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In This Issue

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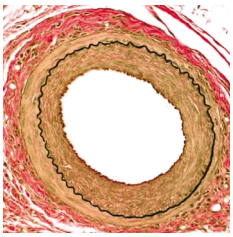
The latest RAGE in restenosis. Expansion of the neointima is a problem in chronic atherosclerosis as well as in response to acute arterial injury. Smooth muscle cells (SMCs) play a key role in the pathologic extension of the neointima that ultimately impinges on the vascular lumen. RAGE, the receptor for advanced glycation end products, is upregulated at sites of vascular pathology, and its blockage is beneficial in mouse atherosclerosis models. Yoshifumi Naka and colleagues have examined RAGE's role in acute arterial injury. As they report (pages 959–972), inhibition of RAGE suppressed neointimal formation in mice upon arterial injury and decreased SMC proliferation, migration, and expression of ECM proteins. Inhibition of RAGE specifically in SMCs yielded similar results. The data point to a key role for RAGE in regulating SMCs after arterial injury and suggest the receptor as a target for therapeutic intervention in heart disease.Spreading mucosal immunity. Local mucosal immunization leads to antigen-specific IgA production at distant mucosal sites, presumably through the migration of activated B cells. Because of the important implications for vaccine development, Eric Kunkel and colleagues are working to understand the mechanisms of IgA-secreting B cell trafficking between distant mucosal sites. Having previously identified a chemokine called MEC, which is expressed by epithelial cells in a variety of mucosal tissues, they report now (pages 1001–1010) that the […]



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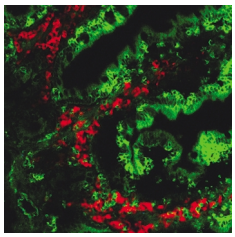

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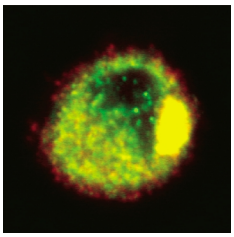
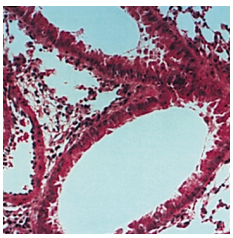
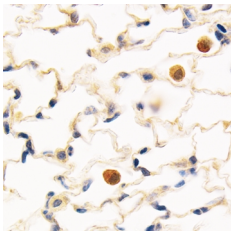


Atopy-promoting dendritic cells. The γ chain of the high-affinity IgE receptor (FcεRIγ) is selectively expressed on antigen-presenting cells from atopic individuals and has been implicated in the pathophysiology of atopic diseases. Interested in the regulation of this receptor on DCs, Thomas Bieber and colleagues have examined the expression of the different components of the receptor during DC maturation (pages 1047–1056). While FcεRIα is present at high levels throughout DC development in atopic and nonatopic individuals, expression of FcεRIγ, which is essential for surface expression of the multimeric receptor, is normally downregulated upon DC differentiation. DCs from atopic individuals, however, show significant levels of FcεRIγ expression, and express the receptor on the surface of mature DCs. In addition to established anti-IgE treatments, modulation of FcεRIγ expression in DCs might prove useful in the management of atopic diseases.



PTEN: a new player in allergen-induced inflammation. Eosinophil accumulation and activation are important events in the development of asthma and involve the enzyme PI3K. The phosphatase PTEN, a major player in cell survival signaling, is known to oppose the action of PI3K. Interested in the role of PTEN in bronchial asthma, Yong Lee and colleagues studied the effects of PI3K inhibitors and PTEN in a mouse model of allergen-induced bronchial inflammation and airway hyperresponsiveness. On pages 1083–1092 the authors show that PTEN expression is diminished in airway epithelial cells of antigen-sensitized and -challenged mice. Intratracheal administration of PI3K inhibitors or adenovirus carrying PTEN cDNA remarkably reduced eosinophil levels and inflammation. One likely mechanism for this reduction is PTEN-mediated eosinophil degranulation and suppression of IL-4 and IL-5. The data support the potential use of PTEN or other PI3K inhibitors for the regulation of allergic inflammation.



Neuronal and inflammatory cell interplay during lung injury. Neurogenic inflammation — the initiation or amplification of the inflammatory response to noxious stimuli by injured or irritated sensory nerves — is mediated by *PPT-A* gene–encoded neurokinins stored primarily in unmyelinated nerve fibers. Recent reports have also indicated the presence of PPT-A mRNA and neurokinin-like immunoreactivity in airway neurons and inflammatory cells. Interested in the interaction between these two cellular reservoirs of neurokinins in the lung, J. Julio Pérez Fontán and colleagues examined their role in protection against both immune-complex–mediated and mechanical lung injury in a murine model (pages 973–980). The data revealed that the *PPT-A* gene must be functional in both sensory nerves and hematopoietic cells to propagate neurogenic inflammation and injury in the lung — an unexpected synergy between sensory nerve fibers and *PPT-A* gene–expressing inflammatory cells.