



INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Programme of Study : **Ph.D.**

Thesis Title: **Silk biomaterial based islet encapsulation platform conferring immunoisolation and immunomodulation toward bio-artificial pancreas development**

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SHORT ABSTRACT

This thesis deals with silk biopolymer based approaches for islet macroencapsulation to overcome the limitations associated with conventional treatment modalities for Type 1 diabetes. These approaches overcome host inflammation via local macrophage polarization and immunomodulation. Primary rat islets were encapsulated in immuno-informed silk matrices of different formats, and explored for immunoisolation and immunomodulation toward bio-artificial pancreas development. The developed immuno-informed silk matrices supported enhanced islet viability with glucose responsive insulin secretion. For combating local inflammation, silk matrices were primed with Dexamethasone and Interleukin-4 (IL-4) for tailoring local biological response via *in vivo* polarization of macrophages towards anti-inflammatory (M2) phenotype. The thesis also explored the potential of silk-based injectable hydrogels for sequential release of encapsulated cytokines (IFN- γ and IL-4) for macrophage polarization (M0 to M1 and M2) and plasticity (M1 to M2 and vice versa) study. The physicochemical properties of injectable silk hydrogels (silk-sonicated, silk-poly ethylene glycol and silk-horseradish peroxidase) were tailored and critically assessed for immunomodulation and biological responses. Also, a novel, rapid gelling, minimally invasive, and cross-linker-free silk-blend hydrogel was developed utilizing two silk varieties, *Bombyx mori* (mulberry) and *Antheraea assama* (non-mulberry). The developed hydrogel maintained prolonged islet viability and glucose responsive insulin secretion with *in vitro* and *in vivo* macrophage polarization towards M2 phenotype. The inherent Arg-Gly-Asp (RGD) sequence of non-mulberry silk improved the islet viability and insulin secretion. Overall, the work demonstrates the potential of silk biomaterial-based approaches for islet encapsulation and also projects the non-mulberry *Antheraea assama* silk as an alternative biomaterial for islet macroencapsulation and silk based bioartificial pancreas.