Bcl6 Regulates Production of SLAM-Associated Protein in Follicular Helper T Cells

（Bcl6 は濾胞性ヘルパー T 細胞における SLAM-Associated Protein の産生を制御する）

千葉大学大学院医学研究院
先端生命科学専攻 分化制御学
（主任： 徳久剛史教授）

谷口 俊文
Abstract

A transcriptional repressor, Bcl6, is known to be the master regulator of follicular helper T (Tfh) cells, but the role of Bcl6 in its regulation still remains unclear. SLAM-associated protein (SAP) is required for the differentiation of Tfh cells and subsequent antigen-specific germinal center formation. In this study, we show that c-Myb is a transcriptional activator for SAP, and that Bcl6 positively regulate c-Myb and subsequently SAP by repressing Myb binding protein (Mybbp1a) and microRNA (miR)-155. Microarray analysis of Th2 cells cultured in vitro from Bcl6 transgenic mice shows increased expression of SAP and decreased expression of Mybbp1a and miR-155. We confirmed the binding of Bcl6 to the promoter region of the Mybbp1a gene and the binding of c-Myb to the promoter region of the SAP gene. CD4⁺ T cells with Mybbp1a knockdown and miR-155 inhibition resulted in increased germinal center (GC)-Tfh in vivo. Knockdown of c-Myb resulted in decreased GC-Tfh. Transduction of the c-Myb gene and the Mybbp1a gene to CD4⁺ T cells in vitro enhanced and repressed the differentiation of Tfh-like cells, respectively. Taken together, Bcl6, by repressing Mybbp1a and miR-155, indirectly regulates c-Myb, which activates SAP expression in Tfh cells.