

Poster presentation

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## Activation of NF- $\kappa$ B by nitric oxide/cGMP in human blood CD14<sup>+</sup> cells

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Nuclear factor  $\kappa$ B (NF- $\kappa$ B) is a common transcription factor regulating expression of multiple genes relevant for immune reactions. It may be activated by numerous stimuli and a number of data have indicated a relationship between its activity and intracellular concentration of cGMP. Increased levels of the nucleotide have been shown to affect expression of TNF $\alpha$ , IL-1, IL-6 and NOS2 in various immune cells. Particularly, cGMP has been shown to affect several important functions of cells belonging to a monocyte/macrophage lineage. Recently, we reported that in freshly isolated human peripheral blood mononuclear cells (PBMC) the NF- $\kappa$ B activity was modulated through a cGMP-dependent pathway. The aim of this study was to determine whether and how cGMP may affect an activity of NF- $\kappa$ B in human CD14 monocytes. They express soluble guanylyl cyclase (sGC) as well as cGMP-dependent protein kinase I (PKG I). We show that in these cells nitric oxide (NO) stimulates the NF- $\kappa$ B activity at low and inhibits it at high doses. This effect is mimicked by membrane-permeable analogues of cGMP. Using specific inhibitors, we also show that stimulatory effect of NO/cGMP on the NF- $\kappa$ B activity is mediated by PKG I. This observation is additionally supported by the fact that stimulatory effect of NO disappears in cultured cells lacking PKG I. Therefore, our results show that at least some reported effects of NO/cGMP on monocytic cells directly involve PKG I and NF- $\kappa$ B.

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