

Effects of cyclosporine A and rapamycin on pro-inflammatory cytokine production by dendritic cell *in vitro*



Maja Machcińska¹, Katarzyna Bocian¹, Grażyna Korczak-Kowalska^{1,2}

¹Department of Immunology, Faculty of Biology, University of Warsaw, Poland ²Transplantation Institute, Medical University of Warsaw, Poland

Objectives:

The most important antigen-presenting cells (APCs) are dendritic cells (DCs), which present antigen to T cells during the immune response to transplantation antigens. It was noted that immature DC cell plays an important role in peripheral tolerance, whereas mature DC induces a complete immune response. Depending on the state of maturation DCs produce a variety of pro- and anti-inflammatory cytokines. This is very important in transplantation, especially in allograft rejection. Immature DCs or DCs with tolerogenic properties may prolong allograft survival. The manipulation of dendritic cells to become insensitive to maturation signals *in vivo* or activation tolerogenic DCs may improve transplant tolerance.

It is important to achieve this aim using the parallel immunosuppressive therapy with cyclosporine A (CsA) and rapamycin (Rapa).

The aim of this study was to evaluate the effect of immunosuppressive agents: rapamycin and cyclosporine A on immature DC pro-inflammatory cytokine production and after LPS stimulation.

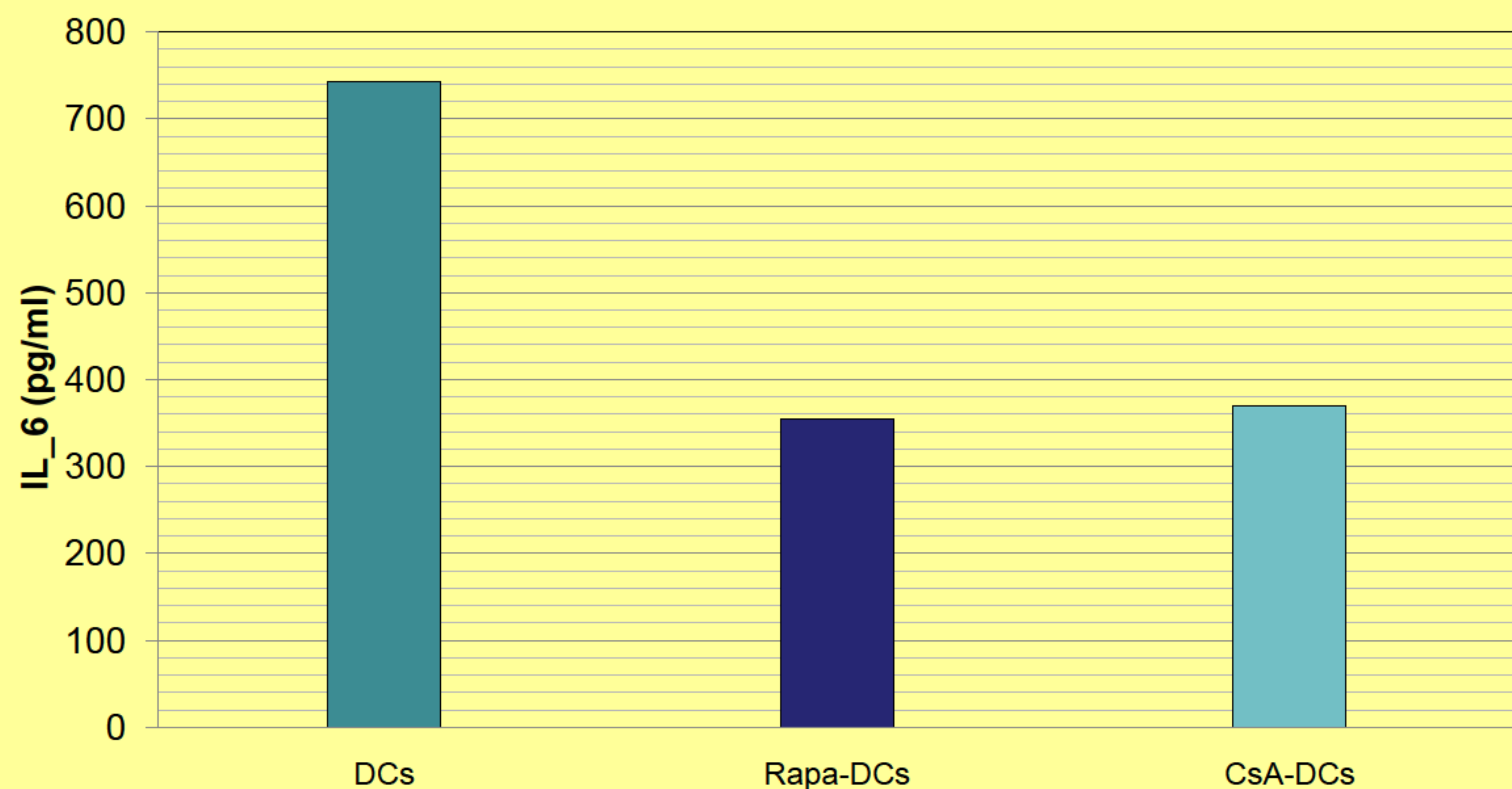
Methods:

Human peripheral blood monocytes were induced by using cytokines: IL-4 and GM-CSF, in the direction of DCs in the presence of rapamycin (Rapa-DCs) and cyclosporine A (CsA-DCs) or without drugs (control, DCs). Then these immature DCs were stimulated with LPS to create mature DCs.

