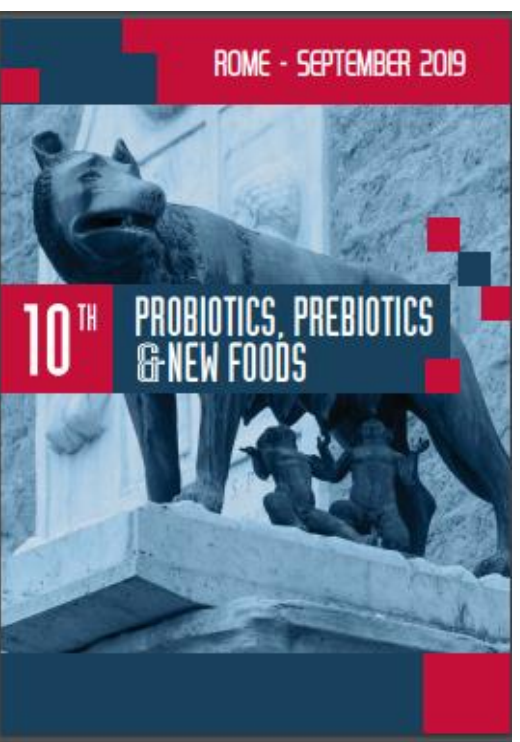


Investigating Potential Chemoprotective Role of Pomegranate Juice Through Analyzing Its Reciprocal Interactions with the Gut Microbiota.



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Introduction

Cancer incidence is increasing in many developing countries as a result of demographics and the adoption of cancer-associated lifestyle choices. The global cancer burden has risen to 18.1 million new cases and 9.6 million deaths in 2018.

Colorectal cancer (CRC) is the second leading cause of cancer death in the world and its