Biomechanical Adaptation of Lewis Lung Carcinoma (LLC) Cells to Circulation Conditions and Metabolic Stress

Olenchuk M.V. [1], Gnatyuk O.P. [1], Romanenko S.V.[2], Kolesnik D.L.[3], Solyanik G.I.[3], Dovbeshko G.I. [1]

[1] Institute of Physics, NASU, 46 Nauky Ave., 03028, Kyiv, Ukraine

[2] O.O. Bogomoletz Institute of Physiology, NASU, 4 Akademik Bogomolets St., 01601, Kyiv, Ukraine

[3] R.E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, NASU, 45 Vasylkivska St., 03022, Kyiv, Ukraine

INTRODUCTION & METHODS

Background: Metabolic stress (glucose deprivation) and loss of matrix attachment (deadhesion) are critical checkpoints during cancer metastasis. However, the mechanical adaptations of cancer cells to these harsh conditions remain poorly understood.

Aim: To evaluate the impact of glucose deficiency on the cell membrane tension of Lewis Lung Carcinoma (LLC) cells under different culturing conditions.

Model: LLC cells maintained in adhesive (2D) and deadhesive (suspension) states under either normoglycemic or glucose-starved conditions.

Methodology: Biophysical properties were quantified via micropipette aspiration using a custom experimental setup (see Fig. 1).

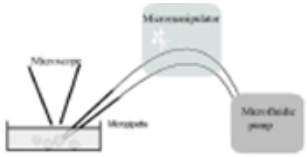

Fig. 1. Micropipette aspiration setup

Quantification: Cell membrane tension (ϒ) was calculated using the modified Laplace law based on the aspiration geometry (see Fig. 2):

$$\gamma = \frac{P_c}{2\left(\frac{1}{R_p} - \frac{1}{R_c}\right)}$$

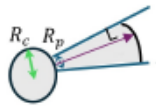

Fig. 2. Aspiration geometry and Laplace law parameters

where P_c is the critical aspiration pressure, R_p is the pipette radius, and R_c is the cell radius.

DISCUSSION

Geometry vs. Metabolism: 3D analysis of single cells demonstrated that variations in cell (R_c) and pipette (R_p) radii are fully standardized by the Laplace law. The observed shifts in membrane tension (ϒ) reflect genuine biophysical remodeling of LLC cells.

Adhesive Baseline: Under standard conditions, adhesive cells exhibit the lowest and most variable tension (0.12–0.76 mN/m) due to dynamic lamellipodia formation. The transition to suspension (deadhesion) stabilizes a baseline spherical tone (0.19–0.53 mN/m).

Stress-Induced Rigidity: Glucose deprivation moderately elevates membrane tone in adherent cells (0.44–0.83 mN/m). Crucially, the combination of deadhesion and starvation triggers an anomalous tension spike to 1.72 mN/m, requiring critical aspiration pressures up to (6.5 mbar) due to extreme deformation resistance.

Surface Stickiness: Severe energy deficit alters membrane glycosylation and enhances non-specific cell stickiness, which was experimentally observed as persistent cell adhesion to the glass micropipette tip.

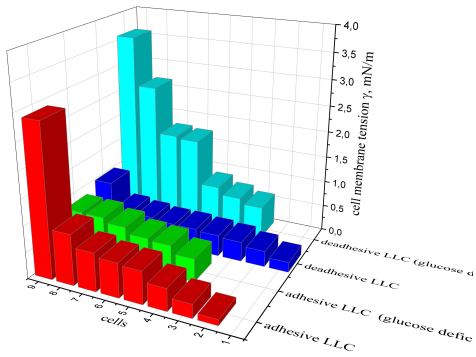

Fig.3. Cell membrane tension

CONCLUSIONS

The synergy of glucose deficiency and loss of adhesion drastically alters the mechanical phenotype of LLC cells, increasing cell membrane tension by 3–6-fold compared to baseline controls.

Biophysical Mechanism: Under suspension starvation, LLC cells likely trigger uncoordinated contraction of the actomyosin cortex (presumably via the RhoA/ROCK pathway). This dramatically increases internal turgor and pulls the plasma membrane taut.

Biological Significance: This extreme membrane "hardening" (> 1.72 mN/m) acts as a mechanical shield, protecting starved cells from hydrodynamic shear stress in the bloodstream, halting energy-consuming endocytosis, and promoting cell aggregation into anoikis-resistant 3D spheroids.

ACKNOWLEDGEMENT

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