

## Tissue Science and Molecular Biology, Stem Cells & Separation Techniques

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# Caroline Hoemann

*George Mason University, USA*

### Articular cartilage engineering with innate immune-modulating biomaterial implants deposited in the subchondral bone marrow

**F**ocal articular cartilage lesions are often treated by bone marrow stimulation, a surgical procedure in which the surgeon debrides all damaged cartilage in a lesion, then creates controlled bone fractures that bleed and induce a spontaneous wound repair response. Because the resulting repair tissues are heterogeneous and often incomplete, new methods are under intense investigation that improve the quality and quantity of repair tissue elicited by bone marrow stimulation. Original attempts to enhance microfracture repair used solid scaffolds designed to form a 3-D scaffold that remains intact, degrades very slowly and ultimately interferes with spontaneous repair processes. We have developed an entirely different regenerative medicine approach, based on the concept that cartilage repair can be enhanced by engineering bioactive microparticles into the hematoma that forms in the subchondral bone. Chitosan is a biocompatible and bioactive polysaccharide composed of glucosamine and N-acetyl glucosamine that is well-known for its ability to attract neutrophils and macrophages to healing wounds. A freeze-dried chitosan implant was designed to disperse into microparticles in bleeding subchondral bone. Data from preclinical rabbit and skeletally aged sheep models show that chitosan microparticles are resident in the hematoma, stimulate macrophage recruitment and angiogenesis in the granulation tissue, induce remodeling of the subchondral

bone plate and significantly enhance the resulting articular cartilage repair tissue volume and integration with subchondral bone. These data serve as an important proof-of-concept that soft materials implanted in the bone marrow can be used to shift endogenous innate immune responses to regenerate a structurally improved cartilage tissue.

#### Speaker Biography

Caroline Hoemann is a full professor of bioengineering at George Mason University, USA. She is highly regarded internationally for her work on cartilage and bone tissue engineering and biomaterial-induced blood and innate immune responses. She is the recipient of 2 NIH-Fogarty post-doctoral fellowships, four career fellowships, is a fellow member of the International Cartilage Repair Society and serves on the editorial boards of *Cartilage* and *The Open Orthopaedics Journal*. She is co-founder and on the board of directors of ORTHO-RTI, an orthopedic biotech company specializing in implants that repair joint tissues. Her research program focuses on understanding how to use biomaterial-guided immune responses to regenerate bone and cartilage tissues. She has published 68 peer-reviewed papers, 14 book chapters/expert opinion papers, 171 conference abstracts and 8 patent inventions. Her translational research program aims to bring new treatment options to patients with arthritis. In addition to strengthening and expanding the department's research portfolio, she brings specific teaching expertise in biomaterials, molecular cell biology and tissue engineering that will enhance and broaden the department's educational programs at both the undergraduate and graduate levels.

e: choemann@gmu.edu

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