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Understanding crosstalk between acidic phospholipids present in bacterial membranes and DnaA, the initiator of *Escherichia coli* chromosomal replication

Rahul Saxena
Georgetown University Medical Center, USA

Abstract

In vivo evidence links proper cellular levels of acidic phospholipids, such as phosphotidylglycerol (PG) and cardiolipin (CL), with continued cell growth and normal chromosomal replication in *Escherichia coli*. Reduced levels of acidic phospholipids, result in arrested-growth and inhibited chromosomal replication in otherwise wild-type *E. coli*. *In vitro* acidic phospholipids such as PG and CL present in a fluid bilayer promote the conversion of inactive ADP-DnaA to replicatively proficient ATP-DnaA. DnaA protein, a member of the AAA+ (ATPase associated with various cellular activities) family, initiates DNA synthesis at the chromosomal origin of replication, *oriC*, and regulates the transcription of several genes, including its own. Interestingly, DnaA with a point mutation in its membrane-binding amphipathic helix, DnaA(L366K), supports growth in cells with deficient in acidic phospholipids. We recently established that DnaA(L366K) can adopt architectures that are independent of its bound nucleotide, and instead the locus determines the functionality of higher order DnaA(L366K)-DNA nucleoprotein complexes. Ongoing studies are examining whether deficient levels of acidic phospholipids adversely affect initiation of chromosomal replication in a manner beyond the loss of nucleotide exchange on DnaA. Future goals include better defining the cross-talk between DnaA protein and acidic phospholipids in the bacterial membrane that helps control the spatial and temporal regulation of chromosomal replication in bacteria.

Biography

Rahul Saxena received his Ph.D. in Biochemistry from the Institute of Microbial Technology, India in 2007, where he made important contributions on the structural-functional characterization of peptide deformylase (PDF), an enzyme involved in post-translational modification of proteins in the pathogenic organism *Mycobacterium tuberculosis*. He pursued postdoctoral studies at Georgetown University School of Medicine where his research has focused on understanding the role of acidic phospholipids present in the bacterial cell membrane in controlling chromosomal replication spatially and temporarily. Recently he was appointed to the faculty in the Department of Biochemistry and Molecular & Cellular Biology at Georgetown University Medical Center. His findings have been published in several peer-reviewed journals, as well as a portion of his work has been accepted to grant a US patent.