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Dr. Caroline Hoemann

Ecole Polytechnique, Canada

Scaffold-guided cartilage repair using chitosan-engineered blood clots : Role of therapeutic inflammatory responses in tissue regeneration

Cartilage repair is a critical un-met need in our aging population. The current standard-of-care is marrow stimulation therapy, where holes are pierced in the bone below the cartilage lesion to promote bleeding and a marrow-derived repair response. However this approach frequently leads to a biomechanically unstable repair tissue that incompletely fills the lesion. We previously conceived that chitosan, a polysaccharide biomaterial known to stimulate wound repair, could be used to make an implant that stimulated microfracture repair. Using animal cartilage repair models, we showed that the therapeutic response to marrow stimulation is significantly improved when a mixture of liquid chitosan and whole autologous blood is solidified over the microfracture defect. Timely clearance of chitosan particles from the lesion by neutrophils leads to local therapeutic effects, including attraction of osteoclasts which remodel the subchondral bone, and alternatively activated macrophages which release angiogenic factors. The implant also draws bone marrow mesenchymal stromal cells (BMSC) near the surface of the repairing defect, which triggers cartilage regeneration at later stages of repair. In vitro experiments using fluorescent chitosan derivatives show that many cell types internalize the polysaccharide polymer (BMSC, neutrophils, macrophages). However chitosan particles alone are unable to promote osteoblast differentiation of BMSCs, or alternative activation of macrophages. Instead, our data show that chitosan facilitates the release of chemokines, instead of catabolic factors, which simulates bone marrow stromal cell migration to the repairing surgically-induced lesion.

Biography

Dr. Hoemann (PhD, MIT, 1993), spent 5 years as an R&D director, in a Montreal-based biomedical device company, where she co-invented a novel medical device for articular cartilage repair, BST-CarGel®. The product was recently tested in an 80-patient randomized clinical trial, with promising interim data at 1 year post-treatment. Dr. Hoemann is an associate professor of Chemical Engineering, has over 40 publications, 6 patents, and serves on the editorial board of Cartilage, and The Open Orthopaedics Journal. Her translational research program aims to understand the mechanisms of cartilage repair, in order to bring new treatment options to patients with arthritis.