AUTOIMMUNE CONNECTIVE TISSUE DISEASES

LOSS OF NUCLEAR-LOCATED AIM2 IMPAIRS SYSTEMIC LUPUS ERYTHEMATOSUS VIA ALTERING TFH CELL FATE

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Absent in melanoma 2 (AIM2) is a component of inflammasome, which is engaged in caspase-1 and IL-1beta-mediated inflammatory responses via sensing cytosolic dsDNA. However, in our observation, we found an increased nuclear-located AIM2 in CD4+ T cells, especially in follicular helper T (Tfh) cells from both peripheral blood and tonsil. In pristane induced and chronic graft versus host disease (cGVHD) lupus models in CD4 cre AIM2 f/f mice, deficiency of nuclear-located AIM2 is capable of impairing lupus progress by reducing Tfh cell differentiation. The mechanism has been revealed as that AIM2 regulates C-Maf and STAT3 by direct binding, thereby regulating the IL-21 production and CXCR5 and PD-1 expression. IL-21 has been found to increase AIM2 via up-regulating TET2 enrichment on the AIM2 promotor region and down-regulating the DNA methylation level of AIM2. Our findings reveal a brand-new regulation pathway of AIM2 in T cells and provide new therapeutic targets for SLE treatment.

Keywords: SLE, AIM2, Tfh, STAT3, C-MAF, TET2