ABSTRACT

Helicobacter pylori's blood group antigen binding adhesin BabA is an important virulence determinant that helps the bacterium to maintain strong adherence to the gastric mucosa. Here, we successfully cloned and over-expressed the BabA extracellular domain in *E. coli* and revealed its two-domain architecture composed of an α-helical head domain and a coiled-coil stem domain poised to connect to its trans-membrane β-barrel domain.

We solved the X-ray structures of the recombinant BabA ectodomain bound to its natural glycan receptor Lewis b (Le^b). We identified a receptor-binding site located in a small β-strand sub-domain grafted into the conserved head domain and demonstrate the binding of ABO Le^b- antigens depends on a disulfide-clasped loop (Cys189/Cys197) that embraces a key fucose residue in Le^b. We also show that *generalist* binding to ABO blood group antigens versus *specialist* binding to blood group O antigens only, depends on the paired occurrence of a bulky residue in position 198 (Asp/Asn/Leu) combined with Pro in position 199.

We expect the high sequence and structural conservation of the disulfide-clasped loop that binds the Le^b secretor fucose forms an ideal target for the design of structure-based anti-adhesives.