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The beneficial effects of probiotic in colorectal cancer mice and their gut microbes: a systematic evaluation and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 September 2024 and was last updated on 26 September 2024.

INTRODUCTION

Review question / Objective Subjects: Colorectal cancer models constructed in C57BL/6 or BALB/c mice (age range 6-8w). Intervention: probiotic and/or probiotic mixture therapeutic intervention. Control or comparison measures: equivalent to receive saline or PBS treatment. Study outcomes (original study must have assessed at least one of the following outcomes): treatment efficacy, microbiome changes, and expression levels of short-chain fatty acids. Study design: to investigate the effects of probiotic interventions in a mouse model of colorectal cancer in compliance with animal ethics.

Condition being studied The incidence and mortality rates of colorectal cancer are estimated to be increasing, with significant geographic variation. Europe, Australia and New Zealand have the highest incidence rates and Eastern Europe has the highest mortality rates. By 2040, the burden of colorectal cancer is projected to increase to 3.2 million new cases and 1.6 million deaths per year. It is therefore particularly important to explore the factors that influence the outcome of colorectal cancer.

METHODS

Participant or population Patients: Colorectal cancer models constructed in C57BL/6 or BALB/c mice (age range 6-8w).

Intervention Intervention: probiotic and/or probiotic mixture therapeutic intervention.

Comparator Control or comparison measures: equivalent to receive saline or PBS treatment.

Study designs to be included English-language research papers will be included if they meet the following criteria: 1) the type of study is a mouse model of CRC with an age range of 6-8w, 2) the intervention: the duration of the probiotic intervention is greater than one week. It must include an experimental group (treated with probiotics and/or probiotic mixtures), and a control

group (treated with saline or PBS under the same conditions); 3) the outcome of the study (the original study must have evaluated at least one of the following outcomes): treatment effect, changes in the microbiome, and SCFAs expression levels.

Eligibility criteria Studies were excluded if they met any of the following criteria: 1) did not comply with animal ethics; 2) were not mouse models of CRC; 3) lacked the target metrics, 4) the experimental group had received FMT prior to the intervention; 5) had no control or the control group had received the drug; and 6) were part of a review, a case report, a clinical study, a synthesis, and a meta-analysis.

Information sources We anticipated a systematic search of electronic databases such as PubMed/MEDLINE, Cochrane Library, Embase, Web of Science, etc., for the period up to August 2024, which was conducted independently by two researchers. We used the following MeSH and non-MeSH terms in our search strategy to identify potentially relevant studies: ((Probiotic or Probiotics) AND (Colorectal Neoplasm or Neoplasm, Colorectal or Colorectal Tumors or Colorectal Tumors or Tumor, Colorectal or Tumors, Colorectal or Neoplasms, Colorectal Neoplasm or Neoplasm, Colorectal or Colorectal Neoplasm or Neoplasm, Colorectal or Colorectal Neoplasm or Neoplasm, Colorectal or Colorectal Neoplasm or Neoplasm).

Main outcome(s) The primary outcomes were colon length, tumor number and tumor volume.

Additional outcome(s) The secondary outcomes were changes in the microbial composition of the tumor microenvironment and its metabolites (e.g., SCFAs) and inflammatory factors.

Quality assessment / Risk of bias analysis The Syrcle risk of bias assessment tool for judging the quality of randomized controlled trials was assessed by two authors alone, before further screening of study titles and abstracts. If the relevance of the study was uncertain, the full text was obtained for further assessment. The tool consists of 10 items (selection bias, implementation bias, measurement bias, loss to visit bias, reporting bias, and others) and has a total score of 10. In the event of differential scoring, a third author scored again and discussion took place.

Strategy of data synthesis Data sets with comparable outcome measures were pooled for meta-analysis using standard statistical procedures in RevMan 5.2, and standard deviations (SMDs) were calculated to compare efficacy. Heterogeneity between studies was assessed for I2 values using I. An I2 value of ≥ 50% was considered to indicate significant heterogeneity, and the combined standard deviation (SMD) was estimated using a random effects model. If no significant between-study heterogeneity was detected (I2 ≤ 50%), a fixed-effects model was used. p-values ≤ 0.10 were considered to be significant for heterogeneity, whereas I2 = 0% indicated no heterogeneity, and we kerned the results when they presented high heterogeneity. Subgroup analyses were performed when significant differences in outcomes were detected. In addition, we used funnel plots to assess potential publication bias.

Subgroup analysis When analyzed, the outcome was found to suffer from high heterogeneity. First we will use rechecking of the data to ensure that the extracted data is accurate. Second, we will use subgroup analysis to reanalyze the data, and the groups will be initially divided into probiotic species, probiotic concentration, administration method, and gender of mice.

Sensitivity analysis When the subgroup analyses are completed and the results are still characterized by high heterogeneity, we will perform sensitivity analyses by STATA software to evaluate the robustness of the outcomes in the literature.When, after subgroup analysis, the results still suffer from high heterogeneity, we will perform a sensitivity analysis by STATA software to evaluate the robustness of the literature's results.

Country(ies) involved China.

Keywords Probiotics, Colorectal Cancer, Combination therapy, Tumor Microenvironment.

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