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KINETICS OF DIFFERENT PROCESSES IN HUMAN ANP AMYLOID FORMATION

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Atrial Natriuretic Peptide (ANP), a soluble circulating protein, can be amyloidogenic and features ANP-containing amyloid deposits are found primarily in the heart [1]. The cause for this transition from soluble to insoluble protein in Isolated Atrial Amyloidosis (IAA) is yet to be determined, and specific structural features that might favour ANP fibrillogenesis have not yet been identified. The molecular basis of ANP aggregation is thus relevant for modelling the amyloidogenesis process as well as for improving delivery systems used for amyloidosis treatments. Consequently, the precise characterization of *in vitro* fibril deposits might provide insight the true biochemical nature of deposited ANP. In this study, we provide detailed analyses of both the soluble and deposited forms of ANP in different solution conditions. The structure and the morphogenesis of aggregates have been monitored by using different experimental techniques: Transmission electron microscopy, spectrophotometric Congo Red assay, thioflavin T fluorescence, FTIR spectroscopy. ANP aggregation displays a wide variety of morphologies, from small oligomeric filaments to voluminous floccules, and therefore different specific processes are likely to be intertwined in the overall aggregation. Fibrillar aggregates grow following a concentration dependent heterogeneous coagulation mechanism, including both protofibril elongation and lateral thickening until formation of strictly interconnected amyloid material.

References:

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PROTEOMICS INVESTIGATION OF HUMAN PLATELETS IN HEALTHY DONORS AND CYSTIC FIBROSIS PATIENT BY SHOTGUN NUPLC-MSE AND 2DE: A COMPARATIVE STUDY

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Platelets are the smallest blood circulating cells involved in several pathophysiological events such as haemostasis, wound repair, inflammation and cardiovascular disease. Although platelets are anucleated particles and inherit their protein content from megakaryocytes, they can undergo translation events and synthesize selected proteins. Thus, the analysis of the platelet proteoma may provide significant information on the role that platelets may play in human pathology.
Cystic fibrosis (CF) is a genetic disease evoked by mutations in the CFTR gene, located in the long arm of chromosome 7 and coding for a protein with ion channel activity. Inflammatory lung disease is the primary cause of morbidity and mortality in CF, nonetheless mechanisms of CF inflammation are still incompletely known. Enhanced platelet activation in vivo and ex vivo has been documented in CF patients which display also increased circulating platelet/PMN and platelet/monocyte complexes, suggesting that platelets may be involved in CF inflammation.
In this work, we pursued a comparative proteomic analysis of platelets obtained from healthy donors and CF patient, employing two different, but complementary approaches, namely the classic 2-DE in association with mass analysis and nanoscale ultra-performance LC-MSE. We compared these techniques for sensibility, accuracy and data reproducibility. We consistently observed that the combination of these techniques gives a more detailed characterization of the platelet proteome and identified, a restricted group of protein differentially expressed in CF platelets.
A comparative analysis of the Gene Ontology was performed to evaluate the overall molecular function and the potential pathophysiological relevance of these proteins within the context of CF inflammation

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