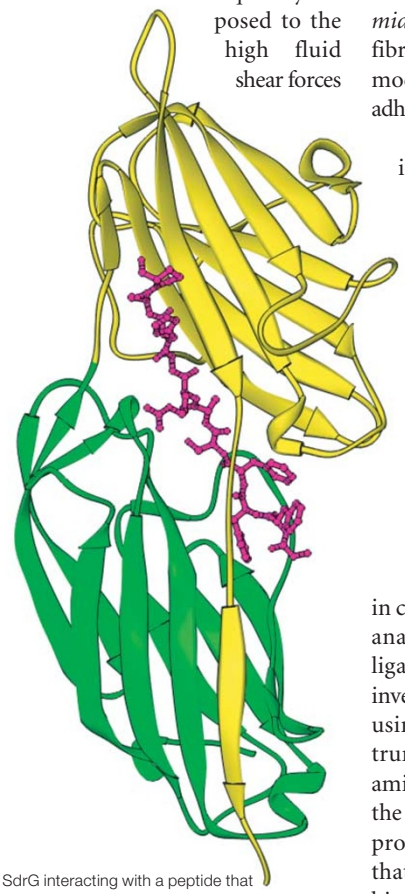
MICROBIAL ADHESION

Dock, lock and latch

The attachment of microorganisms to host tissue represents a first crucial step in most bacterial infections and involves direct interaction between a bacterial surface adhesin and a host ligand. For extracellular pathogens like *Staphylococcus epidermidis*, frequently exposed to the high fluid shear forces present in the bloodstream, a strong, robust interaction is required to initate colonization and ultimately infection. Reporting in *Cell*, Sthanam Narayana, Magnus Höök and colleagues have elucidated the molecular basis for one such interaction — between a cell-wall-anchored protein from *S. epidermidis* (SdrG) and the host protein, fibrinogen — and propose a general mode of ligand binding for related adhesins in Gram-positive bacteria.



SdrG interacting with a peptide that corresponds to its binding site in the human fibrinogen β-chain (residues 6-20; in purple). Courtesy of Sthanam Narayana, University of Alabama at Birmingham, USA.

SdrG is one of a family of bacterial surface proteins that mediate interaction with the host extracellular matrix. Known as MSCRAMMS (microbial surface components recognizing adhesive matrix molecules), this family of adhesins have a similar modular design and an IgG-like folded domain organization, and are implicated as being important for microbial virulence. Ponnuraj *et al.* solved the structure of the ligand-binding domain of SdrG, both as an apoprotein, and in complex with a synthetic peptide analagous to the binding site in its ligand, fibrinogen. They further investigated the binding mechanism using site-directed mutagenesis, truncation mutagensis and peptide amino acid replacement. Analysis of the structure revealed that the SdrG protein has an open conformation that allows access of the ligand to a binding cleft. Following binding of the ligand, a structural rearrangement is induced at the C-terminus of the protein such that access to and from the binding cleft is blocked, and the 'docked' peptide is 'locked' in place. To stabilize the structure, the rearranged C-terminal β-sheet inserts between two β-sheets in an adjacent domain, 'latching' the protein-ligand complex together. Investigation of the interaction using mutant proteins and peptides provided strong support for this multi-step model of microbial adhesion.

The Höök and Narayana groups have also recently solved the structures of the ligand-binding domain of fibrinogen-binding MSCRAMMS from *Staphylococcus aureus*. Investigation of these data in conjunction with a survey of the available genomes of other pathogenic Gram-positive bacteria, revealed the presence of key features of the dock, lock and latch mechanism in a wide variety of MSCRAMM candidates. These anaylses suggest that this interaction mechanism is likely to represent a general mode of ligand-binding in this group of related adhesins from Gram-positive bacteria.

David O'Connell

References and links

ORIGINAL RESEARCH PAPER Ponnuraj, K. *et al.* A "dock, lock, and latch" structural model for a staphylococcal adhesin binding to fibrinogen. *Cell* **115**, 217–228 (2003)

FURTHER READING Foster, T. J. & Höök, M. *et al.* Surface protein adhesins of *Staphylococcus aureus*. *Trends Microbiol.* **6**, 484–488 (1998)

WEB SITES

Magnus Höök's laboratory:
http://www.tamu.edu/cemb/

Sthanam Narayana's laboratory:
http://origin.cbse.uab.edu/faculty_staff/narayana/index.html