DELETION OF THE BAFF RECEPTOR TACI FULLY PROTECTS AGAINST SLE WITHOUT REDUCTION OF B CELL NUMBERS AND FUNCTION

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Methods

To test the role of TACI in driving BAFF-mediated autoimmune disease, we reconstituted BAFF Tg mice with TACI-/- mice and crossed BAFF Tg mice onto TACI-/- mice. Deficient bone marrow and also crossed BAFF Tg mice onto autoimmunity, we reconstituted BAFF Tg mice with a TACI-/- background and aimed to investigate if TACI, a BAFF receptor dispensable for B cell survival and is approved for use in patients with SLE. Surprisingly, the efficacy of rituximab in SLE raises the question of whether B cell depletion is really the mechanism of action of belimumab. In BAFF transgenic (BAFF-Tg) mice, SLE development is T cell-independent but relies on innate activation of B cells in cooperation with the BAFF receptor TACI. Therefore, in this study we tested whether TACI, a BAFF receptor dispensable for B cell survival may have a role in the pathogenesis of SLE.

Results

We show that loss of TACI on B cells protected against BAFF-mediated autoimmune manifestations while preserving B cells, suggesting that loss of BAFF signalling through TACI, rather than loss of B cells, may underpin the effect of belimumab in the clinic. Moreover, a multimeric form of BAFF, is very effective at activating TACI, suggesting that this abnormal form of BAFF may also be a pathogenic factor in SLE.

Conclusions

B cell-sparing blockade of TACI may offer a more specific and safer therapeutic alternative to broad B cell depletion in SLE.

THE CONTRIBUTION OF INTERFERON LAMBDA TO SLE

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Methods

Mouse and human DC subsets were stimulated ex vivo and the IFN-λ expression was measured.

The maturation and the capacity of DC to cross-prime T cells was compared in WT and IFN-λ-/- mice. T cell cross-priming by human DCs was measured ex vivo in the presence of exogenous IFN-λ.

Conclusion

The contribution of interferon lambda to SLE warrants further investigation.

IMPACT OF CD200-FC ON DENDRITIC CELLS IN LUPUS-PRONE NZB/WF1 MICE

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Methods

Female NZB/WF1 mice were treated with CD200-Fc or control for 4 weeks. Plasma samples were collected to measure autoantibody levels. The expression levels of CD200/CD200R1 in peripheral blood mononuclear cells (PBMCs) and splenocytes were examined.

Results

The percentage of CD200/CD200R1-positive cells in splenocytes from NZB/WF1 mice was lower than that of C57BL/6 mice (p<0.05). The plasma level of anti-dsDNA was significantly higher in NZB/WF1 mice than C57BL/6 mice (p<0.001). However, the anti-dsDNA levels decreased (p=0.047) after CD200-Fc treatment. Finally, CD200-Fc reduced the levels of IL-6 (p=0.017) and IL-10 (p=0.03) in the dendritic cell culture supernatant.

Conclusions

The immunosuppressive effect of CD200/CD200R1 signaling pathway might be involved in the immunopathology of NZB/WF1 mice; the present results merit further exploration of agents that can modulate the CD200/CD200R1 pathway as a therapy for human lupus.