The nature of early structural events during protein folding and misfolding is poorly understood. The misfolding events often lead to the aggregation of the proteins, typical of most of the neurodegenerative diseases. Transactive response DNA binding protein 43 (TDP-43) is an important protein in RNA processing and known to be involved in various neurodegenerative diseases categorized as TDP-43 proteinopathies. The cytoplasmic depositions, also known as inclusion bodies, of TDP-43 and its fragments, are pathologic hallmarks of two such fatal neurodegenerative disease: amyotrophic lateral sclerosis (ALS) and frontotemporal lobar dementia (FTLD). However, the mechanism of aggregation and the nature of aggregated state is yet unclear. A detailed understanding of the steps involved in the misfolding and aggregation is very important in order to understand the conformational changes which convert a stable native structure into a disease-prone intermediate/misfolded state. By using various spectroscopic methods, we are trying to determine the characteristics of the native, misfolded and aggregated state and the mechanism of protein aggregation.