OFFICIAL ABSTRACT and CERTIFICATION

Determining the Kinetics of IRF4 and IRF5 in B- and T-Cell Activation

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Innate and adaptive immune responses to foreign antigens result in part from specialized B- and T-cells, which develop with the aid of several transcription factors and signaling pathways, namely B-cell receptor (BCR), Toll-like receptor (TLR) and T-cell receptor (TCR) signaling. Immediately after BCR and TCR stimulation, B- and T-cells begin an activation process that leads to further development and differentiation. Dysfunction of many immune cell subsets and immune-regulatory transcription factors has been implicated in autoimmune disease pathogenesis. The transcription factors interferon regulatory factor (IRF4) and IRF5 of the IRF family have been identified in different B- and T-cell processes, along with autoimmunity. However, a comprehensive analysis of the kinetics of both proteins in both cell types has not been done. This study aimed to analyze the kinetics of IRF4 and IRF5 expression in response to B- and T-cell stimulation using total splenocytes from wild-type (WT) and Irf5 full-body-knockout (Irf5-/-) mice. IRF5 and IRF4 showed early peak expression in B- and T-cells, respectively, while the other protein was more highly expressed in the later stages of activation and differentiation in both cell types. Compared to WT cells, cells from Irf5-/- mice demonstrated defective cell activation and lower IRF4 expression levels, indicating a role for IRF5 in the activation of both cell types and the regulation of IRF4. Together, results identified distinct and overlapping roles for IRF4 and IRF5 in B- and T-cell activation and maturation that may contribute to dysregulated immune cell development in autoimmune disease.

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