Autotransporter proteins (AT) are the biggest family of secreted and outer membrane proteins in Gram-Negative bacteria. These proteins play a major role in pathogenesis as they promote phenotypes such as cell adhesion, toxicity and aggregation, which allow bacteria to resist the effect of antibiotics and immune responses from hosts. ATs consist of an N-terminal signal peptide, a functional α-domain with a linker region and a C-terminal β-domain that translocates the functional domain to the cell surface. The most abundant group of ATs promote cell aggregation and biofilm formation; these surface proteins are known as the AIDA-I-type adhesins. Our research on the adhesin Antigen 43 (Ag43) from uropathogenic Escherichia coli aims at investigating the processing and cell attachment of this AT, as well as defining the structure-function relationships in Ag43 homologues. We expressed and purified the functional α-domain of an Ag43 homologue, E. coli CFT073 Ag43b. The structure of the α-domain of Ag43b was solved, revealing slight structural differences with the previously characterised Ag43a, which can partially explain their different function.

One of the main objectives of this study is to develop an approach to block the function of Ag43. This is being pursued using single-domain antibodies derived from the variable region (vNAR) of a shark antibody known as the IgNAR. Screening of a vNAR phage-displayed library resulted in the identification of two different binders that recognise three Ag43 homologues. This work will provide initial data for future studies on the function and, more importantly, inhibition of this key Autotransporter protein.


Keywords: Autotransporter Proteins, Bacterial Aggregation, vNARs