Angiotensin II receptor type 1 blockers suppress the cell proliferation effects of angiotensin II in breast cancer cells by inhibiting AT1R signaling.


Source

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Abstract

Chronic stress and a high-fat diet are well-documented risk factors associated with the renin-angiotensin system in the development of breast cancer. The angiotensin II type 1 receptor (AT1R) is a novel component of the renin-angiotensin system. Several recent studies have focused on the function of AT1R in cell proliferation during cancer development. Thus, we hypothesized that angiotensin II (Ang II) can promote proliferation of breast cancer via activated AT1R; the activation of AT1R may play an important role in promoting breast cancer growth, and AT1R blocker (ARB) may suppress the promotional effect on proliferation by antagonizing AT1R. The expression level of AT1R was found to be significantly upregulated in breast cancer cells by immunohistochemistry, but no correlation between AT1R expression and ER/PR/Her-2 expression was observed. The AT1R(+) MCF-7 cell line exhibited high expression of AT1R protein, and we generated the AT1R(-)-MCF-7 cell line using RNA interference. ARBs, and in particular irbesartan, effectively inhibited the effects of Ang II on cell proliferation, cell cycle development and downstream AT1R signaling events, including the activation of the Ras-Raf-MAPK pathway and the transcription factors NF-κB and CREB. Irbesartan also significantly altered p53, PCNA and cyclin D1 expression, which was also influenced by activated AT1R in AT1R(+) MCF-7 cells. These results suggest that ARBs may be useful as a novel preventive and therapeutic strategy for treating breast cancer.

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