Macrophages and estrogen action: a positive interplay for inflammation-related disorders

E. Vegeto

Center of Excellence on Neurodegenerative Diseases, Dept. Pharmacological and Biomolecular Sciences,University of Milan, Via Balzaretti 9 - 20133 Milan, Italy

Macrophages are innate immune cells which serve many functions including immune surveillance of the microenvironment for pathogen invasion, damage signals and tissue dysfunction. The dual task of defenders and re-constructors of tissue homeostasis is achieved by activating two main programs: the classical pro-inflammatory phenotype, which is associated with cytokine secretion, immunological activation and cytotoxicity, and the subsequent alternative activation program, which helps in resolving inflammation and restoring tissue homeostasis. In normal aging, the extrinsic changes in systemic and local environment together with cell-intrinsic mechanisms provoke variations in macrophage cell density and, notably, in their immunophenotype which predisposes to an exaggerated pro-inflammatory response against dangerous challenges and a reduced anti-inflammatory and reparative capacity, leading to failure in restoring tissue homeostasis.

It is increasingly evident that the interplay between estrogens and macrophages represents a protective factor for women's health, whereas the menopause is recognized to be itself a key determinant for the decline in immune and functional capacity of macrophages and for the increase in diseases, such as osteoporosis, atherosclerosis and neurodegenerative diseases, which are sustained by inflammation.

Our studies show that tissue resident macrophages are influenced by the estrogen status through the activation of specific receptor-dependent signaling pathways that converge on promoting the resolution of inflammation under normal and pathological conditions, during ageing or in experimental settings that mimic the menopause. Further understanding of the molecular bases of estrogen action will help finding new targets and avoiding adverse effects, thus opening novel therapeutic opportunities for improved women health.