World Academy of Science, Engineering and Technology
International Journal of Biomedical and Biological Engineering
Vol:14, No:07, 2020

Engineering a Tumor Extracellular Matrix Towards an in vivo Mimicking 3D Tumor Microenvironment

Authors : Anna Cameron, Chunxia Zhao, Haofei Wang, Yun Liu, Guang Ze Yang

Abstract : Since the first publication in 1775, cancer research has built a comprehensive understanding of how cellular components of the tumor niche promote disease development. However, only within the last decade has research begun to establish the impact of non-cellular components of the niche, particularly the extracellular matrix (ECM). The ECM, a three-dimensional scaffold that sustains the tumor microenvironment, plays a crucial role in disease progression. Cancer cells actively deregulate and remodel the ECM to establish a tumor-promoting environment. Recent work has highlighted the need to further our understanding of the complexity of this cancer-ECM relationship. In vitro models use hydrogels to mimic the ECM, as hydrogel matrices offer biological compatibility and stability needed for long term cell culture. However, natural hydrogels are being used in these models verbatim, without tuning their biophysical characteristics to achieve pathophysiological relevance, thus limiting their broad use within cancer research. The biophysical attributes of these gels dictate cancer cell proliferation, invasion, metastasis, and therapeutic response. Evaluating the three most widely used natural hydrogels, Matrigel, collagen, and agarose gel, the permeability, stiffness, and pore-size of each gel were measured and compared to the in vivo environment. The pore size of all three gels fell between 0.5-6 µm, which coincides with the 0.1-5 µm in vivo pore size found in the literature. However, the stiffness for hydrogels able to support cell culture ranged between 0.05 and 0.3 kPa, which falls outside the range of 0.3-20,000 kPa reported in the literature for an in vivo ECM. Permeability was ~100x greater than in vivo measurements, due in large part to the lack of cellular components which impede permeation. Though, these measurements prove important when assessing therapeutic particle delivery, as the ECM permeability decreased with increasing particle size, with 100 nm particles exhibiting a fifth of the permeability of 10 nm particles. This work explores ways of adjusting the biophysical characteristics of hydrogels by changing protein concentration and the trade-off, which occurs due to the interdependence of these factors. The global aim of this work is to produce a more pathophysiologically relevant model for each tumor type.

Keywords : cancer, extracellular matrix, hydrogel, microfluidic
Conference Title : ICHM 2020 : International Conference on Hydrogel Materials
Conference Location : Rome, Italy
Conference Dates : July 23-24, 2020