Background: Neoplastic cells, in communication with stromal cells, most notably cancer-activated fibroblasts, initiate a reaction called desmoplasia that causes the proliferation of extracellular matrix components around the primary tumor. This collagen-rich capsule actively inhibits the effective delivery of chemotherapeutic drugs and contributes to the induction of metastasis. Desmoplasia is mediated in part by the renin-angiotensin system through angiotensin-II activation of the angiotensin type-I receptor (AT1R). A second receptor, the angiotensin type-2 receptor (AT2R) has been shown to down-regulate the proliferative activity initiated by AT1R activation. The AT2R agonist compound 21 (C21) has not been previously studied in relation to metastasis and desmoplasia in breast cancer.

Methods: AT2R expression on human mammary fibroblasts (HMF) was visualized by immunofluorescence. The anti-fibrotic and anti-angiogenic potential of C21 were evaluated in HMFs and standard murine fibroblasts (3T3). RNA isolation and cDNA synthesis from untreated and C21-treated HMF and 3T3 cells were performed to determine the relative expression of a number of pro-fibrotic genes including PDGF, TGF-beta, FAP, FSP, SMAD3, SMAD4, and a regulatory gene, SMAD7 via qRT-PCR.

Results: Expression of the AT2R on HMFs was confirmed using immunofluorescence. Treatment with C21 significantly reduced FAP and SMAD4 transcript expression in HMFs.

Conclusions: This study demonstrates that in vitro AT2R is expressed on fibroblasts in the mammary stroma, and that C21 reduces pro-fibrotic gene expression in cell lines. This preliminary data points to the potential use of C21 as a complementary therapy to traditional chemotherapy in the treatment of breast cancer.

Themes:

Check (highlight) the most applicable theme according to the abstract.

- Innovation and Technology
- Health and Wellness
- Culture and Society
- Sustainability and Conservation

Comments: An excellent and well-written abstract!