

P5. The role of *Pseudomonas aeruginosa* culture fractions and purified quorum sensing signaling molecules on human mesenchymal stem cells morphophysiology

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Mesenchymal stem cells (MSCs), the symbol of regenerative medicine, are a major tool for the therapy of lung damaging diseases. The opportunistic pathogen *Pseudomonas aeruginosa* is the most encountered etiologic agent of lung infections, severely affecting patients with cystic fibrosis and also representing the main hitch in the damaged tissue repair and lung transplant related complications.

The aim of this study was to investigate the effects of *P. aeruginosa* culture fractions and purified quorum sensing signaling molecules (QSSMs) on human MSCs death signaling pathways and cytokine profile. The bone marrow isolated MSCs, incubated for different periods of time with one of the seven *P. aeruginosa* PAO1 culture fractions or QSSMs (low density whole cultures, heat inactivated bacterial cultures sediments, sterile supernatants, N-(3-Oxododecanoyl)-L-homoserine lactone (OdDHL), N-butanoyl-L-homoserine lactone (C4-HSL), 2-heptyl-3-hydroxy-4(1H)-quinolone (PQS) and 2-heptyl-4-quinolone (HHQ)) were subjected to the following assays: i) fluorescence microscopy evaluation of cellular morphology and viability; ii) flow cytometry analysis of apoptotic/necrotic MSCs, iii) apoptosis related genes expression analysis by qRT-PCR; iv) quantification of the level inflammatory cytokines released in the MSCs supernatants determined by ELISA. Results were statistically analyzed using the GraphPad In Stat software. The PAO1 whole cultures exhibited the most relevant influences, impacting on MSCs morphology and viability, interfering with apoptotic pathways and significantly stimulating the production of IL-1 β and IL-10, while decreasing the production of IL-6 and IL-8. Our results demonstrate that all tested QSSMs significantly impacted on several core signaling mechanisms of MSCs in a specific and time dependent manner. Even if all tested autoinducers interfered with the MSCs apoptotic genes expression, only OdDHL and HHQ significantly promoted MSCs apoptosis, this aspect being confirmed by the flow cytometry assay. These results demonstrate that *P. aeruginosa* infections may complicate the success of tissue repair by interfering with the normal function of the MSCs in the human body, and eventually, impair or abolish the success of the stem cells therapy.