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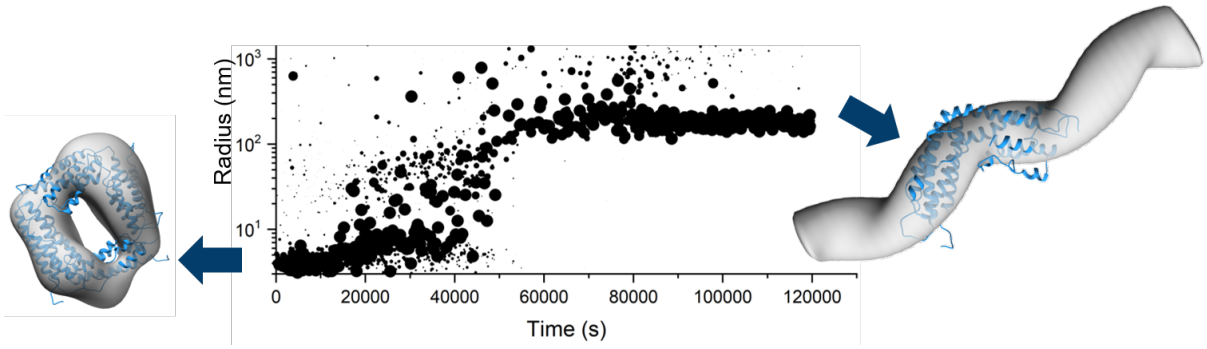
"DISC(1)erning the structural & functional attributes of the Disrupted-in-Schizophrenia 1 protein in chronic mental illnesses"



Abhishek Cukkemane, Ph.D.
Forschungszentrum Jülich, Germany

08.03. 2022. 12:00h

O-030, Department of Biotechnology

Host: Nicholas J. Bradshaw

DISC(1)erning the structural & functional attributes of the Disrupted-in-Schizophrenia 1 protein in chronic mental illnesses

Abhishek Cukkemane, Ph.D.
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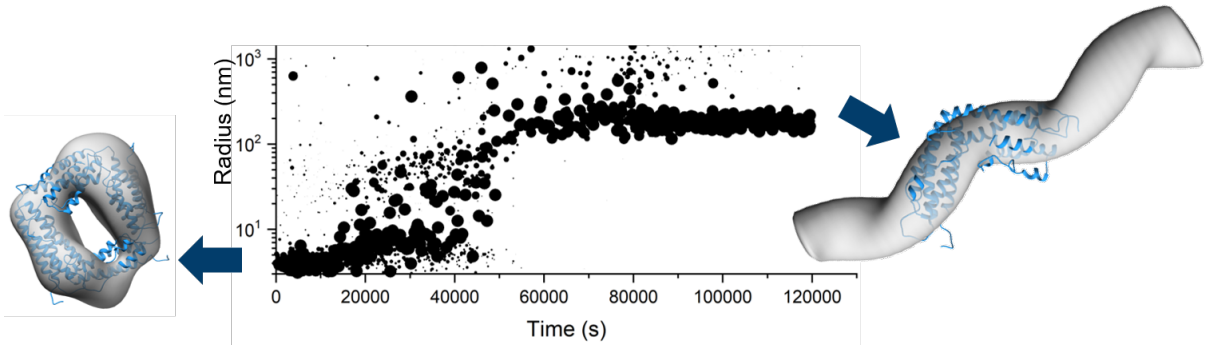
Schizophrenia continues to perplex scientists and clinicians alike, as its aetiology and pathophysiology remain poorly understood due to the complex nature of risk factors arising due to environmental, social and biological origins. One established biological risk factor is the Disrupted in Schizophrenia 1 (DISC1) protein, which has been observed as aggregates in the post-mortem brain tissue of patients suffering from CMIs. However, the notion of schizophrenia as a proteinopathy has been subject to intense speculation and criticism



.Recently, we demonstrate that pathophysiology of psychotic disease bears hallmarks of protein conformational disorder akin to its neurodegenerative cousins. Our major findings using biophysical and structural biology approaches highlight that one of the major regulatory domains (the C-region) forms β-fibrils. By using thermodynamics and aggregation kinetics we were able to map the oligomerization, fibrillization and aggregation pathways of the protein. Also, we demonstrate the cooperative interaction of oligomeric C-region of DISC1 with proteins relevant to the dynein mitotic complex *viz.* Lissencephaly 1 (LIS1) and NDE-Like 1 (NDEL1), which themselves are protein risk factors and are critical for neurodevelopment and cell proliferation.

Cukkemane, A. et al. (2021) Conformational heterogeneity coupled with beta-fibril formation of a scaffold protein involved in chronic mental illnesses. Transl. Psychiatry 11, 639, doi:10.1038/s41398-021-01765-1.