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► To cite this version:

Emmanuèle Helfer, Cécile Jebane, Alice-Anais Varlet, Marc Karnat, Annie Viallat, et al.. Enhanced cell viscosity as a new phenotype associated with lamin A/C alterations. Biophysical Society Annual Meeting BPS2024, Feb 2024, Philadelphia (PA), United States. pp.177a, <10.1016/j.bpj.2023.11.1161>. <hal-04882407>

HAL Id: hal-04882407

<https://hal.science/hal-04882407v1>

Submitted on 13 Jan 2025

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Enhanced cell viscosity as a new phenotype associated with lamin A/C alterations

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Lamin A/C is a crucial component of the nucleus and the impact of lamin A/C alterations has been extensively described at the molecular and nuclear scales, notably on nucleus mechanical properties. However, its impact on whole-cell mechanics has been poorly addressed, even less so in terms of measurable physical parameters.

In the present study, we combined microfluidic experiments with theoretical analyses to provide a quantitative estimation of the whole cell mechanical properties. This allowed us to characterize the mechanical changes induced in cells by lamin A/C alterations and prelamin A accumulation resulting from Atazanavir treatment, a protease inhibitor which alters lamin A/C production, or from lamin A/C R482W mutation associated to type-2 familial partial lipodystrophy (FPLD2). We unveiled a distinctive increase in the long-time viscosity as a signature of cells affected by lamin A/C alterations. We showed that this change cannot be explained solely by mechanical changes in nuclei. Rather, by destabilizing the actin and microtubule networks, we showed a major contribution from the cytoskeleton and uncovered an unexpected role of microtubules in lamin A/ altered cells. Altogether, our results suggest that the whole-cell response to mechanical stress is driven not only by the nucleus but also by the nucleo-cytoskeleton links and the microtubule network. The enhanced cell viscosity assessed by our microfluidic assay could serve as a valuable diagnosis marker for lamin-related diseases.