[P-10]

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