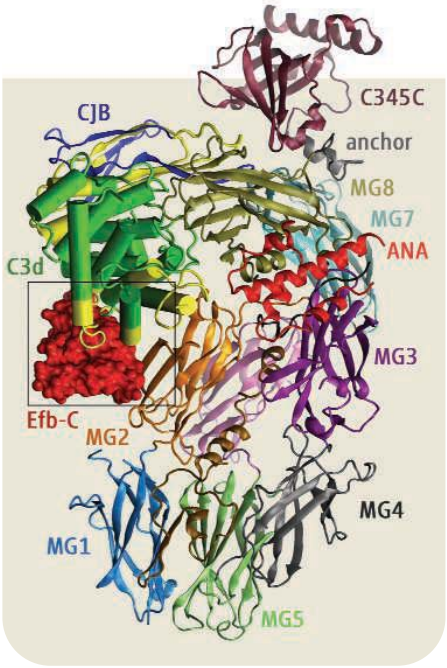
IMMUNOLOGY

A Bacterial Anticomplement



The complement system generates a finely regulated, yet potent antimicrobial response, making it an attractive target for bacterial virulence factors. Most commonly, endogenous regulatory proteins of the complement system are usurped to switch off complement activation, but the widespread human pathogen *Staphylococcus aureus* can inactivate the complement cascade by a more direct means. Previous work has shown that the extracellular fibrinogen-binding protein (Efb-C) generated by *S. aureus* blocks the complement pathway by binding to the thioester-containing domain of the complement C3b protein; indeed, *S. aureus* strains that lack Efb-C display reduced virulence. Hammel *et al.* resolve the crystal structures for the C3-binding domain of Efb-C in its unbound state and in complex with the C3d domain of C3 (shown at right). Structure-based functional studies suggest that native C3 is bound by Efb-C in a way that alters its conformation. As a consequence, conversion to C3b is prevented, and participation in the subsequent activation of the complement cascade is also blocked. As well as binding native C3, Efb-C also had high affinity for C3b, again appearing to induce conformational changes, this time in the already activated form of the complement component. Effective targeting of the interface between Efb-C and the C3d domain by a small molecule could be useful in the treatment of *S. aureus* infection. — SJS

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