suppresses the proliferation of cultured lymphocytes. They proposed then that this peptide (DQ 65-79), like a corresponding MHC I-derived peptide that they had studied, might prove useful for suppressing graft rejection. Here, the same group explores the effects of DQ 65-79 on the sig-naling pathway that activates T-cells in response to IL-2, comparing the effects of this peptide with those of the immunosuppressive drug rapamycin. They find that both treatments block a downstream event in IL2 sig-naling, the activation of the S6 kinase, but that DQ 65-79 interferes at an earlier step than does rapamycin. Not-ing a similarity between the sequence of the peptide and a conserved catalytic region of the phosphatidylinositol (PI) 3-kinase—an enzyme that is activated at an early and critical step of IL2 signaling—Boytim et al. tested the effect of DQ 65-79 on PI 3-kinase in vitro. They report here that the peptide acts by a still-uncertain mechanism to inhibit this lipid kinase in a dose-dependent manner. This peptide could therefore repre-sent a cryptic immunomodulatory sequence within the class II MHC. The challenge remains to determine whether the MHC protein […]

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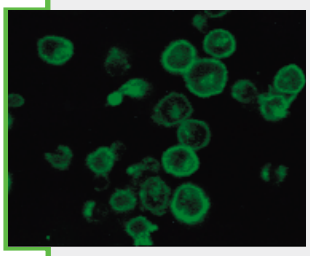

Subtle IFN-γ receptor defects that abolish receptor function

(*See article on pages 1429–1436.*)

Binding of interferon (IFN)-γ to its receptor IFNγR1 represents a crucial early event in immune responses to bacteria and viruses, as seen in the occasional person genetically deficient in IFNγR1. Such individuals typically die in childhood, and, since the fatal illness is often an uncontrollable mycobacterial infection caused by vaccination with live attenuated bacille Calmette-Guérin, it would be of great value to identify children with homozygous defects in the *IFNγR1* gene before vaccination. Jouanguy and coworkers have identified 3 children, of diverse ethnic backgrounds, who experienced severe mycobacterial disease after vaccination. These authors now report that the *IFNγR1* alleles segregating in these families are of a novel class that would not be detected by standard assays. Unlike previously defined strong mutations in this gene, which introduced premature termination codons and would be expected to block IFNγR1 surface expression entirely, the 4 alleles described here are missense mutations or short in-frame deletions, and their products reach the surface of lymphocytes and monocytes. Despite their efficient surface expression and generally normal conformation, as judged by binding to various monoclonal antibodies, these mutant forms of the receptor fail to bind IFN-γ. The authors discuss the structural changes in the mutant IFNγR1 protein in light of other data on ligand- and antibody-binding sites in this receptor, and they propose that ligand-binding or other functional assays for the receptor, in addition to antibody-based detection assays, should be standard tools used to diagnose IFNγR1 deficiency.

In vivo activation of dendritic cells to promote antitumor immunity

(*See article on pages 1383–1393.*)

Dendritic cells (DCs) are specialized antigen-presenting cells that activate T cell responses against specific antigens. The potential use of DCs as an adjuvant to provoke cellular immunity against tumor antigens has inspired considerable excitement, and here Fushimi et al. describe a simple strategy by which to provoke the desired response by DCs and cytotoxic T lymphocytes (CTLs). The chemokine MIP-3α attracts DCs in cell culture experiments and also promotes their maturation to a form that efficiently primes CTL responses against antigens presented by the DCs. By instilling tumors of several types with an adenoviral vector carrying the MIP-3α cDNA, Fushimi and colleagues show that they can activate DC migration into tumors and thereby extend the life of the host animal significantly. As expected, the protection against these tumors depends on CTLs, since it does not occur in CD8 deficient mice. Naïve mice, in addition, can be protected from growth of the relevant tumor type by passive transfer of splenocytes from tumor-bearing mice that received the recombinant adenovirus. Crucially, treated animals enjoy protection systemically, not only at the site at which the virus was introduced, suggesting that CTLs activated by this means can target both metastases and cells of the primary tumor.