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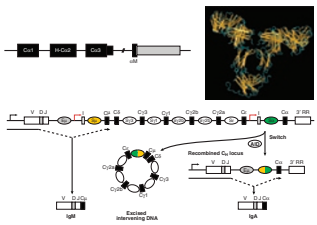

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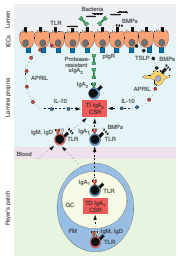
IgA: the current state of play

As is befitting the launch of a journal dedicated to mucosal immunology, there are three items in this issue that focus on quite different aspects of one of the most historically rich areas of this discipline: the field of IgA biology. First there is a review article from two of the seminal contributors to both the "old" and the "new" literature, Per Brandtzaeg and Andrew Macpherson, and their colleagues. The authors describe the evolution of discoveries that have shaped our current understanding of the immunological sites and mechanisms important for IgA B-cell differentiation and IgA production and secretion. Furthermore, they present an insightful perspective on the critical functionality of IgA antibodies in host defense and control of commensal bacteria. **See pages 11 and 31**



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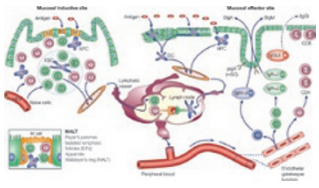
IgA switching in the lamina propria?

Complementing the review article on IgA is a Commentary from Andrea Cerutti on the recent, and somewhat controversial, reports of the lamina propria as a site for IgA class switching—a process formerly thought to be restricted to traditional inductive sites in the mucosa, such as the Peyer's patch. Cerutti eloquently weighs the supporting evidence for this new observation in the context of challenging existing dogma. **See page 8**



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"White paper" on terminology

The final IgA-related article in this issue is a "white paper" that serves to recommend and standardize terminology for describing the molecules and tissues associated with providing immune protection at mucosal surfaces. It is intended to bring consistency to the nomenclature used in publications and discussions, and to be of guidance to investigators new to this field. The accompanying figures brilliantly describe the key compartments and components important for mediating and regulating mucosal immunity—and also provide a great teaching tool for anyone lecturing in the field. **See page 31**

Peyer's patch dendritic cells on the move

Peyer's patches are small intestinal lymphoid tissues commonly used as a portal of entry by numerous oral pathogens. Understanding the initiation of an immune response at this particular anatomic location should therefore assist the development of vaccines and therapeutics against some of the most deadly infectious diseases. Previous studies have demonstrated that bacterial products such as cholera toxin induce dendritic cells at the external epithelial layer to migrate more deeply into the Peyer's patch, where pathogen-specific T cells are found. In an important new study, Anosova *et al.* demonstrate that at much earlier time points Peyer's patch dendritic cells actually migrate toward the epithelial layer in response to bacterial products. This rapid transit of dendritic cells to the external surface of the Peyer's patch probably promotes rapid capture of antigens and microorganisms, which may serve to enhance protective immunity to pathogens and improve the efficacy of mucosal vaccines. **See page 59**

Mucosal site–dependent CD4$^+$ T-cell depletion in HIV infection

An understanding of how HIV is controlled by T cells at mucosal sites is important for the development of effective vaccines. Brenchley and colleagues describe how the immune response to HIV differs at different mucosal effector sites and document how CD4$^+$ T-cell loss differs between compartments such as the terminal ileum and lung (in bronchoalveolar lavage samples). T-cell loss was greatest in the gut, and the authors report that virus levels were highest in this locale. Measurements of interleukin-2, tumor necrosis factor-α, and interferon-γ produced by HIV-specific T cells suggest a greater breadth of response in the bronchoalveolar lavage than in blood or gut. Thus, differences in the quality of the immune responses to HIV and in the extent of CD4$^+$ T-cell depletion are not equivalent at different mucosal sites. **See page 49**

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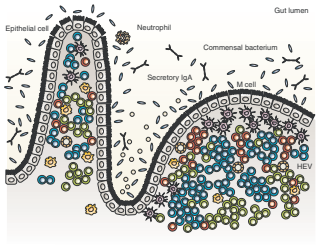

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Breaking barriers with HIV infection

The ability of HIV to cause CD4 depletion and intestinal enteropathy have long been known, although the mechanisms responsible for these effects remain unclear. Here Brenchley and Douek review the potential means by which epithelial integrity may be compromised in HIV infection and discuss how resulting inflammation and bacterial translocation may exacerbate CD4 depletion via local and systemic immune activation. The authors conclude that, when considering new therapeutic approaches for HIV, the importance of restoring both the immunologic and epithelial integrity of the gut should be borne in mind. **See page 23**

Recombinant adenovirus protects against rectal and vaginal HSV-2 infection

Despite extensive efforts over many years, identification of the most effective route(s) and vectors for inducing immune responses at mucosal surfaces remains to be determined. Zhu and colleagues used colorectal immunization with recombinant replication-deficient adenovirus to successfully induce antigen-specific CD8 T cells and IgA-specific antibodies that protect against colorectal challenge of herpes simplex virus type 2 in the large intestine and vagina. Of particular interest in this study is the finding that a single dose of vaccine gives rise to both cellular and humoral immune responses. Previous studies using the mouse model have shown that the effects of vaginal immunization without the appropriate adjuvant are limited and are confined to the site of immunization. The ability of the authors to vaccinate the large intestine to confer protection in the lower genital tract has the potential—if the technique is transferable to humans—to lead to an innovative strategy that protects at multiple levels against viral pathogens, including HIV. **See page 78**

Mucosal traffic controls for distal IgA responses

Both selectins and integrin receptors have roles in lymphocyte trafficking. For homing to the gastrointestinal compartment, lymphocyte expression of $\alpha_4\beta_7$ is critical, with mucosal addressin cell adhesion molecule-1 being the intestinal ligand. Pascual and co-workers indicate the possible contribution of an alternative integrin $\alpha_E\beta_7$ in sustaining IgA responses in the upper respiratory tract following oral immunization. These observations may be used to better design future vaccines targeted to non-intestinal mucosal tissues. **See page 68**

Gut dendritic cells, retinoic acid, and CD8$^+$ T-cell trafficking

There has recently been significant interest in the role of CD103$^+$ dendritic cells and retinoic acid in imprinting T cells with homing receptors specific for directing trafficking to intestinal tissues. In this report, Svensson and coauthors use a novel transgenic mouse system to further delineate the pathways involved in the induction of the gut homing receptors $\alpha_4\beta_7$ and CCR9 on CD8$^+$ T cells and identify retinoic acid signaling and antigen dose as important contributing factors in driving gut tropism. **See page 38**