P1108

Abstract (poster session)

Biofilm formation is a key virulence strategy of Proteus mirabilis during catheter-associated urinary tract infection

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Objective: Catheter-associated urinary tract infections (CAUTI) are the most frequent infections in hospitals and other health care facilities. Proteus mirabilis is the most important pathogen that colonizes the bladder during long-term catheterization. Colonization of the bladder is associated with formation of a crystalline biofilm leading to catheter blockage, stone formation and severe complications for the patient. The relevance of Proteus mirabilis biofilm formation on urethral catheters for CAUTI pathogenicity as well as the mechanisms underlying efficient biofilm formation of Proteus mirabilis are largely unknown. We aimed to identify genetic factors crucial for biofilm formation on urethral catheters. Methods: To identify genetic factors crucial for biofilm formation on urethral catheters, a random mutagenesis approach was applied. 5500 individual Tn5 mutants of Proteus mirabilis HI4320 were evaluated for loss of biofilm formation in a static biofilm model system. In parallel, signature-tagged mutagenesis was used to identify novel virulence determinants of P. mirabilis crucial for colonization of urethral catheters during CAUTI in a dynamic catheterized bladder model in vitro. Attenuated mutants of both libraries were co-challenged with the parent strain in the dynamic catheterized bladder model. Mutants that were significantly outcompeted by the parent strain were identified by sequencing the transposon insertion sites and further tested for growth deficiencies and phenotypes like swarming, hemagglutination, and urease activity. Expression of affected genes during CAUTI infection in vitro was evaluated. Results: Of 7300 mutants, we identified 28 mutants that were significantly outcompeted by the parent strain in the catheterized bladder model, 16 of which were out-competed more than 100-fold for colonization of bladder and catheter, and 10 of which were also attenuated for biofilm formation in a static biofilm model. Swarming was not found to be necessary for catheter colonization. We identified genes affecting MR/P pili synthesis, urease activity, aerobic respiration control, osmolarity control, extracytoplasmic stress, and key metabolic pathways as requirements for P. mirabilis colonization. Discussion: Our results suggest that biofilm formation is a key virulence strategy of Proteus mirabilis and indicate molecular pathways that support Proteus mirabilis biofilm formation, providing therapeutic targets for combating CAUTIs.