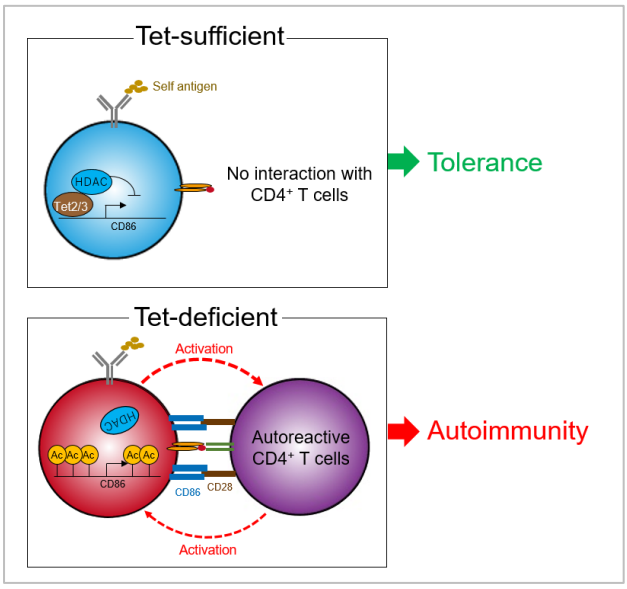
# Tet2 and Tet3 in B cells are required to repress CD86 and prevent autoimmunity

- Functional deficiency of the epigenetic regulator Tet expressed in B cells causes a systemic lupus erythematosus-like autoimmune disease.
- The Tet molecules suppress autoimmune diseases by inactivating B cells attacking our bodies.
- Regulating the functions of the Tet molecule and their related molecules is expected to lead to breakthrough treatments for controlling autoimmune diseases.

Wataru Ise, Tomohiro Kurosaki (Lymphocyte Differentiation, IFReC), Shinya Tanaka, Yoshihiro Baba (Kyushu University) and their research group reported that deficiency of ten-eleven translocation (Tet) DNA demethylase family members, Tet2 and Tet3, in B cells led to hyperactivation of B and T cells, autoantibody production and lupus-like disease. Mechanistically, in the absence of Tet2/Tet3, down-regulation of CD86, which normally occurs following chronic exposure of self-reactive B cells to self-antigen, did not take place. The importance of the dysregulated CD86 expression in Tet2/Tet3-deficient B cells was further demonstrated by restraining, albeit not completely, aberrant T and B cell activation by anti-CD86 blocking. Tet2/Tet3-deficient B cells had a decreased accumulation of histone deacetylase 1 (HDAC1) and HDAC2 at the Cd86 locus. Their findings suggest that Tet2/Tet3-mediated chromatin modification participates in repression of CD86 on chronically stimulated self-reactive B cells, which, at least partly, contributes to preventing autoimmunity.




**Tet-mediated B cell tolerance**

Tet2/3-deficient B cells are activated by self-antigen and express exaggerated amount of CD86. Then those B cells stimulate autoreactive $CD4^+$ T cells, resulting in autoimmune response.

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