

## AT1R Blockade and Treatment for Endometrial Cancer

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We were interested in the recent article entitled "Effect of AT1R knockdown on Ishikawa cell proliferation induced by estrogen [1]". In that research, it is tempting to assume that Angiotensin II Type 1 Receptor (AT1R) can promote the proliferation of estrogen-induced Ishikawa human endometrial cancer cell line.

The Renin-Angiotensin System (RAS) includes Angiotensin-Converting Enzyme (ACE), Angiotensin II (Ang II) and AT1R, etc., and plays a critical role in the control of cardiovascular function [2]. Numerous studies in the past several decades have firmly established that RAS blockade prevents the development of cardiovascular disease [3,4]. Recently, AT1R has drawn considerable interest, not only in the field of cardiovascular risk but also in several types of gynecological malignancies, such as ovarian cancer [5,6], cervical carcinoma [5,7] and endometrial cancer [5,8]. Notably, Shibata et al. showed a correlation between the expression of Ang II and AT1R, and poor disease-free survival of endometrial cancer patients [9]. Similarly, Choi et al. suggested that the AT1R blocker losartan has an antiproliferative effect on endometrial cancer cells [10]. The available data indicate that AT1R blockers may be an effective method of treatment for endometrial cancer, but the mechanisms underlying this response remain to be determined. Although accumulating evidence demonstrates that Ang II-AT1R is a key pathway involved in tumor cell proliferation, angiogenesis and metastasis in many human cancers [5], limited published evidence deciphered the role of AT1R in the progression of endometrial cancer.

Yang et al. attempted to observe the effects of AT1R on the proliferation of human endometrial cancer cell line, which is an interesting idea, but there are still many issues that need to be solved. First, it has been known that estrogens can affect the expression and activity of RAS [11]. As such, two types of endometrial cancer (estrogen-dependent and estrogen-independent) should be studied separately. Second, primary endometrial cancer cells are a suitable biological model to study the effects of AT1R in comparison Ishikawa cell lines. Thirdly, there is no direct evidence that estrogen can promote the proliferation of Ishikawa cells through AT1R, rather than via the estrogen receptor [1]. Although several critical questions remain, the study has provided valuable insight into the relationship between AT1R and endometrial cancer, and may be helpful in predicting the etiology of endometrial cancer.

These data correlate with the increasing evidence that AT1R

blockers have tumor-suppressive effects in various experimental models [5]. In addition, AT1R blockers, such as candesartan, valsartan, telmisartan and losartan are effective antihypertensive agents, and may therefore be readily applied in a clinical setting. AT1R blockers may be a novel approach for the treatment of endometrial cancer.

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