

**P057** The structure of the C-terminal actin-binding domain of talin

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Talin is a large dimeric protein that couples integrins to cytoskeletal actin. Here, we report the structure of the C-terminal actin-binding domain of talin, the core of which is a 5-helix bundle linked to a C-terminal helix responsible for dimerisation. The NMR structure of the bundle reveals a conserved surface exposed hydrophobic patch surrounded by positively charged groups. We have mapped the actin-binding site to this surface and shown that helix 1 on the opposite side of the bundle negatively regulates actin binding. The crystal structure of the dimerisation helix reveals an anti-parallel coiled-coil with conserved residues clustered on the solvent exposed face. Mutagenesis shows that dimerisation is essential for F-actin-binding and indicates that the dimerisation helix itself contributes to binding. We have used these structures together with small angle X-ray scattering, to derive a model of the entire domain. Electron microscopy provides direct evidence for binding of the dimer to F-actin and indicates that it binds to three monomers along the long pitch helix of the actin filament.