STRUCTURAL DOMAINS OF HUMAN SEPTIN 2: STABILITY AND AGGREGATION STUDIES

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Septins are a conserved group of GTP-binding and filament-forming proteins. While originally discovered in yeast, they are involved in a variety of cellular processes, such as polarity determination, membrane dynamics, vesicles trafficking and exocytosis. All the members of the family of septins can be divided into three domains: a variable N-terminal, a GTPase domain, and a C-terminal region, that includes generally sequences characteristic of coiled-coil. The function of Septin 2 (SEPT2) remains unclear, however, SEPT2 together with SEPT1 and SEPT4 are accumulated in deposits known as neurofibrillary tangles and glial fibrils in Alzheimer's disease. In this study, the three structural domains of human SEPT2 (SEPT2, SEPT2-GC and SEPT2-G) were expressed in *E. coli* and purified by affinity and size-exclusion chromatographies. The purified products were analyzed by circular dichroism spectroscopy, rigth-angle light scattering and intrinsic and extrinsic fluorescence spectroscopy. In all the cases, the products forms homodimers *in vitro*, suggesting that the oligomerization occurs for the SEPT2-G. Thermal unfolding of the recombinant products revealed the rapidly formation of aggregates under physiological conditions. In addition, the aggregates have the ability to bind specific dyes such as Congo red and Thioflavin-T, suggesting them to be amyloid in nature. Thus, the present study contributes for the knowledgment of the stability and aggregation kinetic of the SEPT2, leading to a better understanding of its function in neurodegenerative disorders.

Key words: GTP-binding, neurofibrillary tangles, glial fibrils, homodimers, amyloid.

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