

P016 Regulation of adhesion-mediated survival by Focal Adhesion Kinase.

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Focal Adhesion Kinase (FAK) is a non-receptor protein tyrosine kinase that colocalises with integrins in adherent cells, influencing a wide range of biological responses including proliferation, migration and survival. Signalling pathways downstream of FAK that suppress the cells apoptotic machinery have not been fully elucidated although a variety of models have been proposed. Our aim is to explore these pathways through the use of FAK mutants that lack the ability to bind specific effector proteins. Data from FAK C-terminal deletion mutants shows that intact paxillin-binding sites (PBS) are necessary for FAK localisation and survival signalling. Conversely, absence of the proline-rich regions that bind to p130Cas and Graf had little effect on survival. Our data also suggests that survival signalling may not require FAK kinase activity. To complement this approach, we have also generated full-length FAK constructs that contain mutations in the PBS and proline-rich regions. Their localisation and effect on apoptosis in a FAK-null background is currently under investigation.