burden is expected to increase by 60% to more than 2.2 million new cases and 1.1 million cancer deaths by 2030. In Egypt, higher incidence of CRC than other countries has been reported among the younger population (< 40 years).

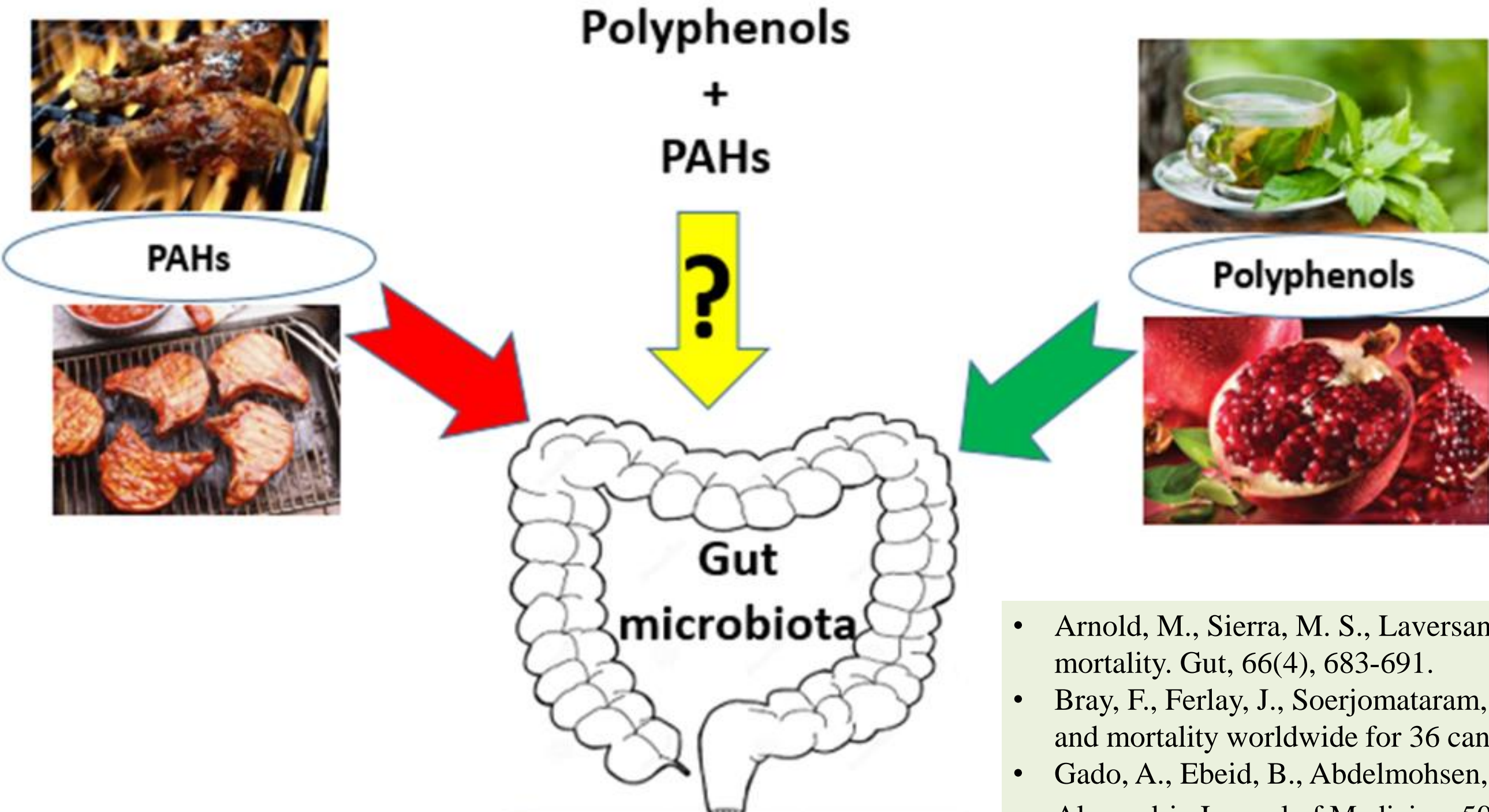
While plants and their constituents have traditionally been used for preventing diseases, including cancer, the emerging concept of combination chemoprevention by multiple agents or “whole foods” is becoming increasingly attractive, opening up the possibility for dietary modification of colon cancer risk.

