Pseudomonas aeruginosa TonB-dependent transporters: *in vivo* expression and relevance

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Pseudomonas aeruginosa is an important opportunistic pathogen. Treatment options become increasingly limited because of rapidly emerging multi-drug resistance. New drugs are urgently needed, but a major problem is to get small molecules across the outer membrane. The *Pseudomonas aeruginosa* genome encodes 36 active transporters that carry out high-affinity binding and energy-dependent uptake of poorly permeating and scarce substrates. These transporters are so-called TonB-dependent transporters (TBDTs) because they require energy transduction from the TonB protein. To determine the relevance of these TBDTs during infection, we used proteomics to quantify 36 different TBDTs in various animal disease models and specimens from human patients. The results show that *Pseudomonas* uses only a small part of its large repertoire of TBDTs during infection. Among those, only a subset is actually required for virulence in mouse infections. *In vivo* functional analyses of mutants lacking multiple TBDTs also question the relevance of *Pseudomonas aeruginosa* main siderophores in virulence. The clinical data reveal tremendous diversity, but also commonalities in *Pseudomonas* nutrient access during human infections. Therefore, TBDTs appear to have an important system-level impact on Pseudomonas *in vivo* physiology and virulence.