Premature senescence by lamin A/C alterations correlates to changes in cell viscoelastic behavior

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Lamin A/C, a protein of the nuclear envelope, contributes to the mechanical properties of the nucleus such as stability, shape, and rigidity. Mutations in lamin A/C gene *LMNA* induce pathologies called laminopathies, with common phenotypes such as nuclear abnormal shape or cell premature senescence. Laminopathies display varying severity and can be tissue-specific, like Type 2 Familial Partial Lipodystrophy (FPLD2) where only adipose tissues are affected, or multi-systemic, like Progeria where the entire body ages prematurely. The relationship between *LMNA* mutations, mechanical alterations in cells and laminopathy severity remains unknown, resulting in a lack of diagnosis and treatment. So far, most studies focused on Progeria and whether the observed alterations are Progeria-specific or common to all laminopathies is not answered yet. Here, we combined high-throughput microfluidic measurements on the second timescale with semi-automated image analysis and a rheological model to extract mechanical properties of human fibroblasts. We showed that fibroblasts prematurely senescent due to lamin A/C alterations (associated to FPLD2 or artificially induced) exhibit a more viscous behavior. The cell mechanical response depends both on the nucleus and on actin and microtubule networks. Our results suggest that lamin A/C alterations impact the nucleus and its link to the cytoskeleton.