The supernatants have been collected and measurements of DC pro-inflammatory cytokine (IL-6 and IL-12) levels were performed by ELISA.

Results:

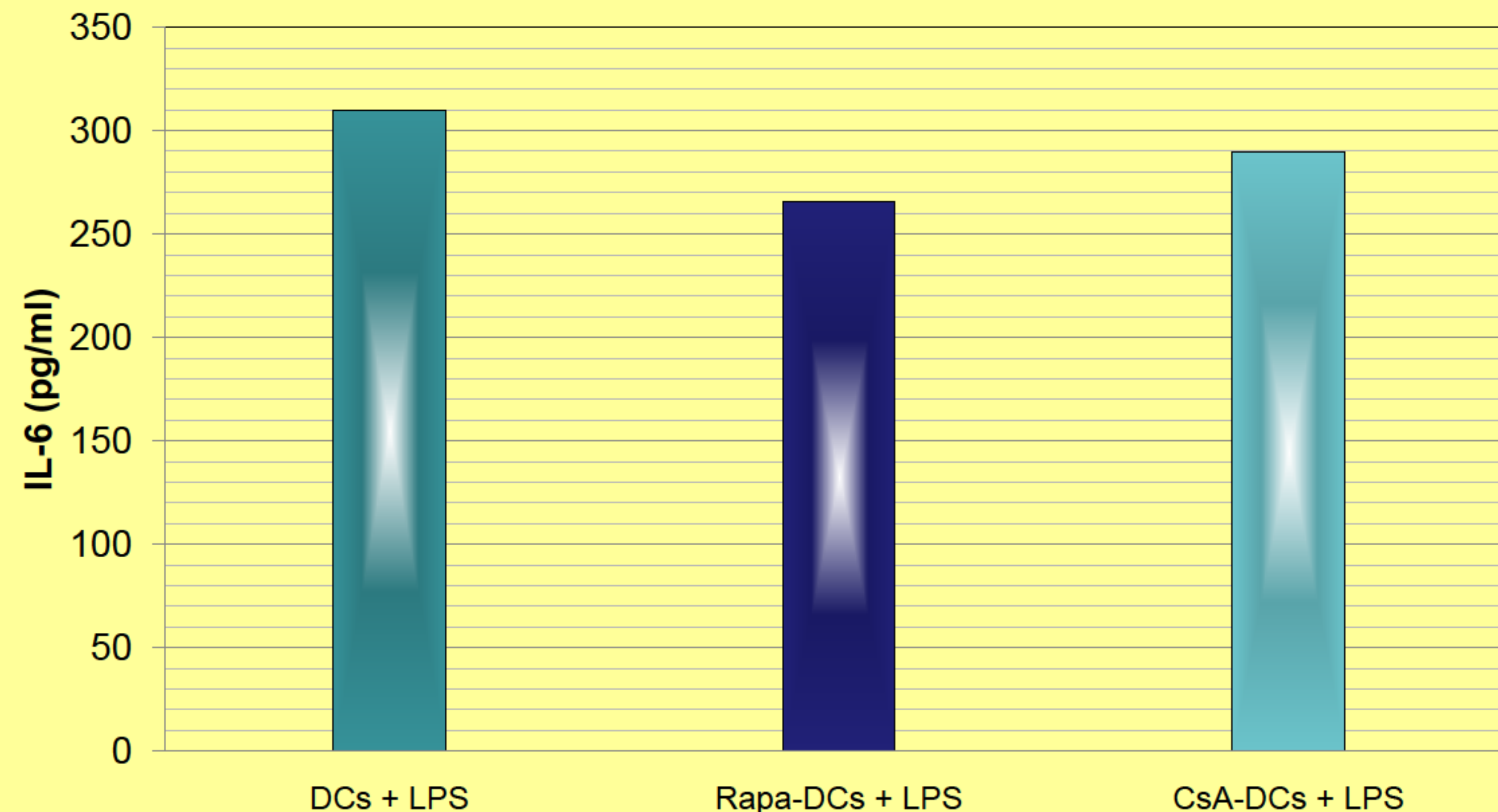
Fig. 1 IL-6 production by immature dendritic cells



We have observed a diminished production of IL-6 by immature dendritic cells when these cells were differentiated in the presence of immunosuppressive drugs: cyclosporine A and rapamycin, compared to control.

The lowest production of IL-6 was noted in the environment of rapamycin..

Fig. 2 IL-6 production by LPS-activated dendritic cells



We have observed that LPS-activated DCs also produced less IL-6, when these cells were differentiated in the presence of immunosuppressive agents.

The lowest production of LPS-induced IL-6 was noted in the environment of rapamycin..

Production of IL-12 by immature DCs and LPS-activated DCs was notably undetectable in all culture conditions.

Conclusions:

We have shown that the immunosuppressive agents: rapamycin and cyclosporine A change the dendritic cells pro-inflammatory cytokine production during their differentiation.

