Uncovering the mechanisms of cell cycle regulation: The link between DnaA and ParA.

The survival of a cell relies on maintaining intact chromosomes after the completion of each cell cycle. Unlike eukaryotic cells, bacterial cells replicate and segregate their chromosome simultaneously. However, the mechanisms involved in temporally coordinating the onset of chromosome replication prior to the onset of chromosome segregation remain unclear. This talk discusses three aspects of an integrated network that links the regulator of chromosome replication initiation (DnaA) with the regulator of chromosome segregation (ParA) in the bacterium *Caulobacter crescentus*. First, we have shown that chromosome replication and segregation can be un-coupled by lowering DnaA to sub-physiological levels. Limited levels of DnaA insufficient to initiate replication can trigger the onset of ParA-dependent chromosome segregation, suggesting a new role for DnaA in chromosome segregation. Second, our data revealed that the activities of DnaA and ParA are not restricted to specific subcellular locations. We have demonstrated that the ParA gradient can be flipped in orientation to trigger segregation in the opposite direction upon rearrangement of key chromosomal loci. Third, our most recent data suggest that ParA can promote DnaA's activity and disturb the once per cell cycle initiation of chromosome replication. In sum, our work on DnaA and ParA has revealed the complexities and interconnections of the systems involved in regulating the progression of the cell cycle in bacteria.