**CA2+-DEPENDENT SIGNALING IN EFFECTOR T-LYMPHOCYTES**

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**Objectives**

Asthma is a chronic inflammatory respiratory disease affecting around 10% of people in Western Countries. Th2 lymphocytes producing interleukin (IL)-4, IL-5 and IL-13 are likely to initiate and amplify the disease in humans and in experimental models. Calcium signaling is essential for most of biological function in lymphocytes but the regulation of intracellular calcium concentration ([Ca]i) depends upon the subset of effector lymphocytes.

Our objectives are to identify calcium channels selectively expressed in Th2 lymphocytes which could represent a potential new therapeutic target in asthma.

**Th2 cells selectively express Ca$_{1}$ channels**

OVA specific transgenic T cells were differentiated along the Th1 and the Th2 pathway and tested for the expression of Ca$_{1}$ channels.

Ca$_{1}$ channels are encoded by 4 genes conferring some tissue specificity; GATA-3 = Th2 specific transcription factor.

**Knocking down Ca$_{1}$ channels impair Ca$^{2+}$ signaling and cytokine production by Th2 cells**

OVA specific transgenic Th2 cells were transfected with Ca$_{1}$ specific antisense oligonucleotides (Cav1AS) and stimulated through the TCR. The increase in [Ca]i and cytokine production were measured. Cav1AS decreased the expression of Ca$_{1}$ channels by 50 to 70%.

**Ca$_{1}$ antisense ONs prevent experimental asthma**

LTh2 transfected with Ca$_{1}$ antisense ONs lose their ability to induce asthma.

**Conclusion- Valorisation**

- Mouse Th2 cells selectively express functional Ca$_{1}$ channels required for cytokine production and effector functions.
- Th2 cells transfected with Cav1AS lose their capacity to induce asthma and Cav1AS may be given by the intranasal route for preventing asthma.
- Human Th2 cells express Ca$_{1}$ channels -> Ca$_{1}$ channels might represent a potential target in asthma (brevet EP09306160.4, INSERM transfert).

**Publications**


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