

Physical Contact Modulation of Macrophage-Mediated Anti-Inflammatory Response in Osteoimmune Microenvironment by Pollen-Like Nanoparticles

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Abstract : Introduction: Nanomaterial-based bone regeneration is greatly influenced by the immune microenvironment. Tissue-engineered nanomaterials mediate the inflammatory response of macrophages to regulate bone regeneration. Silica nanoparticles have been widely used in tissue engineering-related preclinical studies. However, the effect of topological features on the surface of silica nanoparticles on the immune response of macrophages remains unknown. Purposes: The aims of this research are to compare the influences of normal and pollen-like silica nano-surface topography on macrophage immune responses and to obtain insight into their potential regulatory mechanisms. Method: Macrophages (RAW 264.7 cells) were exposed to mesoporous silica nanoparticles with normal morphology (MSNs) and pollen-like morphology (PMSNs). RNA-seq, RT-qPCR, and LSCM were used to assess the changes in expression levels of immune response-related genes and proteins. SEM and TEM were executed to evaluate the contact and adherence of silica nanoparticles by macrophages. For the assessment of the immunomodulation-mediated osteogenic potential, BMSCs were cultured with conditioned medium (CM) from LPS pre-stimulated macrophage cultures treated with MSNs or PMSNs. Osteoimmunomodulatory potential of MSNs and PMSNs in vivo was tested in a mouse cranial bone osteolysis model. Results: The results of the RNA-seq, RT-qPCR, and LSCM assays showed that PMSNs inhibited the expression of pro-inflammatory genes and proteins in macrophages. SEM images showed distinct macrophage membrane surface binding patterns of MSNs and PMSNs. MSNs were more evenly dispersed across the macrophage cell membrane, while PMSNs were aggregated. PMSNs-induced macrophage anti-inflammatory response was associated with upregulation of the cell surface receptor CD28 and inhibition of ERK phosphorylation. TEM images showed that both MSNs and PMSNs could be phagocytosed by macrophages, and inhibiting nanoparticle phagocytosis did not affect the expression of anti-inflammatory genes and proteins. Moreover, PMSNs-induced conditioned medium from macrophages enhanced BMP-2 expression and osteogenic differentiation mBMSCs. Similarly, PMSNs prevented LPS-induced bone resorption via downregulation of inflammatory reaction. Conclusions: PMSNs can promote bone regeneration by modulating osteoimmunological processes through surface topography. The study offers insights into how surface physical contact cues can modulate the regulation of osteoimmunology and provides a basis for the application of nanoparticles with pollen-like morphology to affect immunomodulation in bone tissue engineering and regeneration.

Keywords : physical contact, osteoimmunology, macrophages, silica nanoparticles, surface morphology, membrane receptor, osteogenesis, inflammation

Conference Title : ICBMBTE 2024 : International Conference on Bioactive Materials for Bone Tissue Engineering

Conference Location : Berlin, Germany

Conference Dates : July 22-23, 2024