A LYSOSOMAL HIGH MOLECULAR WEIGHT MULTIENZYME COMPLEX

HALINA OSTROWSKA, WIOLETTA JEDYNASTA-KOZŁOWSKA and JOANNA KALINOWSKA
Department of Biology, Medical Academy, 15-230 Bialystok, Poland

Three acidic glycosidases: β-galactosidase (E.C. 3.2.1.23), α-neuraminidase (sialidase, E.C.3.2.1.18), N-acetylaminoalacto-6-sulfate sulphatase, and serine carboxypeptidase cathepsin A (E.C.3.4.16.1) exist within lysosomes as functional high molecular weight complexes [Pshezhetsky and Ashmarina, Prog. Nucleic Acid. Res. Mol. Biol. 69 (2001) 81]. It has been shown by many authors that the major constituent responsible for the integrity of this complex is cathepsin A, the so-called 'lysosomal protective protein'. By forming a multienzyme complex, it protects β-galactosidase and neuraminidase from rapid intralysosomal proteolysis, and it is also necessary for the intracellular sorting and proteolytic processing of their precursors. In Homo sapiens, a deficiency of cathepsin A leads to the combined β-galactosidase and neuraminidase deficiency called 'galactosialidosis', characterized by the accumulation of various sialyloligosaccharides and gangliosides in patients' tissues and body fluids [D’Azzo et al., The Metabolic and Molecular Bases of Inherited Disease 2 (1995) 2825]. Galactosialidosis is therefore the first known lysosomal storage disease caused by a protease deficiency, and the molecular basis of this disorder is multiple mutations identified in the cathepsin A gene. In addition to its protective role, cathepsin A also functions as a carboxypeptidase at acidic pH and a deamidase/esterase at neutral pH [Hiraiwa, Cell. Mol. Life. Sci. 56 (1999) 894]. In vitro it hydrolyses various biologically active peptides, including substance P, endothelin I, angiotensin I and oxytocin; however, the physiological importance of its enzymatic function is still unknown.