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Induction of Invasive and Migrative Phenotypes by MAP kinase kinase 6 (MKK6) in Human Breast Epithelial Cells

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We previously showed that p38 is a key signaling molecule differentially regulated by H-ras and N-ras, leading to H-ras-specific cell invasive and migrative phenotypes in MCF10A human breast epithelial cells. In this study, we further investigated the role of p38 pathway in the induction of metastatic potential in MCF10A cells as a "gain of function" study. We tested whether the activation of p38 can confer invasive and migrative abilities in MCF10A cells which were originally non-invasive and non-migrative. By transfecting MCF10A cells with constitutively active mutant of MAP kinase kinase (MKK)-6, the direct upstream activator of p38, we established stable transfectant MCF10A cell lines. The results show the induction of invasion and cell migration with a specific up-regulation of MMP-2 in these cells, demonstrating the role of p38 MAPK pathway in the metastatic potential in MCF10A cells. We are currently investigating the transcriptional regulation of MMP-2 gene in p38-activated MCF10A human breast epithelial 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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