NIH 3T3 fibroblast adhesion to a fibronectin substrate: The role of the arachidonic acid signaling pathway

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Abstract

Cell adhesion to the extracellular matrix initiates a cascade of intracellular signaling pathways via integrin activation. Activation of the arachidonic acid (AA) signaling pathway has been shown to be an important early signaling event in both HeLa and fibroblast cell adhesion. The purpose of this research is to study the regulation of adhesion of fibroblasts to a fibronectin substrate by AA signaling. This dissertation is divided into three specific aims: (1) To investigate how the AA signaling pathway, specifically the lipoxygenase and cyclooxygenase metabolites, leuktriene B4 and prostaglandin E2, respectively, modulate directed cell spreading and migration, using a wound healing model. It was concluded that the differential effects of arachidonic acid metabolites produced by lipoxygenase and cyclooxygenase regulate sequential aspects of fibroblast wound closure *in vitro*, cell spreading in to the wound, cell bridges across the wound and cell migration in to the wound. (2) To investigate how changes in intracellular calcium levels regulate AA initiated cell spreading and migration. It was concluded that the presence of extracellular calcium is necessary for intracellular calcium mobilization. Futhermore, while the epsilon isoform of protein kinase C (PKC) is sufficient to facilitate partial cell spreading in the absence of extracellular calcium, PKC alpha is activated by the influx of extracellular calcium to optimize cell spreading and enable cell migration. (3) To investigate how upstream AA signaling events are linked to downstream activation of PKC. It was concluded that phosphatidylinositol specific phospholipase C activation and diacylglycerol production are intermediary signals linking upstream AA signaling to PKC activation. ^

Subject Area

Biology, Molecular|Biology, Cell|Chemistry, Biochemistry