

Regulation of the allergic TH2 T Cell response at the level of $\gamma\delta$ T cell subsets

Laura Sharp*, Youn-Soo Hahn*, Christian Taube⁺, Niyun Jin*, JM Wands*, Arihiko Kanehiro⁺, Michael Lahn*, Rebecca O'Brien*, Erwin Gelfand⁺ and Willi Born*

*Department of Immunology, ⁺Department of Pediatrics
National Jewish Medical and research Center, Denver, Colorado

Murine $\gamma\delta$ T cells, expressing different TCR-V δ genes, represent subsets which arise at different times in ontogeny, are segregated among tissues and exhibit different functions (1). Regulation of the allergic TH2 T cell response appears to be a subset-specific functional effect which manifests itself by default.

We have found that V δ 4⁺ T cells in the lung prevent airway hyperreactivity (AHR) following airway challenge with ovalbumin (OVA). This is evident under conditions of innate reactivity in non-sensitized mice when $\gamma\delta$ T cells are absent, and under conditions of an allergic, $\gamma\delta$ T cell-dependent response in mice sensitized to OVA (2, 3). The regulatory effect requires interferon- γ (IFN- γ) and transporter associated with antigen processing-1 (TAP-1) and appears to be based on an innate challenge-response in the lung.

However, when $\gamma\delta$ T cells are present and are induced to an allergic response by sensitization and challenge with OVA, V δ 4⁺ T cells inhibit the challenge-induced TH2-shift of cytokine producing $\gamma\delta$ T cells in the lung. In contrast, V δ 1⁺, V δ 6⁺ and V δ 7⁺ T cells in the lung do not prevent AHR. Their effect on cytokine producing $\gamma\delta$ T cells is currently under investigation.

1. O'Brien et al., Chem. Immunol. 79: 1-28 (2001)
2. M. Lahn et al., Nature Medicine 5: 1150-6 (1999); PNAS 99:8850-5 (2002)
3. Y.-S. Hahn et al., submitted