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"CARBOHYDRATE-BINDING PROTEINS AS TARGETS FOR ANTI-INFECTIVES: PSEUDOMONAS AERUGINOSA AND ITS LECTIN LECB"

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INM, Leibniz-Saal, Campus D2 5
Host: Prof. Dr. Aránzazu del Campo

Pseudomonas aeruginosa causes a substantial number of nosocomial infections and is the leading cause of death of cystic fibrosis patients. This Gram-negative bacterium is highly resistant against antibiotics and further protects itself by forming a biofilm. Moreover, a high genomic variability among clinical isolates complicates therapy. Its lectin LecB, a carbohydrate-binding protein, is a virulence factor and necessary for adhesion and biofilm formation.[1] We analyzed the sequence of LecB variants in a library of clinical bacterial isolates and demonstrate that it can serve as a marker for strain family classification. LecB from the highly virulent model strain PA14 presents 13% sequence divergence with LecB from the well characterized PAO1 strain. Despite several amino acid variations at the carbohydrate binding site, glycan array analysis showed a comparable binding specificity for both variants.[2] Based on the crystal structures of the lectin with its glycan ligands, we dissected the contributions of individual functional groups to protein binding in a biophysics-guided approach. This knowledge was then used for the development of small and drug-like glycan-based molecules as LecB inhibitors as future anti-biofilm compounds in chronic P. aeruginosa infections.[3-7] In summary, the different LecB sequences serve as marker for strain classification, but due to comparable ligand selectivity, LecB is a highly promising target for anti-virulence therapies, addressing members from both P. aeruginosa families, PAO1 and PA14.

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KONTAKT

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