Dear Editor,

we received Your communication where You inform us on that the Submission Reference #: 79724 "*The microbiota revolution: How gut microbes regulate our lives*", a requires some additional minor revisions before publication in the World Journal of Gastroenterology.

We thank the Editor and Reviewers for the considerable attention and the valuable comments that certainly helped us to improve the quality of the present paper. We have revised the manuscript according to the referee's comments.

Please let us know if the revised paper satisfies requirements for publication.

Thank you very much for your attention and courtesy.

Yours Sincerely,

Luigi Santacroce

REVIEWERS' 1 COMMENTS:

SPECIFIC COMMENTS TO AUTHORS

This work is summarized comprehensively enough. I have two comments: 1. It is better to make Abstract summarize of the entire article. 2. It is better to show more figures or tables in the manuscript.

R

R: We thanks the Reviewer for her/his suggestion. The Abstract section was revised and improved, as well additional figures were added, according to referee's comments. Thank you.

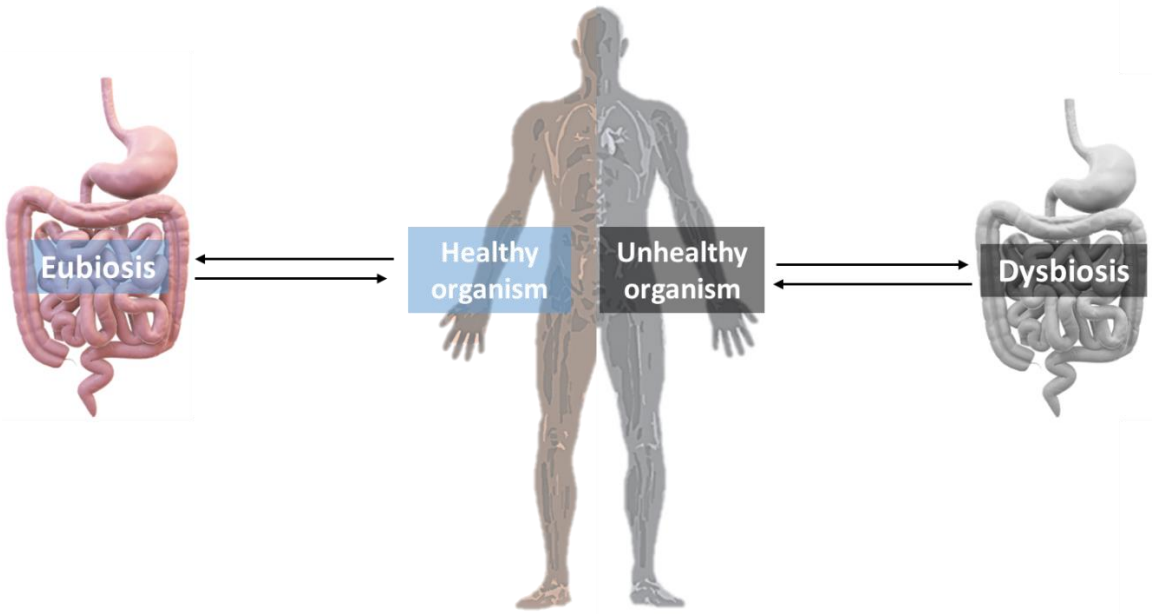

Figure 1. The cross-talking axis host/gut microbiota: The gastrointestinal microbiota plays an important role in host physiology, metabolism, and nutrition. An organism with a regular maintenance of the physiological homeostasis leads to eubiosis of the gut microbiota and vice versa. Conversely, an altered physiological homeostasis leads to gut microbiota dysbiosis and vice versa. An alteration in the gut microbial community is linked to several disturbances gut conditions, including cancer, obesity, and a variety of gut disorders. The contribution of beneficial components

of the gut microbiota to host physiology, metabolism, and immune function has become the focus of scientific research and will undoubtedly lead to new therapeutic approaches.

