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Exploring the Therapeutic Potential of the Hsp70 Chaperone in Light Chain Amyloidosis

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Light chain amyloidosis is a protein misfolding disorder characterized by the deposition of monoclonal immunoglobulin light chains as insoluble amyloid fibrils in tissues and organs, leading to progressive dysfunction. Current treatments mainly focus on reducing amyloidogenic light chain production through chemotherapy or monoclonal antibody therapies, yet effective methods to directly prevent or reverse amyloid fibril formation remain limited. The Hsp70 chaperone system plays a crucial role in protein homeostasis by assisting protein folding, preventing aggregation, and facilitating the degradation of misfolded proteins. This study aims to explore Hsp70 chaperone-based strategies to mitigate light chain aggregation and their potential for future therapeutic development. In the first step, we developed an effective method for producing soluble Hsp70-SBD in sufficient quantity and quality, allowing us to perform basic biophysical characterization, including anti-aggregation properties against the JTO light chain involved in multiple myeloma. We are now developing new variants with higher specificity and improved anti-aggregation properties using evolutionary techniques like yeast display. This work is funded by the EU NextGenerationEU through the Recovery and Resilience Plan for Slovakia under the project No. 09I03-03-V04-00116.