One such family of plant products is the polyphenols, represented by green tea, green coffee, and pomegranate.

The health benefits of pomegranate (*Punica granatum* L), as a main source of dietary polyphenols, have been mostly attributed to hydrolyzable tannins, including ellagitannins, and gallotannins.

Objective

This work aims to examine the chemopreventive role of polyphenol-rich pomegranate on the rat gut microbiota, as a step towards investigating its ability to neutralize polycyclic hydrocarbons-induced carcinogenesis.



Methods

Six seven-week-old male Sprague Dawley rats were randomly allocated to a control group (n = 3), only fed a standard AIN76 diet, and a pomegranate group (n =3) , fed the standard diet + 2.5ml/kg/day pomegranate juice.

Pooled fecal samples from each group were collected twice weekly for eight weeks.

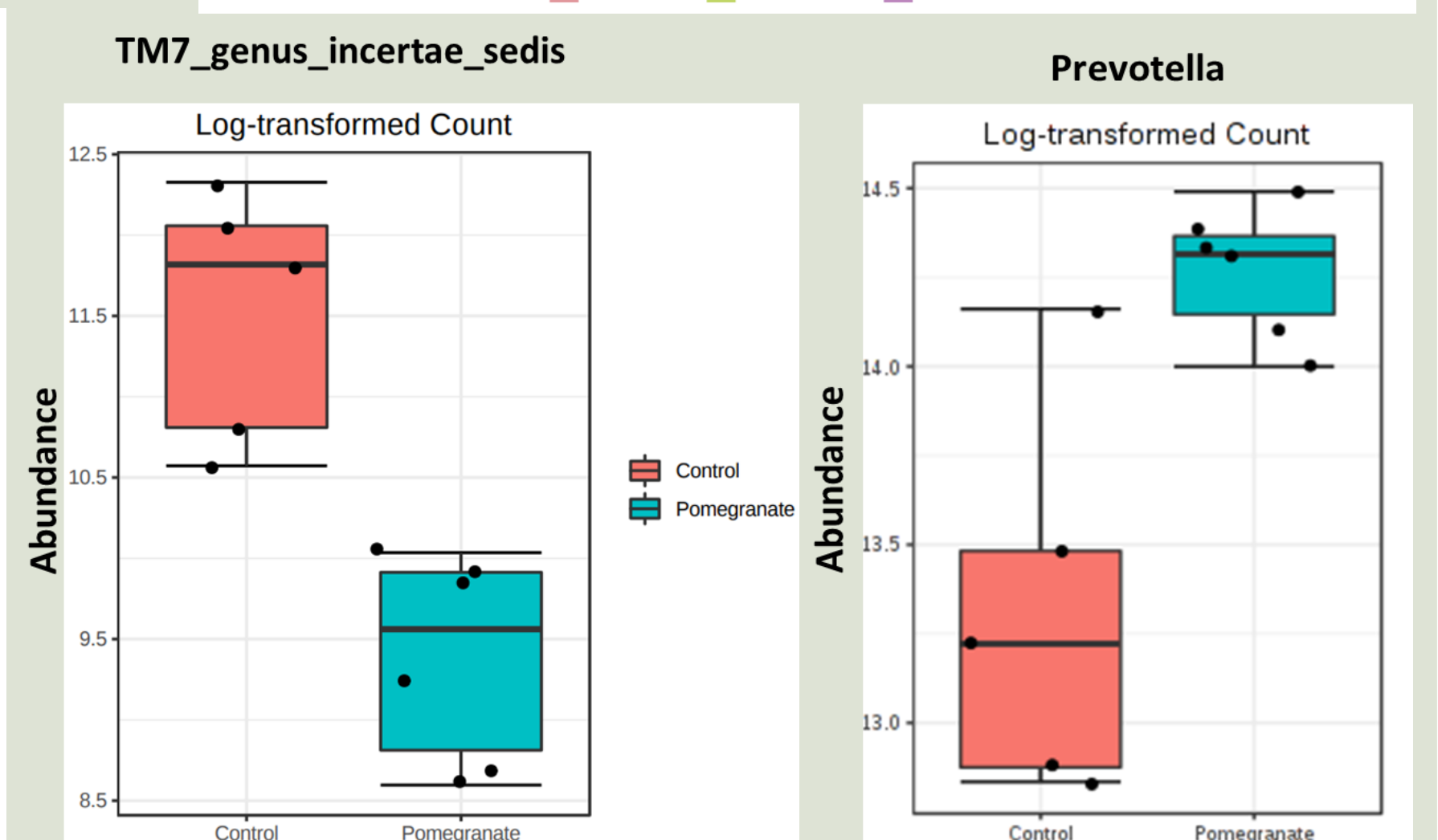
