XII JORNADA DE JÓVENES INVESTIGADORES/AS DEL I3A

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Chromatin Condensation Variation during Confined Cell Migration

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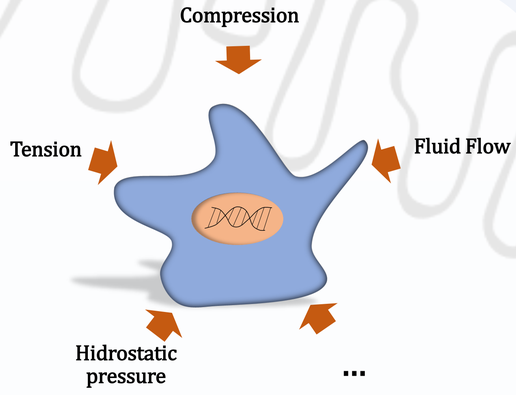
INTRODUCTION

Cells are constantly exposed to a spectrum of mechanical stimuli to which they adapt through mechanotransduction mechanisms. So that they can adapt to the needs of deformation of the nucleus, altering nuclear mechanics for proper cellular functioning.



The deformation of the cell nucleus during confined migration is thought to be one of the mechanosensing mechanisms used by the cell, which affects its gene expression.

Confined migration → Alterations in cytoskeletal mechanical state → Nucleus deformation → Changes in gene expression

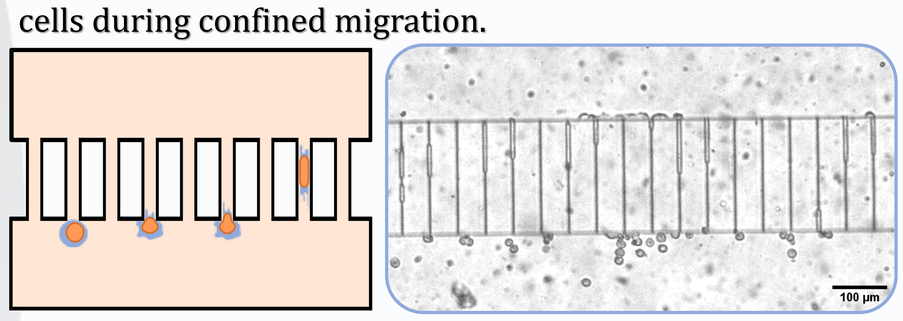
The possible relationship between them could help to understand the expression mechanism that allows cancer cells to migrate through narrow channels during metastasis.

OBJECTIVES

To study chromatin condensation during confined cell migration.

METHODS

We use microfluidic devices with microchannels width from 2 to 12 µm and 6 µm height to simulate the mechanical confined environment of the neuroblastoma cells during confined migration.



To obtain images from the nuclei we use inverted fluorescence optical microscope with a 63x oil immersion objective (Zeiss Axio Observer).

RESULTS & ANALYSIS

Software: ImageJ + MATLAB

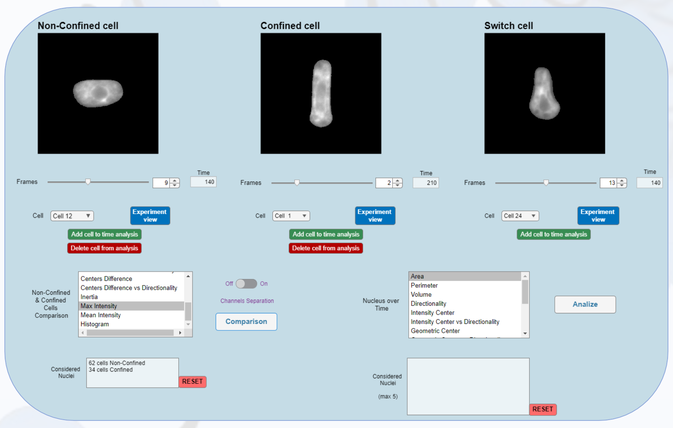


Figure 1. Design of the data comparison application

Cell nuclei are shown (top).
Several cell nuclei can be added for comparing them over time.
Two menus bottom allow analysis by group or by individual cells.

