J Bioengineer & Biomedical Sci 2016, 6:5 (Suppl)
http://dx.doi.org/10.4172/2155-9538.C1.012

Translation of basic materials research into orthopaedic implants

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In this presentation we will discuss the translation of a diverse set of new material technologies into orthopaedic applications. In all of the applications, the implementation of the new materials was accelerated by basic research leading to a new fundamental understanding of the relationship between processing, structure, and mechanical properties of the constituent materials. The examples span devices and new materials that have been successfully used in thousands of patients, to materials yet to be cleared in a device by the FDA. The topics to be overviewed include: The development and understanding of deployable shape memory polymers to mitigate damage when reattaching soft tissue to bone. A fundamental breakthrough on the processing and machinability of shape memory alloys to enable a paradigm shift in the success of large bone intramedullary fusion devices. A 3D printed titanium alloy that alters the standard therapy for bunion treatment from the cutting and fusing of bone to facilitating the creation of a new artificial ligament in the foot. A new approach to the formation of surface porosity in a high strength polymer that results in the first ever FDA clearance of an all polymer spinal fusion cage with porosity. Finally, a high strength bio-mimetic elastomer is shown to have early promise as a reliable and long-term soft tissue replacement.

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Experimental evaluation of discoidin domain receptor 2 as an ideal target for development of disease-modifying osteoarthritis drugs

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Introduction: Currently, no targets for disease-modifying osteoarthritis drugs exist. Co-localized expression of discoidin domain receptor 2 (DDR2) and matrix metalloproteinase 13 (MMP-13) has been found in degenerative articular cartilage of both human OA tissues and mouse models of OA. In healthy articular cartilage, DDR2 is kept inactivated by the peri-cellular matrix; however, once lost, DDR2 is activated and induces expression of MMP-13, resulting in joint destruction and OA.

Methods: We generated aggrecan-CreERt2 mice and floxed Ddr2 mice and used conditional knock out techniques to remove Ddr2 from articular cartilage of knee joints in 8 week old mice via intra-peritoneal Tamoxifen injection (Group A). Destabilization of the medial meniscus (DMM) or sham surgery was performed at 10 weeks of age. Group B mice were subjected to DMM or sham surgery at 10 weeks of age, followed by DDR2 removal 8 weeks later. Knee joints from mice in Group A were harvested at 8 weeks or 16 weeks post-surgery and from Group B at 16 weeks post-surgery. Histology was performed and the OARSI Modified Mankin Score was used to evaluate articular cartilage degeneration. Statistically significant differences were determined via T-test.

Results: The average modified scores were as follows: Group A 8 week control, 1.64 (n=7); Group A 8 week experimental, 0.64 (n=7) [P<0.05]; Group A 16 week control, 4.67 (n=7); Group A 16 week experimental, 1.27 (n=9) [P<0.05]; Group B, 1.1 (n=5).

Conclusion: In conclusion, conditional removal of Ddr2 in articular cartilage attenuated articular cartilage degeneration in mature knee joints of mouse models of OA.

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