DISSECTING GERMINAL CENTER B CELL RESPONSES IN COMMON VARIABLE IMMUNODEFICIENCY

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Abstract

Common Variable Immunodeficiency (CVID) represents the most common human primary immunodeficiency. It is characterised by hypogammaglobulinemia and displays signs of immune dysregulation, such as lymphadenopathy, autoimmunity and inflammatory organ manifestations in over 30% of patients. Low numbers of class switched memory B cells and plasmablasts in peripheral blood reflect a heterogenic germinal center (GC) dysfunction, providing the opportunity to dissect essential steps during memory and effector differentiation. We combine deep phenotyping by multi-parameter cytometry, transcriptome analysis and microscopy on secondary lymphoid organs in order to identify underlying dysregulated expression profiles, molecular pathways and cellular interactions in individual CVID patients.
Preliminary analysis of RNAseq data revealed T-bet-regulated gene expression in centroblast, centrocytes and memory B cells derived from CVID patient's secondary lymphoid organs confirming Th1/TfH1-driven immune dysregulation previously identified in peripheral blood. Identification of informative altered molecular, cellular and histological findings in patients with immunodeficiency will shed new light on the complex GC responses in humans.