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Gut Microbial Dynamics in a Mouse Model of Inflammation-Linked Carcinogenesis as a Result of Diet Supplementation with Specific Mushroom Extracts

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Abstract : The gut microbiota plays an important role as gut inflammation could contribute to colorectal cancer development; however, this role is still not fully understood, and tools able to prevent this progression are yet to be developed. The main objective of this study was to monitor the effects of a mushroom extracts formulation in gut microbial community composition of an Azoxymethane (AOM)/Dextran sodium sulfate (DSS) mice model of inflammation-linked carcinogenesis. For the in vivo study, 41 adult male mice of the C57BL / 6 strain were obtained. 36 of them have been induced in a state of colon carcinogenesis by a single intraperitoneal administration of AOM at a dose of 12.5 mg/kg; the control group animals received instead of the same volume of 0.9% saline. DSS is an extremely toxic polysaccharide sulfate that causes chronic inflammation of the colon mucosa, favoring the appearance of severe colitis and the production of tumors induced by AOM. Induction by AOM/DSS is an interesting platform for chemopreventive intervention studies. This time the model was used to monitor gut microbiota changes as a result of supplementation with a specific mushroom extracts formulation previously shown to have prebiotic activity. The animals have been divided into three groups: (i) Cancer + mushroom extracts formulation experimental group: to which the MicoDigest2.0 mushroom extracts formulation developed by Hifas da Terra S.L has been administered dissolved in drinking water at an estimated concentration of 100 mg / ml. (ii) Control group of animals with Cancer: to which normal water has been administered without any type of treatment. (iii) Control group of healthy animals: these are the animals that have not been induced cancer or have not received any treatment in drinking water. This treatment has been maintained for a period of 3 months, after which the animals were sacrificed to obtain tissues that were subsequently analyzed to verify the effects of the mushroom extract formulation. A microbiological analysis has been carried out to compare the microbial communities present in the intestines of the mice belonging to each of the study groups. For this, the methodology of massive sequencing by molecular analysis of the 16S gene has been used (Ion Torrent technology). Initially, DNA extraction and metagenomics libraries were prepared using the 16S Metagenomics kit, always following the manufacturer's instructions. This kit amplifies 7 of the 9 hypervariable regions of the 16S gene that will then be sequenced. Finally, the data obtained will be compared with a database that makes it possible to determine the degree of similarity of the sequences obtained with a wide range of bacterial genomes. Results obtained showed that, similarly to certain natural compounds preventing colorectal tumorigenesis, a mushroom formulation enriched the Firmicutes and Proteobacteria phyla and depleted Bacteroidetes. Therefore, it was demonstrated that the consumption of the mushroom extracts' formulation developed could promote the recovery of the microbial balance that is disrupted in the mice model of carcinogenesis. More preclinical and clinical studies are needed to validate this promising approach.

Keywords : carcinogenesis, microbiota, mushroom extracts, inflammation
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