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# Cathepsin B-Induced Degradation of Lysozyme Amyloid Fibrils †

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Diseases associated with the accumulation of ordered protein aggregates, amyloid fibrils, once thought to be rare, are predicted to soon become epidemics. However, there are still no effective drugs without serious side effects for the degradation of amyloid plaques, which is currently considered a promising therapeutic strategy. We tested the proteolytic enzyme cathepsin B, involved in the cellular immune response, as a potential amyloid-degrading agent.

Our investigation focused on model lysozyme amyloid fibrils that accumulate in systemic non-neuropathic hereditary amyloidosis. Various microscopic, biochemical, and spectroscopic approaches were used to study the properties of amyloids and their degradation products. We showed that cathepsin B-mediated proteolysis of amyloid-forming proteins led to fibril fragmentation. In some amyloid fragments, the loss of an ordered structure was also observed. The identified effects can be attributed to the disruption of intra- and intermolecular hydrogen bonds in the fibril core. At the same time, with the stepwise addition of cathepsin B (as opposed to a one-step enzyme addition at the same concentration), we observed a lower number of "fluffed" fragments, although the efficiency of amyloid degradation remained practically unchanged. Cathepsin B deactivation did not lead to fibril reassembly (as is the case with other amyloid-degrading factors) for at least 5 days. Despite the observed cathepsin B-induced degradation of amyloids, cell viability was not increased in its presence, indicating an equally high cytotoxicity of intact amyloids and of their degradation products.

The results of our study show that the visible destruction of amyloid fibrils does not always lead to a decrease in their cytotoxicity. However, the transformation of amyloids into smaller and less stable aggregates with an altered structure (as effected by cathepsin B) is an important step in the development of effective and safe anti-amyloid agents.

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