Estrogen promotes macrophages proliferation and polarization

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Macrophages are resident immune cells that play a key role in host defense against pathogenic infections and in inflammatory responses. They are able to respond to a variety of microenvironmental stimuli, adopting different activation states depending on the activating signal and context, in order to eliminate the pathogen and restore homeostasis.
Humans show strong sex differences in immunity to infection and autoimmunity, suggesting that sex hormones modulate immune responses. Indeed, estrogens regulate cells and pathways of the innate and adaptive immune systems, as well as immune cell development.
Previous studies showed that 17β-estradiol (E_2) 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. To evaluate estrogen physiological activity on macrophages we performed a genome-wide gene expression study through RNA-sequencing analysis of peritoneal macrophages isolated from female mice both with different endogenous estrogen levels and following short and long term estrogen administrations.
The bioinformatic data suggest that E_2 modulates important biological processes in macrophage physiology; among these, proliferation and the induction of an anti-inflammatory and pro-resolution phenotype emerge as mostly significant. We thus confirmed this evidence by proving, through gene expression, FACS analyses and BrdU incorporation, that the proliferative index and macrophage cell number are induced by estrogen surge. Furthermore, we demonstrated that a prolonged hormone administration induces a dynamic activation process that evolves towards a pro-resolving phenotype through the synthesis of IL10. Altogether, these results deepen our 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.