Lamins and bone disorders: current understanding and perspectives.


Abstract
Lamin A/C is a major constituent of the nuclear lamina implicated in a number of genetic diseases, collectively known as laminopathies. The most severe forms of laminopathies feature, among other symptoms, congenital scoliosis, osteoporosis, osteolysis or delayed cranial ossification. Importantly, specific bone districts are typically affected in laminopathies. Spine is severely affected in LMNA-linked congenital muscular dystrophy. Mandible, terminal phalanges and clavicles undergo osteolytic processes in progeroid laminopathies and Restrictive Dermopathy, a lethal developmental laminopathy. This specificity suggests that lamin A/C regulates fine mechanisms of bone turnover, as supported by data showing that lamin A/C mutations activate non-canonical pathways of osteoclastogenesis, as the one dependent on TGF beta 2. Here, we review current knowledge on laminopathies affecting bone and LMNA involvement in bone turnover and highlight lamin-dependent mechanisms causing bone disorders. This knowledge can be exploited to identify new therapeutic approaches not only for laminopathies, but also for other rare diseases featuring bone abnormalities.

KEYWORDS: LMNA-related congenital muscular dystrophy (L-CMD); bone turnover; hutchinson-gilford progeria syndrome (HGPS); lamin A/C; mandibuloacral dysplasia (MADA, MADB)