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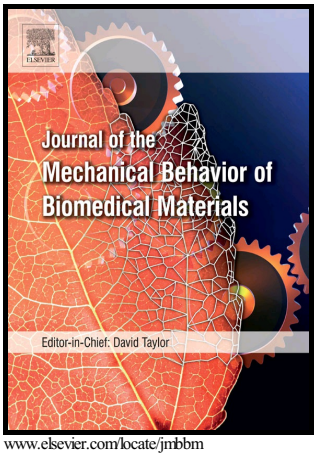

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An Investigation of the Viscoelastic Properties and the Actin Cytoskeletal Structure of Triple Negative Breast Cancer Cells

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Abstract

An improved understanding of the evolution of cell structure and viscoelasticity with cancer malignancy could enable the development of a new generation of biomarkers and methods for cancer diagnosis. Hence, in this study, we present the viscoelastic properties (moduli and viscosities) and the actin cytoskeletal structures of triple negative breast cancer (TNBC) cells with different metastatic potential. These include: MCF-10A normal breast cells (studied as a control); MDA-MB-468 cells (less metastatic TNBC cells), and MDA-MB-231 cells (highly metastatic TNBC cells). A combination of shear assay and digital imaging correlation (DIC) techniques is used to measure the local viscoelastic properties of live breast cells subjected to constant shear stress. The local moduli and viscosities of the nuclei and cytoplasm are characterized using a generalized Maxwell model, which is used to determine the time-dependent creep responses of cells. The nuclei are shown to be stiffer and more viscous than the cytoplasms of the normal breast cells and TNBC cells. The MCF-10A normal breast cells are found to be twice as stiff as the less metastatic MDA-MB-468 breast cancer cells and over ten times stiffer than the highly metastatic MDA-MB-231 breast cancer cells. Similar trends are also observed in the viscosities of the nuclei and the cytoplasms. The measured differences in cell viscoelastic properties are also associated with significant changes in the cell cytoskeletal structure, which is studied using confocal fluorescence microscopy. This reveals significant differences in the levels of actin expression and organization in TNBC cells as they become highly metastatic. Our results suggest that the shear assay measurements of cell viscoelastic properties may be used as effective biomarkers for TNBC diagnosis and screening.

Graphical abstract