CELL PHASE IDENTIFICATION IN A THREE-DIMENSIONAL TUMOR CELL CULTURE MODEL BY FOURIER TRANSFORM INFRARED (FT-IR) SPECTROSCOPIC IMAGING

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Cell cycle progression plays a vital role in regulating proliferation, metabolism and apoptosis. Specifically, assessing cell phase is of significant importance since the development of cancer is tightly linked with the dysregulation of cell cycle. However, investigating the cellular status in three-dimensional in vitro models and tissue is often limited to the complexity of sample preparation and the loss of structural integrity. The most common technique nowadays is flow cytometry, which requires a full disintegration of cellular organization and additional fluorescence staining. To overcome these challenges, Fourier transform infrared (FT-IR) spectroscopic imaging is introduced in this study. It is a powerful approach for analyzing biological samples by detecting the vibrational modes of indigenous molecules, thereby eliminating the need for stains and greatly expanding information beyond phase or intensity contrast of optical imaging. Drawing upon these advantages, we apply FT-IR imaging integrated with unsupervised learning technique to distinguish subtle biochemical compositions between cell phases while retaining a spatial distribution of the innate constituents. The spectral variation in DNA quantity from 2D cell culture is served as an indicator to understand the relative cell cycle stages in a 3D MCF10A acini model. We further evaluate the temporal dependence of these spectral changes throughout the acini formation and validate that cells present to be more proliferative in the early stages of acini formation compared to fully developed acini. Taken altogether, our study presents a computational approach to provide a comprehensive cell phase in tissue-like structure without any requisite for specific biomarker staining, which has the potential to accelerate pharmaceutical agents design with more defined targeted effects. Moreover, the integration of FT-IR spectroscopy and computational methodologies could also expand to the field of pathology and lead to an improvement for clinical diagnostics.