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.

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[1] K. Lewis, *Annu Rev Microbiol* **2010**, *64*, 357-372.

[2] E. Maisonneuve, K. Gerdes, *Cell* **2014**, *157*, 539-548.

[3] M. Civera, S. Sattin, **2019**, *manuscript in preparation*.

[4] G. Conti, M. Minneci, S. Sattin, *Chembiochem*, **2019**, *20*, DOI: 10.1002/cbic.201900013