CHAPTER 18

Synthetic Hydrogels for 3D Cell Culture

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Introduction

Using two-dimensional (2D) tissue-culture dishes, *in vitro* cell/tissue culture has become a common practice in biomedical laboratories worldwide. Through adding defined supplements (i.e., growth factors, carbohydrates, lipids, or other soluble nutrients) in cell culture media, one can readily examine the effects of soluble biochemical cues on cell behaviors. However, evidence and intuition suggest that 2D cell cultures are less physiologically relevant since cells plated on a rigid 2D surface do not receive proper environmental stimuli that are presented from a three-dimensional (3D) extracellular matrix (ECM) (Cushing and Anseth 2007; Tibbitt and Anseth 2009). Since the early 21st century, there has been a paradigm shift in cell culture *in vitro*, where 3D culture techniques are being developed to overcome the shortfalls of conventional 2D methods. The advancements in 3D cell culture have benefited modern biomedical sciences, molecular and cellular biology, cancer cell biology, regenerative medicine, and tissue engineering. For example, matrices derived from animal ECM (e.g., Matrigel®, gelatin, and collagen gels) are widely used for 3D cell culture by biomedical researchers (Benton et al. 2014). The easy preparation of these animal-derived matrices has allowed researchers to verify 2D cell culture results in 3D, a step closer to mimicking the *in vivo* microenvironment. However, these 'natural' matrices are often mechanically weak when comparing with the mechanics of many tissues *in vivo*. Furthermore, these matrices often contain batch-dependent properties, including the compositions of matrix proteins and residual growth factors. Hence, they might not be ideal for studying molecular pathways elicited by mechanical stimuli, cell-matrix interactions, and growth factor signaling.

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