IL-1 signaling through focal adhesions

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Focal adhesions are very small adhesion plaques on the surfaces of adherent cells that allow them to attach to their underlying protein substrates (Carragher and Frame 2004, *Trends Cell Biol.*). The pro-inflammatory signaling molecule interleukin 1 (IL-1) generates signals as a result of binding to IL-1 receptors. These receptors are enriched in focal adhesions (Arora et al. 1995; *J. Biol. Chem.*). Focal adhesions grow in size as long as the cells can remain adherent to their underlying substrates and this behaviour is influenced by IL-1 (Qwarnström et al. 1991; *PNAS*). If focal adhesions are not allowed to form on the underside of anchorage-dependent cells, IL-1 signaling does not occur (Luo et al. 1997; *Biochem. J.*). The binding of IL-1 to its signaling receptors leads to activation of the mitogen-activated protein kinase ERK (Lo et al. 1998; *J. Biol. Chem.*) and to expression of enzymes like matrix metalloproteinases (MMPs) that break down the extracellular matrix. For IL-1 signaling to occur, not only must the IL-1 receptors be enriched in focal adhesions but the focal adhesions must be of a size that is large enough (> 1 μm^2). We are interested in relating the formation and growth of focal adhesions and the restriction provided by focal adhesions on IL-1 signaling to downstream activation of ERK and expression of collagenase. The data provided show the kinetics of ERK activation and MMP-3 expression in response to IL-1 when cells form different sizes of focal adhesions. In the focal adhesions there are a number of proteins that are both structural and provide important signaling functions. We seek to understand how different focal adhesion proteins, when present or not, affect focal adhesion size and IL-1-related downstream signals.

Background literature

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