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Antitumor effects of a combination of interferon-alpha and sorafenib on human renal carcinoma cell lines

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ABSTRACT

To support the role of interferon (IFN)-α and sorafenib combination therapy against renal cell carcinoma (RCC), the effects of IFN-α and sorafenib on tumor growth, vascular endothelial growth factor (VEGF) production, and phosphorylation levels of extracellular signal-regulated kinase (ERK) and mitogen-activated protein/ERK kinase (MEK) were examined using several cultured RCC cell lines (ACHN, Caki-1, Caki-2, SMKT-R1, SMKT-R2, SMKT-R3 and SMKT-R4). IFN-α or sorafenib alone inhibited the proliferation of all the cell lines except Caki-2, while combined treatment with the two agents showed enhanced inhibitory effects compared to treatment with each agent alone. VEGF production was inhibited by IFN-α alone in ACHN and SMKT-R2 cells and by sorafenib alone in ACHN, Caki-1, SMKT-R1 and SMKT-R2 cells. However, sorafenib increased VEGF production by Caki-2 cells. Interestingly, combined treatment with the two agents suppressed VEGF production by SMKT-R1 and SMKT-R2 cells more strongly than IFN-α or sorafenib alone. Although phosphorylated ERK (p-ERK) was increased after 30 min of treatment with IFN-α alone, no difference was observed between control and IFN-α-treated cells after 2 h. Sorafenib decreased p-ERK in ACHN, Caki-1, SMKT-R1 and SMKT-R2 cells, but increased p-ERK in Caki-2, SMKT-R3 and SMKT-R4 cells, after 2 h. Combined treatment with IFN-α and sorafenib decreased p-ERK compared to treatment with each agent alone in all cell lines except Caki-2. However, IFN-α did not inhibit the p-ERK increase induced by sorafenib in Caki-2 cells. Phosphorylated MEK

showed similar patterns to p-ERK after the various treatments. In conclusion, combined treatment with IFN-α and sorafenib suppressed cell proliferation and VEGF production more strongly than treatment with each agent alone in several RCC cell lines.

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