The Effects of Orthopaedic Wear Particles on Natural Killer T Cells in vitro

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Disclosures:

Introduction: Two major issues in total joint arthroplasty are loosening of implants and osteolysis caused by wear particle-induced inflammation. Wear particles stimulate the release of pro-inflammatory cytokines, chemokines and other inflammatory mediators from macrophages and other cells. Although the biological response of macrophages to wear debris is well established, the role of other cell types such as natural killer T lymphocytes (NKT) and dendritic cells is limited. Upon activation, NKT cells are known to modulate the immune system by rapidly secreting either pro-inflammatory cytokines such as IFN-γ, or anti-inflammatory mediators such as IL-4. This ability to either further activate or suppress the inflammatory response makes these cells unique. The purpose of current study is to evaluate cytokines released by NKT cells in response to phagocytosable polymer particles with/without dendritic cells.

Methods: NKT cells were isolated from the spleens of C57BL/6J male mice (6-8 weeks old) and cells were exposed to two different particle types, ultra-high molecular weight polyethylene (UHMWPE) and poly-methyl-methacrylate (PMMA) with or without lipopolysaccharide (LPS). In addition, particle/LPS stimulated dendritic cells were co-cultured with NKT cells in specific groups. The expression profiles of IFN-γ and IL-4 were analyzed at both mRNA and protein levels using qPCR and ELISA respectively. The NKT cells activation ligand α-galactosylceramide (GalCer) was used as a positive control.

Results: Both the UHMWPE and PMMA particles alone failed to stimulate the NKT cells to secrete IFN-γ or IL-4. Furthermore, particles with/without LPS did not stimulate cultures of both NKT cells and antigen presenting dendritic cells to produce increased levels of cytokines; α-GalCer treatment in the co-culture system significantly enhanced the IL-4 expression by NKT cells (Figure1, p<0.005).

Discussion: Our results suggest that activation of NKT cell is not initiated in the inflammatory reaction to polymer wear particles, irrespective of the presence of antigen presenting cells (dendritic cells) or LPS. This finding is consistent with the fact that polymer particles stimulate the innate rather than the adaptive immune system. Our results do not preclude the possibility that NKT may play a role later on in the events associated with wear debris and periprosthetic osteolysis. Indeed, previous studies have shown that NK cells are a principal tissue-infiltrating lymphocyte subset in patients with OA and patients with periprosthetic inflammation who are undergoing revision joint replacement surgery (Huss et al. 2010). These NKT cells display a quiescent phenotype that is consistent with post-activation exhaustion.

Significance:

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in osteoarthritis and periprosthetic inflammation. " Arthritis & Rheumatism 62(4): 3799-
Figure. Secretion of IL-4 cytokine by NKT cells were determined by ELISA. The cells were exposed to UHMWPE (PE) only (+) or different treatment.