# ImmunoTools IT-Box-Cy55M-Award 2013


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### Sensing Iron: molecular responses of $CD8^+$ T lymphocytes to iron overload

Blood cells are in the direct contact with circulating iron. The interaction between this immune cells and non-transferrin-bound iron (NTBI) was firstly addressed by De Sousa in 1978 based on her observations on lymphocyte traffic and positioning it was suggested that the immune system could have a role in monitoring tissue iron toxicity as part of its surveillance function. Furthermore, abnormalities in the relative proportions of the two major T lymphocyte populations, $CD4^+$ and $CD8^+$ (mainly due to low $CD8^+$ T cells) were described in the clinical iron overload context of Hereditary Hemochromatosis (HH) observations that preceded the discovery of the HH gene (*HFE*).

The mechanism(s) underlying the participation of lymphocytes in iron homeostasis remain mostly unknown. The aim of my PhD is to contribute to the elucidation of the mechanisms how lymphocytes may act as modifiers of iron balance. To address that question we performed a genome-wide gene expression analysis using murine $CD8^+$ T-lymphocytes RNA under iron overload condition induced by iron rich diet in comparison with a normal diet control group in both genetic background of C57BL/6 and *HFE*($^{-/-}$).

The genes found to be more significantly differentially expressed between the two genetic backgrounds were: S100a8 and S100a9. These proteins form a heterocomplex (also known as calprotectin) with an important antimicrobial activity function. S100a8 and the S100a8/a9 complex are secreted upon stimulation with inflammatory mediators. It has been shown that the pro-inflammatory cytokine calprotectin is involved in innate immunity, leukocyte adhesion, endothelial transmigration and chronic inflammation busted by IL-1 and TNF activation. Moreover, S100a8 and S100a9 transcripts were previously found to be substantiattly up-regulated in skeletal muscle, heart and liver of iron-loaded mice. Nothing was reported regarding lymphocyte expression under iron-induced conditions.

The ImmunoTools *IT-Box-Cy55M* box will allow us to access the regulation of S100a8 and S100a9 expression by $CD8^+$ T lymphocytes in conditions of stimulation by several inflammatory cytokines such as: IL-1, TNFα, MCP-1 and IFNδ. The data obtained with this ImmunoTools box will give us a better understanding about the differential gene expression of $CD8^+$ T lymphocytes in the two genetic backgrounds (C57BL/6 and *HFE*$^{-/-}$).

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**ImmunoTools** *IT-Box-Cy55M* for **Mónica Costa**

includes 55 recombinant mouse cytokines

rm EGF, rm Eotaxin / CCL11, rm FGF-a / FGF-1, rm FGF-b / FGF-2, rm FGF-8, rm Flt3L / CD135, rm G-CSF, rm GM-CSF, rm GRO-a / CXCL1, rm GRO-b / CXCL2, rm IFNgamma, rm IL-1alpha, rm IL-1beta, rm IL-2, rmIL-3, rm IL-4, rm IL-5, rm IL-6, rm IL-7, rm IL-9, rm IL-10, rm IL-11, rm IL-13, rm IL-15, rm IL-16, rm IL-17A, rm IL-17C, rm IL-17F, rm IL-19, rm IL-20, rm IL-21, rm IL-22, rm IL-25 / IL-17E, rm IL-27, rm IL-31, rm IL-33, rm IP-10 / CXCL10, rm LIF, rm MCP1 / CCL2, rm M-CSF, rm MIP-1α/ CCL3, rm MIP-1β / CCL4, rm MIP3α / CCL20, rm MIP3β / CCL19, rm NGF-beta, rm PDGF-AA, rm PDGF-BB, rm RANTES / CCL5, rm sCD40L / CD154, rm SCF, rm SDF-1α / CXCL12a, rm SDF-1β / CXCL12b, rm TNFα, rm TPO, rm VEGF DETAILS

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