B cell class switch recombination is regulated by DYRK1A through MSH6 phosphorylation

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Abstract

Protection from viral infections depends on immunoglobulin isotype switching, which endows antibodies with effector functions. Here, we found that the protein kinase DYRK1A is essential for B cell-mediated protection from viral infection and effective vaccination through regulation of class switch recombination (CSR). *Dyrk1a*-deficient B cells were impaired in CSR activity in vivo and in vitro. Phosphoproteomic screens and kinase-activity assays identified MSH6, a DNA mismatch repair protein, as a direct substrate for DYRK1A, and deletion of a single phosphorylation site impaired CSR. After CSR and germinal center seeding, DYRK1A was required for proper clonal expansion of antigen-specific B cells through attenuation of proliferation. These findings reveal DYRK1A-mediated biological mechanisms of B cell immune responses that may be used for manipulation in antibody-mediated autoimmunity.