

## **Initiating Allergic Immunity**

Richard M. Locksley, Howard Hughes Medical Institute, Departments of Medicine and Microbiology/Immunology, University of California San Francisco, San Francisco, California

Methods for tracking the key functional mediators of different immune responses are limited by the short half-lives and spatial restriction of effector molecules. We have used a gene knockin strategy that relies on replacement of target genes with genes linked via internal ribosomal entry sites to heterologous markers. In this way, cells transcribing a given locus can be identified in tissue sections or after their dispersal using flow cytometry. Key cytokines induced during allergic immunity include the proteins whose genes are closely linked in the genome, IL-4 and IL-13. Additionally, alternatively activated macrophages, which can be identified by expression of arginase-1, have been seen in these types of host responses. Cells that express IL-4 and IL-13, as well as alternatively activated macrophages, have been functionally implicated in the elaboration of allergic immunity, in that these responses become attenuated in their absence. Using mice whose cells are marked to allow identification of these responses at the individual cell level, we have followed the cells marked in this way during allergic immune responses induced by helminth infection or by allergic lung sensitization. These observations have allowed us to identify early events in the elaboration of this type of host response.

### **References**

- Voehringer D, et al. 2004. Type 2 immunity reflects orchestrated recruitment of cells committed to IL-4 production. *Immunity* **20**:267-277.
- Scheu S, et al. 2006. Activation of the integrated stress response during T helper cell differentiation. *Nat Immunol* **7**:644-651.
- Voehringer D, et al. 2006. Type 2 immunity is controlled by IL-4/IL-13 expression in hematopoietic non-eosinophil cells of the innate immune system. *J Exp Med* **203**:1435-1446.