

Hypoxia-induced invadopodia formation : a role for β -PIX

ABSTRACT

During tumour progression, oxygen tension in the microenvironment surrounding tumour cells is reduced, resulting in hypoxia. It is well established that cancer cells resist the negative effects of hypoxia by inducing angiogenesis predominantly via the activity of transcription factor hypoxia-inducible factor-1 (HIF-1). However, more recently HIF-1 α has also been linked to increased invasive potential, although the molecular mechanisms remain to be defined. Invasive cancer cells are thought to employ membrane protrusions, termed invadopodia, to achieve matrix degradation. While many invadopodia components have been identified, signalling pathways that link extracellular stimuli to invadopodia formation remain largely unknown. Indeed, the relationship between invadopodia formation and HIF-1 α has not been explored. We now report that HIF-1 α is a driver of invadopodia formation. Furthermore, we have identified an important, direct and novel link between the Rho family activator β -PIX, HIF-1 α and invadopodia formation. Indeed, we find that β -PIX expression is essential for invadopodia formation. In conclusion, we identify a new HIF-1 α mechanistic pathway and suggest that β -PIX is a novel downstream signalling mediator during invadopodia formation.

Keyword: β -PIX; Hypoxia; Invadopodia