

## NUCLEAR DYNAMICS IN LAMIN PERTURBED HUMAN FIBROBLASTS

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The human cell nucleus is a highly organized architectural entity with chromatin as well as proteins occupying distinct and functionally relevant nuclear domains, jointly confined by the nuclear envelope. Directly below the inner nuclear membrane, lies an interconnected meshwork composed of intermediate filaments – the lamina – which provides structural support for the nucleus and has a central role in defining nuclear organization [1]. Defects in its components (lamins) lead to a class of diseases collectively referred to as laminopathies [2]. Lamin mutations affect the physical integrity of nuclei, resulting in increased susceptibility to mechanical stress and alterations in (mechanosensitive) gene expression.

Most studies regarding the mechanical properties of the nucleus with respect to lamin-irregularities are based on the induction of extracellular stress, such as strain or compression, and mainly focus on the aspects of nuclear integrity and nucleo-cytoskeletal interaction [3]. Far less is known about the role of chromatin organization and mobility in nuclear mechanics.

In this study, we quantitatively compared nuclear deformation and chromatin mobility of fibroblasts from a Hutchinson-Gilford progeria patient with cells from a lamin A/C-deficient patient and wild-type dermal fibroblasts. We thereby made use of inherent chromatin markers, telomeres, which we visualized with telomere-binding fusion proteins. In order to minimize phototoxicity we reduced illumination to a minimum by means of controlled light exposure microscopy (CLEM). We found that the absence of lamin A/C increased nuclear plasticity and intranuclear mobility dramatically in contrast with progeria cells, which show reduced dynamics.

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