SYNVIVO - Revealing dendritic cell-CD4+ T cell communication by using synthetic biology in vivo

CD4+ T cells are crucial component of our immune system: they support distinct types of proinflammatory responses key for pathogen clearance, maintain tolerance and suppress harmful inflammation. To perform this multitude of functions, naïve CD4+ T cells first undergo activation through direct contact with dendritic cells (DCs), a highly heterogeneous compartment including several populations of migratory and resident cells. These interactions lead to selection of antigen specific T cell clones, followed by their proliferation and differentiation into distinct subsets showing specialized effector programs or polarizations. Despite the essential role of dendritic cells in the activation and polarization of naïve CD4+ T cells, we have limited information available on both the identity of DC involved in priming and the molecular messages exchanged upon DC-CD4+ T cell interaction in different types of response. Recently, I developed an innovative technology that allows us for the first time to label interactions between immune cells in vivo. This method, which we called LIPSTIC, relies on the labeling of genetically engineered receptor–ligand pairs mediated by the enzyme Sortase A. After the enzymatic reaction takes place in vivo, the history of ligand–receptor interactions is revealed by the presence of reporter tags easily detected by flow cytometry. This proposal aims to determine how interactions between dendritic cells and T cells instruct CD4+ T cells toward distinct fates using LIPSTIC and by implementing other technologies designed ad hoc to measure and understand the biological consequences of relevant cell-cell interactions on T cell fate decision. The combined approaches described here will contribute to the characterization of the molecular signals governing CD4+ T cell response in vivo.

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