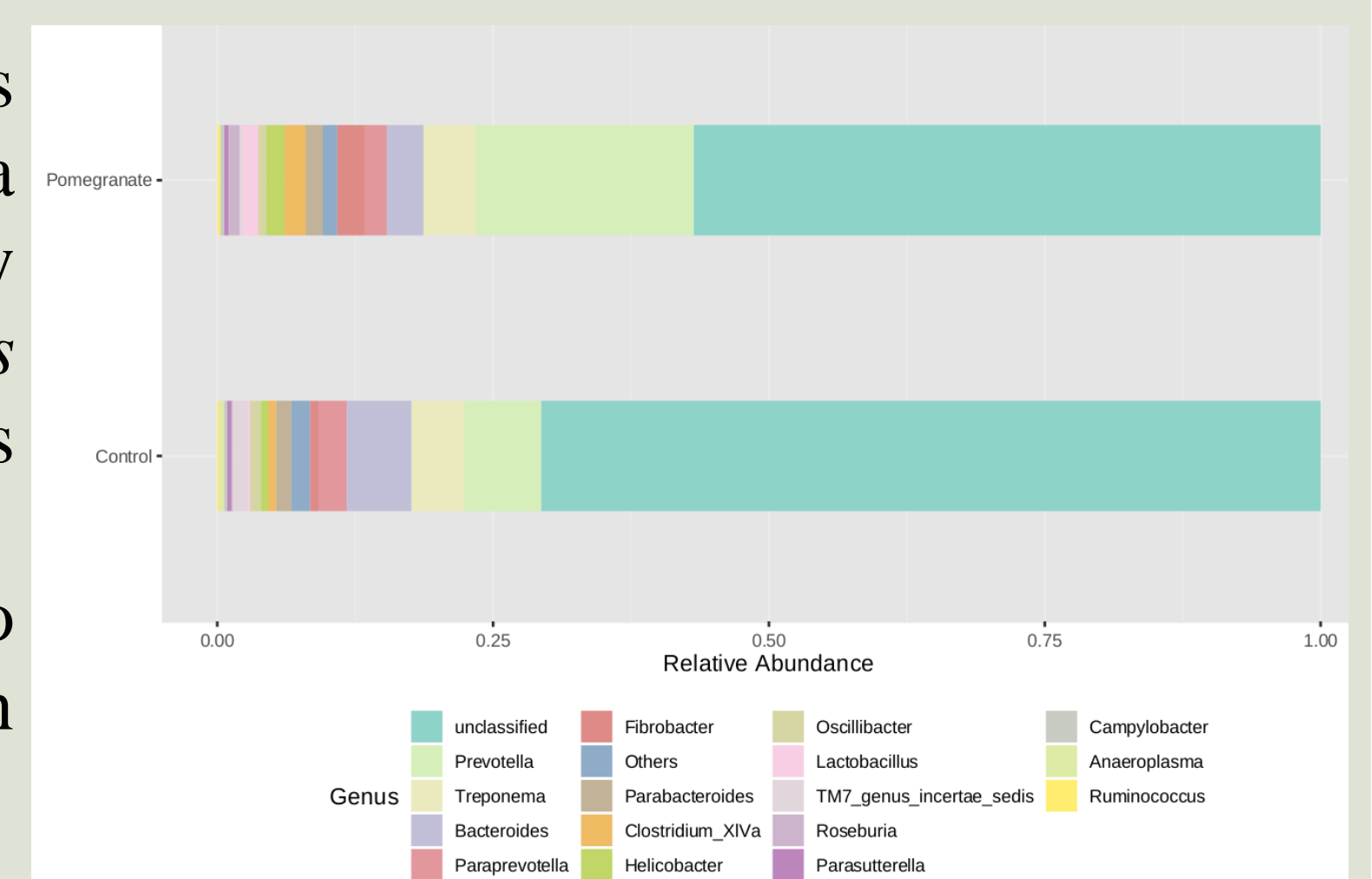
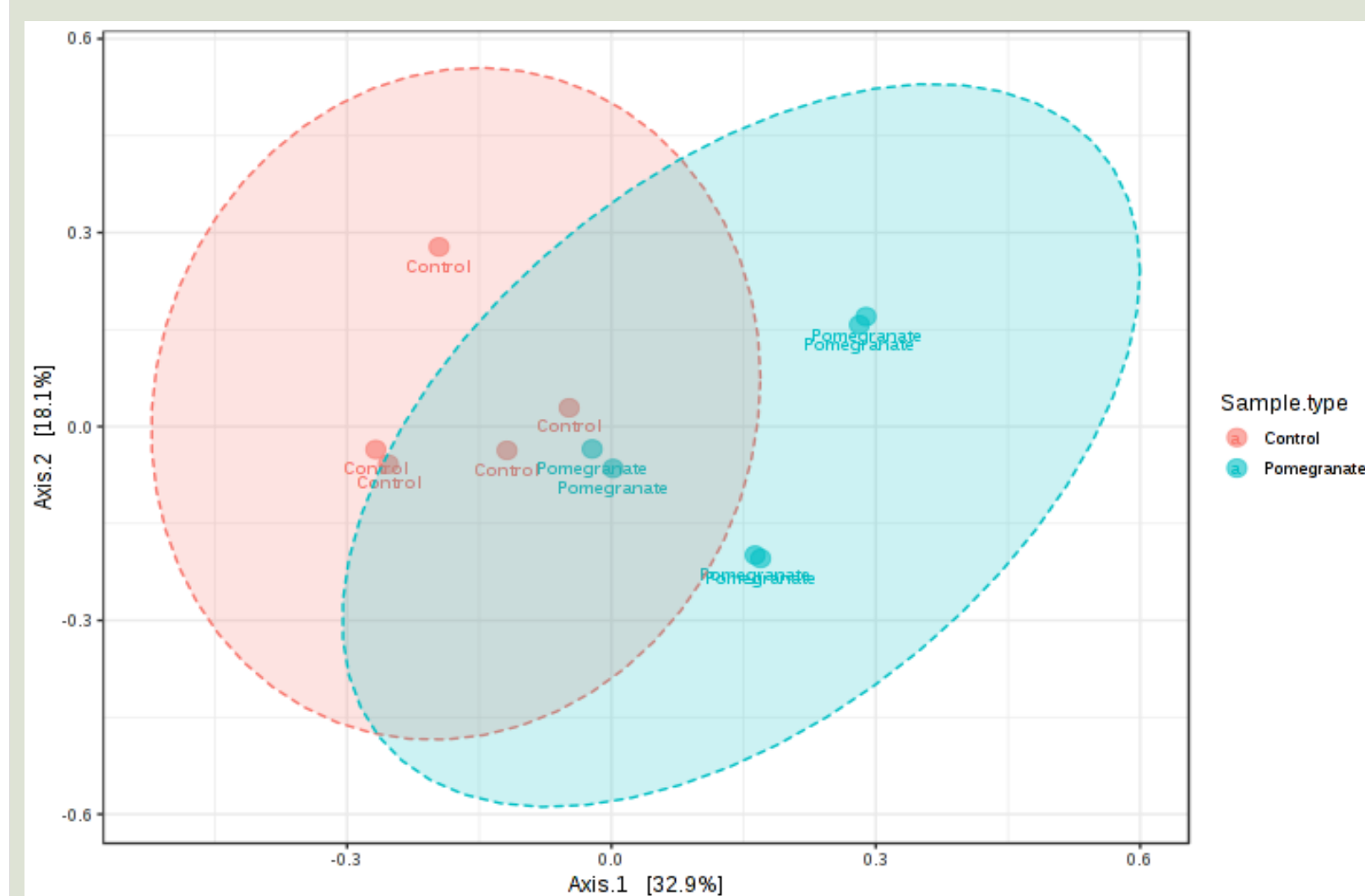
DNA from 12 samples was extracted, quantified, and subjected to 16S rRNA amplicon sequencing by Illumina MiSeq. Sequencing data were analyzed by MG-RAST and MOTHUR. Microbiome Analyst (<https://www.microbiomeanalyst.ca/MicrobiomeAnalyst/faces/home.xhtml>) was used for downstream analysis of MOTHUR output, including statistics and visualization.

