The residues in the hydrophobic core of Staphylococcus aureus Fatty acid Kinase B1 determine fatty acid specificity.

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Fatty acid (FA) kinase is a two-component system that produces acyl-phosphate for the synthesis of membrane phospholipids in Gram-positive pathogens. FA kinase consists of a kinase domain protein (FakA) that phosphorylates its fatty acid substrate bound to a fatty acid binding protein (FakB). We report four crystal structures of Staphylococcus aureus FakB1 each bound to different saturated fatty acids (myristate (14:0), palmitate (16:0), anteiso 15:0 and anteiso 17:0). The different FA structures are accommodated within the fluid hydrophobic interior of FakB1 that re-organizes to accommodate the different chain lengths and anteiso branching. The structural reorganization in the protein interior is not propagated to the protein's surface. The conformational rigidity of the FakB1 surface coupled with the flexibility of the FakB1 interior allow it to bind different saturated fatty acid structures while maintaining a constant protein surface to preserve its protein-protein interactions with FakA and the downstream enzymes that utilize FakB(acyl-phosphate) as substrates in bacterial lipid metabolism (PlsX and PlsY).