Evolution of J-domain proteins (JDPs) function and relatedness

Milena Stolarska, Department of Molecular and Cellular Biology, Intercollegiate Faculty of Biotechnology

Supervisor: prof. Jarosław Marszałek

Hsp70 chaperones play critical roles in protein homeostasis. By transiently binding many different substrates, they assist in diverse cellular processes, from *de novo* protein folding to protein trafficking to disassembly of protein complexes. Transiently interacting with ATP-bound Hsp70 via their defining J-domain, J-domain protein (JDP) co-chaperones are crucial players in the Hsp70-substrate interaction cycle - facilitating stimulation of Hsp70's ATPase activity, which in turn drives large scale conformational changes that stabilize substrate binding.

In my studies I performed evolutionary analysis of two Hsp70s: mitochondrial - Ssq1 and bacterial - DnaK and their JDP co-chaperone partners Hsc20 and DnaJ, respectively. Because structurally interactions of both Hsp70s with JDP are similar, I checked if residues involved in this interaction are conserved. I aligned the amino acid sequences of both J-domains and Hsp70s, what shows that residues forming the interfaces are not identical. Therefore, I performed more detailed analysis for Hsc20/Ssq1 and DnaJ/DnaK interfaces separately. First, I analyzed the conservation patterns at both interfaces, what revealed that the interfacial positions are variable both across phylogeny and within evolving lineages.

Moreover, I performed the coevolution analysis of both interfaces, assuming that coordinated changes across binding interface could allow them to maintain J-domain/Hsp70 interaction despite sequence variability. I used the phylogenetic approach. The analyses were restricted to JDP/Hsp70 interaction pairs from Ascomycota species for Hsc20/Hsp70 and from bacteria species for DnaJ/DnaK, as enough sequence variation was observed within these data sets. With phylogenetic trees of Hsp70s I used the probabilistic Coev model of sequence evolution, to discriminate between coevolving and non-coevolving positions homologous to those occupied by contacting residues for the Hsc20/Ssq1 and DnaJ/DnaK interactions. I identified 16 coevolving positions for the Hsc20/mtHsp70 interaction and 20 coevolving positions for the DnaJ/DnaK interaction. As a control, I tested the same dataset using a model of 'independent' evolution. Based on these results I concluded that coevolution is a major force that drives both specificity and strength of the J-domain protein/Hsp70 interaction.

KSZTAŁCIMY NAJLEPSZYCH *– kompleksowy program rozwoju doktorantów, młodych doktorów oraz akademickiej kadry dydaktycznej Uniwersytetu Gdańskiego. Zad. 2. Life Sciences and Mathematics Interdisciplinary Doctoral Studies (LiSMIDoS)*

HUMAN CAPITAL
NATIONAL COHESION STRATEGY

EUROPEAN UNION
EUROPEAN
SOCIAL FUND

Project co-funded by European Union under the European Social Fund