COMPUTATIONAL BIOLOGY WEBINAR @ IMSc

CHAPERONING FOUR BILLION YEARS OF PROTEIN EVOLUTION

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Along evolutionary time, starting from simple a beginning, the repertoire of life's proteins has widely expanded. A systematic analysis across the Tree of Life (ToL) depicts that from simplest archaea to mammals, the total number of proteins per proteome expanded ~200-fold. In parallel, proteins became more complex: protein length increased ~3-fold, and multi-domain proteins expanded ~300-fold. Apart from duplication and divergence of existing proteins, expansion was driven by birth of completely new proteins. Along the ToL, the number of different folds expanded ~10-fold, and fold-combinations ~40-fold. Proteins prone to misfolding and aggregation, such as repeat and beta-rich proteins, proliferated ~600-fold. To control the quality of these exponentially expanding proteomes, core-chaperones, ranging from HSP20s that prevent aggregation, to HSP60, HSP70, HSP90 and HSP100 acting as ATP-fueled unfolding and refolding machines, also evolved. However, these core-chaperones were already available in prokaryotes ~3 billion years ago, and expanded linearly, as they comprise ~0.3% of all genes from archaea to mammals. This challenge—roughly the same number of core-chaperones supporting an exponential expansion of proteome complexity, was met by: (i) higher cellular abundances of the ancient generalist core-chaperones, and (ii) continuous emergence of new substrate-binding and nucleotide-exchange factor co-chaperones that function cooperatively with core-chaperones, as a network.

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