PROTEIN FOLDING AND CONFORMATIONAL DISEASES

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The protein molecules take the shape of a globule in the aqueous environment. The spontaneous folding processes are explained broadly by two models, such as structural and kinetic. The structural models aim at the actual structure of intermediates which appear before the formation of dominant intermediates prior to the formation of native globular protein. The kinetic models emphasize on the formation of native globular protein as well as dominant intermediates and the rate of the folding process. Variants of kinetic models include biased random search, nucleation growth and sequential folding pathways. Structural models propose that 'H' bonded structures occupy the lowest position in the hierarchical order of the native protein formation pathway. Though the information necessary for the correct folding of polypeptide chain is nascent in the primary structure of polypeptide, still 15% of the globular proteins require the help of chaperones and chaeronins.

Conformational diseases are a gorup of disorders, which share common molecular pathology. Each disease arises from the same destabilizing mutations and polymerization of conformationally unstable protein occurs intracellularly at the site of synthesis leading to accumulation of protein aggregates, such as alpha$_1$ antitrypsin in hepatocytes and neurotropin in neurons. The intracellular polymer formation is common determinant of neurodegeneration in Inclusion body dementias such as spongiform encephalopathies, sporadic and familial Parkinson's disease and Alzheimer's disease. Similarly onset and severity of the hepatic cirrhosis is associated with the aggregation of alpha$_1$ antitrypsin in hepatocytes. The challenge of the day is to design suitable diagnostic technique prior to the appearance of cellular inclusion body and develop suitable drug delivery system either to prevent the polymerization of aberrant protein or to increase the secretion of cellular protein aggregates.