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Up-regulation of Matrix Metalloproteinase (MMP)-2/9 by Type I Collagen

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Acquisition of matrix metalloproteinase (MMP) and activity has been reported to be associated with increased migration and invasiveness of cancer cells. We have previously shown that H-ras, but not N-ras, induces invasive and migrative phenotypes in MCF10A human breast epithelial cells. To examine whether differential activation of proMMP-2 by H-ras and N-ras is responsible for the H-ras-specific induction of metastatic potential, we compared the activation of pro-MMP-2 by type-I collagen in H-ras- and N-ras MCF10A cells. Type-I collagen induced MMP-2 activation only in H-ras MCF10A cells but not in N-ras MCF10A cells. Since the activation of proMMP-2 requires multimolecular complex assembly involving proMMP-2, membrane type 1-matrix metalloproteinase (MT1-MMP) and tissue inhibitor of metalloproteinase (TIMP)-2, their expressions were examined in these cells. While endogenous level of TIMP-2 was decreased by type-I collagen in both H-ras and N-ras MCF10A cells, MT1-MMP was selectively induced by H-ras. These results suggest that type I collagen-induced MMP-2 activation in MCF10A cells is H-ras-dependent and that the active species of MT1-MMP expression may be involved in this event.

Keyword: MMP, TIMP, Ras, MT1-MMP