ACTIVATION OF P38 AND EGFR ARE REQUIRED FOR OUABAIN ACTION ON HUMAN MONOCYTES

Valente, R.C.[1]; Nascimento, C.R.[1,2]; Affonso-Mitidieri, O.R.[1]; Araujo, E.G.[3]; Rumjanek, V.M.[1]

[1]IBqM, UFRJ; [2]IBCCF, UFRJ – Rio de Janeiro; [3]Depto. Neurobiologia, UFF – Niterói – RJ, Brasil.

First described in plants, the steroid ouabain was also observed in plasma and several mammalian tissues. In the immune system, ouabain was shown to decrease lymphocyte proliferation and to sinergyze with glucocorticoids enhancing thymocyte apoptosis. However, little is known about its action on monocyte function. Providing these cells play a pivotal role on the recognition of foreign antigens, we aimed to analyse ouabain action on human monocytes, through the measurement of several surface molecules related to macrophage state of activation, such as Mac-1, CD80, CD86 and CD14 using flow cytometry. Peripheral blood mononuclear cells were collected from healthy individuals and monocytes were separated. After 24h incubation, ouabain decreased the expression of the integrin Mac-1, in a dose-dependent fashion. Moreover, 24h incubation with 10^{-7}M ouabain increased the population of $CD80^-/CD86^-$ double negative cells, indicating that ouabain might impair monocyte-induced lymphocyte activation, and also decreased CD14 expression (nearly 50%). In order to address the cellular mechanisms involved, we employed SB202109 and tyrfostin, inhibitors of p38 and EGFR, respectively. We observed that both inhibitors abolished ouabain action on CD14 expression. Hence, our data suggest that ouabain downregulates monocyte effector function, decreasing Mac-1, CD80/CD86 and CD14 expression, and also that its action on CD14 expression is related to activation of both p38 and EGFR.

Support: CNPq and FAPERJ.