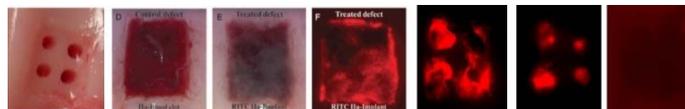
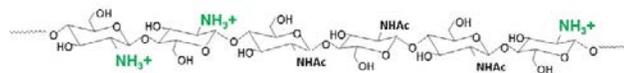


Biomaterials for Cartilage and Bone Tissue Engineering : Paradigms and Clinical Translation

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This seminar will explain a paradigm shift in the use of polymers to repair tissues that led to the successful translation of a novel cartilage repair medical device to the clinic. In traditional tissue engineering paradigms, a 3-D polymer scaffold is intended to serve as a temporary structure in which cells can produce a new tissue. Chitosan is a naturally-derived polysaccharide composed of glucosamine and N-acetyl glucosamine, whose unique hemostatic and wound-healing properties were recognized over 30 years ago. Because bone bleeding is ineluctably present in surgically-debrided articular cartilage lesions, instead of working against blood in the wound environment, we took an entirely new approach. We mixed the chitosan polymer into whole blood to create a novel hybrid blood clot implant. This represented a significant departure from prior use of polymers in biomaterials, in that the blood clot fibrin became the structural scaffold, and chitosan microparticles with negligible mechanical properties were intended to stabilize the clot structure. Implant testing in small and large animal cartilage repair models revealed safety and efficacy of the implant. These data helped obtain regulatory approval for a randomized controlled clinical trial where Level 1 evidence was produced showing that the implant improves the structural quality of the cartilage repair tissue. Meanwhile, extensive studies were carried out to reveal underlying mechanisms-of-action. Our novel data showed that chitosan guides innate immune cells to repairing bone defects, and that cell-driven clearance of the chitosan polymer provokes aseptic inflammatory angiogenesis and bone tissue remodeling, a beneficial repair response that we call “wound bloom”. Wound bloom is a phenomenon where transient resorption and repair of the damaged bone attracts mesenchymal stem cells that can regenerate cartilage. Based on these findings, subchondral chitosan implants were next developed and shown to induce a more potent articular cartilage repair response in skeletally aged animal models. Finally, through another traditional and evolving paradigm, we are designing biodegradable soft materials to help a porous 3-D bioplastic scaffold interface with the bone wound environment through innate immune-guided mechanisms. By merging paradigms, we are investigating whether soft bioactive materials could help transform an inert bioplastic implant into a living tissue capable of turning over into native bone over time.



“from Molecules to Tissues”