ACRONYM: **TransPred**

Title: **Predicting cell-cell horizontal transmission of antibiotics resistance from genome and phenome**

Keywords: **Horizontal transmission, antibiotics resistance, conjugation, modelling, Gram negative, experimental evolution, omics**

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Abstract:

We propose to disclose candidate drug targets controlling the horizontal cell-cell transmission of anti-microbial resistance (AMR) and to predict AMR and its transmission dynamics from bacterial genome composition. We will integrate leading expertise from bacteriology, -omics and mathematical biology in the development of an integrated theoretical-empirical framework of plasmid borne transmission of AMR cassettes.

We will employ massive-scale experimental evolution of Escherichia coli and Salmonella enterica gene deletion and overexpression collections, where adaptation requires transfer of AMR carrying conjugative plasmids. In addition, we will select for, identify and functionally dissect de novo mutations that promote horizontal transmission during long-term experimental evolution. Both approaches will disclose cellular functions controlling horizontal AMR transmission that are candidate targets for helper drugs delaying AMR development and spread.

Second, we will sequence vast swaths of the genotype space inhabited by clinical bacterial isolates and disclose variants likely to alter transmission properties. DNA sequence data will be complemented by data on transcriptome, proteome and antibiotics resistance, allowing causally cohesive reconstruction of the history of antibiotics resistance.

Third, we will integrate the omics data into a mathematical framework capable of predicting AMR transmission in clinical isolates, thereby laying the foundations for a future personalized medicine that tailors antibiotic choice to infection.