ACRONYM: **PNEUMOSPREAD**

Title: **Mechanisms for acquisition and transmission of successful antibiotic resistant pneumococcal clones pre- and post-vaccination**

Keywords: **Antibiotic resistant successful pneumococcal clones, transmission, host respiratory microbiome, nasopharyngeal carriage, CRISPR/cas9, in vitro and vivo models**

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Abstract:

AMR in Streptococcus pneumoniae is spread globally by a limited number of clones. PCV vaccination has decreased AMR among vaccine-type strains. AMR now emerges by expansion of non-PCV types. The project focuses on genetic/functional properties of AMR clones with the goal to target their success and transmission in the carrier population.

The goals are to: 1) Perform whole genome based analyses on emerging AMR after PCV introduction, comparing with pre-PCV. Sequence data will be correlated to host factors including clinical patient information. Phylogenetic and general machine learning methods will be applied and a data base will be created to identify microbial traits that link success of AMR to transmission, colonization and ability to cause invasive disease 2) A set of animal models will be used to study transmission, colonization and disease capability of AMR clones. Different endogenous and environmental cues will be applied to these studies by altering host immune defense, by sensitizing with influenza A virus, by exposure to long term antibiotics, and by affecting physical or chemical parameters in the environment 3) Drivers affecting transmission/colonization/invasive disease will be identified using appropriate mutants, and monitoring the influence of the host microbiome using germ free mice 4) Resistance transfer and role of competence pili, conjugative transfer and lack of CRISPR/Cas9 interference will be studied in the presence and absence of a respiratory microbiome 5) Clonal elimination will be attempted in mice models using antigens targeting AMR clones and by generating a CRISPR/Cas9 delivery system for interference of AMR clones during carriage.