

P015 Dicer-dependent regulation of development and gene expression in T cells

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To investigate the role of miRNAs in T cell development, we generated a T cell lineage-specific conditional Dicer knock-out. Positive selection of thymocytes was un-impaired in the absence of Dicer but differentiation towards mature T cells was delayed. Consistent with this, genes required for maturation were not fully up-regulated in Dicer-deficient cells. Furthermore, we show that the development of regulatory T cells in the thymus is dependent on Dicer.

To address the impact of miRNAs on gene expression during thymocyte development we have compared the gene expression profiles of wildtype and Dicer-deficient thymocytes. This analysis revealed that many of the genes up-regulated in Dicer-deficient DP cells were specific for the SP stage in wild type thymocytes. Bioinformatics analysis revealed an enrichment of binding sites of three miRNA families in the 3'UTRs of up-regulated genes. Our data suggest that in DP thymocytes post-transcriptional regulation by miRNAs co-operates with transcriptional regulation to refine the expression patterns of developmental stage-specific genes. De-regulation of these genes in the absence of miRNAs leads to severe impairment of thymocyte survival and differentiation.