

Jennifer Mytych – "*The search for novel properties of klotho protein in the fight against bacterial infections*"

ABSTRACT

Monocytes play an important role in host defense to bacterial pathogens. In monocytes, under physiological conditions, after eradication of the threat, apoptotic cell death is activated. However, under abnormal conditions, when bacterial endotoxins are not fully neutralized, the lifespan of monocytes is prolonged and the acute inflammatory reaction becomes chronic. Taking into account observed changes in monocytes phenotype and functions, it seems highly probable that in these cells, the program of premature senescence is initiated. Further, this phenomenon can also adversely affect the interaction of monocytes with non-immune cells. At the same time, research on the anti-aging and anti-inflammatory properties of klotho protein suggests that it can play a key role in these processes.

Obtained in this study results suggest that *E. coli* lipopolysaccharide, depending on the dose used, activates various regulatory pathways i.e. premature senescence, macrophage differentiation and apoptotic cell death in monocytes. Thus, the possibility of bacterial antigen-induced immunosenescence in monocytes was confirmed. Also, the exact mechanism of this process was proposed: observed redox and calcium/zinc imbalance led to changes in secretory phenotype, DNA damage and permanent cell cycle arrest. Furthermore, monocytes undergoing premature senescence lost their key properties crucial for mediating both specific and non-specific immune responses. Overexpression of secreted and membrane form of klotho protein in monocytes protected them from bacterial antigen-induced premature senescence. It was also confirmed, that incubation of activated and prematurely senescent monocytes with epithelial cells led to cytotoxic and genotoxic events in epithelial cells resulting in apoptosis or premature senescence. Also in this case, klotho overexpression in epithelial cells protected them from changes caused by dysfunctional monocytes.