

MacroTheranostics: A Macrophage-based Therapeutic and Diagnostic Wound Care Company

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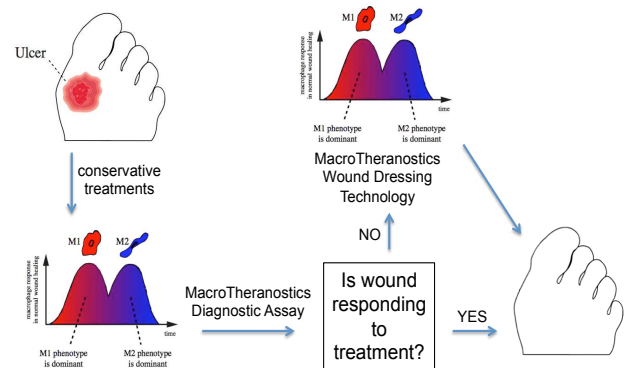
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Technology: Managing the diabetic foot is a complex process and includes antibiotic therapy, regular and thorough wound debridement, and the application of appropriate wound dressings. Wound dressings range from simple saline-soaked cotton pads, hydrocolloids, foams, and gels to more advanced wound care treatments such as skin substitutes. Although successful for some, many patients do not respond to conservative treatment modalities. As a result, the selection of an appropriate wound dressing from the dozens of choices available on the market is critical to success. However, currently there is no method to obtain consistent, timely, and actionable data related to wound progression. Moreover, those patients who do not respond to conservative treatment modalities may benefit from a more active treatment. Yet, the majority of currently available wound dressings are designed to merely protect the wound and keep it moist, with little to no bioactive elements. Therefore, a multi-functional hydrogel dressing that can deliver bioactive healing compounds that correct the underlying problem in diabetic wounds - dysfunctional inflammation - holds great potential for the treatment of nonhealing wounds.

In normal wound healing, inflammatory cells (monocytes) are recruited to the site of injury, where they differentiate into macrophages, release inflammatory cytokines and recruit other inflammatory cells. In early stages of wound healing, macrophages exhibit a “classically activated” phenotype, also referred to as “M1,” which secrete pro-inflammatory cytokines and are destructive, clearing the wound of debris. In later stages, macrophages switch to an “alternatively activated” or “M2” phenotype. M2 macrophages promote extracellular matrix synthesis, matrix remodeling, and angiogenesis. If the M1-to-M2 transition is disrupted, depicted by persistent numbers of M1 macrophages, the wound suffers from chronic inflammation and impaired healing.

At MacroTheranostics, we have developed two revolutionary technologies based on the underlying biology of macrophages in wound healing to address current unmet needs in the wound care industry. In one technology, we have developed a predictive assay that measures the behavior of macrophages, the major regulators of healing, and can be easily incorporated into the normal wound treatment regimen. Debrided wound tissue is analyzed by real time polymerase chain reaction (RT-PCR), and a proprietary algorithm converts gene expression data using a panel of biomarkers to a single score that identifies the inflammatory state of the wound. By tracking the changes in the inflammatory state over time, we are able to accurately predict if a wound is healing or not. The results obtained from this assay suggest that those patients who did not respond to conservative treatments may benefit from more aggressive, bioactive treatments. To this end, we have developed an immunomodulatory wound dressing technology that can restore the balance of macrophage

phenotype in diabetic wounds. This will be accomplished by using a proprietary controlled release system to present pro-healing cytokines in a temporally controlled manner from a hydrogel wound dressing. In addition to the traditional roles of hydrogel wound dressings of protecting the wound from infection while keeping it moist, these immunomodulatory hydrogels will directly aid wound healing by targeting the macrophage, a master regulator of tissue repair.



Market: Diabetes affects 29 million Americans, with approximately 1.7 million new cases diagnosed each year. More than one third of Americans are obese, a leading cause of type 2 diabetes. Dysfunctional wound healing is a major complication of both type 1 and type 2 diabetes. Foot ulcerations, which occur in 15% of diabetic patients, lead to over 82,000 lower limb amputations annually in the United States, with a direct cost of \$9 billion per year. The average cost to treat a diabetic ulcer has been estimated as \$5,000 per ulcer episode, \$28,000 over a two-year period, over \$60,000 total, and upwards of \$100,000 if the limb requires major amputation. Moreover, the presence of a foot ulcer is correlated with increased mortality.

Commercialization Strategy: Both technologies developed at MacroTheranostics have considerable commercialization potential because of the large number of patients with chronic wounds and current projections of market growth in the foreseeable future. A significant level of interest in our technologies has already been achieved in both the wound care and diagnostic industries, as a result of presentations at conferences and networking. Several large wound care companies have already expressed interest in collaborating on clinical trials. Therefore, our commercialization strategy is to first develop a revenue model with a CLIA lab in order to further de-risk our diagnostic technology and attract potential partners. We will later proceed with launching our wound dressing technology as it requires a Biologics License Application (BLA), whereas a de novo reclassification to the 510(k) pathway is likely for our diagnostic assay, since this assay is a low-to-moderate risk diagnostic that can be used as an aid to physician assessment.