Characterization of nanomechanical properties of normal and cancer prostate cells

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Introduction
Cancer metastasis involves the detachment of cells from the primary tumor, migration through the extracellular matrix, entry into the blood stream, exit through the extracellular matrix, and colonization in a distal organ site. The cells experience different types of mechanical stress such as compression (tumor mass), hydrostatic (blood vessels), shear (blood flow), and osmotic (extracellular matrix) during this process. These extracellular forces could be expected to have a significant influence on cancer metastasis.

Understanding the role of mechanical stress in cancer metastasis involves characterization of the membrane mechanical properties of normal and cancer cells and studying the response of cells after subjected to mechanical stress.

Central hypothesis
The central hypothesis of this research is that mechanical stress influences cancer metastasis through changes in membrane properties.

Methods
Prostate cell lines (normal and cancer) have been used as the model system to substantiate the central hypothesis.

1. The prostate cancer cell lines were obtained from ATCC and subcultured by established protocols. These are RWPE-1 (normal), RWPE-2 (nonmetastatic), DU145 (moderately metastatic from brain metastasis), and PC3 (highly metastatic from bone metastasis).
2. The invasiveness of these cell lines were measured using cell invasion assay to confirm their representation of cancer progression stages.
3. Their cell membranes were studied with a Veeco Multi-mode Picoforce instrument in Tapping Mode (noncontact) with a SiN cantilever. Force distance curves were recorded in the approach and retraction modes.
4. The cell adhesion proteins were analyzed for their expression levels in the presence and absence of osmotic stress using In-Cell Western blot analysis (Pierce®).

Results

AFM based characterization

Distribution of pre-tension term

Distribution of Young’s modulus term

Distribution of dilation modulus term

Response of cell adhesion proteins

Architecture of cell adhesion proteins

Cell-cell and cell-matrix adhesions formed by E-cadherin and αVβ3 integrin.

Cell-cell and cell-matrix adhesion expression

Osmotic stress exerted by 50 mM PEG.

The cell invasion assay indicates high invasiveness upon subjecting the cells to osmotic stress.

Conclusions
Prostate cancer cells from different cancer progression states have varying mechanical properties. These prostate cancer cells respond to osmotic stress differently in terms of cell-cell and cell-matrix adhesion protein expression.

Future directions
The study of cell adhesion protein expression in detail in response to osmotic stress. Study of the change in cell membrane properties by AFM when subjected to osmotic stress. Investigate pathways by which mechanical stress is transmitted through the cellular architecture.

References