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Combination of trastuzumab and gastrin inhibited growth of HER2-negative gastric cancer

Guo-Hui Fu
Shanghai Jiao Tong University School of Medicine, China

Epidermal Growth Factor receptor 2 (HER2) is expressed in 6%-23% gastric cancer tissues. Administration of Trastuzumab, a fully humanized monoclonal antibody targeted to the HER2, is associated with survival rate in HER2-positive gastric cancer (GC) patients. Gastrin is a major gastrointestinal hormone proven to have an inhibitory effect on GC *in vitro* and *in vivo*. Here, we report the synergistic inhibitory effects of Trastuzumab and Gastrin on HER2-negative GC cells through the Gastrin/Cholecystokinin B receptor (CCKBR) pathway. Trastuzumab upregulated CCKBR protein levels but could not initiate its signal transduction, whereas Gastrin increased the levels and activation of CCKBR. Molecular experiments indicated that Trastuzumab and Gastrin co-treatment synergistically enhanced the stability of CCKBR. Moreover, their combined treatment synergistically arrested GC cells at G0/G1 phase, down-regulated levels of GC-related proteins, including anion exchanger (AE) 1, Cyclin D1, β-catenin and Cytoplasmic p16, and promoted nuclear translocation of p16. In addition, combination treatment upregulated AE2 levels, which are reduced in GC tissues. The *in vivo* synergistic anti-GC effect of combined treatment was confirmed in xenograft experiments. The results demonstrated the synergistic effect of Gastrin and Trastuzumab in the suppression of GC.

Biography

Guo-Hui Fu has completed her MD from Jiamusi Medical College, China and then completed PhD from Harbin Medical University, China and Post-doctoral studies from Kyushu University School of Medicine, Japan. She is the Dean and Professor of Pathology Center, Shanghai Jiao Tong University School of Medicine. She has published more than 81 papers in reputed journals and has been serving as an Editorial Board Member of repute.

fuguhu@263.net, guohuifu@shsmu.edu.cn