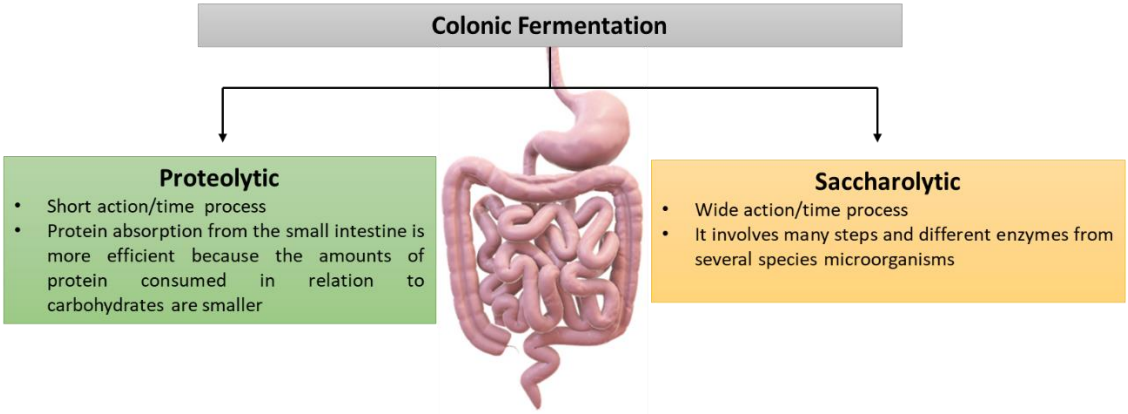

Figure 2. The metabolism activity by the colonic microbiota. The intestinal microbiota finds an environment rich in polysaccharides which are not digested by stomach enzymes. Fermentation of polysaccharides by intestinal bacteria leads to the production of acetate, butyrate, and propionate, which are used as a carbon source by intestinal mucosal cells. The initial fermentation of the carbohydrate that escaped digestion in the small intestine is followed by the utilization and cross-distribution of metabolites by various members of the microflora, and then the synthesis of short-chain fatty acids (butyrate, propionate, acetate). Proteolytic fermentation differs from saccharolytic fermentation because it releases many potentially toxic nitrogen and sulfur metabolites, such as ammonia, amines, nitrates, nitrites, and hydrogen sulfide [32,40].

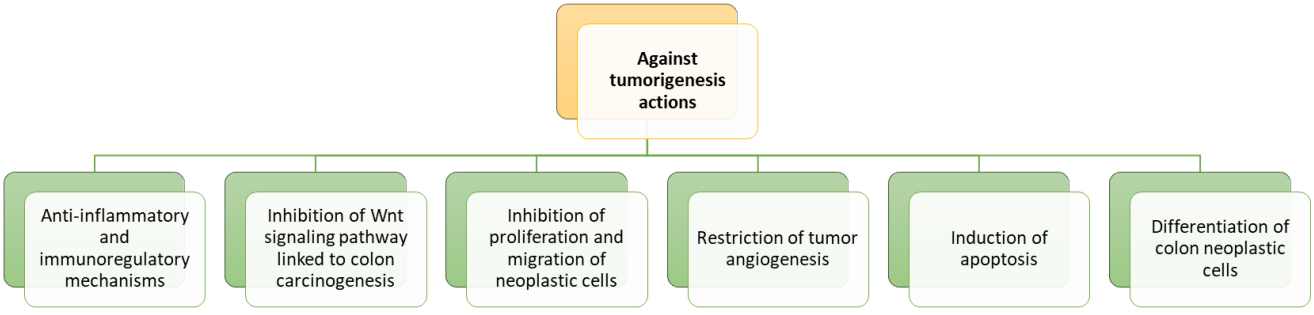

Figure 3. The inhibitory properties of butyrate on tumorigenesis through various mechanisms by the colonic microbiota. Many of the metabolites of protein fermentation can be taken up by other microorganisms and synthesized into active carcinogens. For example, amines and nitrates can be used by facultatively anaerobic and anaerobic colonic bacteria and catalysed the formation of N-nitrosamines, which are among the strongest procarcinogens. Reduced levels of butyrate in the body

are not only an indication of the possibility of cancer, but also indicate the severity of the cancer and its course in the body.

REVIEWERS' 2 COMMENTS:

SPECIFIC COMMENTS TO AUTHORS

The topic is huge and diverse. Literature coverage is incomplete and misses many critical studies. Integration of multiple fields is incomplete. For example, please see Inamura K et al. Gut 2022 for scientific integration.

R: We thanks the Reviewer for her/his suggestion. The manuscript was revised and improved, according to referee's comments. Thank you.

REVISION REVIEWER'S COMMENTS:

SPECIFIC COMMENTS TO AUTHORS

The authors improved the paper.

R: Thanks for your comments.