PROTEASE INHIBITOR CYSTATIN C IS DIFFERENTIATION DEPENDENT IN HUMAN DENDRITIC CELLS

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1. INTRODUCTION
Dendritic cells possess a big capacity to elicit immune response. Their maturation occurs as they migrate to lymphoid organs, where they present captured antigens to T cells. The central role of endosomal/lysosomal proteolytic enzymes in generating antigenic peptides and controlling major histocompatibility complex class II (MHC II) traffic defines these enzymes as an important area of investigation. The involvement of natural protease inhibitors has been supported by the study on cystatin homologue, secreted from the filarial parasite *Brugia malayi*, which was shown to down-modulate MHC II-restricted antigen presentation.

2. AIMS AND METHODS
Our study has been focused on another cystatin homologue, i.e. human cystatin C. In order to modulate the proteolytic capacity of intracellular proteases in human dendritic cells, our first goal was to characterize the endogenous cystatin C during the differentiation of monocytes to immature dendritic cells and their further maturation with TNF-alpha and LPS, respectively. Quantification of inhibitor cystatin C and its target enzyme cathepsin S has been performed by immunogold electron microscopy, performed on labelled cryo sections of monocytes, immature and mature dendritic cells.

3. RESULTS
We showed that in immature dendritic cells cystatin C content was highly elevated compared to their precursors - monocytes. The low content of cystatin C in monocytes resulted from lower expression, but not from its elevated secretion. On the other hand, increased expression of cystatin C and high content in Golgi apparatus were observed in immature dendritic cells. The transport of cystatin C was shown from Golgi apparatus towards the cell membrane, where cystatin C accumulated in fully mature dendritic cells.

4. CONCLUSIONS
Differentiation and maturation dependence of endogenous cystatin C supports its intracellular regulatory potential and suggests it new role in Golgi apparatus of immature dendritic cells.