



DEPARTMENTAL SEMINAR

Chemical, Biological & Macro-Molecular Sciences

30th November'2021

4.00 PM

ONLINE

SPEAKER

Dr. Santosh Kumar Jha
Principal Scientist & Associate Professor (AcSIR)
Physical and Materials Chemistry Division
CSIR-National Chemical Laboratory

TITLE OF THE TALK

Mechanistic insights into the stress-induced aggregation of TDP-43 in ALS

ABSTRACT

Chronic environmental stress modulates the physiochemical and solvation environment of the cellular milieu and leads to the amyloid-like aggregation of proteins in neurodegenerative diseases. However, how the stress is sensed by proteins at the molecular level and consequent steps during their aggregation is not well understood for any protein. One such vital nucleic-acid binding protein is TDP-43, whose aggregation is implicated in \sim 97 % of cases of amyotrophic lateral sclerosis (ALS), an incurable motorneuron disease.

In this talk, I will discuss about our discovery of TDP-43 as a physiochemical stress-sensor. I will also discuss about how the amyloid-like misfolding of the protein could begin from site- specific triggers and how the energy landscapes of folding and aggregation of the functional domain of the protein is coupled by a metastable molten-globule like oligomeric form. Finally, the site-specific step-wise mechanism of the formation of amyloid-like aggregate of the protein will be discussed.

HOST FACULTY