Expression of Peroxisome Proliferator-Activated Receptor Gamma in *Helicobacter* Pylori-associated Mouse Gastric Cancer Tissue and Human Gastric Epithelial Cells.

Sang-yeon Oh, Ki-taek Nam¹, Dong-deuk Jang¹, Ki-hwa Yang¹, Ki-baik Hahm² and Dae-yong Kim Department of Veterinary Pathology, Seoul National University

¹National Institute of Toxicological Research, Korea ²Genome Research Center for Gastroenterology, Ajou University School of Medicine, Suwon, Korea E-mail: pearlynn@naver.com

Introduction

Peroxisome proliferator-activated receptor (PPAR) is nuclear hormone receptors that can be activated by a variety of compounds. Two PPAR gamma isoforms are expressed at the protein level in mouse, gamma 1 and gamma 2. And PPAR gamma is intimately associated with cell differentiation and proliferation[1]. So aim of this study, investigated where express PPAR gamma in mouse gastric cancer tissues, including human gastric cancer cell lines and expression pattern of PPAR gamma.

Materials and Methods

To generate stomach cancer, female C57BL/6 mice were treated with N - methyl - N - nitrosourea (MNU) and $Helicobacter\ pylori$. All mice were sacrificed at the 50th week after carcinogen treatment, and histopathology, immuno- histochemistry(IHC), and Western blotting for PPAR gamma was performed. In vitro experiment was performed using gastric epithelial cells and administration of PPAR gamma ligands and H. pylori. Cell viability after drug treatment was assessed by measures of MTT reduction. Detection of apoptosis is using DNA fragmentation.

Results

The pattern of PPAR gamma expression in stomach lesions, which was localized primarily in gastric epithelial cells. PPAR gamma protein was expressed normal gastric epithelial cells, and more highly expressed in gastric adenoma and adenocarcinoma. PPAR gamma protein expression in gastric adenoma and adenocarcinoma was higher than normal mouse glandular stomach. In gastric

epithelial cells PPAR gamma protein expression decreased in treatment of PPAR gamma agonists but in treatment of PPAR gamma antagonist was more highly expressed PPAR gamma protein. In MTT assay and detection of DNA fragmentation shows that PPAR gamma agonists induced apoptosis cancer cells, but not PPAR gamma antagonist.

Discussion

In this study, we confirmed that PPAR gamma protein more highly expressed in gastric cancer tissue. But other study show that in human esophageal cancer tissues, the expression of PPAR gamma was decreased compared normal esophageal epithelium. So, PPAR gamma expression level does not seem to show a consistent tendency, suggesting tissue-specific expression of PPAR gamma[2]. And recently, PPAR gamma agonists are potential chemopreventive agents for colon and prostate cancer [3]. Thus, PPAR gamma agonists may be the target for the prevention or treatment of gastric cancer.

References

- Gupta, R. A., Polk, D. B., Krishna, U., Israel, D. A., Yan, F., DuBois, R. N. and Peek, R. M. Jr. J. Biol. Chem. 2001, 17, 31059-66.
- Segawa, Y, Yoshimura, R., Hase, T., Nakatani, T., Wada, S., Kawahito, Y., Kishimoto, T. and Sano, H. Prostate. 2002, 1, 108-16.
- Terashita, Y., Sasaki, H., Haruki, N., Nishiwaki, T., Ishiguro, H., Shibata, Y., Kudo, J., Konishi, S., Kato, J., Koyama, H., Kimura, M., Sato, A., Shinoda, N., Kuwabara, Y. and Fujii, Y. Jpn. J. Clin. Oncol. 2002, 32, 238-43.