Partner 11

A compartmentalized protein-protein interaction network as a novel model of aging

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Protein-protein interaction networks (interactomes) help to understand cellular function at the systems level. The nodes of these networks are proteins, while the links are their physical interactions. In currently used interactomes the subcellular localization of proteins was not included, thus several interactions were false-positive, because the interacting proteins of the interactome did not have the same cellular localization in living cells.

D'Angelo *et al.* (Cell, 136:284) showed that the permeability of the nuclear pore complexes increases during the aging process. Encouraged by this observation, we defined three states of aging of the compartmentalized cellular interactome as a new aging model: A.) The "young" cell has only the interactions, where both proteins have the same subcellular localization. B.) To the interactome of the "elderly" cell we add all those interactions, where one of the proteins had a nuclear, while the other had a cytoplasmic localization mimicking the state described by D'Angelo *et al.* C.) We call the generally used interactome, which does not take into account any cellular localization as "very old", since this models the state, where already all intracellular barriers have become permeable.

We examined the interaction networks of four model organisms (*S. cerevisiae, C. elegans, D. melanogaster, H. sapiens*), starting from the protein-protein interaction databases STRING and BioGRID (as model C.) and modify them in models A.) and B.) using the integration of the subcellular localization data of the BaCelLo, eSLDB, pTARGET and PA-GOSUB databases to our new ComPPI database. We analysed the interactome topology with Pajek, and the modular structure with our new ModuLand program (www.linkgroup.hu/modules.php). The visualization was made with Gephi, while the statistical analysis was made using R-programming.

The number of nodes and links increased from model A.) to C.) and with increasing evolutional complexity. Network diameter decreased through the aging models, and increased with evolutionary complexity. The degree distributions showed a scale-free character in all cases. Our results show that the inclusion of localization data fundamentally changes the properties of the interactome. The decrease on network diameter shows an increased vulnerability of aged networks for noise and damage propagation. In contrary, the cells adaptability and damage-tolerance increased with evolutionary complexity.