ERC-2014-CoG

DevoTed_miR

MicroRNA determinants of the balance between effector and regulatory T cells in vivo (DevoTed_miR)

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Project Beneficiaries

Instituto de Medicina Molecular João Lobo Antunes João Lobo Antunes (iMM)

Researcher Bruno Silva Santos

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Overview

THE PROBLEM

This project aims to dissect the microRNA (miRNA) networks that control the differentiation of effector and regulatory T cell subsets in vivo, in various experimental models of infection and autoimmunity. We are focusing on three critical mediators of T cell functions: interferon- (IFN-) and interleukin-17A (IL-17), highly pro-inflammatory cytokines; and Foxp3, the transcription factor that confers suppressive properties to regulatory T cells. We envisage the identification of specific miRNAs that can modulate the balance between effector and regulatory T cell subsets, and thus impact on protective immune responses and/ or immune-mediated pathology.

SPECIFIC OBJECTIVES

1. Characterize the miRNA repertoires of in vivo-generated effector and regulatory T cell subsets, isolated from infection or autoimmune models established in a reporter mouse for Ifng, Il17 and Foxp3.

2. Define the individual miRNAs that impact selectively on effector or regulatory T cell differentiation, based on loss- and gain-of-function experiments.

3. Determine the impact of miRNA expression modulation on effector or regulatory T cell subsets in vivo, using infection and autoimmune models, thus attest-ing the physiological relevance of the miRNA-mediated mechanisms.

4. Dissect the external cues and intracellular mechanisms that regulate candidate miRNA expression in specific effector or regulatory T cell subsets.

5. Identify the mRNA networks controlled by candidate miRNAs using a combination of bioinformatics and biochemical assays, and couple the effects of miRNA and mRNA manipulation on effector or regulatory T cell subsets in vivo.

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