ID der Kurzfassung : **75**

# Interleukin-1β paves the way for protective lung-resident memory T cells: implications for a universal flu vaccine?

## Inhalt

Tissue-resident memory T-cells (TRM) are increasingly recognized as important, cross-reactive immune component in the protection against influenza A viruses (IAV). However, there is a lack of specific vaccine strategies to elicit potent TRM responses. Here, we evaluated vector-encoded IL-1β as genetic adjuvant in intranasal adenoviral vector immunizations against IAV.

First of all, we showed that IL-1β enhances antibody and T-cell responses, most pronounced in lung TRM populations. In consequence, vaccination with the adjuvant established superior protection against divergent H1N1, H3N2 and H7N7 infections. Specifically, a coordinated action of both CD4+ and CD8+ T-cells was required to mediate optimal cross-reactive immunity, but this protection was independent of circulating T-cells. From a mechanistic perspective, we demonstrated that IL-1β activates several essential checkpoints in the formation of lung TRM including (i) immediate infiltration of immune cells into the lung, i.e. TRM-priming CD103+ DCs, (ii) broad lung inflammation consisting of cytokines, chemokines and adhesion molecules and (iii) lung infiltration of TRM precursors with an increased expression of CD69 und CD103 but only in presence of local antigen. Bone marrow transfer experiments showed that IL-1β-induced TRM-development requires IL-1 receptor signaling in both stromal and hematopoietic cells but with stronger contribution of the latter ones. Importantly, analysis of respiratory parameters and lung barrier function showed no detrimental effects of the adjuvanted immunization.

Our data reveal the multifaceted effects of mucosal IL-1β on the induction of TRM and thus contribute to the basic understanding of local immunity which might pave the way for efficient TRM-inducing IAV vaccines.

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