

## Regulation of Focal Adhesions by PI(4,5)P2 and PI(3,4,5)P3 in Cancer Cells

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### Abstract

Phosphoinositides and their downstream signalling molecules are involved in adhesion, proliferation and invasion. In this study, MDA-MB-231 breast cancer has been used to investigate the possible role of PI(4,5)P2 and PI(3,4,5)P3 in the regulation of FA turnover. Firstly, PI(4,5)P2 and PI(3,4,5)P3 have been visualised by PLC $\delta$ 1-PH-GFP or mCherry and Btk-PHGFP or mCherry respectively. Then, the spatial organisation of PI(4,5)P2 and PI(3,4,5)P3 with FA proteins was directly studied. PI(4,5)P2 and PI(3,4,5)P3 were moderately co-localised with FA proteins, such as talin, vinculin, FAK, paxillin and zyxin. PLC inhibition reduced co-localisation between PI(4,5)P2 and FA, while PI3K inhibition had no effect. Temporal organisation between PI(4,5)P2 and PI(3,4,5)P3 and FAs was studied. The local levels of PI(4,5)P2 within a single FA increased gradually during assembly and declined gradually during the disassembly process. Whereas, PI(3,4,5)P3 levels within FA were almost at a constant level during FA assembly and disassembly. PLC inhibition significantly reduced the decline in PI(4,5)P2 levels within single FA disassembly, while PI3K inhibition had only a small effect. Additionally, PLC and PI3K significantly inhibited FA turnover, cell migration and wound healing. Finally, Co-IP studies showed that PI3K p110 $\alpha$  and PLC  $\beta$ 1 directly associated with vinculin and talin, while PI3K p85 did not interact with them. Reverse co-IP was used to confirm the interaction of PLC and PI3K with FA proteins.

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### Biography

Dhurgham Al-Fahad has completed his PhD at the age 30 years from University of Reading, UK. He is member staff in Al-Yen university at collage of medical and health technology and the head of Optics technology department.

Currently he has a project that uses some extracts such as cannabinoids with chemotherapy that are used as a treatment for type of cancers and what is the cause of spread of cancer in Iraq.