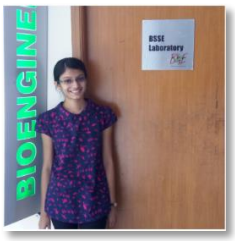
Indian Institute of Science
Centre for BioSystems Science and Engineering

BSSE Annual Work Presentation

25th February 2019, 4:00 PM, MRDG Seminar Hall, 1st floor, Biological Sciences Building

Immune profiling of Diabetic Foot Ulcers and development of a drug delivery strategy to promote healing



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ABSTRACT

Diabetic Foot Ulcer (DFU) is a common complication in Type II Diabetes patients. Failure to appropriately manage these wounds leads to gangrene formation and ultimately lower limb amputation. Several reports suggest the presence of prolonged inflammatory state in DFU, with two recent articles showing that the presence of Neutrophil Extracellular Traps (NETs) in DFUs is an indicator of poor healing. In addition to local inflammation at wound site, few studies also confirm the existence of systemic inflammation in patients with DFUs. To investigate the role of NETs as well as systemic inflammation in healing of DFUs, we planned to do the following: study NETs in wounds by collecting biopsy samples of wounds in patients with DFU; and characterize systemic immune cell phenotype by collecting their peripheral venous blood. The objective of the study is twofold: a) Correlate presence of NETs in biopsy samples to stage of wounds and healing of ulcers in patients b) Compare the immune cell phenotype characterized from peripheral venous blood to healing of ulcers.

In addition to answering questions pertaining to failure in wound-healing of DFUs, we also aim to develop therapeutics that assist healing. Therapeutics that aid in tissue regrowth and remodeling have been attempted as potential treatment options for DFU, but they are usually not sufficient to heal the wounds as they fail to address the issue of inflammation. We hypothesize that healing of diabetic ulcers may be promoted by reducing the local inflammation and providing the necessary factors for tissue regrowth. To test this hypothesis, we are developing a sequential drug delivery system to deliver an immunosuppressant for suppressing the inflammation followed by growth factors (GF) to assist the proliferation of endothelial cells and fibroblasts. Specifically, a chitosan-based scaffold system loaded with immunosuppressant rapamycin and growth factors have been developed. Rapamycin is dispersed homogenously throughout the scaffold whereas, growth factors are first encapsulated into chitosan microspheres which is further entrapped inside the same scaffold allowing a dual release. Preliminary data of dual release of rapamycin and a model protein for GF, BSA-FITC suggests a two-day fast release of 80% of encapsulated rapamycin as desired. About 50% of the protein was found to be released in 24 hours wherein, a delay of 24-36 hours was anticipated before start of protein release. Alternate strategies are being attempted to delay the release of protein after which the efficacy of the in-vitro release system will be tested in-vivo for healing of surgically induced dermal wounds in streptozotocin induced db model of rat and lepr-/- diabetes mice model.