

Title: Regulation of Focal Adhesions by PI(4,5)P2 and PI(3,4,5)P3 in Cancer Cell Migration

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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 δ 1-PH-GFP or mCherry and Btk-PH-GFP 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 α and PLC β 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.



Speaker Biography:

Dhurgham 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. He has two papres in progress for publication. He in collaboration with the professor Falasca at the University of Curtin of Australia and with the Professor Phil Dash at the University of reading in UK. 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.

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