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Glatiramer Acetate and Nanny Proteins Restrict Access of the Multiple Sclerosis Autoantigen Myelin Basic Protein to the 26S Proteasome

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Abstract

© 2014 Ekaterina Kuzina et al. We recently showed that myelin basic protein (MBP) is hydrolyzed by 26S proteasome without ubiquitination. The previously suggested concept of charge-mediated interaction between MBP and the proteasome led us to attempt to compensate or mimic its positive charge to inhibit proteasomal degradation. We demonstrated that negatively charged actin and calmodulin (CaM), as well as basic histone H1.3, inhibit MBP hydrolysis by competing with the proteasome and MBP, respectively, for binding their counterpart. Interestingly, glatiramer acetate (GA), which is used to treat multiple sclerosis (MS) and is structurally similar to MBP, inhibits intracellular and in vitro proteasome-mediated MBP degradation. Therefore, the data reported in this study may be important for myelin biogenesis in both the normal state and pathophysiological conditions.

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