
Lamin A/C Mechanotransduction in Laminopathies

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Abstract

Mechanotransduction translates forces into biological responses and regulates cell functionalities. It is implicated in several diseases, including laminopathies which are pathologies associated with mutations in lamin and lamin-associated proteins. These pathologies affect muscle, adipose, bone, nerve, and skin cells and range from muscular dystrophies to accelerated aging. Although the exact mechanisms governing laminopathies and gene expression are still not clear, a strong correlation has been found between cell functionality and nuclear behavior. New theories base on the direct effect of external force on the genome, which is indeed sensitive to the force transduced by the nuclear lamina. Nuclear lamina performs two essential functions in mechanotransduction pathway modulating the nuclear stiffness and governing the chromatin remodeling. Indeed, A-type lamin mutation and deregulation has been found to affect the nuclear response, altering several downstream cellular processes such as mitosis, chromatin organization, DNA replication-transcription, and nuclear structural integrity. In this review, we summarize the recent findings on the molecular composition and architecture of the nuclear lamina, its role in healthy cells and disease regulation. We focus on A-type lamins since this protein family is the most involved in mechanotransduction and laminopathies.

Keywords: Emery-Dreyfuss muscular dystrophy; Hutchinson Gilford progeria syndrome; gene regulation; lamin A/C; lamin partners; laminopathy; mechanotransduction.

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