

**P032** Prefibrillar oligomers of human stefin B (cystatin B) interact with membranes  
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Protein aggregation to amyloid fibrils is central to most neurodegenerative diseases. More and more evidence is obtained that the initial insult to cells comes from prefibrillar species, such as protofibrils, globular oligomers and even smaller oligomers, rather than mature fibrils. The »channel« hypothesis states that oligomeric species, as shown for A- $\beta$ ,  $\alpha$ -synuclein or prion fragments, exert toxicity by forming channels into membranes, which initiates a cascade of detrimental events for the cell. Interaction of the granular aggregates and globular oligomers of human stefin B, an amyloidogenic protein not involved in any known amyloid pathology, with model lipid membranes was studied. Results have shown that prefibrillar oligomers of stefin B, cause concentration dependent membrane leaking. In addition, the prefibrillar oligomers increase the surface pressure at air-water interface, i.e. they have amphipatic character and are surface seeking. They interact predominantly with acidic phospholipids, such as DOPG or DPPS as shown by calcein release experiments and surface plasmon resonance. These effects are specific to the weakly toxic stefin B, contrasting the homologue - stefin A, which does not transform into prefibrillar aggregates under any of the conditions studied, neither is toxic.