Pathogenic role of fibroblast like synoviocyte in the particle induced periprosthetic osteolysis

Ashish Ranjan Sharma, Supriya Jagga, Yeon-Hee Lee, Ju-Suk Nam, Sang-Soo Lee
Institute for Skeletal Aging & Orthopedic Surgery, Hallym University-Chuncheon Sacred Heart Hospital, Chuncheon, Korea

INTRODUCTION

The buildup of particulate debris from the interface of orthopedic and dental implants is widely recognized as the major initiating event in development of periprosthetic osteolysis and aseptic loosening. Wear debris from the prosthesis affects a diverse kind of cells, including macrophages, synoviocytes, lymphocytes, osteoblasts and osteoclasts. Among them, fibroblast-like synoviocytes (FLS) are unique cells that populate the intimal lining of the synovium. FLS maintains the dynamic integrity of joints by controlling the composition of the synovial fluid and extra cellular matrix. However, under inflammatory condition, FLS displays pathogenic behavior by releasing a number of pro-inflammatory cytokines and are crucial for the pathogenesis of chronic inflammatory joint diseases. In here, we have tried and examined the effect of Ti particles on human FLS and the mechanism by which it might participate in the process of periprosthetic osteolysis.

DESIGN & METHODS

RESULTS

1. Treatment of Ti particles to FLS increased the expression of Cox-2 while suppressed that of IκBα, implicating the activation of NFκB signaling pathway.

2. Treatment of Ti particles to human FLS increased the mRNA expression of pro-inflammatory cytokines and Rankl.

3. Conditioned medium from Ti particles (Ti CM) stimulated FLS induced the mRNA expression of osteoclastogenic markers like TRAP and Rankl. Ti CM stimulated the osteoclast formation.

4. Ti CM suppressed osteogenic markers like transcriptional factors (Osterix & Runx-2), ALP activity, collagen synthesis and mineralization in osteoblasts.

5. Ti CM suppressed WNT and BMP signaling pathways. Ti particles stimulated FLS showed induced mRNA expression of antagonists of WNT and BMP signaling pathways.


CONCLUSIONS

FLS responds to wear debris from implants by demonstrating inflammatory characteristics like releasing pro-inflammatory cytokines and Rankl. Ti CM enhances osteoclastogenesis and impedes osteogenic ability of osteoblasts. Moreover, Ti CM suppressed bone forming signals like WNT and BMP signaling pathways in osteoblasts. An increased expression of WNT and BMP signaling antagonists were observed in Ti particles treated FLS. Inhibition of SOST in Ti CM partially restored bone signaling pathways as well osteogenic activity in osteoblasts. Further studies focused on the role of other released antagonists in CM by Ti particles stimulated FLS might explain the complete reasons for the suppressed impeded osteogenic activity of osteoblasts during periprosthetic osteolysis.

REFERENCES


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