

## THE ROLE OF MICROBIOTA ENTEROTOXIGENIC *BACTEROIDES FRAGILIS* IN ETIOLOGY OF COLORECTAL CANCER

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**ABSTRACT :** In a search to detect a relation between the gut microbiota with colorectal cancer; this study aims to find a link of microbiota Enterotoxigenic *Bacteroides fragilis* (ETBF) in the colorectal cancer (CRC) tissues along with its relation with other clinical-pathological variables. The presented research utilized quantitative real time polymerase chain reaction (qRT-PCR) technique for the purpose of revealing constant of ETBF abundance in normal and CRC tissues; along with its association with other clinical-pathological variables (gender and age). The study results confirm that ETBF has been considerably higher in CRC tissues of patients in comparison to controls collected from adjacent normal tissues of the same patients and the tissues of another healthy individuals. The results indicated enrichment in ETBF in CRC samples using qRT-PCR technique. No significant association was found between ETBF with other clinical-pathological variables (age and gender), whereas it was highly elevated in CRC tissues; this may be considered as a hazard factor for the growth of metastasis and CRC.

**Key words :** Colorectal cancer, Enterotoxigenic *Bacteroides fragilis* (ETBF), qRT-PCR.

### INTRODUCTION

Globally, CRC is considered to be the 3<sup>rd</sup> major cancer, with about 1.4 million new conditions identified in the year 2012 (Ferlay *et al*, 2015). Based on the statements of the Ministry of Health (2012, 2013, 2014) New Zealand experienced one of the most elevated rates per capita of colorectal cancer, with median yearly standardized rate per 100,000 for males of 55.2 (range, 50.8 – 56.2) and for females 44.1 (range, 42.5 – 45.0). Most CRC conditions (>90%) are considered to be sporadic and follow a pattern that could be expected from an as however unknown environmental sources. The present reasoning regarding the carcinogenesis hypothesizes, indicate that the cancer is originated from sequence of events which consist of pathogenic stimulus, for example, a bacterial infection, and after that by chronic inflammation, that result in variations in cellular micro-environment, causing pre-cancerous and ultimately cancerous changes (Brücher and Jamall, 2014). In the condition when the presented hypothesis is true, most of cancer's indicated genetic findings are considered to be epiphenomena or late events which happen following precancerous stage, which increase the risk of cancer

development by secreting bacterial toxins via toxin-mediated DNA spoilage (Wu *et al*, 1998; Wu *et al*, 2006). Also by expression of chemokines and cytokines (pro-inflammatory) (Ismail *et al*, 2003). There are two molecular subtypes related to the anaerobic *Bacteroides fragilis*: enterotoxigenic *Bacteroides fragilis* (ETBF) and nontoxigenic *Bacteroides fragilis* (NTBF); *Bacteroides fragilis* (*B. fragilis*) is related to the intestinal tumors and intestinal inflammation because of the enterotoxin production (Ignacio *et al*, 2015; Kim *et al*, 2002; Weikel *et al*, 1992). ETBF strains considered to be enteric pathogen that is currently proved as a source of diarrheal disease in animals and human (Sears, 2009). ETBF's pathogenicity is consequent to *B. fragilis* toxin (BFT; also referred to as fragilysin), a 20 kDa zinc-dependent metalloprotease toxin with 3 isotypes (BFT-1, BFT2 and BFT3) and *bft* gene is unrivaled, only identified in *Bacteroides fragilis* (Sears, 2009). The BFT join to a specific epithelial receptor of colon, which activate Wnt and NF-κB signaling pathways through splitting of cell adhesion and tumor suppressor protein (E-cadherin) (Kim *et al*, 2005; Sanfilippo *et al*, 2000; Wu *et al*, 1998). Hence, a morphological cell alterations, activation of signaling