Angiotensin II promotes tumor growth and metastatic lesion formation of murine TNBC 4T1 cells through the fibroblasts around cancer cells

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The effect of angiotensin II (Ang II) on metastatic lesion formation and tumor microenvironment were analyzed by in-vivo and in-vitro experiments. Triple negative breast cancer 4T1 cells constitutively expressing luciferase were subcutaneously injected into mammary fat pad of BALB/c mice. Ang II was administered using osmotic pump and valsartan (Val) was administered orally once a day. Four weeks after cell injection, primary tumor was removed for analysis. Lung metastasis was also evaluated by micro-CT imaging and the measurement of luciferase activity. Ang II infusion significantly accelerated the growth of primary tumor and lung metastatic lesion formation, however Val treatment significantly attenuated them. Snail and c-Myc protein expressions were significantly increased in primary tumors of Ang II-infused mice but Val treatment reversed them. However, in vitro, Ang II did not affect proliferation, migration, invasion or protein expressions of 4T1 cells. In contrast, Ang II significantly increased Snail and c-Myc protein expressions when 4T1 cells were co-cultured with dermal fibroblasts. These results indicate that Ang II affects tumor microenvironment to accelerate the tumor growth and metastatic lesion formation.