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MUCOSAL IMMUNOLOGY

Air miles for T cells

Effector and memory T cells show an increased propensity to traffic back to the tissue sites in which they were originally activated. Dendritic cells (DCs) have been shown to drive the selective trafficking of T cells to the skin and small intestine by inducing T cell expression of tissue-specific homing molecules. Two studies now describe the mechanisms by which lung DCs can promote T cell migration to both the lungs and the small intestine.

Luster and colleagues found that $CD4^+$ T cells homed more efficiently to the lungs if they were activated by lung DCs than if they were activated by DCs from various other tissue sites. They showed that lung DCs promote homing to the lungs partly through the induction of CC-chemokine receptor 4 (CCR4) expression by T cells, which enables T cell recruitment to the lungs in response to CC-chemokine ligand 17 (CCL17) and CCL22.

> “lung DCs can promote immunity to mucosal pathogens by driving T cell homing to the lungs and intestines”

The physiological relevance of this process was shown by transferring antigen-specific wild-type or CCR4-deficient $CD4^+$ T cells that had been activated by DCs from different tissue sites into mice infected with influenza virus. Mice that received wild-type T cells activated by lung DCs showed reduced weight loss and cleared their infection more rapidly than mice that received CCR4-deficient T cells activated by lung DCs or than mice that received wild-type T cells activated by DCs not from the lungs. Thus, DC-mediated imprinting of T cell homing to the lungs is important to drive more effective immune responses to pathogens in the airways.

Mehandru and colleagues compared the ability of DCs from different tissues to imprint gut-homing molecules on $CD4^+$ T cells and found that DCs from the lungs, but not from the spleen or skin-draining lymph nodes, could induce T cell expression of the gut-homing molecules CCR9 and α4β7 integrin as efficiently as DCs from the mesenteric lymph nodes (MLNs). Similarly to what has been shown for DCs from the MLNs, the induction of α4β7 integrin expression on T cells by lung DCs was dependent on retinoic acid and transforming growth factor-β-mediated signalling. However, although imprinting with intestinal homing molecules has been reported to be exclusively driven by $CD103^+$ intestinal DCs, both $CD103^+$ and $CD103^-$ DCs from the lungs induced CCR9 and α4β7 integrin expression on T cells.

In addition, the authors showed that T cells activated in an antigen-specific manner by lung DCs could migrate to the intestinal lamina propria. Furthermore, intranasal immunization with antigens expressed by the gastrointestinal pathogen *Salmonella enterica* subsp. *enterica* serovar Typhimurium was more effective than subcutaneous immunization in protecting mice against subsequent enteric infection with this pathogen.

Taken together, these studies show that lung DCs can promote immunity to mucosal pathogens by driving T cell homing to the lungs and intestines. They also add further support to the much older concept of a common mucosal immune system.

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ORIGINAL RESEARCH PAPERS Mikhak, Z., Strassner, J. P. & Luster, A. D. Lung dendritic cells imprint T cell lung homing and promote lung immunity through the chemokine receptor CCR4. *J. Exp. Med.* **210**, 1855–1869 (2013) | Ruane, D. *et al.* Lung dendritic cells induce migration of protective T cells to the gastrointestinal tract. *J. Exp. Med.* **210**, 1871–1888 (2013)