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ORAL

Notch-mediated control of memory T cells against cancer cells

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Abstract

T cells recognize an antigen presented by self-MHC, and the part of initially activated T cells differentiate toward memory T cells. T cells also recognize cancer cells leading to generation of memory T cells against cancer-derived antigens although the activity of T cells are frequently suppressed by various factors. The release from T cell inhibitory factors could allow T cells to respond to cancer cells. However, it remains unclear which molecules are required for long-term survival of memory T cells and generation of memory T cells against cancer cells. Notch functions as a regulator for fate decision, activation and survival of immune cells. We have demonstrated the roles of Notch in mature T cell differentiation and found that Notch signaling is essential for the maintenance of memory CD4 T cells. The inhibition of Notch disturbs the survival of memory CD4 T cells. The effect of Notch on T cell survival depended on glucose uptake through cell surface Glut1 expression. We revealed that Notch is crucial for the long-term survival of memory T cells against cancer cells and suppression of Notch signaling reduced the tumor antigen-specific killing of cancer cells. Those data demonstrate that Notch is pivotal for the maintenance of memory T cells against cancer cells and suggest that activation of Notch signaling might be advantageous to cancer immunotherapy.

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