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Control of T cell effector functions by miRNAs

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Abstract

The differentiation of effector T cells is a tightly regulated process that relies on the selective expression of lineage-defining master regulators that orchestrate unique transcriptional programs, including the production of distinct sets of effector cytokines. miRNAs are post-transcriptional regulators that are now viewed as critical players in these gene expression networks and help defining cell identity and function. This review summarises the role of individual miRNAs in the regulation of the differentiation of effector T cell subsets, including $CD4^+$ T helper cells, cytotoxic $CD8^+$ T cells and innate-like NKT cells. Moreover, we refer to miRNAs that have been identified to affect simultaneously two or more effector T cell populations, impacting on the balance between effector T cells *in vivo*, thus constituting potential biomarkers or targets for therapies aiming at boosting immunity or controlling autoimmunity.

Key words: miRNAs, T cell differentiation, effector T cells, T cell regulation

1. Introduction

T lymphocytes develop in the thymus to acquire a T cell receptor (TCR) that undergoes key selection processes to attest productive somatic rearrangement (positive selection) while avoiding self-reactivity (negative selection). For most T cells, this is the result of molecular interactions between the TCR and peptide-major histocompatibility complex (MHC) complexes, although for a minor subset of Natural Killer (NK)-like, NKT cells, the selecting element is CD1d presenting glycolipids [1]. For conventional T cells, the outcome of the preferential TCR binding to MHC class I or II is the selection into the $CD8^+$ or $CD4^+$ T cell lineages, respectively. $CD8^+$ T cells leave the thymus to become cytotoxic T lymphocytes (CTLs) upon cognate antigen recognition in the periphery. Most $CD4^+$ T cells retain a naïve phenotype in the thymus, and will only differentiate into T helper (Th) cells upon activation in secondary lymphoid organs; however, 5-10% of $CD4^+$ thymocytes undergo commitment to the regulatory T cell lineage, characterized by the expression of the master transcription factor (TF), Foxp3.

The peripheral differentiation of T cells relies on the selective expression of other lineage-defining master regulators that orchestrate unique transcriptional programs allowing the different T cell populations to secrete distinct sets of effector cytokines and other effector