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Prevalence of *Mycoplasma hyorhinis* contamination in tissues samples from cancer patients : A Brief Report

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ABSTRACT

Infectious agents cause 15-20% of cancers worldwide. The contamination of infectious agents may be caused by a local chronic inflammatory response or tumorization. Mycoplasma contamination can interfere with biological agents and cause DNA damage which affects gene expression, disrupts the cell-cycle control and apoptotic responses. Mycoplasmas are widely distributed in nature; some mycoplasmas have the ability to penetrate into the cell and cause sever disease. Most mycoplasmas are known to infect the cell culture media, which is difficult to detect the contamination.

M. hyorhinis is one of the main reasons the Mycoplasma contamination in tissues samples from cancer patients. Mycoplasma is related to human cancers and some other human diseases. Several studies have shown that *M. hyorhinis* potentially plays a role in esophageal, gastric, lung, breast, glioma, colon, and prostate cancers. The prevalence of *M. hyorhinis* in various tissues leads to cancer progression. Therefore, it is necessary to pay more attention to this mycoplasma agent in order to control and understand its mechanism.

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Introduction

Infectious agents cause 15-20% of cancers all around the world (1,2). The contamination of infectious agents may be caused by a local chronic inflammatory response, or by tumorization through viral or bacterial protein products (3-5). Different types of infectious agents have been identified for various cancers (6). Mycoplasma contamination can interfere with biological agents and cause DNA damage which affects gene expression, disrupts the cell-cycle control and apoptotic responses (7-9). *M. hyorhinis* can increase the invasion and migration of prostate epithelial cells which is associated with arthritis, cervicitis, infertility and human cancer that is a common contamination of stem cells (10–14). *M. hyorhinis* belongs to the class Mollicutes that are small and wall-free. In the 1960s, the first study has reported the association between mycoplasma infection and leukemia (15).

It has been reported that *M. hyorhinis* is the most usual contamination of cell cultures in association with human cancers, such as (esophageal, gastric, lung, breast, glioma, colon cancer, and prostate) (10, 16-17). Namiki and colleagues reported the occurrence of *M. hyorhinis* infection in malignant of the benign human prostate (BPH-1) in cell culture (10, 17-18). Besides, Urbanek and his colleagues, using serological test showed positive tests of *M. hyorhinis* for more than

thirty percent benign prostatic hyperplasia (BPH) and more than fifty percent prostatic cancer tissues (19). Moreover, these bacteria are able to increases the cell migration and cell invasion of gastric cancer cells and melanoma cells (10, 16-17).

Dong and his research group in 1980 performed studies on monoclonal PD4 antibody via mice immunization with the gastric cancer cell, then the mycoplasma antigen was detected by PD4, which is a lipoprotein of *M. hyorhinis* called P37 and does not have any homology with human proteins (17-21).

In a study by Huang et al., using this antibody for immunohistochemistry, the prevalence of the mycoplasma species was evaluated in tissues, the prevalence of this bacterium was more than fifty percent in gastric cancer, twenty-eight percent in chronic superficial gastritis, thirty percent in gastric ulcer and thirty-seven percent in intestinal metaplasia. However, in colon cancer, the prevalence was fifty percent but 20% reported in the adenomatous polyp, which showed the increased prevalence of *M. hyorhinis* as a disease progressive (16).

The study of Duan displayed that this mycoplasma infection depends on the interaction of p37 protein, which is a major membrane protein of *M. hyorhinis* and host ANXA2 through the N-terminal. Also, polyclonal antibodies can block p37 and cause decreasing contamination and promoting the migration of *M. hyorhinis* from the gastric cancer cell, respectively (22).

Studies have shown a direct interaction between the mycoplasma contamination and cancer metastasis such that p37 invasion and metastatic gastric cancer cells will increase both in vitro and in vivo (19, 23).

