MS08-P08 | Bacterial Nucleosidase is regulated by the alarmone (p)ppGpp

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Bacteria are exposed to ever-changing environments and have evolved responsive systems to address this. In times of low availability of nutrients, or the presence of antibiotics, they reduce their growth rate. One way that bacteria signals stress is via the hyperphosphorylated guanosine nucleotides ppGpp and pppGpp, collectively called (p)ppGpp, that have been shown to regulate replication, transcription, translation, and metabolic pathways. PpnN, a pyrimidine/purine nucleotide 5'-monophosphate nucleosidase from *Escherichia coli,* has previously been determined to be able to bind (p)ppGpp.

In our recent publication we were able to show the crystal structures of PpnN, both in an apo form and pppGpp-bound state. When bound to pppGpp it undergoes a dramatic conformal shift, exposing its active site, which we also show translates to an increased catalytic activity. By performing mutations in the pppGpp-binding site we were able to show that loss of pppGpp binding lead to antibiotic sensitivity, but also an improved fitness in competition against other bacteria in a state of abundance. By making a Δ*ppnN*-strain we saw the opposite effect.

We have since then been able to crystallize new forms of PpnN shedding light on the interaction between (p)ppGpp and PpnN, and will expand upon the complexities of bacterial meahcnisms leading to tolerance. This information becomes increasingly important when discussing the emerging threat of multiresistant bacteria, since antibiotic tolerance is a necessary step for the evolution of antibiotic resistance, and that *ppnN* is conserved amongst most Proteobacteria.