TARGETING BACTERIAL PERSISTERS IN THE POST-ANTIBIOTIC ERA

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Persister cells[1] are a dormant bacterial phenotype temporary tolerant to antibiotic treatment; this distinctive trait distinguishes them from well-known genetically resistant variants, and hints their role in chronic and recurrent infections. Inhibition of the intracellular accumulation of guanosine tetra- or pentaphosphate ((p)ppGpp), the triggering event of the signalling cascade that allows bacteria to activate this phenotypic switch (i.e. the stringent response), may prevent the insurgence of persisters and therefore the incomplete sterilization that is often responsible of relapsing infections[2].

In particular, we aim to interfere with (p)ppGpp production by gaining control of the key upstream regulatory proteins RSH (RelA/SpoT-Homologue superfamily, a.k.a. Rel). To this end, we are adopting a multidisciplinary approach, comprising computational studies,[3] synthesis[4] and ligand-protein interaction assays. Our recent insights into the many facets of this problem will be presented.