Structural Analysis of Disease-related Proteins by NMR

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The genome contains the DNA code which specifies the amino acid sequence of a protein. In order to perform the protein's function, the polypeptide chain must fold into a well-defined tertiary structure. Therefore, experimental determination of the protein structures is of high importance for a detailed understanding of protein functions. Recently, nuclear magnetic resonance (NMR) spectroscopy has developed into an extremely powerful tool for solving solution structure of proteins. We have been studying the three-dimensional structures of various proteins by NMR spectroscopy.

Under some circumstances, however, several proteins fail to achieve their functional structures and assemble into large insoluble aggregates. These insoluble protein aggregates include amyloid fibrils, which are fibrous protein aggregates having highly organized cross-β structure. Amyloid fibrils are known to cause human amyloid disorders, including Alzheimer's disease and familial amyloid polyneuropathy. On the other hand, there have been a number of proteins that inhibit the amyloid fibril formation. We have been studying the amyloid fibrils from two points of view, namely (i) the relationship between the structural change of proteins and amyloid fibril formation, and (ii) the inhibition of the amyloid fibril formation.