FGF10/FGFR2 signaling induces pancreatic cancer cell movement through actin cytoskeleton remodeling

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ABSTRACT

Background: Fibroblast growth factor (FGF) 10 from stromal cells induces cell migration and invasion through FGF receptor (FGFR) 2-IIIb in pancreatic cancer. Here, we examined the mechanism of cancer cell migration induced by FGF10/FGFR2-IIIb signaling, focusing on morphological changes of the cancer cells.

Methods: Morphological changes of several pancreatic cancer cell lines were examined after treatment with recombinant FGF10 in two-dimensional and three-dimensional cultures. Changes of intracellular actin filament organization were studied using fluorescent phalloidin staining. Microarray analysis was performed to evaluate mRNA expression induced by FGF10, with confirmation by quantitative RT-PCR analysis and immunocytostaining.

Results: FGF10 induced lamellipodial protrusions and branching tubules in AsPC-1 and CFPAC-1 cells, which express FGFR2-IIIb. Phalloidin staining showed that FGF10 promoted actin cytoskeleton remodeling in the lamellipodial region. Microarray analysis detected integrin-α1 and integrin-β1 as possible regulators of actin filament formation by FGF10. Upregulation of mRNA for these genes by FGF10 was confirmed by quantitative RT-PCR and immunocytostaining showed overexpression of the integrins after FGF10 treatment.

Conclusion: These results show that FGF10 induces characteristic morphological changes that lead to cell migration and may be mediated through FGFR2-IIIb and integrin-α1 and β1. Suppression of this signaling may be a novel therapeutic approach in pancreatic cancer.
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