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AIRE, a key factor in the unequal impact of autoimmune diseases on men and women

Nadine Dragin, a researcher from an Inserm/UPMC/CNRS/AIM team codirected by Sonia Berrih-Aknin and Rozen le Panse at the Institute of Myology, based at Pitié-Salpêtrière Hospital, AP-HP, has demonstrated the central role of AIRE, a key factor in immune tolerance, in the unequal impact of autoimmune diseases on men and women. This work, published in The Journal of Clinical Investigation on 1 April 2016, was funded by AFM-Téléthon.

Autoimmune diseases result from a malfunction of the immune system that attacks normal constituents of the body known as “autoantigens.” They affect 5–8% of the population, and affect women more than men. They thus represent the fifth leading cause of death in women of childbearing age.

To explain this inequality, the researchers from the Institute of Myology focused on thymic tolerance mechanisms, i.e. this state of immune non-response to an antigen. The research teams observed that the Auto-Immune REgulator (AIRE), a key factor in immune tolerance, is less strongly expressed in women than in men.

AIRE controls the expression of tissue-specific antigens on the epithelial cells of the thymus (a lymphoid organ that produces components of the immune system in humans). On contact with epithelial cells expressing these specific antigens, potentially pathogenic cells receive signals that lead to their destruction. A decrease in AIRE expression leads to reduced expression of these specific antigens, and hence to less efficient elimination of the cells. This phenomenon is observed after puberty, when the thymus in both women and female mice expresses less AIRE than that in males, leading to poorer immune tolerance, and hence to greater susceptibility to autoimmune disease. The researchers also showed that oestrogen was the hormone responsible for this effect, since oestrogen treatment of thymic epithelial cells from humans and mice resulted in a decrease in AIRE expression in these cells.

Taken together, these results therefore indicate that, in females, oestrogen induces changes in the expression of the AIRE gene, thereby increasing the sensitivity of women to autoimmune diseases. AIRE expression levels may therefore indicate a predisposition to an autoimmune disease, and make the oestrogen level a potential therapeutic target.

Publication

“Estrogen-mediated downregulation of AIRE influences sexual dimorphism in autoimmune diseases”

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