DBT-NCCS study reveals evolutionarily conserved plasticity of nuclear pore complexes

New Delhi, Nov 27: Three domains - Archaea, Bacteria, and Eukarya, make up the tree of life. The first two are prokaryotic microorganisms, whose cells do not have a nucleus. The third domain comprises eukaryotes, i.e. organisms that have cells with a well-defined nucleus, which includes diverse lifeforms from simple, single-celled yeasts to plants, to human beings.

The nucleus is a very important organelle of the cell, given that it serves to store and organize genetic information present in the hereditary material, DNA. The DNA is coiled around nuclear proteins called histones that collectively form the chromosomes. The nucleus is enclosed within a nuclear envelope (NE), which serves to separate and protect the chromosomes from the other cellular components.

However, at the same time, the nucleus also needs to communicate and exchange molecules with the rest of the cell. This is necessary for cellular processes to take place within and outside the nucleus in a coordinated manner, which is required for the cell to function normally. For this purpose, the nuclear envelope has nuclear pore complexes (NPCs), which selectively mediate and regulate the exchange of biomolecules, between the nucleus and the cytoplasm, which lies outside the nucleus.

Each NPC is an assembly of multiple copies of about 20-30 different proteins called nucleoporins (Nups), that surround a central pore. While small molecules diffuse through NPCs, larger molecules are recognised and transported through the central pores by the Nups.

Mutations in Nups are often linked with cellular defects and diseases, which are thought to result from a disturbance in nuclear transport. Defects in NPCs are correlated with many diseases, such as cancer, nervous system diseases and immune system disorders. Therefore, NPCs have been the subject of research, since understanding the relation between NPC

function and these diseases could help develop treatment regimens for the mitigation of these diseases.

Dr. Radha Chauhan and her team at DBT-National Centre for Cell Science (DBT-NCCS) in Pune, an autonomous institute of the Department of Biotechnology, have been studying various aspects of the structure of NPCs, using cutting edge research tools, to learn the about these important cellular structures at the molecular level. The central transport channel (CTC) of NPCs is made up of three nucleoporins Nup62, Nup58, and Nup54. How these nucleoporins form the CTC was earlier not clear.

Recently, Dr. Chauhan and her group explored the CTC Nups from various species and observed that distinct biochemical characteristics of CTC Nups are evolutionarily conserved. Moreover, comparative biochemical analyses of CTC complexes revealed various combinations of Nup62, Nup54, and Nup58 coexisting.

They also observed that the end of the mammalian Nup93 protein molecule, called the "amino-terminal domain", is conserved, and is crucial for anchoring the CTC and keeping it localized at the NPCs. Their investigations using techniques like "small angle X-ray scattering" and electron microscopy revealed a 'V' shape of the CTC-Nup93 complex. These studies have for the first time demonstrated the evolutionarily conserved plasticity and stoichiometric diversity in CTC Nups. These research findings were recently published in the international journal, Protein Science.

* Link to the paper: https://onlinelibrary.wiley.com/doi/abs/10.1002/pro.3983

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