**Application of Drug Delivery System to Cytomedicine**

# Abstract

Hydrogel coatings have been proposed as a promising strategy to improve the biocompatibility of therapeutic cells and biomedical devices. However, most of the developed coating methods are only applicable for simple geometries, typical sizes, and limited substrates. In addition, its applications in therapeutic cell encapsulation have been hampered by inadequate construction of the hydrogel capsules such as off-center encapsulation, a low fraction of cell-laden capsules, immense volume, and lack of control over the thickness of capsules. To address these issues, we report a method called surface-triggered in situ gelation (STIG) for universal hydrogel coating of multiscale objects ranging from single cells to mini-organs (pancreatic islets) to biomedical devices with arbitrary shapes and heterogeneous components. By covering cells or devices with calcium carbonate particles, we achieved progressive propagation of alginate hydrogel from their surface under the stimulation of D-(+)-gluconic acid-δ-lactone (GDL). The thickness of the hydrogel layers was easily controlled from several micrometers to hundreds of micrometers by adjusting the gelation time and the release rate of calcium ions. Importantly, STIG facilitated accurate, complete (cell-centering), and individual cell encapsulation, which potentially overcomes the pitfalls of conventional strategies. Conformal hydrogel encapsulation by STIG successfully prolonged survival of xenogeneic pancreatic islets in immunocompetent mice for >120 days. We further proved that our low-cost and facile method could potentially lead to advances in different fields by rendering a precisely controlled microscale alginate layer on various a wide variety of biomedical substrates.