Interactions of the plasma cell membrane with wear particles generated from artificial hip replacements

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Abstract

Since the 1960s, total hip replacements (THRs) have been used to successfully restore the mobility of diseased hip joints. Hard bearing materials, such as ceramic-on-ceramic and metal-on-metal were introduced to reduce wear rates and extend implant longevity[1]. Cobalt chromium (CoCr) and alumina-based ceramic wear particles, generated from the bearing surface, are predominately nanoscale in size and adverse biological reactions to the wear particles, both *in vitro* and *in vivo*, have been reported[2]. In particular, CoCr wear particles have been associated with hypersensitivity reactions, pseudotumors, and extensive necrosis in the tissues surrounding the implants[3]. Whilst a number of studies have investigated the effects of CoCr and ceramic wear particles, little is known about the interaction of wear particles with the cell plasma membrane and subsequent internalisation. This is particularly important in determining how particle binding to the cell membrane manifests to larger scale adverse reactions, especially with metal implants. Therefore, this project aims to determine if nanoparticles are able to damage the cell membrane with toxic consequences or whether they pass the membrane and exert toxic effects intracellularly.

In order to investigate the project aims, the use of model membranes was implemented. Vesicle leakage assays on clinically relevant CoCr and ceramic wear particles were performed. Ceramic wear particles increased vesicle leakage in a dose response manner, but surprisingly CoCr wear particles did not extensively induce vesicle leakage suggesting that the latter particles do not induce pore formation within the membrane. Quartz crystal microbalance with dissipation (QCM-D) was also used to assess the ability of the particles to bind to solid-supported bilayer lipid membranes (sBLM) on SiO_2. This technique demonstrated that both the ceramic and CoCr wear particles bind to the membrane, although the interaction between the particles and lipid membrane is very weak, leading to a strong effect on the energy dissipation in the QCM-D. Furthermore, the addition of fetal bovine serum (10% v/v) with CoCr nanoscale wear particles demonstrated a reduced incidence of particle binding to the membrane. This may be caused by the effects of a protein corona, shielding the surface of the wear particles. From these initial results, further work is required to fully assess wear particle toxicity including using isolated plasma membranes from fibroblasts and macrophages to investigate the effect of particle:membrane protein interactions.

[1] Dowson *et al.* 2004. J Arthroplast 19:118-123
[2] Brown *et al*. 2006. Proc Inst Mech Eng Part H – J Eng Med 220:355-369
[3] Willert *et al.* 2005. J Bone Joint Surg-Am Vol 87A: 28-36