Additionally, GC/MS metabolomic profiling was applied to pomegranate juice before and after its *in vitro* exposure to selected bacterial strains representing the gut microbiota.

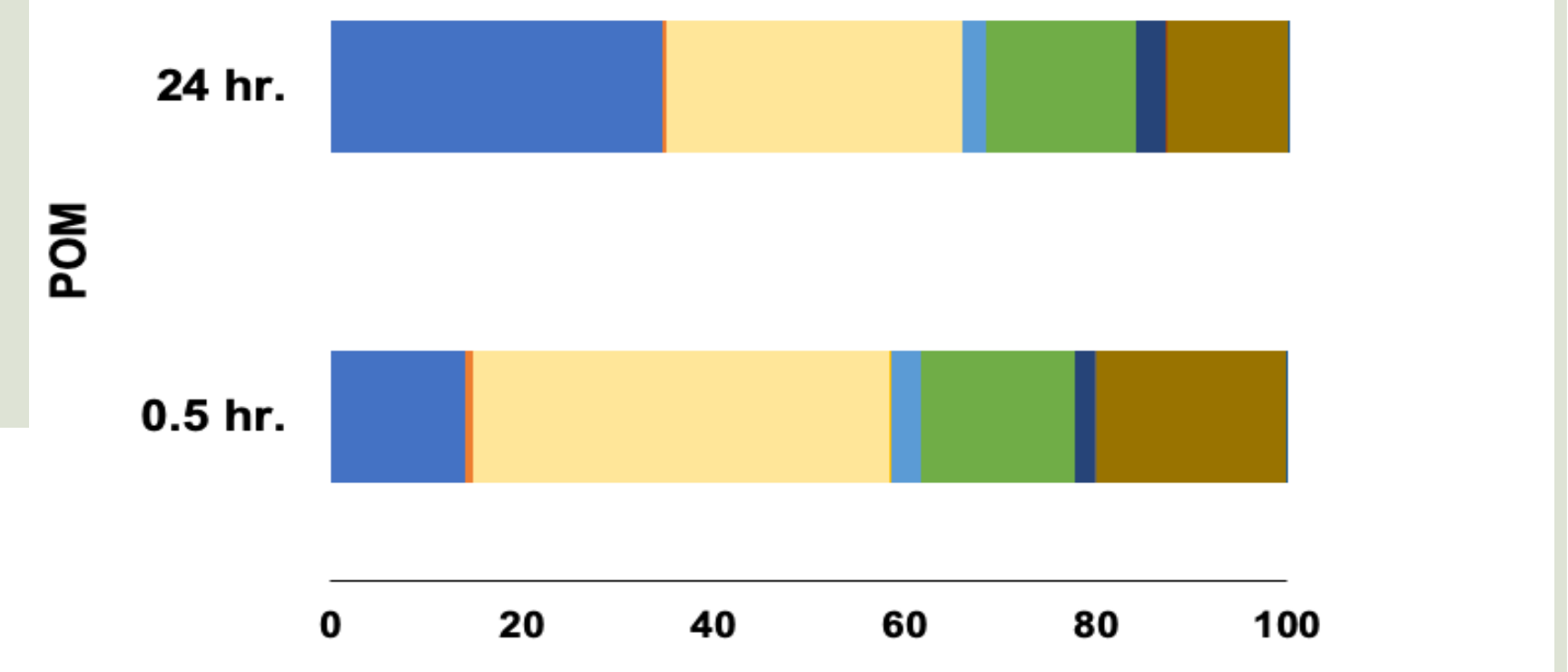
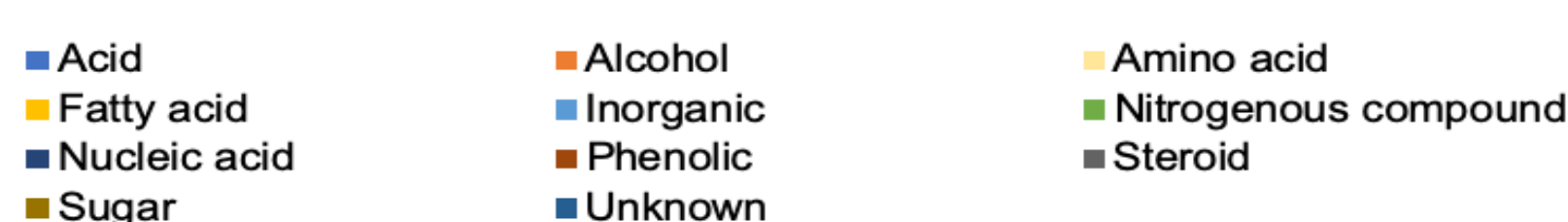
Results

In pomegranate-fed rats, phylum Bacteroidetes (particularly genus *Prevotella*) and genera *Fibrobacter* and *subdoligranulum* were substantially more abundant, while *TM7* genus *incertae sedis* and *Dorea*, among other Firmicutes, were less abundant.

Overall, the Firmicutes-to-Bacteroidetes ratio increased by age and was also significantly lower in the pomegranate-fed rats.



Additionally, a significant decrease in amino acids and sugars was observed in the microbiota-treated juice, while organic acids significantly increased.



Future plan

This pilot work serves as a standardization step for a model to test the potential chemoprotective effect of pomegranate (and other natural polyphenols) against the carcinogenic effect of selected polycyclic hydrocarbons.

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