The conversion of a polypeptide backbone into a native protein is a key element in the translation of the genetic information of an organism. As the organism ages, folding seems to deviate, which signals for several diseases (mainly neurodegenerative ones). Protein misfolding causes its deposition in the cell in the form of aggregates or amyloid fibrils, both of which have toxic effects. Molecules, that play an important role in cell protection, are molecular chaperones, which help protein folding and protein disaggregation. Therefore, chaperones seem to have a fundamental role in the organism by increasing the success of physiological functions and protecting cells from becoming ill. Our proposal has the main objective of understanding protein folding by: 1) studying the folding pathway and the stability of proteins, mainly globins; 2) characterizing the forces and the mechanisms of amyloid fibril formation; 3) structurally and functionally characterizing chaperones; and 4) studying the mechanisms by which chaperones help folding, stop aggregation, resolubilize aggregates, and interact with proteins involved in cell malignization. Our goal is to understand protein folding inside the cell: such knowledge will generate important new ways of thinking, and may help lead to new therapies.
SUMMARY OF RESULTS TO DATE AND PERSPECTIVES

Human chaperones have been cloned and purified in their folded conformation, as measured by circular dichroism and fluorescence spectroscopy. The hydrodynamic properties of the proteins are under investigation by hydrodynamic techniques (analytical ultracentrifugation, gel filtration chromatography and dynamic light scattering). Ab initio calculations are underway and will give further insights on quaternary structure.

Xanthomonas secretion chaperone and target: two sets of secretion chaperones and their respective targets were selected by two-hybrid studies. Proteins were purified and their interaction measure by in vitro techniques.

Sugarcane chaperones: we initiated further characterization of chaperones that are part of the HSP70-HSP90 complex (involved in abiotic and biotic stress in plants – a pathogen causes biotic stress).

Results on protein folding showed that the information that is present on the amino acid sequence is also important to avoid aggregation. Permutation mutants may still exhibit native structure and function, but aggregate easily.

MAIN PUBLICATIONS


Carlos Henrique Inácio RAMOS
Instituto de Química
Universidade Estadual de Campinas (Unicamp)
Caixa Postal 6154 - Cidade Universitária
13084-862 – Campinas, SP – Brasil
+55-19-3521-3144
cramos@iqm.unicamp.br