Imparting Anti-Cancer Properties to Orthopedic Materials: The Role of Selenium Nanoclusters

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Statement of Purpose: It is estimated that 2,380 individuals will be diagnosed with bone and joint cancers and 1,470 individuals will die from primary bone and joint cancers in 2008 in the US [1]. A common technique to treat bone cancer is the surgical removal of cancerous tissue followed by insertion of an orthopedic implant. Therefore, it would be beneficial to have implants specifically designed to prevent the occurrence and reoccurrence of bone cancer and promote healthy bone tissue growth. Current orthopedic implant materials do not possess anti-cancer properties and, thus, can not keep cancer from reoccurring. The objective of the present in vitro study was to create an orthopedic implant with anti-cancer chemistry to simultaneously promote healthy bone cell functions and inhibit cancerous bone cell functions. Elemental selenium was chosen as the biologically active agent in this effort because of its known chemopreventative properties. Nano-structured surface features in selenium were employed to promote bone cell functions since numerous studies have shown greater osteoblast (bone-forming cells) functions on nano-structured surfaces than on conventional, micron structured surfaces. Previous studies also have shown that selenium compacts with nano-structured surfaces increased osteoblast densities after 1 day of culturing compared to the compacts with micro- or submicro-structured surfaces [2]. To demonstrate the versatility of using selenium nanoclusters to transform current orthopedic implant materials which do not inhibit cancer growth, selenium nanoclusters were coated on three common orthopedic implant materials here: titanium (Ti), stainless steel (SS), and ultra high molecular weight polyethylene (UHMWPE).

Methods: The three common orthopedic materials, Ti (Alfa Aesar), SS (Alfa Aesar), UHMWPE (Interstate Plastics) were individually degreased and cleaned. The substrates were then exposed to 4:1 molar mixtures of glutathione (GSH, reduced form, TCI America) and sodium selenite (Na_2SeO_3, Alfa Aesar). Selenium nanoclusters formed on the substrates after 1N NaOH was introduced to bring the mixture to the alkaline regime. To study the morphology of both uncoated and coated (with selenium nanoclusters) substrates, scanning electron microscopy (SEM) was used. To study the biocompatibility of the substrates, primary human osteoblasts (ScienCell Research Laboratories, population numbers 2-4) were cultured on the substrates for 4 hours, 1 day and 3 days. To test the anti-cancer properties of the substrates, rat osteosarcoma (bone cancer cells, ATCC, population numbers 15-17) were cultured on the substrates for 1 and 3 days. Cell densities were determined by counting using a fluorescence microscope. Seeding density was 3,500 cells/cm^2. The culturing media was Dulbecco's Modified Eagle Medium supplemented with 10% fetal bovine serum and 1% penicillin/streptomycin. Experiments were run in triplicate and repeated 3 times.

Results: SEM images showed clearly that selenium nanoclusters (referred to as nSe) were successfully coated on Ti, SS and UHMWPE substrates (Figure 1). The nSe are hemispherical and have a size of around 80nm in diameter. Healthy osteoblast cell densities increased on the substrates with higher densities of nSe after 1 and 3 days of culturing. In contrast, cancerous osteoblast cell densities decreased on the substrates with higher densities of nSe after 3 days of culturing.

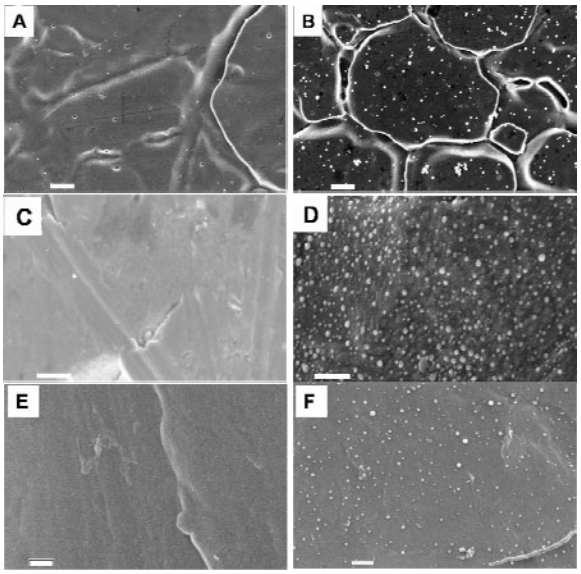

Figure 1. SEM images of uncoated SS (A), nSe-coated SS (B), uncoated Ti (C), nSe-coated Ti (D), uncoated UHMWPE(E) and nSe-coated UHMWPE (F). Bars in A, B, C, D are 500nm, Bars in E, F are 1 μm.

Conclusions: This study presents a method to coat common orthopedic materials (i.e. Ti, SS and UHMWPE) with nSe to impart anti-cancer properties to the orthopedic materials. The mechanisms why cancer cells were inhibited on the coated substrates are complex and need more investigation. This form of selenium, i.e. nanocluster selenium, may be a promising coating material in applications where anti-cancer properties are desired. More in depth studies are needed to further explore the mechanisms of the selenium nanocluster coatings **References:**

[1] (American Cancer Society statistic data 2008.)
[2] (Tran P. International Journal of Nanomedicine 2008:3(3) 391–396.)