Group Analysis

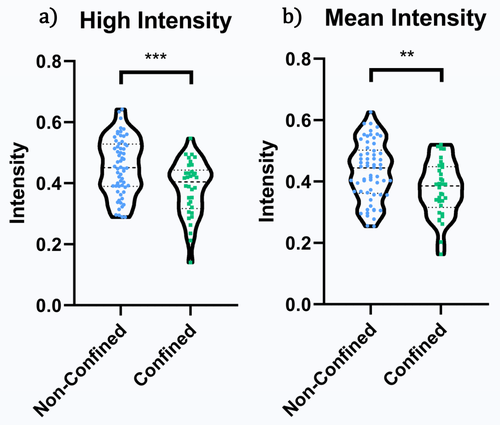


Figure 2. Violin plot intensity comparison

a) High intensity comparison:
Non-Confined cells: 0.45 ± 0.09
Confined cells: 0.38 ± 0.09
P-value: <.001

b) Mean intensity comparison:
Non-Confined cells: 0.43 ± 0.09
Confined cells: 0.37 ± 0.09
P-value: .004

Individual Analysis

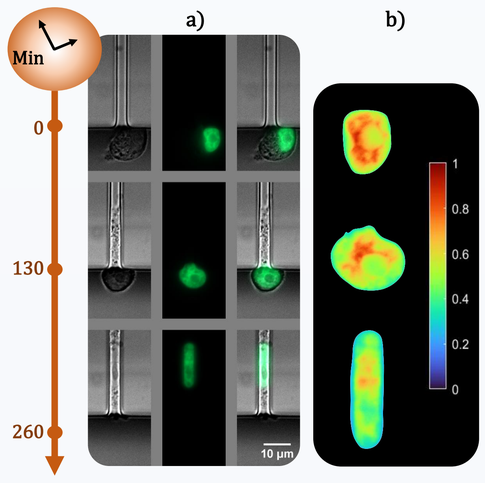


Figure 3. Cell nucleus during confined migration in a 4 µm channel

a) Brightfield and fluorescence microscopy.

b) Segmented nucleus with a colour map of highlighting chromatin distribution.

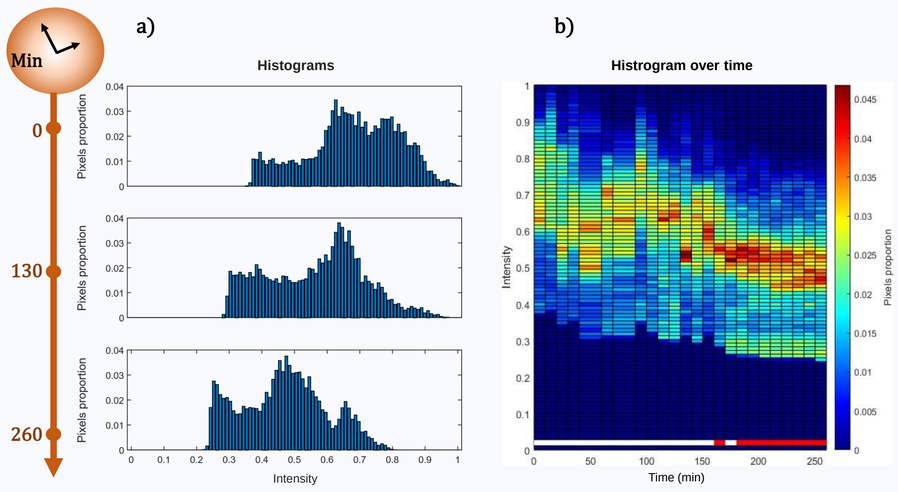


Figure 4. Cell nucleus histogram of fluorescence intensity over time

a) 2D histograms of the nucleus intensity at three points in time.

b) 3D histogram of the nucleus intensity. The bottom line shows when the cell is considered unconfined (white) or confined (red).

These results demonstrate a different distribution of chromatin under confinement compared to non-confinement, both at the group level (confined vs non-confined) and at the individual level (cells transitioning between states). It seems that fluorescence intensity decreases with confinement, suggesting a chromatin condensation variation that must be proved in the future using specific techniques.

CONCLUSIONS

Our findings indicate that cellular nucleus deformation can impact chromatin reorganization, which is relevant for understanding mechanotransduction mechanisms in metastasis and may aid to design new therapeutic targets.

ACKNOWLEDGEMENTS

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[1] WAGH, K. ISHIKAWA, M. GARCIA, D.A. STAVREVA, D.A. UPADHYAYA, A. HAGER, G.L. Mechanical Regulation of Transcription: Recent Advances. *Trends Cell Biol*. 2021, 31(6), pp. 457-472.
[2] FRIEDL, P. WOLF, K. LAMMERDING, J. Nuclear Mechanics during Cell Migration. *Curr Opin Cell Biol*. 2011, 23(1), pp. 55-64.
[3] JACOBSON, E. C., PERRY, J. K., LONG, D. S., OLINS, A. L., OLINS, D. E., WRIGHT, B. E., VICKERS, M. H., & O'SULLIVAN, J. M. Migration through a small pore disrupts inactive chromatin organization in neutrophil-like cells. *BMC biology*. 2018, 16(1), pp. 142.

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