Inositol hexafosfato inibe metástases e invasão no câncer de mama I


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Abstract

BACKGROUND: The anti-cancer agent inositol hexaphosphate (IP6) is an abundant intrinsic component of both plant and mammalian cells. In addition to inducing differentiation and inhibiting growth of numerous cancer cell lines in vitro, IP6 has been demonstrated to prevent and abrogate both primary tumor and metastasis in vivo.

MATERIALS AND METHODS: Using MDA-MB 231 human breast cancer cells, we studied the potential of IP6 to inhibit cell adhesion, migration and invasion, the key steps in cancer metastasis, utilizing the extracellular matrix (ECM) proteins, a culture wounding assay, modified Boyden chambers, immunocytochemistry and zymography.

RESULTS: IP6 treatment caused a 65% reduction of cell adhesion to fibronectin (p = 0.002) and a 37% reduction to collagen (p = 0.005). To determine whether a decrease in cell adhesion leads to a decrease in cell motility, migration assays were performed; IP6 decreased both the number of migrating cells and the distance of cell migration into the denuded area by 72% (p < 0.001). Haptotatic cell migration in a modified Boyden chambers was also reduced in a dose-dependent manner. While cell migration on fibronectin was inhibited by 65% (p < 0.001), migration on collagen and laminin was decreased by 32% (p < 0.01) and 13% (p < 0.05), respectively. Immunocytochemistry revealed the absence of lamellipodia structure in IP6-treated cells as compared to untreated cells, corresponding to a diminished ability of cancer cells to form cellular network as determined by Matrigel outgrowth assay. Likewise, cell invasion also was decreased (by 72% after IP6 treatment, p = 0.001) in a dose-dependent fashion. Additionally, IP6 significantly (p = 0.006) inhibited the secretion of matrix metalloproteinase (MMP)-9 as assessed by zymography.

CONCLUSION: The results of this study show that IP6 inhibits the metastasis of human breast cancer cells in vitro through effects on cancer cell adhesion, migration and invasion.

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