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TGF-β INDUCES INVASIVE PHENOTYPE OF MCF10A HUMAN BREAST EPITHELIAL CELLS

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Transforming growth factor-β (TGF-β), a hormonally active polypeptide found in normal and transformed tissues, regulates cellular growth and phenotyphic plasticity. We have previously shown that H-ras, but not N-ras, induces invasive phenotype in MCF10A human breast epithelial cells. In this study, we wished to examine the effect of TGF-β on H-ras-induced invasion and motility in MCF10A cells by performing in vitro invasion assay and wound migration assay. TGF-β significantly induced invasive phenotype of non-invasive parental MCF10A and N-ras MCF10A cells. Since matrix metalloproteinase (MMP)-2 and MMP-9 play critical roles in cellular invasion, we investigated MMP-2 and MMP-9 activities in TGF-β-treated cells. A prominent upregulation of MMP-2 and a slight increase of MMP-9 were detected upon TGF-β treatment, suggesting that TGF-β-induced invasive phenotype may possibly be mediated by MMP-2 rather than MMP-9. TGF-β enhanced migration of H-ras MCF10A and N-ras MCF10A cells in a dose-dependent manner while it did not affect non-transformed MCF10A cell migration. The data suggest that the stimulatory effect of TGF-β on migration is seen only in cells where the ras signaling pathway is activated but not in the parental MCF10A cells. In order to study the molecular mechanisms under which TGF-β enhances cell migration, activation of ras downstream effector molecules by TGF-β is currently being investigated.

Keyword : TGF-β, H-ras, invasion, MMP, MAPK