Molecular Genomics, Proteomics and Bioinformatics

Reading Assignment #1

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In the Fraser paper entitled *Evolutionary Rate in Protein Interaction Network,* the correlation between protein interactions, the protein fitness effect and evolutionary rate, is described in *Saccharomyces cerevisiae* and *Caenorhabditis elegans*. Functional genomic data was compared to determine the conservation of orthologs and the amount of interactions in yeast proteins. Evolutionary distance (K) was used to quantify well-conserved domains in terms of substitutions after animal divergence. A negative correlation was observed between the number of interactions and the evolutionary rate of the protein. This relationship is illustrated in the scatter plot of Figure 1 in *C.elegans*. Several hypotheses emerged to explain this phenomenon. First, if a protein has more interactions in an organism, then the arrangement of the protein is limited in the amount of substitutions that can occur. The second hypothesis is that the proteins with more interactions had a greater impact on the fitness of the organism, which causes these proteins to evolve more slowly However, this is not proven by a relationship between interactions and the protein fitness effect. This model is shown in Figure 2. In order to assess the fitness effect of interacting proteins, the difference between the evolutionary rate of the yeast protein and nematode ortholog was calculated and distributed based on the average of these values. The result of this distribution shown in Figure 3A is that interacting proteins evolve at similar rates supporting the idea of co-evolution. This is further supported by the same method of distribution with the fitness effect of these orthologs (Figure 3B). A possible explanation for the similarity between fitness effect and the evolutionary rate of interacting proteins is shown in Figure 3C with the calculation of observed correlations between the fitness effects and evolutionary rates of interacting proteins. This demonstrates the small role that the fitness effect plays in the evolutionary rates of interacting proteins. Further directions include the relationship between the number of interactions or structural homology in the evolutionary rate of various proteins.