Секция «Экспериментальные исследования»

Noradrenaline switch mesenchymal stem/stromal cells to proinflammatory phenotype

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Inflammation - is a typical pathological process induced by a pathogenic factor. Inflammation includes destruction of a pathogenic agent and regeneration of the surrounding tissues. Mesenchymal stem/stromal cells (MSC) are important components of inflammation and regeneration. MSC are part of many tissues in an organism. MSC are capable to differentiate into several types of cells, therefore MSC play an important role in reparation and regeneration of an injury. Since MSC influence activity of cells of the immune system, they also regulate process of inflammation by secreting cytokines and inducing an anti-inflammatory response. Hormones and neuromediators regulate functional activity of MSC. Noradrenaline, which controls secretory activity and differentiation of MSC, is one of the important neuromediators for MSC. Earlier we showed an interesting phenomenon of switching of the intercellular signaling, in response to adrenergic receptors stimulation: noradrenaline stimulates beta-adrenergic receptors in MSC and induces heterologous sensitization of alpha 1A-adrenergic receptors.

In our work we studied influence of noradrenaline on secretory activity of MSC, associated with regulation of inflammation. Using NanoString we examined changes in expression of over 700 cytokines and other proteins, that are associated with regulation of the immune reaction. Using PanCancer Immune Profiling Panel we showed that noradrenaline induces elevation in RNA expression of many proinflammatory cytokines (as well as receptors and members of signaling pathways, activated by these cytokines) and decrease in expression of anti-inflammatory molecules. We have also explored changes in expression of 17 proinflammatory cytokines using BioRad BioPlex. We observed that stimulation by noradrenaline leads to an increased expression of proinflammatory cytokines, such as IL-6, IL-8, G-CSF, IFN-G and MCP-1. Repeated stimulation of alpha 1A-adrenergic receptors by noradrenaline did not change expression of cytokines. Therefore, stimulation of beta-adrenergic receptors and not the alpha1A adrenergic receptors leads to MSC switching to a proinflammatory phenotype.

Thus we established that stimulation by noradrenaline induced elevation of pro inflammatory cytokines secretion as well as increased sensitivity of cells to these molecules. MSC switched from anti-inflammatory to proinflammatory phenotype. The work was supported by the Grant of the President of the Russian Federation for the state support of young Russian scientists - candidates of sciences MK-3167.2017.7