ISGE
GYNECOLOGICAL ENDOCRINOLOGY
THE 18TH WORLD CONGRESS
7-10 MARCH 2018 FLORENCE, ITALY

P20. Sexual differences in macrophage physiology

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Context. Beyond their role in immunity against infections, macrophages are being widely recognized to participate in physiological functions in the absence of infective signals. Through the acquisition of specialized phenotypes, these cells adapt to various microenvironment signals, secrete specific molecules or present surface receptors that orchestrate intercellular interactions that maintain tissue homeostasis. Since progesterone and androgen receptors are not expressed by macrophages, estrogen is the only sex steroid signal that directly modulates macrophage activity.
Women display stronger immune responses than men, as confirmed by the different incidence of infective and autoimmune diseases, which may involve a sexually distinct activity of macrophages possibly caused by estrogen action in these cells. However, sex differences in macrophages and the involvement of estrogen action have not been explored yet.
Objective. The purpose of this study is to evaluate differences in gene expression and activity between male and female macrophages.
Methods. Peritoneal macrophages are isolated from male and female mice and analyzed by transcriptomics, followed by bioinformatics analyses and functional validation.
Results. Our data show that a great number of genes are differentially expressed in macrophages isolated from male and female animals; strong differences are observed in biological processes such as proliferation, immune activation and energy metabolism, as shown by bioinformatics and biochemical assays of mitochondrial function. Moreover, our data show that some of these different genes are responsive to estrogen in females. These data show that female and male macrophages possess strongly different phenotypes and energetic expenditure and that the estrogen signaling pathway in macrophages may be responsive, at least in part, for such differences.
Conclusions. The strongly different phenotype of macrophages in the two sexes provides an explanation for the sexual dimorphism in the incidence and progression of inflammatory pathologies, such as cardiovascular diseases, infections and wound healing, while a derangement of the estrogen-macrophage interplay may similarly represent a risk factor. Our results also support the need to refine the use and development of anti-inflammatory therapies by taking into account patients' sex and estrogen responsiveness.

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