Nuclear pore complexes have species-specific molecular architecture

Dr. Radha Chauhan and her team at autonomous institute of the Department of Biotechnology, the National Centre of Cell Science (NCCS), carried out a comparative analysis of the amino acid sequences of nucleoporins (Nups) from several different species using high throughput bioinformatics methods, to identify crucial differences in their Nup-subcomplexes. They found that from the entire repertoire of about 30 Nups in species like yeast and humans, a few are unique to each species. Some of the 30 Nups are highly conserved across species, while others show wide variations between species, due to divergent evolution.

Dr. Chauhan's findings indicate that though the number of Nups may be similar, nuclear pore complexe (NPC) assembly likely takes place in a manner that is unique and specific to the species, and this may be linked to the unique structural features of Nups of that particular species. Therefore, although there are some similarities between human and yeast NPCs, including the number of Nups, the structural details of the machinery are likely to be significantly different in humans to accommodate more complex eukaryotic cell functions. The structures of NPCs revealed by recent studies done by others, using newer tools like electron tomography which reveal molecular structures at much greater resolution, also corroborate these findings.

Studies done by Dr. Chauhan's team led them to conclude that the protein-protein interactions in NPCs are species-specific, rather than being similar across all eukaryotic organisms, and that their structure and function should therefore be studied in an organism-specific manner. These studies thus highlight the unprecedented concept of species-specific architecture of NPCs, which has only now slowly started gaining acceptance. The research findings of this team were published in the journal, Protein Science. This research article was among the top 10% of the most downloaded papers, which underscores the immediate impact generated by this research. In recognition of this, each author of the paper was recently awarded with a certificate of achievement by the journal publishers.

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, 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 NE 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). 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. Therefore, NPCs have been the subject of many studies.

An NPC is one of the largest protein complexes in eukaryotic cells, and is also structurally complex. Carrying out structural studies on proteins of NPCs from higher organisms like humans is challenging due to their large size and the prevalence of unstructured regions. Therefore, individual proteins and/or complexes from lower eukaryotes like yeast, which are easier to work with in the laboratory, have often been studied as a proxy for human NPCs. This is based on the premise that Nups are broadly conserved over evolutionary times across eukaryotic species, and that NPC structures appear to be similar in different eukaryotes, based on earlier observations. However, aalthough the primary architecture of the NPC is evolutionarily conserved; there are significant variations at the level of individual Nups. Like all other protein molecules, Nups are composed of a chain of different building blocks called amino acids, which are strung together in a specific sequence.

Source**:** https://onlinelibrary.wiley.com/doi/full/10.1002/pro.3558