Research suggests core nuclear pore elements shared by all eukaryotes

July 13 2009

(PhysOrg.com) -- For perhaps 1.8 billion years after life first emerged on Earth, a sort of evolutionary writer's block stalled the development of organisms more complicated than single cells. Then, a burst of experimental creativity about 1.7 billion years ago brought the cell nucleus onto the scene, stashing the cell's genetic material inside a protective inner membrane and setting the stage for the evolution of more sophisticated creatures from yeast, say, to plants and human beings. Now research shows that one of the most basic design principles of this new eukaryotic life-form — the gatekeeper to the cell nucleus known as the nuclear pore complex — is largely shared across the most distantly related eukaryotes. Its core components likely evolved once and for all and would be found in the nuclear pore complex of what is known as the last common eukaryotic ancestor.

The findings, by Rockefeller University researchers Brian T. Chait, Michael P. Rout and colleagues, add details to an unfolding picture of cellular evolution that shows a common architecture for the nuclear pore complex and the vehicles that evolved around the same time to transport cargoes between different parts of the cell, called coated vesicles. As early as 1980, Rockefeller professor Günter Blobel proposed that the internal membranes of cells — such as those encompassing the nucleus and vesicles — evolved from invaginations of the outer cell membrane. Rout and Chait suggested in 2004 that the nuclear pore complex and vesicle coats, which both contain α-solenoid and β-propeller protein folds, evolved from ancient molecules called protocoatomers that stabilized the membranes of these primordial internal structures.

“This work shows that the pore contains the signature of this ancient evolutionary event,” says Rout, head of the Laboratory of Cellular and Structural Biology. “Some evolutionary biologists have argued that the resemblance is only superficial. This paper shows that that is not true. The resemblance is not skin deep. Indeed, it goes all the way to the core.”

Published June 13 in *Molecular & Cellular Proteomics*, research performed by former graduate student Jeffrey A. DeGrasse, now at the United States Food and Drug Administration, picked apart the proteins that make up the nuclear pore complex of Trypanosoma brucei, a deadly, single-celled parasite responsible for African sleeping sickness. In the evolutionary tree of eukaryotic life, T. brucei is about as far removed from vertebrates like ourselves as possible, far more distant than commonly used model organisms such as yeast, fungi and plants. “The trypanosomes were at the wedding of the eukaryotes but were divorced the day after,” says Rout, quoting his University of Cambridge colleague Mark C. Field, who also worked on the research. The idea is that if the nuclear pore complex proteins of trypanosomes are the same as those in vertebrates, then they almost certainly are also in the hypothetical cell known as the last common eukaryotic ancestor. “They are defining features of eukaryotes, just as warm blood plus hair form a defining feature of mammals,” says Rout.

Prior research had led other scientists to question whether the nuclear pore complex proteins are in fact conserved because they had found that the amino acid sequences that make up the proteins are quite different among far-flung eukaryotic species. DeGrasse and colleagues, working with highly enriched samples of nuclear pore complexes from our distant parasitic relative, also found that the amino acid sequences are not well conserved, based on a Basic Local Alignment Search Tool analysis of mass spectroscopy data. But they took the analysis a step further. Working with Andrej Sali at the University of California, San Francisco,

DeGrasse applied a variety of other bioinformatic tools including algorithms describing protein folds and sorted through an initial pool of 757 proteins to identify 30 candidate nuclear pore complex proteins, roughly the same number that makes up the nuclear pore complexes of yeast and vertebrates. The researchers were able to genomically tag 22 of the 30 proteins and establish that they are deeply related, or homologous, to known proteins in yeast and vertebrate nuclear pore complexes, specifically those proteins that form the core scaffold of the complex and other well-described structures.

“These proteins are conserved at the structural level, especially the pore coat and the core scaffold, but also the unfolded proteins that traffic molecules through the complex between the nucleus and cytoplasm,” says Chait, the Camille and Henry Dreyfus Professor and head of the Laboratory of Mass Spectrometry and Gaseous Ion Chemistry. “All of the main elements are there.”

More information: Molecular & Cellular Proteomics, June 13, 2009
Evidence for a shared nuclear pore complex architecture that is conserved from the last common eukaryotic ancestor
Jeffrey A. DeGrasse, Kelly N. DuBois, Damien Devos, T. Nicolai Siegel, Andrej Sali, Mark C. Field, Michael P. Rout and Brian T. Chait

Provided by Rockefeller University (news : web)