# A STRUCTURAL APPROACH TO THE STUDY OF SEPT4 AND THE HUMAN 'SEPTINOME'

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Septins are a widely distributed group of filament forming GTPases which play central roles in membrane reorganization during cell division, exocytosis, vesicle trafficking etc. Despite their importance, little is known about their molecular organization or atomic structures. No crystal structure of any septin or part thereof has been reported in the literature. The human genome contains at least 13 genes (SEPT1 – SEPT13) coding for different septins which suffer from both alternative splicing and post-translational modification to render a large number of products. We have adopted a multi-center approach to studying the human 'septinome' in which a large scale effort is under way to clone, express, purify and crystallize several constructs of each of the human septins, of which nine are already undergoing crystallization trials. In parallel SEPT4-G has been the subject of structural studies which demonstrate it to be dimeric in solution and to readily suffer rapid thermal unfolding at physiological temperature and pH leading to the formation of amyloid aggregates. This observation may simultaneously clarify the current controversy concerning the formation of homo-*versus* hetero-filaments and represent a physiological mechanism for eliminating excess components during the formation of physiologically relevant filaments.
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