JCI The Journal of Clinical Investigation

In This Issue

John Ashkenas

J Clin Invest. 2001;107(12):1479-1479. https://doi.org/10.1172/JCI119928.

In this issue

Immune costimulation and the Kaposi's virus (See article on pages 1599–1606.) Viruses of the herpesvirus family have developed numerous innovative strategies to establish themselves in their host by evading, destroying, or redirecting host immune cells. Here, Coscoy and Ganem define a novel pathway through which the human herpesvirus associated with Kaposi's sarcoma (KSHV) acts on the B cells that it infects to block the protective response of cytotoxic T lymphocytes (CTLs). B cells are a major target of KSHV and are key to host defenses against the virus, because they act as antigen-presenting cells (APCs) to activate CTL responses against infected cells. As is generally seen in APC-T cell interactions, efficient activation of CTLs against KSHV requires not just that the B cells present a viral peptide in an appropriate MHC context, but also that they express one or more costimulatory proteins. Coscoy and Ganem show that the viral protein K5 acts specifically on the surface expression of two costimulatory proteins, ICAM and B7-2, causing them to be internalized rapidly and routed to the lysosome. In the absence of these proteins on the B cell surface, interacting T cells fail to induce the usual program of gene expression that is associated with active CTL responses. Because K5 resides in the ER protein of infected cells, its specific and profound effect […]

In this issue

By John Ashkenas, Science Editor

Immune costimulation and the Kaposi's virus

(See article on pages 1599–1606.)

Viruses of the herpesvirus family have developed numerous innovative strategies to establish themselves in their host by evading, destroying, or redirecting host immune cells. Here, Coscoy and Ganem define a novel pathway through which the human herpesvirus associated with Kaposi's sarcoma (KSHV) acts on the B cells that it infects to block the protective response of cytotoxic T lymphocytes (CTLs). B cells are a major target of KSHV and are key to host defenses against the virus, because they act as antigen-presenting cells (APCs) to activate CTL responses against infected cells. As is generally seen in APC–T cell interactions, efficient activation of CTLs against KSHV requires not just that the B cells present a viral peptide in an appropriate MHC context, but also that they express one or more costimulatory proteins. Coscoy and Ganem show that the viral protein K5 acts specifically on the surface expression of two costimulatory proteins, ICAM and B7-2, causing them to be internalized rapidly and routed to the lysosome. In the absence of these proteins on the B cell surface, interacting T cells fail to induce the usual program of gene expression that is associated with active CTL responses. Because K5 resides in the ER protein of infected cells, its specific and profound effect on the fate of surface-expressed ICAM and B7-2 remains a puzzle.

Re-examining iron's role in heart disease

(See article on pages 1545–1553.)

Chemically modified forms of the LDL are thought to serve as the direct source of cholesterol in atherosclerotic plaques, but the nature of the chemical modification that converts native LDL to an atherogenic species in vivo is a matter of much debate. LDL can be oxidized in vitro by treatment with iron or other metal ions to generate a form that accumulates in cultured cells, mimicking the genesis of foam cells in the early atherosclerotic lesion. The potential importance of iron in atherogenesis has been suggested frequently, and some epidemiological evidence suggests that high serum iron levels can promote heart disease. Arguing against such an association is the finding that people with the iron-overload disorder hemochromatosis seem to develop arterial lesions more slowly than those in the general population, raising the possibility that high serum iron is somehow protective. Kirk et al. now make a similar observation in a more tractable experimental system. Here, they show that high levels of dietary iron are associated with delayed progression of arterial lesions in atherosclerosis-prone mice. The authors speculate about the basis of this paradoxical effect, and they exclude the possibility that iron overload reduces serum lipoprotein levels or induces a systemic increase in protective antioxidants. It remains possible that iron exerts both pro- and antiatherogenic roles, but this work raises considerable doubt that the former predominate in the physiological setting.

Somatostatin in sexually dimorphic gene expression

(See article on pages 1571–1580.)

Male and female mammals are distinguished not just by their primary sexual characteristics, but also by their different postpartum growth rates and by subtle differences in expression of metabolic genes. The best-studied examples of such genes encode isoforms of cytochrome P450 that are expressed in the liver under control of growth hormone (GH). In the rat, the species that has proved most tractable for these studies, it is not the level of GH that dictates whether these genes are expressed in males or females, but rather the timing of GH expression. Providing a continuous level of GH favors the female expression pattern, whereas "pulsatile" expression of GH, with peaks occurring six times per day, leads to the male pattern. Because the hypothalamic peptide somatostatin (SST) helps regulate secretion of GH, Low et al. have studied the effects of SST deficiency on sexual development in the mouse. The authors show that, as in rats, wild-type male mice have more dramatic fluctuations in GH levels than do females. The absence of SST does not seem to alter the frequency of the fluctuation, but it raises the GH level at the low point in the cycle so the liver in males is presumably exposed to at least a moderate level of the hormone at all times. The *SST* mutation leads to a feminized pattern of gene expression in the livers of males, but it has no dramatic effect on the expression pattern in livers of females. Surprisingly, the males and females in this mutant strain maintain their sexually dimorphic sizes and growth rates, suggesting that not all genes that are regulated by pulsatile GH release are equally sensitive to the continued presence of the hormone during the interpulse portion of the cycle.