

A160 EFFECTS OF CTLA4-IG ON MONOCYTE/MACROPHAGE DIFFERENTIATION AND CYTOKINE PRODUCTION

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Background and objectives Cytotoxic T lymphocyte antigen 4 (CTLA4) is a surface protein on T lymphocytes that binds to the surface of antigen-presenting cells through the

CD80/86 molecules regulating their co-stimulation. The authors hypothesised that Abatacept (CTLA4-Ig) might bind to monocyte/macrophages regulating the differentiation of monocytes to macrophages, and the production of pro-inflammatory and anti-inflammatory cytokines by macrophages.

Material and methods Human peripheral blood mononuclear cells were isolated from buffy coats from four normal donors by Ficoll gradient cell separation. Then, monocytes were purified by CD14 positive selection, and they were differentiated in vitro to classic and alternative macrophages by culturing in the presence of granulocyte-macrophage colony stimulating factor or macrophage-colony stimulating factor (M-CSF) respectively. The authors analysed the CTLA4-Ig binding to classic and alternative macrophages by flow cytometry. After demonstrating that CTLA4-Ig binds to classic and alternative macrophages, the effect of CTLA4-Ig on macrophage differentiation and cytokines production were tested.

Results CTLA4-Ig binds to human macrophages. In addition, CTLA4-Ig reduced, in a dose-dependent fashion, the macrophage differentiation in monocytes cultures stimulated with M-CSF. This results did not evidence any effect of CTLA4-Ig on the IL-10 or tumour necrosis factor production by neither classical nor alternative macrophages.

Conclusion These data show that CTLA4-Ig directly affects macrophage differentiation in vitro. Therefore, the beneficial effect of Abatacept in rheumatoid arthritis patients could be achieved at least partially through a direct mechanism of action on the monocyte/macrophage line cell.