Angiotensin II stimulates proliferation and metastasis of murine TNBC 4T1 cells by affecting the tumor microenvironment

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Although it is known that tumor microenvironment affects tumor growth and metastasis, the effect of angiotensin II (Ang II) on tumor microenvironment has not been clarified. The aim of this study was, therefore, to examine the effect of Ang II on tumor microenvironment using a murine model of spontaneous cancer metastasis. Triple negative breast cancer 4T1-Luc cells, lacking Ang II type 1 receptor (AT1R) expression, were subcutaneously injected into mammary fat pad of BALB/c mice. After Ang II was administrated for 4 weeks using an osmotic pump, the primary tumor was weighed and analyzed for protein expressions. Metastasis to the lung was also evaluated by micro-CT and the measurement of luciferase activity. The weight of primary tumor and the number of lung colonies and their luciferase activity were significantly increased in the Ang II-treated mice. The expression levels of epithelial-to-mesenchymal transition markers (snail and vimentin) and cell proliferation markers (cyclin D1 and c-Myc) were also increased in primary tumors of the Ang II-treated mice. On the other hand, Ang II didn't alter the proliferation, migration, or infiltration of 4T1 cells *in vitro*. These results suggest that Ang II stimulates cancer growth and metastasis even in 4T1 cells lacking AT1R expression probably by affecting tumor microenvironment. Therefore, the Ang II signaling pathway could be an appropriate target for cancer therapy.