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Regulation of gene expression networks implicated in B cell homeostasis, germinal center responses, and tolerance by the *micro-ophthalmia* transcription factor (Mitf). My lab is interested in mechanisms of immune tolerance to self that eliminate autoreactive B cells which produce pathogenic, including neurotoxic, autoantibodies in lupus. We have identified an unexpectedly critical role of Mitf – a master regulator of pigmented cell development – in B lymphocyte homeostasis and tolerance, using complementary mouse models of Mitf deficiency: the $Mitf^{mi\text{-}vga9/mi\text{-}vga9}$ loss-of-function (null), and B-cell specific expression of a recombinant trans-dominant negative (TDN) Mitf-inhibitor protein. Both models displayed T_H-dependent spontaneous splenomegaly coincident with elevated lymphocyte and plasma cell numbers, autoantibody titers, and proteinuria, consistent with impaired renal function from autoimmune complexes. In addition, Mitf inactivation in B cells worsened aspects of autoimmune disease on a genetic background that produces only mild lupus ($C57B6^{lpr/lpr}$). RNAseq of *ex vivo* resting B cells from the Mitf-deficient mice – collaborative work with investigators at the University of Iceland – identified novel MiT family candidate target genes and pathways in B cells that could be responsible. In both models, there was transcriptional upregulation of genes that control cell cycle, germinal center responses, and plasma cell differentiation. Interestingly, Mitf null B cells, but not TDN B cells, showed evidence of type I interferon dysregulation, an abnormality caused by the effect of non-B cells impacted by systemic absence of Mitf. These studies reveal Mitf's role as 1) a key regulator of a B cell intrinsic germinal center program that is required to restrain B cell activation and prevent the emergence of pathogenic autoantibodies through novel target genes, and 2) a regulator of systemic inflammatory processes in non-B cells that can impact the B cell microenvironment.

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