of clumping factor A from S. aureus [5] and sdrG from S. epidermidis [6]. Crystallographic studies of several ALS family members are under way and good native data has been obtained. ALS proteins require expression in specific E. coli strains that allow formation of disulphide bridges in the cytoplasm [7], critical for correct folding of the proteins. Combined with the low number of methionines present (<1/150aa), the need for strains that are not methionine auxotrophs significantly lowers the possibility of success using Se-SAD/MAD phasing methods. As observed with other IgG superfamily proteins, particularly considering the low sequence homology with available models, molecular replacement has proved difficult. However, a combination of careful model selection, iodide-soaks data and NMR structure information might prove successful, as on-going studies seem to indicate. We are currently working on determining structural models of NT-ALS9 in the apo and peptide-bound forms (data collected at BM14, ESRF, France) that will allow a better understanding of these adhesin family and their binding mechanisms. Studies of other family members, including different constructs and binding assays with a wider peptide range are also on-going. The structural information obtained will provide insights into C. albicans adherence to host cells, shedding light into the mechanisms underlying pathogenicity of this otherwise harmless human commensal.

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Recognition and Activation of the RTK Met by the Bacterial Invasion Protein InlB. Hartmut H. Niemann[a], Davide Ferraris[b], Ermanno Gherardi[c], Dirk W. Heinz[b]. [a]*Department of Chemistry, Bielefeld University, Germany.* [b]*HZI, Braunschweig, Germany.* [c]*MRC, Cambridge, UK.*
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Listeria monocytogenes targets the human receptor tyrosine kinase Met to induce its own uptake into a variety of normally non-phagocytic cells. We investigate the interaction between Met and its bacterial ligand, the listerial invasion protein InlB, using X-ray crystallography and other biophysical and biochemical methods. The crystal structure of the complex in two different crystal forms defines the details of the interaction revealing two interfaces between InlB and Met. The rigid internalin domain of the leucine-rich repeat protein InlB simultaneously binds to two different domains of Met that are separated by a flexible linker [1]. This two-site interaction probably fixes the otherwise flexible receptor in a signaling competent conformation. However, this postulated conformational change upon ligand binding does not fully explain the mechanism of receptor activation. In general, receptor tyrosine kinases are thought to be activated by ligand induced oligomerization. *In vitro*, we have so far not been able to observe Met dimerization upon binding of InlB. Based on different assemblies present in our crystal structures we discuss the structure of the signaling competent, dimeric activation complex.

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Structure and Assembly of a Bacterial Pilus with Stabilizing Isopeptide Bonds. Edward N. Baker[a], Neil Paterson[a], HaeJoo Kang[a]. [a]*School of Biological Sciences, University of Auckland, Auckland, New Zealand.*
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Pili are long, hairlike protein assemblies that extend from a bacterial surface and mediate colonization and pathogenesis. The pili of Gram-positive organisms are formed by covalent polymerization of a major pilin subunit that forms the shaft of the assembly. The crystal structure of the major pilin from *Streptococcus pyogenes* [1] revealed another striking feature in the form of internal covalent crosslinks (isopeptide bonds) formed between Lys and Asn side chains. Intramolecular crosslinks of this kind had never been seen before in proteins. We have solved the 1.6 Å resolution structure of SpaA, the major pilin protein that forms the shaft of the pili expressed by *Corynebacterium diphtheriae*. The structure shows that SpaA is folded into 3 tandem Ig-like domains, two of which contain self-generated isopeptide bonds between Lys and Asn residues. These bonds have been confirmed by mass spectrometry, which has also been used to identify the intermolecular isopeptide linkages in the native pili. The crystal packing reveals long columns of pilin molecules, modeling the assembly believed to occur in the pili. This structure, with that of the *S. pyogenes* major pilin, reveals key principles in Gram-positive pilus structure and stability: both intermolecular and intramolecular covalent crosslinks for strength and stability, and a modular construction that allows the incorporation of other Ig-like subunits into the pilus for specialized functions such as cell adhesion.

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