Poster C-6

Intracellular transporters evolve slowly

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Short Abstract: The membranous organelles in eukaryotes could affect on the evolution of particular proteins, such as intracellular transporters (ITs) because of particular functional constraints. We compared evolutionary rates of ITs and non-ITs. The results suggest that ITs, especially transporters for large molecules are slowly evolving now.

Long Abstract:

There are three domains (eubacteria, archaea, eukaryota) in the life on the earth, and the origin of eukaryota is one of the most attractive open questions in the research field of evolution. Many hypotheses have been proposed as the origin and the history of eukaryotes, some of them look reliable, some of them look plausible and some of them look too speculative. Numbers of approaches might be, and we believe that the intracellular membranes, structures which divide the cytosol into some sections in eukaryotic cells could be a clue to unveil the secret of eukaryotes. Contrary to prokaryotes (eubacteria and archaea), eukaryotes have a number of organelles inside themselves. For example, they have nucleus, ER (Endoplasmic Reticulum), Golgi apparatus, and so on. One of the characteristics of these organelles is that, they are membranous. And these membranous organelles are believed to be indispensable machineries for extant eukaryotes, in order to keep closed environments for each biochemical steps and keep active but dangerous molecules (some enzymes) away from the other molecules. In short, we can say that the membranous organelles are firewalls in the cells, at present. Then, please imagine the epoch of the eukaryotes (about two billion years ago). Before that, there had been only prokaryotes on the earth. It is roughly believed that eukaryotes came into being by the symbiotic events of prokaryotes, and they have gained membranous organelles and enhanced the eukaryote specific functions inside the cells. The origin and detailed history of the membranous organelles are still unclear, so we do not take care about the origin and history in this study, but anyway, ancient eukaryotes have gained the membranous organelles as a result of the early evolution of eukaryotes. Then let us see this epochal situation from the viewpoint of intracellular topology. In prokaryotic time, cells might have no boundary inside themselves because they did not have membranous organelles, hence, almost all protein molecules might be accessible each other, and variety of chemical condition in a cell might be small. In addition, we can say that the Protein-Protein Interaction (PPI) networks in the bacterial cells are sound, free from walls (membranes). Now the time, and the cells have gained the membranous organelles (nucleus, ER, Golgi apparatus, and so forth) and the eukaryotes have come into existence. After the emergence of eukaryotes, the accessibility between protein molecules inside the eukaryotic cells would be restricted by the membranes because the membranes could be the walls. The PPI networks should be disturbed by the gain of

membranes in the cells, because the membranes could be the barriers for the locomotion of molecules in the cells. Of course there could be density gradients of protein and some other molecules without membranous organelles, but in terms of comparison with eukaryotes, prokaryotes have had boundary-free environments inside themselves. In other words, the gain of membrane system could be one of the most epochal events in the evolution of eukaryotes, and we can say that the membranous organelles are the firewalls at present, but were obstacles in the cells, in past. Here we want to point out the latter one, membranous organelles were the obstacles, and the fact that eukaryotes have surely overcome the obstacles because they are living now. From the viewpoint of molecular evolution, this difficult situation could be a selective pressure for evolution of protein molecules. We speculate that the ancient eukaryotes exposed themselves to danger of extinction by dividing their cytosol into some sections hence they had been under the selective pressure to enhance the intracellular transporting machineries with the intracellular transporters (ITs). We suppose that this promotion of ITs protein molecules was taken place around two billion years ago, and have gone past. Again from the viewpoint of molecular evolution, we speculate that the ITs are now under the strong functional constraint because the intracellular transporting machineries have already developed, and extant eukaryotes should deeply depend on the machineries. In summary, particular eukaryotic protein molecules (ITs) would have been under the specific evolutionary pressure compared with the other protein molecules (non-ITs). In other words, the gain of the membranous organelles would affect on the evolution of particular eukaryotic proteins, such as ITs. Moreover, from the above mentioned speculations the evolutionary rates of the ITs would have been fluctuated with the time course. It looks very difficult to infer the evolutionary rates of protein molecules in two billion years ago, so with motivation to give insight to the evolutionary studies of the current membrane system and intracellular transporting machinery, we are conducting the analyses with the methods of molecular evolution. First, we computed the evolutionary rates of IT proteins involved in large molecule transport (ribosomal subunits, etc.) in the cells, because we assume that ITs involved in larger molecules are under stronger functional constraint than those for small cargos. We used the proteome sequences of budding yeast (Saccharomyces cerevisiae) as a model organism of eukaryote. To compute the evolutionary distances as the (relative) evolutionary rates, we detected the orthologous pairs between the proteome sequences of S. cerevisiae and S. paradoxus, and align the sequence pairs. We referred the GO (Gene Ontology) annotations to classify the proteins according to the functions. Second, we focused on the two groups, ITs and non-ITs, and compared the mean evolutionary rates of the two. The results suggest that ITs, especially the intracellular transporters for large molecules are slowly evolving now. This new finding on the borderline between cell biology and molecular evolution would be a next viewpoint of computational biology. We are examining the results and further analyses are underway.