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Melatonin impedes prostate cancer metastasis by suppressing MMP-13 expression

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Abstract

Prostate cancer has high metastatic potential. Men with higher urinary levels of the sleep hormone melatonin are much less likely to develop advanced prostate cancer compared with men with lower levels of melatonin. Melatonin has shown anticancer activity in experimental investigations. Nevertheless, the therapeutic effect of melatonin in metastatic prostate cancer has largely remained a mystery. Analyses of Gene Expression Omnibus data and human tissue samples indicated that levels of matrix metalloproteinase 13 (MMP-13) expression are higher in prostate cancer patients than in healthy cancer-free individuals. Mechanistic investigations revealed that melatonin inhibits MMP-13 expression and the migratory and invasive capacities of prostate cancer cells via the MT₁ receptor and the phospholipase C, p38, and c-Jun signaling cascades. Importantly, tumor growth rate and metastasis to distant organs were suppressed by melatonin in an orthotopic prostate cancer model. This is the first demonstration showing that melatonin impedes metastasis of prostate cancer by suppressing MMP-13 expression in both in vitro and in vivo models. Thus, melatonin is promising in the management of prostate cancer metastasis and deserves to undergo clinical investigations.

Keywords: MMP-13; MT1 receptor; melatonin; metastasis; prostate cancer.

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