

**ELUCIDATING REAL-TIME CNACER CELL-MATRIX INTERACTION  
IN HETEROGENEOUS 3D GEL MATRIX SYSTEM**

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**KEY WORDS:** Living cells, time-lapsed 3D imaging, cancer invasion, drug testing

A mechanically tunable three-dimensional (3D) collagen-I hydrogel supported cancer cell migration/invasion in the context of heterogeneous microenvironment. Through intensive interactions with the reconstituted extracellular matrix (ECM), cells remodeled ECM while they migrated, resulted in enhanced regional differentiation in collagen network organization. In turn, cells actively adapted their migratory behavior to the heterogeneous microenvironment. Pharmaceutical intervention of microtubule stability and Rho kinase pathways partially inhibited cell migration, and the drug effects depended on the local environment that cells resided in.

Time-lapsed microscopy closely monitored the above processes, through a combination of transmitted light microscopy using DIC and confocal laser scanning microscopy (CLSM), utilizing TE-2000 inverted microscope. Malignant breast cancer cells, MDA-MB-231 were labeled with fluorescence CellTracker dye, and tracked under fluorescence CLSM. Simultaneously, the dynamics of micro-architecture of collagen fibers was monitored using reflective mode of CLSM. Specimens in medium supplied glass-bottom dishes were in an environment chamber mounted on the microscope, keeping cells in physiological conditions throughout the 8 hrs of imaging.

This 3D live imaging model simulated highly heterogeneous extracellular microenvironment, as often found in vivo, and enabled the examination of ECM context-dependent cell-migratory behavior. Drug tests suggested the potential application in anti-migratory cancer drug development.