# Molecular characterization of the interaction between the Hsp70 chaperone Binding immunoglobulin protein (BiP) and the islet amyloid polypeptide for the inhibition of amyloid formation

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Many diseases are associated with insoluble amyloid deposits in various tissues, including Alzheimer's disease and type II diabetes. To achieve its insoluble cross-β structure, the protein precursor undergoes a multitude of transient conformational transitions, making the development of specific therapy against amyloidosis particularly challenging. The chaperones heat shock proteins of 70 kDa (Hsp70) have been identified as potent inhibitors of amyloid aggregation. Herein, the islet amyloid polypeptide (IAPP) is used as a model amyloidogenic peptide to characterize the mechanism of inhibition by the Hsp70 Binding immunoglobulin protein (BiP), which is composed of a nucleotide binding domain (NBD) and of a peptide binding domain divided into two subunits (SBDα and SBDβ). BiP hydrolyzes adenosine triphosphate (ATP) to change its conformation isolating the client protein, but can also work in the absence of ATP, without modifying its conformation. Full-length BiP, SBDα and SBDβ subunits were recombinantly expressed to identify the domain responsible for the inhibition of amyloid aggregation of IAPP in the absence of ATP. Biophysical analyzes supported by computational approaches show that the complete structure of BiP is necessary for amyloid inhibition. By further characterizing the residues implicated in this interaction, this project will support the design of new therapeutics.