

P043 The structure of the F0F1 double domain of the talin head.
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Talin is a large (270kDa) dimeric protein that couples the integrin family of cell adhesion molecules to cytoskeletal actin. Talin comprises an N-terminal head embedded in which is a FERM domain composed of three subdomains, (F1, F2 and F3) and a C-terminal rod made of amphipathic helical bundles. The talin FERM domain is unique in that it contains an extra 85 amino acids at the N-terminus, and a large extended loop within the F1 subdomain. Here, we report the NMR structure of the first 85 amino acids which we refer to as F0 and show that it adopts a ubiquitin-like fold. We have also determined the NMR structure of the F0F1 double domain. The structure reveals two beta-grasp folds joined by an extensive charged interface. The F1 loop is shown to be unfolded even in the whole FERM domain. Using small angle X-Ray scattering and NMR, a model of the whole talin FERM domain is proposed. The potential role of F0 in integrin activation is currently being investigated.