CELL ADHESION

# FAK or talin: who goes first?

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Integrin-containing adhesion complexes mediate cell–matrix interactions and function as signalling platforms during cell spreading and migration. Previous studies have elucidated the protein composition of adhesion sites and the mechanisms by which integrins are activated and interact with the underlying actin cytoskeleton, but the detailed sequence of events leading to the assembly of adhesion complexes remains unclear. Schlaepfer and colleagues now report that the recruitment of focal adhesion kinase (FAK) lies upstream of talin recruitment to integrins, which seems to contradict the sequence of events known so far.

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FAK and talin are two key players in adhesion assembly. Talin is a large cytoskeletal protein that binds integrin cytoplasmic tails and FAK and activates integrins. FAK is a cytoplasmic Tyr kinase that phosphorylates substrates such as paxillin to regulate adhesion dynamics. To study the role of FAK–talin binding at nascent adhesions (formed within 15 min), the authors plated normal and *Fak*$^{-/-}$ mouse embryonic fibroblasts (MEFs) onto fibronectin-coated slides. In normal MEFs, talin and FAK colocalized at nascent adhesions, whereas in *Fak*$^{-/-}$ MEFs talin did not localize to such adhesion sites, although talin levels were normal and nascent adhesions were formed. Interestingly, however, talin localized to more mature adhesions later on, even in the absence of FAK. Thus, FAK appears to enhance early talin recruitment to nascent adhesions.

Talin binds to the cytoplasmic tail of integrins. However, when the authors mutated the talin-binding site on integrin β1 they found that talin associated with FAK and colocalized together with FAK to adhesions. Thus, direct binding of talin to integrin is not essential for talin recruitment to nascent adhesions.

Next, by performing point mutation analysis, the authors identified Glu1015 as a FAK residue required for talin binding. Importantly, talin was unable to localize to nascent adhesions in MEFs expressing a version of FAK mutated at this residue. Moreover, lack of FAK or expression of the FAK mutant led to the accumulation of large adhesions that exhibited slow turnover and impaired cell motility, indicating that FAK–talin binding is important for adhesion turnover, which is required for motility.

Finally, FAK localization to nascent adhesions was found to be independent of talin. Together, these results show that FAK promotes the recruitment of talin to nascent adhesions independently of integrin, and that this is important for adhesion dynamics. Although surprising, as talin is a potent integrin activator and thought to be recruited upstream of FAK, this might reflect a difference between nascent and mature adhesions in terms of assembly–disassembly dynamics.

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**ORIGINAL RESEARCH PAPER** Lawson, C. *et al.* FAK promotes recruitment of talin to nascent adhesions to control cell motility. *J. Cell Biol.* **196**, 223–232 (2012)
**FURTHER READING** Parsons, J. T., Horwitz, A. R. & Schwartz, M. A. Cell adhesion: integrating cytoskeletal dynamics and cellular tension. *Nature Rev. Mol. Cell Biol.* **11**, 633–643 (2010)