ImmunoTools IT-Box-Cy55M-Award 2013

Denise Soutar

PhD Supervisor: Prof. Dr. Isabel Mérida de San Román

Departamento de Inmunología y Oncología Laboratorio 414
Centro Nacional de Biotecnología (CSIC)
Calle Darwin 3, 28049 Madrid

Diacylglycerol-dependent signal intensity determines Effector Versus Regulatory programmes in T Cells

In T cells, after TCR triggering, Diacylglycerol (DAG) acts as a lipidic second messenger in the activation of mTOR through Ras/MAPK pathway. Diacylglycerol kinase Alpha (DGKα) catalyzes the conversion of DAG into Phosphatidic acid (PA) to modulate the activation of these pathways.

Once the T cell is activated, it has to select its fate. The decision of naive CD4 T cells to assume the fate of effector or regulatory cells is dependent on the secreted cytokines , related to the strength of Akt/mTOR signaling .We aimed to analyze the impact of lacking DGKα in the determination of T helper vs Treg fate. To this end we determined in vitro TGFβ-mediated induction of $CD4^{+}CD25^{+}FOXP3^{+}$ iTregs in T cells from WT and DGKα $^{-/-}$ mice.

We stimulated naïve CD4 Tcells with anti CD3, anti-CD28, IL-2 and TFG-β for five days, and we observed that Foxp3 induction is greatly impaired in DGKα $^{-/-}$ mice compared to WT, with an increase in IFN-gamma, IL-17 and IL-10 secretion.

Our results suggest that enhanced activation of the Ras/MAPK and AKT/mTOR pathways in DGKα deficient mice prevents iTreg differentiation, but additional studies are needed to confirm the commitment of those cells.

To reach this objective, we want to perform Th17 and Tr1 polarization from CD4 naïve T cells and a *IT-Box-Cy55M* would be very useful because we need to polarize the cells to Th17 lineage in presence of IL-17, IL-6 and IL-21; and regarding to polarize CD4 naïve to Tr1 lineage we need IL-10 and IL-27.

We would also need IL-15 because we are currently studying the influence of DGKα deficiency and the strength of Akt/mTOR signaling in the generation of memory CD8 T cells. We are carrying experiments with IL-2 in CD8 memory generation, and IL-15 would be very useful to complete our study relating to memory generation in CD8 T cells and DGKα deficiency.

ImmunoTools *IT-Box-Cy55M* for **Denise Soutar**
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.