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Activation of MKK6 Induces Invasive and Migrative Phenotypes in MCF10A Human Breast Epithelial Cells

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Ras expression has been suggested as a marker for tumor aggressiveness of breast cancer, including the degrees of invasion and tumor recurrence. We previously showed that p38 MAPK is a key signaling molecule differentially regulated by H-ras and N-ras, leading to H-ras-specific cell invasive and migrative phenotypes in human breast epithelial cells (Cancer Res.: 63, 5454-5461, 2003). In this study, we further investigated the role of p38 MAPK pathway in the induction of metastatic potential in MCF10A cells as a "gain of function" study. We established stable transfectants of MCF10A expressing constitutively activated mutant of MAP kinase kinase (MKK)-6, the direct upstream activator of p38 MAPK. We show the induction of invasion and cell migration with specific upregulation of MMP-2 in these cells, demonstrating the role of p38 MAPK pathway in the metastatic potential in MCF10A cells. [Supported by a grant (R04-2003-000-10063-0) from the Basic Research Program of the Korea Science & Engineering Foundation]

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