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JNP3, traditional medicine, suppresses PMA-induced invasion via the inhibition of NF-kB-dependent MMP-9 expression in MCF-7 human breast cancer cells

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Objectives

Matrix metalloproteinase-9 (MMP-9) plays an important role in invasion and metastasis of cancer cells. In this study, we examined the inhibitory effect of JNP3, a new compound isolated from a traditional Chinese formulation, on PMA-induced MMP-9 expression in MCF-7 human breast carcinoma cells. Because the expression of MMP-9 has been implicated in invasion and metastasis of cancer cells, we also examined for its molecular mechanism on PMA-induced cell invasion and MMP-9 expression.

Materials and Methods

- Isolation of the JNP3 compound from the traditional Chinese formulation
- MTT assay
- Gelatin zymography
- Transient transfection and luciferase promoter assay
- Reverse transcriptase-polymerase chain reaction (RT-PCR)
- Western blot analysis
- Invasion assay

Results and Discussion

In the present study, JNP3 was examined for its potentials on PMA-induced MMP-9 expression in MCF-7 cells with detailed molecular mechanisms. JNP3 significantly suppresses PMA-induced MMP-9 secretion through inhibition of its transcriptional activity. Here we provide evidence showing that JNP3 inhibits PMA-induced MMP-9 secretion and protein expression through inhibition of the NF-kB dependent transcriptional activity of MMP-9 gene via ERK and JNK signaling pathways. Matrigel invasion assay showed that the inhibition of cell invasion by JNP3 is correlated well with inhibition of MMP-9 expression. These results indicate that JNP3 can be use as the potential anti-metastatic and anti-invasive agents. Futhermore, this beneficial effect of JNP3 may expand future clinical researches on the regulation of tumor invasion and metastasis in vivo.

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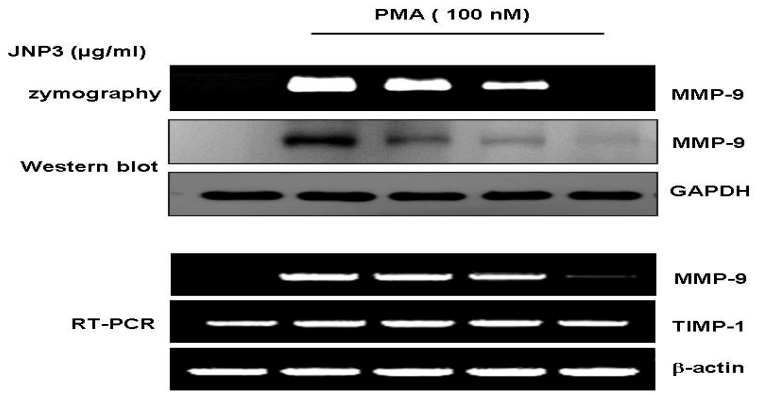

Fig. 1. Effects of JNP3 on PMA-induced MMP-9 activity and expression.

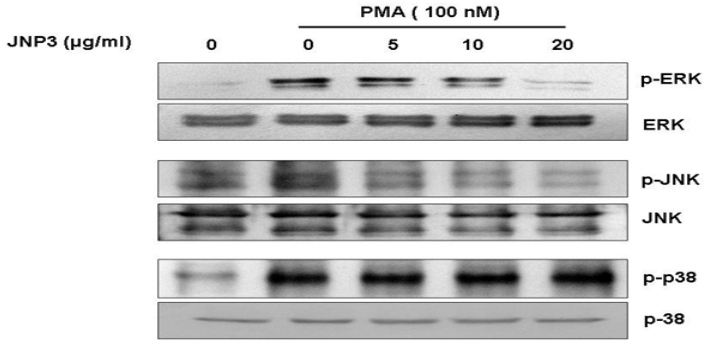

Fig. 2. Effects of JNP3 on the PMA-induced activation of MAPK signaling pathways in MCF-7 cells.

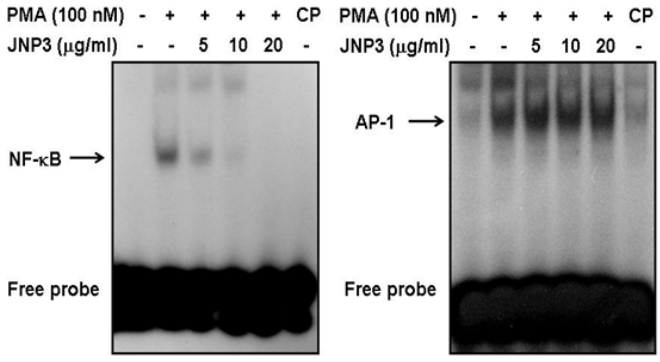

Fig. 3. Effects of JNP3 on the PMA-induced AP-1 and NF-kB activations in MCF-7 cells.