

P003 Structural studies of ligand recognition by the C-terminus of focal adhesion kinase

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Focal adhesion kinase (FAK) plays a central role in the regulation of focal adhesion (FA) assembly and turnover and integrin mediated signalling. The function of FAK as a key regulator depends on its ability to associate with a variety of signalling molecules. The C-terminal non-catalytic domain of FAK mediates such interactions with other focal adhesion proteins. It is comprised of a flexible region containing proline-rich SH3-binding motifs and the four-helical focal adhesion targeting (FAT) domain, which is implicated in the recruitment of FAK to FAs. In this study a C-terminal fragment (residues 867-1052) of human FAK was used to characterise two distinct binding events: 1) binding of SH3 domains to the most C-terminal proline-rich region (residues 871-880) of FAK and 2) binding of short peptides mimicking paxillin LD motifs to the FAT-domain of FAK. These were followed by a combination of techniques including solution NMR, ITC and X-ray crystallography. The molecular basis of ligand recognition and implications for interactions with other known binding partners will be discussed.