



### **Thrust 5. Wound Healing and Biomarker Detection**

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There are two main topics of this thrust on biomedical materials and devices: narrowly focused wound healing and broad impact biomarker detection, as described below.

There is a strong need of new materials to address current limitations in wound healing and in the translational aspects of wound healing. However, there is a void of information at the molecular level addressing cell-material interactions, at the tissue level addressing the evolution of implantable scaffold, and at the organ level addressing the development of new intervention methods to enhance healing. This thrust is in the process of creating novel materials and experimental techniques to improve translational work. By tackling the steps between materials development and implantation, it is generating design rules and predictive models to determine the viability of a material in enhancing wound healing. There are three primary areas of interest:

First, precise delivery of cells using novel implantable materials. While biomaterials are designed with precise initial rheological properties for cell signaling, cells dynamically interact with these materials and reengineer scaffolds over time. During wound healing, cells are attracted to the wound site by chemicals secreted from damaged tissue. The types of cells called to the wound vary, and the timing of their arrival is carefully orchestrated to start and continue healing with maximum efficiency. We aim to understand cellular reengineering in the wound environment and use this knowledge and newly engineered biomaterials to develop a strategy to selectively deliver cells spatially and temporally to enhance wound healing.

Second, designing advanced materials to guide functional cartilage regeneration. Articular cartilage is a highly organized tissue but once damaged, it has limited ability to self-repair because of poor cell migration and slow matrix deposition due to a lack of blood supply. The proposed work introduces a novel materials-based approach to guide articular cartilage regeneration across scales from the cell to tissue level to form organized, functional tissues. The microenvironment surrounding cells is specifically designed to promote cell migration and differentiation in defined spatial locations to guide matrix organization over time.

Third, flexible materials to guide callus formation for bone defect regeneration. The typical pathway for bone fracture healing involves formation of a cartilaginous soft tissue structure called a callus, which gradually ossifies over time as the bone unites. In traumatic injuries when the fracture is accompanied by bone loss, callus formation may be deficient or absent. The objective of this work would be to fill the bony void with a highly porous, low-rigidity, functionalized scaffolding that promotes cell infiltration, differentiation, matrix formation, and ultimately tissue regeneration in large defects that would not otherwise heal on their own.

The second topical area of this thrust is concerned about ultra-low concentration biomarker detection in biological fluid. Biomarkers exist in various types of biological fluid, including saliva, urine, and blood. In recent years, liquid biopsy through detection and analysis of cells, exosomes/liposomes, viruses, and DNA/RNA has emerged as a minimally-invasive tool for diagnosis and personalized medicine. This trend leads to an urgent need for efficient methods of biochemistry analysis and effective diagnosis of various diseases such as cancer, stroke, neural disorder, and HIV. This research thrust is focusing on developing novel and versatile techniques to detect ultra-low concentrations of biomarkers in various biological fluids using multidisciplinary strategies.