Development of photo-crosslinked collagen hydrogels for Tumor-on-Chip (ToC)

(collaboration DBE/AMBER groups)

Keywords: collagen fibrillar gels, cell culture, photo-rheology

Collagen is a naturally abundant structural protein, biocompatible, bioactive and plays an important role in tissue integrity and regeneration. As the main component of the tumor microenvironment, collagen I has been widely used as a biomaterial to mimic diverse tissues, including tumors. Typical collagen I hydrogels are formed by a physical process that involves the self-assembly of collagen triple-helices, process triggered under neutral pH and physiological temperature. This leads to the formation of fibrils, which in turn entangle with each other to form a hydrogel. However, collagen hydrogels prepared through physical crosslinking suffer from weak mechanical properties and rapid degradation,[1] which can severely limit their biomedical application. Thus, new chemical strategies are needed.

Photo-crosslinking uses a photoinitiator to initiate chemical crosslinking reactions in biomaterials upon irradiation. This technique enables precise spatial and temporal control over the crosslinking process and significantly enhances the mechanical strength of hydrogel networks by inducing covalent bonding between polymer chains.[2] Photo-crosslinking of collagen gels has been reported, but most approaches involve considerable synthetic effort to chemically modify the collagen precursor to install photo-crosslinkable functional groups, which is time consuming and costly.

In this project, we will develop photo-triggerable collagen I hydrogels with tunable mechanical properties for use in a Tumor-on-Chip (ToC) platform. Importantly, this strategy will avoid the chemical modification of collagen, thus, it will be easier and cheaper to apply. Non-toxic photoinitiators in combination or not with a co-initiator will be used.[3, 4] A systematic study will be conducted to investigate the effects of (co)-photoinitiator type, concentration, and irradiation conditions on the properties of formed hydrogels. Mechanical strength of these hydrogels will be characterized by photo-rheology, and their morphology will be analyzed using scanning electron microscopy (SEM). Additionally, basic cell toxicity and metabolic activity will be assessed to ensure the cytocompatibility of this novel approach. Finally, the injectability of the precursors in a microfluidic platform will be evaluated to determine the practicality of hydrogel formulation for ToC application.

References

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