Targeting the renin-angiotensin system in gastric cancer therapeutics

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Background

Overactivation of the renin-angiotensin system (RAS) is frequently associated with harmful consequences in various diseases. In the present study, we investigated association between overexpression of the key regulator genes of RAS and overall survival in gastric cancer patients.

Methods

Association between expression levels of key regulator genes of RAS and long-term outcome was investigated by using the web-based gene survival analyzer, Kaplan-Meier Plotter (KM plotter), in gastric cancer patients. Overall survival rates for study cohorts which stratified by best selected expression level of the key regulator genes of RAS including angiotensinogen (AGT) (202834_at), renin (REN) (206367_at), angiotensin converting enzyme-1 (ACE1) (209749_s_at), ACE2 (219962_at), angiotensin receptor-1 (AGTR1) (208016_s_at), AGTR2 (222321_at) and peroxisome proliferator-activated receptor gamma (PPARγ) (208510_s_at) were calculated.

Results

Gene expression and 10-year overall survival were identified for 875 gastric cancer patients. The overexpression of key regulator genes of RAS were significantly associated with increased risk of death AGT (HR=1.55, 95% CI 1.31-1.84), REN (HR=1.33, 95% CI 1.12-1.58), ACE1 (HR=1.85, 95% CI 1.49-2.31), AGTR1 (HR=2.04, 95% CI 1.65-2.51) and AGTR2 (HR=1.72, 95% CI 1.44-2.05) except ACE2 (HR=0.77, 95% CI 0.65-0.92), which attenuates harmful effects of RAS by catalyzing the hydrolysis of angiotensin II. The 10-year overall survival was significantly lower for the cohorts with overexpression of AGT, REN, ACE1 (Figure 1A-C), AGTR1 and AGTR2 (Figure 1E and 1F), while it was significantly higher for cohorts with overexpression of ACE2 (Figure 1D). The PPARγ mediated inhibitory pathway (Figure 1G) could attenuate harmful effects of RAS. The overexpression of PPARγ was significantly associated with reduced risk of death (HR=0.70, 95% CI 0.58-0.85) and associated with better overall survival (Figure 1H).

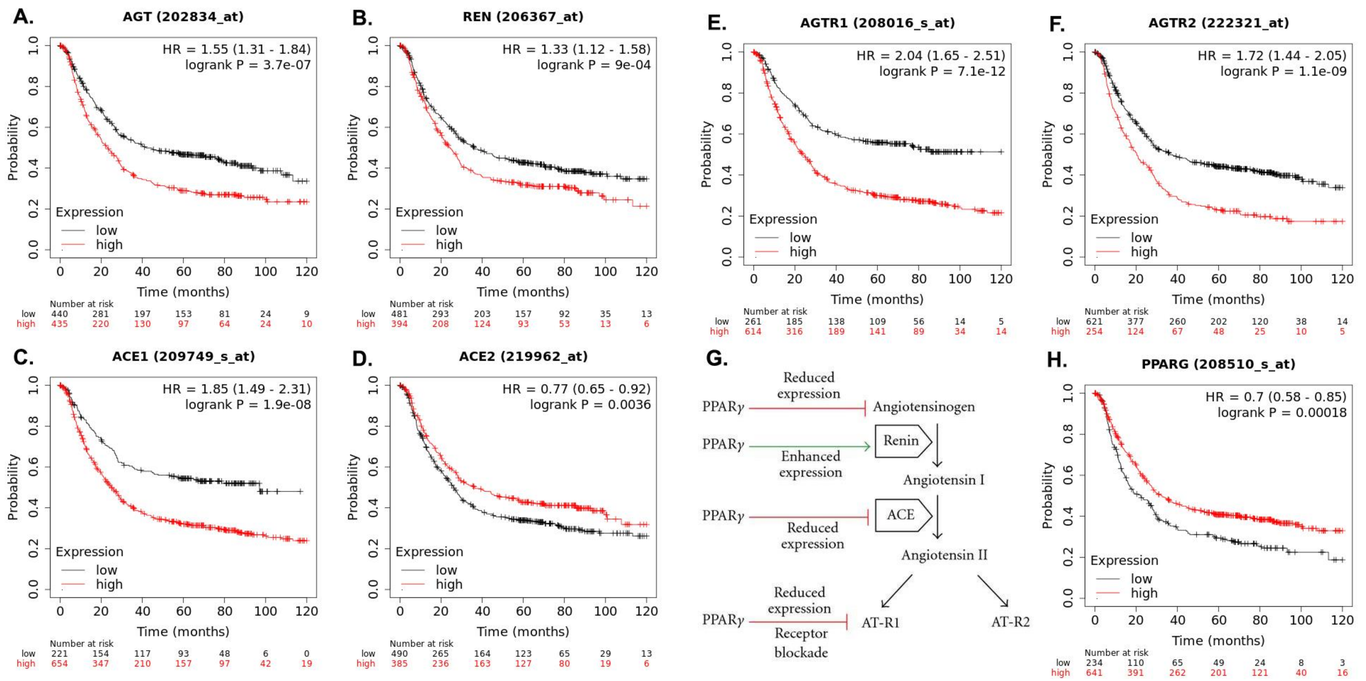

Figure 1. *Overexpression of key regulator genes of RAS and overall survival in gastric cancer patients.*

Conclusions

The overexpression of key regulator genes of RAS are significantly associated with increased risk of death and lower overall survival in gastric cancer patients. While upregulation of PPARγ mediated inhibitory pathways of RAS significantly increases overall survival rate in gastric cancer patients.

Disclosure: Nothing to Disclose