M. hyorhinis in different tissues

Information related to data collection from different cancer registries via *M. hyorhinis* have been published in various articles (Table1). In 1995, in their first study, Sasaki et al. reported a high prevalence of mycoplasmas in tumor tissue and found 48% of gastric adenocarcinoma samples infected by *M. hyorhinis* (24). In 2001, Huang and colleagues conducted a large screening of different cancer tissues using IHC and reported the rates of *M. hyorhinis* infection that was 40-53% in the lung, breast cancer, esophageal and glioma tissue samples. Atogether, increased mycoplasma infection ratios were detected in gastric carcinoma (56%) compared with other gastric diseases (28-37%, depending on the pathology), and colon carcinoma (55%) in comparison to tissue derived from adenomatous polyps (21%). Importantly, the authors found that *M. hyorhinis* infection significantly increased in well-differentiated tissues compared with poorly differentiated tissues whereas the most studies report the increased mycoplasma infection in high versus low-grade samples (16).

In 2010, the statistical analysis of Yang's study indicated that the presence of *M. hyorhinis* was 64% in gastric cancer tissues and significant relationship was observed among Mycoplasma infection. By increasing EGFR and ERK1 / 2 phosphorylation, *M. hyorhinis* can probably promote the migration of tumor cells, invasions, and metastases in vitro and in vivo. The migration of infected cells can be inhibited by an antibody against the *M. hyorhinis* p37 protein (17).

In 2010, Elisabetta Mariotti et al. reported the cancer cells infected by *M. hyorhinis* and there was the highest number of CD133+ cells compared to the same cells, whereas they were not effective when exposed to the antibiotic treatment. Their results showed when M. hyorhinis caused infection the percent of CD133 positive cells increased.. Therefore, *M. hyorhinis* infection plays an important role in the quality of human colon cancer cell lines, leading to false positives in the expression of cancer stem cells, which presents the expression of CD133 (25).

The Mycoplasma infection was compared in prostate biopsies from healthy individuals and BPH patients, patients with elevated PSA levels, high-grade prostatic intraepithelial neoplasy (HGPIN) and prostate cancer. Patients with prostate cancer or HGPIN indicated an increase in seropositivity for *M. hominis* and *M. hyorhinis* antibodies compared with individuals suffering from BPH (19, 26-27).

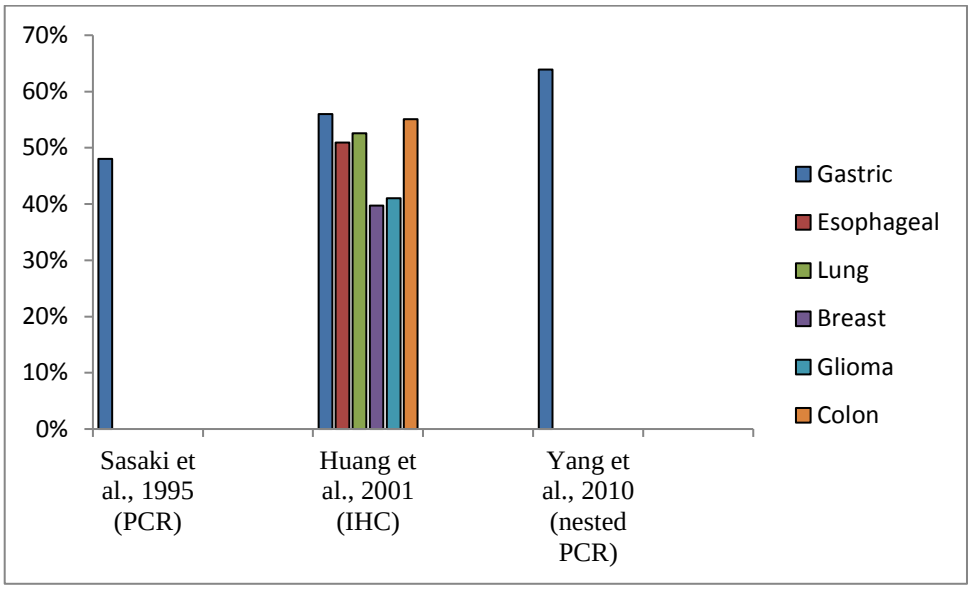

Figure 1: Prevalence of *M. hyorhinis* in tissue samples from cancer patients

Conclusion

The prevalence of *M hyorhinis* in various tissues leads to cancer progression in patients with cancer. Therefore, it is necessary to pay more attention to this mycoplasma agent in order to control and understand its mechanism.

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