

## W0432

**Studies of Antibiotic Resistance in *S. pneumoniae*.** L. Pernot, L. Chesnel, A. Le Gouellec, J. Croizé, T. Vernet, A. Zapun, A. Dessen, O. Dideberg, Microbiology and Molecular Medicine, Medical Faculty-Univ. of Geneva, Switzerland, Microbial Pathogenesis, Yale Univ., New Haven, CT 06511 USA, Inst. de Biologie Structurale, Grenoble, France, Lab. Bactériologie, CHU, Grenoble, France.

The human pathogen *Streptococcus pneumoniae* is one of the main agents causing respiratory tract infections. Clinical isolates of *S. pneumoniae* often exhibit decreased susceptibility towards  $\beta$ -lactams, a phenomenon linked to multiple mutations within the penicillin-binding proteins (PBPs). PBP2x is the first target to be modified under antibiotic pressure. An important polymorphism is found in PBP2x sequences from clinical resistant strains. By comparing 89 PBP2x sequences, we have identified two distinct groups of drug-resistant strains. The first group includes proteins that display high similarity to PBP2x from the resistant strain Sp328. The second group includes sequences in which a signature mutation, Q552E, is found adjacent to the third catalytic motif. We here report the structural and functional analysis of (1) the M339F substitution found in a subset of the first group, originating from highly resistant strains, and (2) of PBP2x harboring the mutation Q552E.

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