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Dissecting the interactome of RNA-binding proteins in post-transcriptional regulatory networks

Messenger RNAs have traditionally been viewed as passive molecules in the pathway from transcription to translation. However, it is now clear that RNA-binding proteins (RBPs) play an important role in RNA metabolism by controlling gene expression at post-transcriptional level. Nevertheless, our understanding of how RBPs control diverse cellular RNA targets within the context of other RBPs is largely unclear. Here, we first show that RBPs as a functional class of proteins exhibit significantly higher proportion of protein-protein interactions compared to non-RBPs in Sacchoromyces cerevisiae. We then extend our results, using RBP-RNA networks for a selected set of RBPs, to demonstrate that the number of RNA substrates bound by a RBP correlates positively with its number of protein interactions suggesting the contribution of RBPs towards this plasticity. Further analysis reveals that RBPs predominantly interact with other RBPs than non-RBPs, supporting the notion that the interplay between RBPs is responsible for the observed plasticity in the number of RNA targets. Functional analysis of the physically interacting proteins of RBPs suggests that RBPs can be grouped into distinct biological processes based on their degree. For example, splicing and translation were associated with highly interacting RBPs and mRNA localization was associated with poorly connected RBPs. Our results also show that RBPs are significantly disordered, with the extent of disorderedness increasing with the RNA degree of an RBP. Further analysis to study post-translational modifications in RBPs clearly revealed that not only are RBPs extensively phosphorylated but also the number of kinases targeting them increases with the number of RNAs controlled. These observations are further supported by the number of predicted disordered binding sites in RBPs, indicating the more general role of post-translational modifications in providing disordered RBPs the plasticity to control a number of RNA targets by combinatorially interacting with diverse RBPs to regulate different cellular processes at post-transcriptional level. Our study suggests a mechanistic basis behind the functioning of RBPs in the context of ribonucleoprotein complexes and provides a novel framework to elucidate the link between different levels of regulation in higher eukaryotes.

Biography

Sarath received his Ph.D in Molecular and Systems Biology from MRC Laboratory of Molecular Biology & University of Cambridge. Following a fellowship at University of Illionis, he is currently an Assistant Professor in the School of Informatics, Indiana and Purdue University Campus and at the Center for Computational Biology and Bioinformatics, IU School of Medicine. He has published more than 35 papers in reputed international journals, has H-index of 15 and serves on the editorial board of the journals Frontiers in Systems Biology, Network Biology and Journal of Biomolecular Research and Therapeutics.

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