

Publication

Urinary Tract Infection: Which Conformation of the Bacterial Lectin FimH Is Therapeutically Relevant?

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)**ID** 3886718**Author(s)** Mayer, Katharina; Eris, Deniz; Schwardt, Oliver; Sager, Christoph P.; Rabbani, Said; Kleeb, Simon; Ernst, Beat**Author(s) at UniBasel** [Ernst, Beat](#) ; [Mayer, Katharina](#) ; [Eris, Deniz](#) ; [Schwardt, Oliver](#) ; [Sager, Christoph](#) ; [Rabbani, Said](#) ; [Kleeb, Simon](#) ;**Year** 2017**Title** Urinary Tract Infection: Which Conformation of the Bacterial Lectin FimH Is Therapeutically Relevant?**Journal** Journal of Medicinal Chemistry**Volume** 60**Number** 13**Pages / Article-Number** 5646-5662

Frequent antibiotic treatment of urinary tract infections has resulted in the emergence of antimicrobial resistance, necessitating alternative treatment options. One such approach centers around FimH antagonists that block the bacterial adhesin FimH, which would otherwise mediate binding of uropathogenic Escherichia coli to the host urothelium to trigger the infection. Although the FimH lectin can adopt three distinct conformations, the evaluation of FimH antagonists has mainly been performed with a truncated construct of FimH locked in one particular conformation. For a successful therapeutic application, however, FimH antagonists should be efficacious against all physiologically relevant conformations. Therefore, FimH constructs with the capacity to adopt various conformations were applied. By examining the binding properties of a series of FimH antagonists in terms of binding affinity and thermodynamics, we demonstrate that depending on the FimH construct, affinities may be overestimated by a constant factor of 2 orders of magnitude. In addition, we report several antagonists with excellent affinities for all FimH conformations.

Publisher American Chemical Society**ISSN/ISBN** 0022-2623 ; 1520-4804**edoc-URL** <http://edoc.unibas.ch/55825/>**Full Text on edoc** No;**Digital Object Identifier DOI** 10.1021/acs.jmedchem.7b00342**PubMed ID** <http://www.ncbi.nlm.nih.gov/pubmed/28471659>**ISI-Number** WOS:000405764900025**Document type (ISI)** Journal Article