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EC GASTROENTEROLOGY AND DIGESTIVE SYSTEM

Perspective

The Possible Role of Microbiome in Gastric Cancer: Perspectives

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Background

A microbiota is an "ecological community of commensal, symbiotic and pathogenic microorganisms" [1] found in and on all multicellular organisms studied to date from plants to animals. In the human intestine, the microbiome comprises about 100 trillion of microorganisms attributable to 500 - 1000 different species, including bacteria, archaea, protists, fungi and viruses [2]. The microbiome lives in symbiosis with the host metabolizing the residues that the human cannot use and controlling an accurate equilibrium of the immune system. Furthermore, it can be considered an environmental component to which we are continually exposed to high doses throughout life. However, the composition of microbiome may vary based on certain factors, such as diets, lifestyle changes and nutrition, and is involved in the development and progression of certain tumors, affecting patients' response to cancer treatments [3].

In recent decades the Microbiome is taking a decisive role in the medical field and, in particular, in the new immunotherapies that aim to strengthen the immune system by making it recognize a tumor, be able to attack it and, consequently, to eliminate it. The human body possesses a large number of microorganisms that influence the susceptibility of cancer both through their prodigious metabolic capacity and for their profound influence on the function of immune cells. Microbial pathogens develop carcinogenesis in 15 - 20% of cancer cases, but an even greater number of malignant tumours are associated with the altered composition of the commensal microbiome. Some studies have shown that microbiome can alter the susceptibility and progression of cancer through different mechanisms. This opens up the possibility of considering the microbiome a risk factor in the development of cancer but, it remains to be determined whether the changes of the microbiome contribute to the onset of the tumor and its progression, or if they are consequence of the disease. Therefore, a possible relation of the microbiome is being established in the development of gastric cancer and, therefore, with *Helicobacter pylori.* Gastric adenocarcinoma is the third cause of cancer-related death globally, with more than 700,000 deaths per year; nearly all of these cases are attributable to *H. pylori* up to 89% [4].

Discussion and Conclusions

The symbiotic relationship between microbiome and the human host is very complex and is largely beneficial but, at times, detrimental to human health. Modifications in the lifestyle cause variable change in the composition of the microbiome between different people and some disorders, such as deregulation of metabolism and inflammation, are particularly relevant since they are recognized as characteristics of cancer [5]. Some studies also provide that microbiome can alter the susceptibility and progression of cancer through different mechanism, such as the modulation of inflammation, the induction of DNA damage and the production of metabolites within the oncogenesis. Nonetheless, recent studies have shown that microbiome can support the immune system in the fight against carcinogenesis: intestinal microbes sometimes respond by promoting growth and the creation of immune cells. The impact of microbiome on cancer treatment has simply begun to be studied but it could lead to a revolution in the medical field.

There is a growing evidence of the key role of the microbiome, principally of the dysbiotic, in the development of gastric cancer [6-8] (Figure 1). The role of the Altered Schaedler Flora with the colonization of H. pylori in the promotion of gastritis and dysplasia *in vitro* has been demonstrated [9]. Recently, it has been described that the bacteria included in the progression of pre-neoplastic gastric lesions are *Peptostreptococcus stomatis, Dialister pneumosintes, Streptococcus anginosus, Parvimonas micra, and Slackia exigua* [10]; and *Clostridium colicanis* and *Fusobacterium nucleatum* are present in the gastric tumor microenvironment [11]. The possibility has arisen that the interaction of the gastric microbiota may play a role in the different ratios of development of gastric cancer, even in populations with the same high prevalence of *H. pylori* [12].

