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## Endoplasmic reticulum stress-mediated inflammatory signaling pathways within the osteolytic periosteum and interface membrane in particle-induced osteolysis

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Aseptic loosening secondary to periprosthetic inflammatory osteolysis results from the biological response to wear particles and is a leading cause of arthroplasty failure. The origin of this inflammatory response remains unclear. We aim to validate the definite link between endoplasmic reticulum (ER) stress and particle-induced inflammatory signaling pathways in periprosthetic osteolysis. We examine the histopathologic changes of osteolysis and the expression of specific biomarkers for ER-stress-mediated inflammatory signaling pathways (IRE1 $\alpha$ , GRP78/Bip, c-Fos, NF- $\kappa$ B, ROS and Ca<sup>2+</sup>). Moreover, pro-inflammatory cytokines (TNF- $\alpha$ , IL-1 $\beta$  and IL-6) and osteoclastogenic molecules (VEGF, OPG, RANKL and M-CSF) were assessed in clinical interface membranes and murine periosteum tissues. We found wear particles to be capable of inducing ER stress in macrophages within clinical osteolytic interface membranes and murine

osteolytic periosteum tissues and to be associated with the inflammatory response and osteoclastogenesis. Blocking ER stress with sodium 4-phenylbutyrate (4-PBA) results in a dramatic amelioration of particle-induced osteolysis and a significant reduction of ER-stress intensity. Simultaneously, this ER-stress blocker also lessens inflammatory cell infiltration, diminishes the capability of osteoclastogenesis and reduces the inflammatory response by lowering IRE1 $\alpha$ , GRP78/Bip, c-Fos, NF- $\kappa$ B, ROS and Ca<sup>2+</sup> levels. Thus, ER stress plays an important role in particle-induced inflammatory osteolysis and osteoclastogenic reactions. The pharmacological targeting of ER-stress-mediated inflammatory signaling pathways might be an appealing approach for alleviating or preventing particle-induced osteolysis in at-risk patients.

### Biography

Guoyin Liu has completed his Master's degree from Medical School of Nanjing University, and is currently a PhD candidate in Nanjing Medical University. He is the doctor-in-charge and associate professor at the Department of Orthopaedics, Jinling Hospital of Nanjing Medical University. He worked mainly on the role of intracellular and extracellular GRP78/Bip in particles-induced periprosthetic osteolysis and rheumatoid arthritis; the clinical application of extracorporeal shock wave therapy, corticosteroid injection, and needle-knife therapy in the treatment of chronic plantar fasciitis; and the application of lamina osteotomy and replantation with miniplate fixation (restorative laminoplasty) in intraspinal occupying lesions. He had been invited as a speaker to the "World Congress on Virology & Infectious Diseases" during November 20-22, 2017 in Miami, FL, USA, and as a speaker to the International Conference on Biomarker Research in Clinical Medicine scheduled for February 19- 21, 2018 in Paris, France (BRCM 2018). He was a member of the Standing Committee of the China Medicine Education Association (CMEA), and a managing director of National Association of Health Industry and Enterprise Management (NAHIEM).

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