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Defective collagen proteostasis and matrix formation in the pathogenesis of lysosomal storage disorders

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Abstract

The lysosome is a catabolic organelle devoted to the degradation of cellular components, such as protein complexes and whole or portion of organelles that reach the lysosomes through (macro)autophagy. The lysosomes also function as signaling organelles by controlling the activity of key metabolic kinases, such as the mechanistic target of Rapamycin complex 1 (mTORC1). Lysosome dysfunction has dramatic consequences on cellular homeostasis and cause lysosomal storage disorders (LSDs). Here we review the recently proposed mechanisms by which impairment of lysosome/autophagy pathway affects extracellular matrix formation and skeletal development and growth. In particular, we will highlight the role of autophagy as a collagen quality control pathway in collagen-producing cells. An impairment of autophagy, such as the one observed in LSDs, leads to a collagen proteostatic defects and can explain, at least in part, the skeletal phenotypes characterizing patients with lysosomal storage disorders.