Nature Reviews Nephrology | Published online 14 Nov 2016; doi:10.1038/nrneph.2016.167

LUPUS NEPHRITIS

B-cell ERα signalling promotes lupus development

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Estrogens have been implicated in the pathogenesis of lupus and approximately 90% of patients are female. Now, Dana Tabor and Karen Gould report that estrogen receptor α (ERα) signalling in B cells promotes lupus development. "We were interested in knocking out ERα in specific immune cell lineages in lupus-prone mice in order to figure out which cells are the critical targets for estrogens during lupus pathogenesis," explains Gould. "We began by knocking out ERα in B cells because of their central importance in lupus and the known effects of estrogens on these cells."

The researchers found that B-cell-specific ERα knockout reduced the production of pathogenic anti-double-stranded DNA autoantibodies and increased the median survival of lupus-prone mice. "The development of lupus nephritis was attenuated even though the Cre–lox system only resulted in ERα deletion in ~50% of B cells, suggesting that we might see a therapeutic benefit with a drug that only partially disrupts B-cell ERα signalling," comments Gould.

In female, but not in male lupus-prone mice, B-cell-specific deletion of ERα resulted in a decrease in the proportion of B cells that were activated prior to autoantibody development and lupus onset. "This observation suggests that estrogens preferentially enhance the development of lupus in females by promoting B-cell activation in an ERα-dependent manner," says Gould.

The researchers conclude that estrogens, acting via ERα in B cells, can promote lupus development. They now plan to investigate how this process occurs at the molecular level with the hope that this work will lead to insights that could fuel the identification of new therapies.

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ORIGINAL ARTICLE Tabor, D. E. & Gould, K. A. Estrogen receptor α promotes lupus in (NZB x NZW)F1 mice in a B cell intrinsic manner. *Clin. Immunol.* http://dx.doi.org/10.1016/j.clim.2016.10.011 (2016)