【P-51】

Role of p38 MAPK in TGF-βInduced MMP-2/-9 Activation

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To address if conversion of TGF-β's growth inhibitory signaling into an oncogenic pathway may occur at the early stage of tumor progression, we investigated the role of TGF-β signaling pathway in phenotypic transformation of MCF10A breast epithelial cells. TGF-β treatment was sufficient to induce migrative and invasive phenotypes in these cells, an important phenotypic conversion during tumor progression. TGF-β rapidly activated ERK-1/2 and p38 leading to up-regulation of MMP-2 and MMP-9. While both p38 and ERKs are required for TGF-β-induced MCF10A cell migration and invasion, TGF-β-induced MMP-2/-9 expression depends on p38 signaling, but is independent of ERKs activity. To investigate how TGF-β and oncogenic H-ras signal transduction pathways interact with each other in the malignant progression of breast epithelial cells, we investigated the role of TGF-β in metastatic potential of H-ras-transformed MCF10A cells. While activation of p38 and ERKs was required for TGF-β-induced cell migration and invasion, only p38 signaling was crucial for MMP-2/-9 up-regulation in H-ras MCF10A cells [Supported by the Korea Food and Drug Administration Grants, KFDA-03092-LIF-000 and KFDA-04092-LIF-002].
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