ESTROGEN PROMOTES MACROPHAGE PROLIFERATION AND POLARIZATION

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Macrophages are resident immune cells that play a key role in host defense against pathogenic infections as well as in tissue remodeling and homeostasis. These cells are able to respond to a variety of microenvironmental stimuli, adopting different phenotypes depending on the activating signal and context.

Humans show strong sex differences in immunity; these can be mainly ascribed to steroid sex hormones. Indeed, estrogens regulate cells and pathways of the innate and adaptive immune systems. Previous studies showed that 17β-estradiol (E2) is able to modulate the reactivity of macrophages during inflammation, down-regulating the expression of inflammatory genes. However, a full comprehension of the molecular details by which estrogens exert their anti-inflammatory activity is still unclear. In order to have a deeper understanding of the physiological activity of estrogen on macrophages we performed a genome-wide gene expression study on peritoneal macrophages isolated from female mice under different endogenous or pharmacological estrogen levels.

The bioinformatic analysis of our data suggested that E2 modulates several biological processes involved in macrophage physiology; among these, proliferation and the induction of an anti-inflammatory and pro-resolution phenotype emerge as mostly significant. We thus first focused on two biological pathways, namely proliferation and immune activation, and confirmed the activity of estrogen, which showed to occur in a dynamic and specific manner. Hormone action was further validated in an in vivo experimental model of peritoneal inflammation based on zymosan injection. Further studies on the biological role and pharmacological regulation of the estrogen-macrophage interplay will be discussed.

Altogether, our results deepen the understanding of endocrine-immune interactions and have relevant implications for the pathogenesis and therapeutic strategies of inflammatory pathological conditions in which the estrogen-macrophage interplay is involved.