The PDZ protein MPP2 interacts with c-Src in epithelial cells

Summary / Zusammenfassung

c-Src is a non-receptor tyrosine kinase involved in regulating cell proliferation, cell migration and cell invasion and is tightly controlled by reversible phosphorylation on regulatory sites and through protein–protein interactions. The interaction of c-Src with PDZ proteins was recently identified as novel mechanism to restrict c-Src function. The objective of this study was to identify and characterise PDZ proteins that interact with c-Src to control its activity. By PDZ domain array screen, we identified the interaction of c-Src with the PDZ protein Membrane Protein Palmitoylated 2 (MPP2), a member of the Membrane-Associated Guanylate Kinase (MAGUK) family, to which also the Discs large (Dlg) tumour suppressor protein belongs. The function of MPP2 has not been established and the functional significance of the MPP2 c-Src interaction is not known. We found that in non-transformed breast epithelial MCF-10A cells, endogenous MPP2 associated with the cytoskeleton in filamentous structures, which partially co-localised with microtubules and c-Src. MPP2 and c-Src interacted in cells, where c-Src kinase activity promoted increased interaction of c-Src with MPP2. We furthermore found that MPP2 was able to negatively regulate c-Src kinase activity in cells, suggesting that the functional significance of the MPP2-c-Src interaction is to restrict Src activity. Consequently, the c-Src-dependent disorganisation of the cortical actin cytoskeleton of epithelial cells expressing c-Src was suppressed by MPP2. In conclusion we demonstrate here that MPP2 interacts with c-Src in cells to control c-Src activity and morphological function.

Publications / Publikationen


Keywords / Suchbegriffe

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