Alpha-B-crystallin modulates physical properties and cytotoxicity of lysozyme amyloids

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The main functions of chaperones are maintaining the native tertiary or quaternary structure of monomeric proteins, as well as the formation and dissociation of protein complexes. The role of chaperones in fibrillogenesis is currently being actively investigated. At the same time, the effect of chaperones on mature amyloid fibrils is paid much less attention. Given that progressive amyloidosis are currently being detected at the stages when mature amyloid fibrils have already formed, the study of the chaperones effect on these protein aggregates are of high relevance for searching the therapeutic agents. It is known that small heat shock protein alpha-B-crystallin, which is found in large quantities in the body of patients as part of amyloid plaques, is able to inhibit the proliferation of amyloid fibrils. We investigated the effect of this chaperon on mature lysozyme amyloid fibrils prepared under various conditions. Transmission electron microscopy of the tested objects indicated the chaperon-induced degradation of lysozyme amyloid fibrils into the large disordered aggregates at the physiological conditions. Simultaneously with the decompactization of amyloid fibrils, a partial degradation of denatured disordered aggregates into smaller aggregates and monomers occurs. We showed that degraded aggregates obtained by treatment with alpha-B-crystallin have a more pronounced cytotoxic effect on the HeLa cell line in comparison to mature fibrils. According the results of MTT test, the presence of the degraded aggregates in the culture medium for 24 h reduced the number of living cells by about 30 % ($p < 0.05$) in comparison with mature fibrils, while chaperone itself had no toxic effect on the cells. Thereby our data support the notion that physical modifications of amyloid fibrils by alpha-B-crystallin are sufficient to enhance their cytotoxicity. This work was supported by grant from Russian Science Foundation (No. 18-74-10100).

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