GelSert: a new frontier of soft tissue culture substrates

Camilla Mussoni*[1], Özge Ekin Akdere[1], Felix Reul[1], Jacopo Di Russo[2], Rahman Omidinia Anarkoli[1], and Laura De Laporte†[1,3,4]

[1]DWI – Leibniz-Institute for Interactive Materials, Aachen – Germany
[2]Institute of Molecular and Cellular Anatomy, RWTH Aachen University – Germany
[3]Institute for Technical and Macromolecular Chemistry, Chair for Macromolecular Materials for Medicine, RWTH Aachen University – Germany
[4]Department of Advanced Materials for Biomedicine (AMB), CBMS—Center for Biohybrid Medical Systems, AME—Institute of Applied Medical Engineering, RWTH Aachen University – Germany

Abstract

In vitro tissue models are an emerging technology that overcomes the need for animal testing. Fundamentally, a base substrate, or scaffold, offers a surface for cells attachment and growth until they can mature to form a tissue. Such substrate should be representative of the physical and chemical properties of the environment that guides cell behavior, the extracellular matrix (ECM). Traditional cultures heavily rely on flat, rigid membrane inserts composed of polycarbonate (PC) or polyethylene terephthalate (PET). These standard materials fail to replicate the complex, fibrous topography and compliant mechanical properties of the native soft-tissue ECM, thereby limiting the physiological relevance of the tissue and its maturation. Over time, electrospinning has offered a high-throughput pathway to produce biomimetic fibrous meshes, that closely mimic the nature of the ECM. However, standard polymer (such as polylactide or polycaprolactone) processing often requires cytotoxic solvents and yields membranes that remain excessively stiff compared to native soft tissues. This study introduces GelSert, a novel synthetic hydrogel-based platform designed to produce soft, porous, and highly biomimetic hydrogel membranes tailored for soft tissue engineering. The GelSert system leverages the reactive click-chemistry crosslinking between amine- and epoxy-functionalized star polyethylene glycol (sPEG) precursors. By optimizing the gelation kinetics and processing parameters of this system, stable hydrogel fiber networks were fabricated via electrospinning. The structural porosity, fiber diameter, and stiffness of the resulting matrices can be systematically regulated by processing parameters. The fabricated PEG-hydrogel membranes successfully converge the high-throughput advantages of electrospinning with the desirable biomimetic elasticity of hydrogel matrices, delivering a highly tunable, cytocompatible, and fibrous substrate capable of replicating the intricate nature of native extracellular matrices. This device establishes a robust platform for physiologically relevant mechanobiology studies and advanced *in vitro* models of complex epithelial tissues, including the retina, nephron, and skin.

Keywords: Electrospinning, Tissue Engineering, Biomedical Applications

*Speaker
†Corresponding author: delaporte@dwi.rwth-aachen.de