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Involvement of p38 mitogen-activated protein kinase in H-ras-induced invasive phenotype and motility

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One of the most frequent defects in human cancer is the uncontroled activation of the ras-signaling pathway. We have previously shown that H-rasm but not N-ras, induces an invasiveness. Here, we show that cell motility was greatly increased by H-ras, but not by N-ras, suggesting that H-ras-induced invasive phnotype involves enhanced cell motility. To unveil the molecular mechanism by which H-ras selectively induces invasive phenotype in MCF10A cells, we investigated whether H-ras and N-ras differentially regulate the ras effector pathways. While both H-ras and N-ras activate ERK-1,2, only H-ras, but not N-ras, effectively activates p38 kinas activity. Activity of JNK-1 was not altered by either H-ras or N-ras. To assess the functional significance of H-ras-activated p38 in inasion, we examined the effect of SB203580, a specific p38 inhibitor and DN p38. Treatment of SB203580 reduced inassive activity and motility of H-ras MCF10A cells. H-ras MCF10A cells were transfection with DN p38, but not DN JNK-1, inhibited cell migration. These results suggesting a possible involvement of p38 in H-ras-induced invasiveness/motility.