Poster

Role of the hepatoprotective citoquine cardiotrophin-1 (CT-1) in macrophages polarization

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ABSTRACT

Motivation: Cardiotrophin-1 (CT-1) is a member of the interleukine-6 (IL-6) family, which signals through gp130/leukemia inhibitory factor receptor (LIFR). Signal transduction via gp130 involves three major downstream pathways: the STAT-3 (signal transducer and activator of transcription-3), the ERK and the AKT pathways, all of them described as antiapoptotics. CT-1 has been described as hepatoprotective.

However, the role of cardiotrophine in inflammation is a non-well studied process. Whenever an inflammation occurs, macrophages are the first cells of the inmune system to respond. These, in respond to various enviromental cues or under different pathophysiologic conditions, can aquire distinct functional phenotypes via by undergoing different phenotypic polarization. Macrophages M1 (proinflammatory) and M2 (antiinflammatory) are two well- separated groups, which describe opposing activities of killing and repairing, respectively.

The aim of our study was to evaluate the role of CT-1 in macrophages polarization.

Methods: To analyze the macrophages polarization into M1 or M2, different proinflammatories and antiinflammatories genes expression were measured, as well as the pathways involved, using molecular biology techniques, such as quantitative PCR (qPCR) and Western Blots.

Results:

1. In vivo model: a septic shock was induced to mice through a LPS injection. By analysis of the expression of proinflammatories genes in hepatic samples, we observed that pretreated mice with CT-1, showed a decrease on the levels of genes expression involved in proinflammation or M1, such as TNFα, IL1β and IL12p40.

2. In vitro model: macrophages polarization into M1 or M2 was induced by using LPS or IL4 respectively. The analysis of pro and antiinflammatories genes expression, showed us that pretreated macrophages with CT-1 had some modifications in the level of genes expression when compared with those non-treated. M1 genes expression diminished in relation to non-treated. On the other hand, M2 genes expression augmented with respect to non-treated. Interestingly, CT-1 can't modify these expression genes by itself.

Conclusions:

1. CT-1 modulates inflammatory response against LPS, by reducing proinflammatories cytokines within an in vivo model.

2. CT-1 modifies macrophage polarization into M1 or M2 induced by LPS or IL4, reducing proinflammatories cytokines and promoting antiinflammatories, but, interestingly, is not able to polarize macrophages by itself.

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