

The nucleotide (p)ppGpp is critical for stress resistance in bacteria. In the bacterium *Escherichia coli*, (p)ppGpp interacts with RNA polymerase to reprogram transcription upon stress. However, *Firmicutes*, a major phylum of Gram-positive bacteria that includes many human pathogens, employ a different strategy. Our recent work using the widely studied firmicute *Bacillus subtilis* identified enzymes in GTP biosynthesis pathways as major targets of (p)ppGpp and unmasked a GTP-(p)ppGpp feedback loop that is critical for cell viability. Our work supports a model that, in firmicutes, (p)ppGpp regulates GTP levels to maintain metabolic homeostasis and to allow stress resistance.