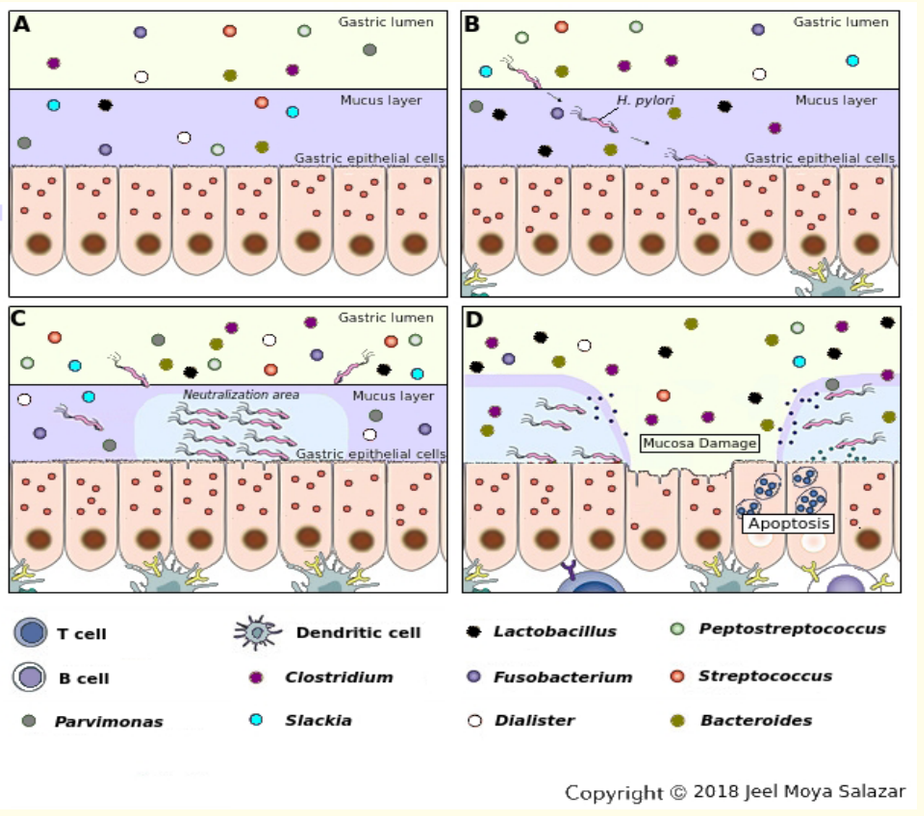

Figure 1. *Interaction model between microbiota and Helicobacter pylori in predisposing the gastric mucosa for the development of cancer. A. In the H. pylori-free stomach, the gastric microbiota coexists in harmony with the gastric mucosa. B. Initial colonization by H. pylori promotes communication with the gastric microbiota. C. After a long time of co-infection and co-colonization, plus the presence of risk factors that determine the gastric dysbiotic, atrophy and inflammation of the gastric epithelium occurs, increase of the pH, and innate immune response that generates changes in the acquisition of nutrients, metabolism and survival of members of the normal microbiota, and however expansion and development of other species (like a Clostridium, Lactobacillus, Peptostreptococcus, Bacteroides, etc.) that promote the progression of pre-neoplastic lesions. D. During the development of the disease the normal ecological niche is lost, and the presence of species that favor this inflammatory state and of constant H. pylori infection, cellular atrophy and mucosal damage persist with the possibility of cancer development.*

Diet plays a distinctive factor among populations throughout the world. The diet has been related to the gut and gastric microbiome with a progressive greater thoughtfulness in recent years [13]. Having so many populations with different diets, even within the same city, and that diets are "moving" between communities due to globalization, with a potential to change the organic balance is something that we should consider in this text. The Hispanic/Latinos, just as the Hindus, have aphrodisiac diets that include products such as chili. The interaction with these elements of the diet have recently been evaluated demonstrating implications in the microbiological homeostasis, and therefore, in the health of the individuals [14-16]. From diets with only the consumption of a food to the use of multiple gastronomic mergers are important to understand the possible microbiological change, and its implications in populations increasingly interested in these foods. We believe that a study on microbiome and gastric cancer should be developed in Peru, mainly in the north of the country, where the prevalence of *H. pylori* and gastritis is significant [17]. We postulate that the diet high in chili peppers (of these subjects) and other foods (high consumption of carbohydrates and sugar) typical of this region are promoting the progressive development of gastric cancer, where the microbiota can play a key role.

Faced with this new and growing conception about the implications of bacteria in gastric homeostasis, the future looks towards the development of treatments that include the use of microbe-based therapies [18,19], especially in countries with poor health-care systems and high-mortality rates due to gastric cancer. In Latin America, for example, the highest incidence of cancer was seen in Chile, Costa Rica, Colombia, Ecuador, Brazil, and Peru [20]. However, these rates not only occur in low-income countries, they also occur within high-income countries and between population groups [21,22]. Hence, gastric cancer becomes a cosmopolitan problem that requires the attention of governments.

In summary, there is enough evidence to relate *H. pylori*, which causes almost all cases gastric cancer worldwide, to the gastric microbiota in the development and progression of gastric cancer. Being a global problem, gastric cancer must remain evaluated to understand its development and to establish, therefore, prevention actions at all health-care levels. Likewise, populations with their own socio-cultural and nutritional patterns should be evaluated; in our opinion, each idiosyncratic action causes a different interaction of the host gastric microbiome with *H. pylori* and its environment.

Author Contributions

All the authors contributed to this paper.

Conflict of Interest

There are no potential conflicts of interest.

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