High-throughput profiling of drug interactions in Gram-positive bacteria

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1. Drug combinations represent a powerful resource to fight the antimicrobial resistance crisis (Chapter 1, this thesis)

2. Combinatorial complexity limits drug interaction screening attempts. Automated platforms and high-throughput data analysis greatly improve feasibility and efficiency of combinatorial screens (Chapter 2, this thesis)

3. Drug combinations can be used as multiple perturbations of cellular processes, analogously to genetic perturbations. Accordingly, drug interactions and genetic interactions exhibit common features (Chapters 3-4, this thesis)

4. Drug interactions are known to be species-specific since the dawn of the antibiotic era. Drug interaction conservation between two species can be linked to their genomic relatedness and to their different permeability to individual drugs (Chapter 4, this thesis)

5. Even when they have no effect on bacterial growth, non-antibiotic drugs can synergize with antibiotics (or with other non-antibiotic drugs) and provide new therapeutic options against multi-drug resistant bacteria (Chapter 5, this thesis)

6. In the age of polypharmacy, non-antibiotic and antibiotic drugs are commonly co-administered. Non-antibiotic drugs can antagonize antibiotics, potentially hindering their action in real-life infection contexts
(Chapter 5, this thesis)

7. Drug-drug and drug-gene interaction data can be combined to decipher the genetic background of drug interactions, predict novel drug-drug interactions and unveil the function of uncharacterized genes (Chapter 6, this thesis)

8. “General questions never lead to more than limited answers. On the contrary, limited questions have often led to more and more general answers” (François Jacob, “La souris, la mouche et l’homme”)