# ABSTRACT

Although the control of DNA replication has been widely studied, how is it arrested when a cell encounters adverse environmental changes is still not fully elucidated. When stress occurs, a stringent response is launched, during which (p)ppGpp (guanosine pentaphosphate or tetraphosphate) accumulates and indirectly leads to the synthesis of an inorganic polyphosphate (PolyP), which binds to Lon protease and stimulates the proteolysis of ribosomal proteins. Although it was demonstrated that the (p)ppGpp binds to the primase and inhibits its activity, it is not known how DNA replication initiation is rapidly arrested in *Escherichia coli*.

I hypothesized that replication initiation arrest is caused by the degradation of the replication initiation protein, DnaA which also plays a role as a transcription regulator. Initially, to test this hypothesis I examined the intracellular level of DnaA when a cell encounters stress. Indeed, I observed the decrease in DnaA level when cells were subjected to stressful conditions. As a result of a further set of *in vivo* as well as *in vitro* experiments, I found out that (i) Lon protease degrades DnaA in a PolyP-dependent manner to arrest DNA replication initiation, (ii) Lon-PolyP complex targets only DnaA-ADP, but not DnaA-ATP, (iii) Lon level transiently increases during stringent response, (iv) DnaA binds to its own promoter during stress.

To conclude, I propose a novel pleiotropic mechanism, that I termed SIDDA (Stress-Induced Degradation of DnaA), which governs the inhibition of replication initiation during stress in *E. coli.* Due to the dual function of DnaA, the proteolysis of the selected fraction of DnaA allows for both the inhibition of replication initiation as well as for blocking *de novo* synthesis of DnaA.