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LPS-stimulated human macrophages displayed sex differences in estrogen receptors α and β

Ilaria Campesi[1,2], Maria Marino[3], Flavia Franconi[1,4] and Andrea Montella[1]

[1] Department of Biomedical Sciences, University of Sassari, Sassari, Italy
[2] Laboratory of Sex-Gender Medicine, National Institute of Biostructures and Biosystems, Sassari, Italy
[3] Cell Physiology Lab, Department of Science, University Roma Tre, Rome, Italy
[4] Assessorato alle Politiche per la Persona, Regione Basilicata, Potenza, Italy

Macrophages play a key role in immunity, inflammation, and atherosclerosis. Moreover, several evidences demonstrate that 17-β-estradiol (E2) plays a key role in inflammation and atherosclerosis through estrogen receptors (ERs) ERα and ERβ, processes that display sex differences. It has been largely demonstrated that male tissues express active ERs, but there is still lack of knowledge on their role in inflammation in males. Macrophages, which have ERα and ERβ, are a good model to evaluate the role of ER levels and activation in inflammation. The aim of our work was to evaluate the ability of lipopolysaccharide (LPS) to modulate, in a sex-specific way, the expression and the activation status of ERα and ERβ in blood monocytes-derived macrophages (MDMs) from healthy men and women. MDMs were isolated from blood of 7 adult men and 7 adult and fertile women (aged 21 - 35 years), and cultured. After 10 days of culture, MDMs were incubated with 100 ng / ml LPS for 24 h and lysed for the analysis of ERα, ERβ, P- ERα, p38 and P-p38 expression by Western Blotting.

We found that in basal conditions, the expression of ERα and ERβ was significantly higher in female MDMs than in male ones. Importantly, LPS stimulation up-regulated ERα and ERα phosphorylation in both sexes, but this regulation was more pronounced in male MDMs. Moreover, LPS down-regulated ERβ level only in female MDMs. The expression of p38 and P-p38 proteins, used as marker of ERβ activity, did not display any sex differences. Finally, the ratios between ERα / ERβ and P-ERα / ERα were significantly higher in male than in female MDMs.

Our findings show, for the first time, that LPS can modulate the activation of ERα but not that of ERβ, identifying a critical role of the subtype ERα in inflammatory responses mediated by LPS, at least in human MDMs. These results represent a starting point in understanding the influence of sex in the relationship between LPS and ERα.

Keywords

sex differences, estrogen receptors, lipopolysaccharide, inflammation

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