The angiotensin II/angiotensin II receptor system correlates with nodal spread in intestinal type gastric cancer. 

We aimed to substantiate the putative significance of angiotensin II receptor type 1 (AT1R) and type 2 (AT2R) for gastric cancer biology by investigating the correlation of their expression with various clinicopathologic variables and patient survival. Local expression of AT1R, AT2R, and angiotensin-converting enzyme (ACE) was investigated by immunohistochemistry in tumor and corresponding nontumor specimens obtained from 100 patients with gastric cancer, and compared with the ACE insertion/deletion gene polymorphism. AT1R and AT2R were found in the tumor epithelial cells of 26 (26%) and 95 (95%) patients, respectively. AT1R was significantly more prevalent (P<0.001) in intestinal type gastric cancer than in diffuse type gastric cancer. In intestinal type gastric cancer, its expression correlated with the N category (P = 0.009) and the International Union Against Cancer tumor stage (P = 0.024). AT1R+ intestinal type gastric cancers had a larger number of lymph node metastases (P = 0.026), a higher International Union Against Cancer tumor stage (P = 0.032), and a shorter survival time (P = 0.009) than AT1R- tumors. Multivariate analysis with lymph nodes as a dependent variable showed that AT1R status and ACE-I/D gene polymorphism are independent risk factors. Irrespective of the genotype, AT1R+ gastric cancers had a relative risk of lymph node metastases.
metastases of 4.40 (95% confidence interval, 1.30-14.86). When the ACE genotype was included, the relative risk of having lymph node metastases increased considerably in AT1R+ tumors being heterozygous or homozygous for the ACE D allele (odds ratio, 19.00; 95% confidence interval, 1.45-248.24). Our study shows that AT1R and AT2R are expressed locally in gastric cancer and that the combination of AT1R expression and ACE I/D gene polymorphism correlates with nodal spread in intestinal type gastric cancer.