

TITLE: TRAIL, DR4, AND DR5 GENE EXPRESSION: APOPTOSIS DYSREGULATION AND GASTRIC TUMORIGENESIS

AUTHORS: GATTI, LL.;¹ PEREIRA, JN².; SANTOS MP².; BARBOSA³, RASMUSSEN, LT^{1,2}

INSTITUTION: ¹ Centro Universitário das Faculdades Integradas de Ourinhos, Ourinhos, SP (Rodovia BR-153, Km 338 S/N Água do Cateto, Ourinhos - SP, 19909-100), ² Faculdade de Medicina de Marília, Marília. SP (Av. Monte Carmelo, 800, Marília SP, 17519-030) ³ Universidade Federal de Goiás (Av. Esperança, s/n - Chácaras de Recreio Samambaia, Goiânia - GO, 74690-900)

ABSTRACT:

Helicobacter pylori (*H. pylori*) is one of the main causes of gastric diseases including Gastric Cancer (GC), which is one of the leading causes of cancer deaths worldwide. In addition to *H. pylori* infection, deregulation of apoptosis process can be a risk factor for cancer. *TNF-related apoptosis-inducing ligand* (*TRAIL*) is responsible for promoting apoptosis by binding to its Death Receptors *TRAIL-R1* (*DR4*) and *TRAIL-R2* (*DR5*). *TRAIL* is selective to neoplastic cells; however, these cells can present resistance to this pathway, especially GC cells. We aimed to evaluate the expression level of *TRAIL*, *DR4*, and *DR5* along with the presence of *H. pylori* in patients with dyspeptic symptoms and GC, to identify the influence of these pro-apoptotic genes in the gastric tumorigenesis. *H. pylori* was detected using PCR, and gene expression analysis was performed by real-time quantitative PCR. The patients were divided in groups according to histopathological analysis (Control, Gastritis, and Cancer groups). Of the 244 gastric biopsy samples analyzed, 103 tested positive for the bacterium, which was most prevalent in the Cancer group (73.1%). *DR4* and *DR5* genes were overexpressed in the Cancer group compared to the Control ($p = 0.0007$) and Gastritis ($p < 0.0001$) groups, whereas the *TRAIL* gene was less expressed when comparing the same groups ($p < 0.0001$). Our results indicate that GC cells express high levels of *DR4* and *DR5* in attempt to stimulate apoptosis while expression of *TRAIL* is decreased in the same type of cancer, confirming the resistance of this cancer to apoptosis via *TRAIL*.

Keywords: *Helicobacter pylori*, gastric cancer, TRAIL, DR4, DR5

Development Agency: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) (Grant Nº. 2018/0848-1)