Mechanobiology in Engineered 3D Microenvironments: Advanced In Vitro Platforms to Decipher Cell–Matrix Interactions

Mechanical cues arising from the extracellular microenvironment play a fundamental role in regulating cell adhesion, migration, differentiation, and disease progression. Elucidating the mechanisms of cellular mechanotransduction requires experimental models capable of precisely controlling the physical and geometrical properties of the cellular niche. In this context, two-photon polymerization (TPP) has emerged as a powerful biofabrication technology, enabling the fabrication of three-dimensional microarchitectures with sub-micrometric resolution and tunable mechanical properties. Beyond serving as structural scaffolds, these engineered microenvironments provide quantitative platforms to investigate how cells sense and respond to defined mechanical stimuli.

This lecture will present recent advances in the design of TPP-fabricated 3D microscaffolds for the study of cell–matrix interactions, highlighting how parameters such as stiffness, topology, curvature, anisotropy, and spatial confinement regulate mechanotransduction pathways and ultimately determine cell fate. Particular emphasis will be placed on experimental strategies to probe traction force generation, contact guidance, confined migration, and invasive behavior, as well as on the integration of engineered microenvironments with responsive biomaterials, microfluidics, and organ-on-chip technologies to reproduce physiologically relevant mechanical niches.

By combining advanced microfabrication with quantitative cell biology, these platforms are redefining in vitro mechanobiology, enabling the systematic investigation of the reciprocal interplay between cells and their physical environment. The convergence of biofabrication, mechanobiology, and microphysiological systems is expected to provide more predictive disease models, accelerate the development of mechanobiology-informed therapeutic strategies, and contribute to the next generation of precision medicine.