CORRELATION OF MECHANICAL PROPERTIES WITH CELL MIGRATION OF NON SMALL-CELL LUNG CANCER CELL LINES

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Introduction

Cancer cells are defined by their ability to invade through the basement membrane, a critical step during invasion and metastasis. Cell stiffness has been postulated to be important in transmigration of cancer cells through a basement membrane [1]. Recent studies have shown that cancer cells themselves are more compliant than normal cells. However, the extent of the correlation between cancer cell mechanical properties and specific aspects as cell migration especially after drugs' treatment has not been determined. Non-small cell lung cancer (NSCLC) accounts for 80% of all cancer mortality cases. Recent evidence suggests that estrogen signaling is critical in the progression of malignancies that express estrogen receptors and may also be involved in the pathogenesis of NSCLC [2]. Aromatase, catalyses the final step in estrogen synthesis locally in tissues, including the lung tissue. Exemestane (EXE) is an irreversible steroidal aromatase inhibitor approved for postmenopausal women with breast cancer.

Method

NSCLC cell lines H23 and A549 were used. A micropipette method was used to determine the mechanical properties of cells prior and after their treatment with EXE.

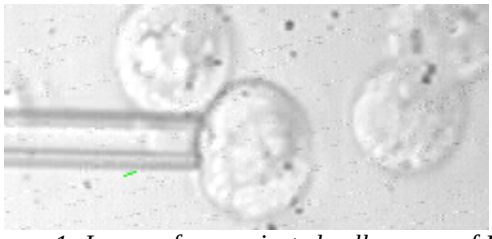

Figure 1: Image of an aspirated cell cancer of H23 cancer cell line.

More specific, we applied negative pressure, P, on individual cells through the pipette and we measured the length of the cell tongue, L, Fig.1. The slope of the curve $\Delta P=f(L/D)$, Fig. 2, reflects the cell stiffness, where D, is the micropipette diameter and the elastic shear modulus (ESM), G, was determined by the equation $\Delta P=4\pi G(L/D)$. [3]. Cells migration was determined with boyden chamber assay.

Results

We found that the ESM of the untreated A549 and H23 cells was 480.0±237.23Pa and 159.10 ±62.10Pa, respectively. Twenty four hours after cells' treatment with EXE, the ESM was decreased at 269.87±43.0Pa and 125.0± 65.05Pa, respectively. Furthermore, treatment of cells with EXE reduced cell migration solely at H23 cells (36.7%±12.4). EXE did not affect A549 cells' migration.

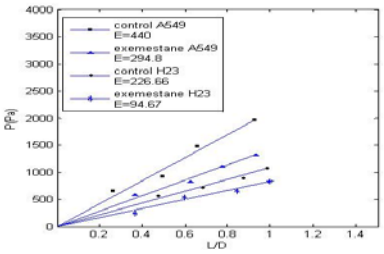

Figure 2: Typical experimental data on ESM of individual cancer cells.

Discussion

Our data showed that the two cell lines had different ESM, and both cell lines reduced their stiffness after treatment with EXE ($p<0.05$). The cells with the higher ESM were resistant to EXE treatment regarding migration implying that lower stiffness might be render cells more sensitive to migration inhibition. However, the reduced ESM by EXE in A549 was not associated with alterations in cell migration. This means that although rheological parameters might have a predictive role, cell migration is a complex process that might regulated also by the cell contractility. The project is still ongoing in order the profile for mechanical properties of cells to be completed.

References

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3.C.T.Lim *et al*, J Biomech, 39:195-216, 2006.