Protein intrinsic disordered and the regulation of transcription of TA operons

Intrinsically disordered regions (IDR) in proteins has been studied in a large number of contexts in eukaryotes. However it has received less attention in prokaryotes even though they form an important part of the proteome of bacteria and archaea and their function impinge beyond simple folding upon binding transitions. Identified as plasmid-stabilising entities, toxin–antitoxin (TA) modules are ubiquitous in the genomes of prokaryotes and archaea. Most commonly they constitute small operons that encode two genes. The downstream gene encodes for a stable toxic protein, while the upstream “antitoxin” gene protects the cell against this toxin. Type II TA modules, the most extensively studied group, consists of many different families with distinct distributions and biochemical activities and with complex evolutionary relationships between them.

TA antitoxins typically contain a significant amount of intrinsic disorder, with variable degrees of pre-structuring. Originally the antitoxin IDR was assumed to be involved in toxin-neutralization and directly linked to the susceptibility of the protein to proteolytic degradation and short in vivo lifetime. In recent years a body of evidence has accumulated that links intrinsic disorder of TA antitoxins to their different in vivo functions and physicochemical properties. As such, they have become a paradigm for the unprecedented variety of roles of intrinsic disorder in the prokaryotic proteome. Therefore, in order to understand the nature and functionality of intrinsic disorder in antitoxins, we have looked at evolutionary unrelated type II TA modules to characterise as much as possible the complex regulatory network that relates toxin synthesis, neutralisation and operon repression. Our data shows that these IDR and their functional plasticity are the linchpin of regulatory process that are completely different otherwise.