Use of "Smart" Materials and Cell Sheet Engineering to Characterize Buried Biological Interfaces

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Interactions between cellular materials and surfaces are critical to the understanding of problems ranging from biologically-induced corrosion of ship hulls to the rejection of implant materials in the human body. For example, implanting stents, intended to improve the circulation of patients suffering from atherosclerosis, can initiate a cascade of cellular events in the host organism, ultimately resulting in device failure from occlusion or thrombosis. The in-situ diagnosis of this sequence of events is inherently complicated, causing many researchers to turn to experiments utilizing in vitro cell material/substrate material interactions. These in vitro experiments allow for correlation of the properties of the cell culture material (e.g., surface chemistry, topography, or film stiffness) with the behavior of the cellular material (e.g., cell adhesion, proliferation, or apoptosis). Although the mechanisms by which surface character influences cell survival are as yet unknown, the proteins in the extracellular matrix (ECM) are thought to play a critical role via mediation of the cellular response to the substrate surface.

Typically, the removal of cells from culture substrates requires harsh methods such as enzymatic digestion or physical scraping, which damage the morphology and function of cells, as well as the ECM. Cell cultures on poly(*N*-isopropyl acrylamide, pNIPAM) offer a particularly promising system for the study of cell/surface material interactions. Surfaces treated with pNIPAM have been observed to undergo a transition at the lower critical solution temperature (LCST) of ~31°C. Above the LCST (i.e., at the cell culture temperature of 37 ºC), the surfaces are hydrophobic, and many cell types adhere and proliferate. Below the LCST (i.e., at room temperature) the surface rapidly hydrates, and cells spontaneously detach as a sheet. In addition, cell sheets harvested from pNIPAM are rapidly incorporated into living material without using sutures, possibly due to the concurrent detachment of at least part of the underlying Extracellular Matrix (ECM), which acts as a "glue" to help cell sheets adhere to the new surface. Until now, this behavior has been empirically observed, but the underlying mechanisms for this response have not been well understood.

Our research focuses on the thorough examination of the cellular response using both biological and surface science techniques. Using cell sheet engineering techniques, we are capable of harvesting cell sheets grown on plasma-deposited pNIPAM (ppNIPAM) while preserving cell sheet orientation and topography. This gives direct access to the buried (and previously inaccessible) interface of the basal cell surface and ECM protein region of the confluent cell sheets. Using surface science techniques, we compare each layer, from the morphology (using scanning electron microscopy, SEM) down to the chemical composition of each layer (using X-ray photoelectron spectroscopy, XPS; and time-of-flight secondary ion mass spectrometry, ToF-SIMS). In this way, we aim to understand the mechanism by which this harvest technique works at the fundamental level, and thereby guide the rational design of the next generation of medical devices based on this technology.