Infection of Female BWF1 Lupus Mice with Malaria Parasite Attenuates B Cell Autoreactivity by Modulating the CXCL12/CXCR4 Axis and Its Downstream Signals PI3K/AKT, NFκB and ERK.

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Abstract:

Systemic lupus erythematosus (SLE) is a prototypic autoimmune disease characterized by abnormal autoreactivity in B cells. Lymphocytes and their soluble mediators contribute to the disease pathogenesis. We recently demonstrated that infecting lupus mice with malaria confers protection against lupus nephritis by attenuating oxidative stress in both liver and kidney tissues. In the current study, we further investigated B cell autoreactivity in female BWF1 lupus mice after infection with either live or gamma-irradiated malaria, using ELISA, flow cytometry and Western blot analysis. The lupus mice exhibited a significant elevation in plasma levels of IL-4, IL-6, IL-7, IL-12, IL-17, IFN-α, IFN-γ, TGF-β, BAFF and APRIL and a marked elevation of IgG2a, IgG3 and ant-dsDNA autoantibodies compared with normal healthy mice. Infecting lupus mice with live but not gamma-irradiated malaria parasite partially and significantly restored the levels of the soluble mediators that contribute to the progression of lupus. Furthermore, the B cells of lupus mice exhibited an increased proliferative capacity; aberrant overexpression of the chemokine receptor CXCR4; and a marked elevation in responsiveness to their cognate ligand (CXCL12) via aberrant activation of the PI3K/AKT, NFκB and ERK signaling pathways. Interestingly, infecting lupus mice with live but not gamma-irradiated malaria parasite restored a normal proliferative capacity, surface expression of CXCR4 and B cell response to CXCL-12. Taken together, our data present interesting findings that clarify, for the first time, the molecular mechanisms of how infection of lupus mice with malaria parasite controls B cell autoreactivity and thus confers protection against lupus severity.

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