Seminar

on

Xenogene silencing, stress response and chromosome architecture in *E. coli*

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Abstract:

A significant proportion of a bacterial genome is predicted to have been acquired horizontally. In *E.coli* and its relatives, these are under pressure to be maintained in a transcriptionally silent state in standard growth conditions by a global gene regulatory system centred around a protein called HNS; de-silencing of these genes could lead to a strong disruption of gene expression homoeostasis. This talk will discuss the effect of horizontal gene transfer on gene expression states, and whether and how a bacterium can adapt to the disruption of their physiological regulation, as follows. H-NS, a global transcription repressor, binds to A+T-rich sequence tracts, many of which are horizontally-acquired, and keeps them transcriptionally silent. The talk will discuss genomic-scale analysis showing that the A+T-rich sequences bound by H-NS are intrinsically capable of high gene expression, which, as a cumulative increase in gene expression over ~20% of the genome, could impose a high metabolic cost on the organism. The gene silencing function of H-NS is directed towards the silencing of highly-transcribable genes at two intertwined levels: (a) sequence specificity – H-NS binding motifs are more enriched in highly transcribable sequences; (b) coregulatory network structure – partial backup of H-NS function by StpA is directed towards highly transcribable genes. An indirect consequence of the disruption of the H-NS-centred gene silencing mechanism is the down-regulation of transcription from a large number (10-12% of all genes) of otherwise highly expressed genes. Thus, de-silencing horizontally-acquired genes results in a global disruption of the gene expression state of the cell. How does the cell adapt to such a circumstance, short of reacquiring the silencing system? This is an important consideration: as a regulator of horizontally acquired genes, H-NS targets different gene functions even across closely-related bacteria, making its regulatory network dynamic, and subject to disruption by rampant horizontal gene acquisition. Genome-scale experimental work in our laboratory has shown that two distinct evolutionary strategies – inactivation of a replaceable component of the RNA polymerase (the σ38 σ-factor for general stress response), as well as a well-structured duplication of ~40% of the genome centred around the origin of replication – converge in partially redressing the transcriptional imbalance of a strain lacking the gene silencing system. The direct effects and the indirect consequences of these mutations appear to target distinct coordinates of the chromosome: stress-responsive and horizontally-acquired genes are encoded around the terminus of replication, and the consequence of their up-regulation being felt closer to the origin of replication, and vice-versa. This work immediately presents an intriguing connection between the contrasting direct and indirect effects of two distinct global regulatory systems and chromosome architecture.

Brief Biosketch:

Dr Aswin Sai Narain Seshasayee is currently working as Young Investigator in Faculty of Biochemistry, Biophysics and Bioinformatics, NCBS, Bangalore. He completed his PhD and postdoc at EMBL, University of Cambridge.

Dr Aswin's main research interest includes :

Genome-scale approach towards investigating bacterial gene regulation.

Future projects of Dr Aswin's in NCBS includes :

1. Genomic analysis of the impact of *E. coli* nucleoid-associated proteins on chromosome topology and global gene expression.
2. Impact of horizontal gene acquisition on the conserved gene regulatory network in enterobacteria.
3. Genomic analysis of the impact of distinct second messenger signalling systems on enterobacterial gene expression.
4. Genomic analysis of factors influencing DNA methylation in bacteria.
5. Generation and analysis of metagenomic data towards understanding genotype-phenotype relationships in the context of adaptation to an environment.
6. Genomic characterisation of clinical strains of enterobacterial pathogens.