Clinical Trials Corner

Dear Readers,

Welcome to the next edition of the Clinical Trials Corner of *Nutrition and Healthy Aging*. The aim of this section is to inform readers of upcoming clinical trials and highlight new findings. If you would like to draw attention to a specific topic or upcoming clinical trials, please email me: leonie.heilbronn@adelaide.edu.au

Alterations in microbial diversity and function are linked to poorer metabolic health. Aging is generally associated with a reduction in species such as bifidobacteria that have health promoting activities, and an increase in the firmicuties phylum. However, these changes are not universally observed, and may be more pronounced with increasing frailty (1). Interestingly, an age dependent increase in the contribution from the sub-dominant species in centenarians and super-centenarians has also been reported (2). In mice, interventions such as intermittent fasting restore microbial diversity and increase lifespan (3). Interest is building as to whether microbiota based interventions will promote healthy aging and increase well-being in the elderly.

A number of clinical trials are currently registered, or are recently completed, that examine the short-term effects of altering diet composition, or utilising prebiotic supplements, on microbiome diversity and function in the elderly, and whether this is associated with improved health.

An acute randomised cross-over trial is being conducted at the University of Colorado to examine the effects of a 1-week of high fat, high sugar, low fiber diet vs. a low fat, low sugar, high fiber diet in 120 younger (aged 18-29y) or older individuals (aged 60-79y) on the gut microbiome. Phases 1 and 2 will be separated by a three week washout. This study will identify whether older individuals will behave similarly to younger individuals, and will identify the temporal aspects of the change in microbiome diversity with collection of daily swabs.

The RAMP study (Rejuvenation of the Aging Microbiota with Prebiotics) is a quadruple blind randomised controlled trial examining the effects of a prebiotic supplement, 2'-fucosyllactose, at 2 doses (1 and 5g/day) on immune status and microbiota composition for 6-weeks. Importantly, this study plans to investigate changes in microbiota function and plasma metabolites, as well as metabolic markers in 90 healthy individuals aged ≥ 60 years.

Investigators at the University of Aberdeen have recently completed a double-blind randomised controlled cross-over trial investigating the effects of 15 grams of wheat bran vs. maltodextrin on microbiota function, diversity, glucose and blood lipids in healthy adults aged >60 years over 35 days.

We await publication of these short-term trials, as well as findings from the NU-AGE trial, which sought to investigate the effects of a nutrient rich whole foods diet (NU-Age whole diet approach) for 1 year on the functional and compositional analysis of the microbiota in 120 healthy elderly men and women aged 65-79 years.

Sincerely,

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References:

[1] An *et al*. Age-dependent changes in GI Physiology and microbiota: time to reconsider? Gut 0:1-10 (2018).

[2] Biagi *et al*. Gut Microbiota and Extreme Longevity. Current Biology 26, 1480-5 (2016)

[3] Li et al. Intermittent Fasting Promotes White Adipose Browning and Decreases Obesity by Shaping the Gut Microbiota. Cell Metabolism; 26(4):672-685 (2017).

[4] Costabile *et al*. Effects of soluble corn fiber alone or in symbiotic combination with Lactobacillus rhamnosus GG and the pilus deficient derivative GG-PB12 on fecal microbiota, metabolism and markers of immune function: A randomised, double blind, placebo controlled, cross-over study in healthy elderly. Frontiers in Immunology 2018 (8):1443.

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https://www.clinicaltrials.gov/

A). Study Title:.The RAMP Study – Rejuvenation of the Aging Microbiota with Prebiotics
Clinicaltrials.gov identifier: NCT03690999;
Sponsor: Stanford University.
Collaborator: Abbott
Primary Outcome: Immune Status and Function [Time Frame: Baseline and 6 weeks].
Secondary Outcomes: Microbiota composition, Microbiota function, Weight, Waist, Blood Pressure, Blood lipids, Fasting glucose, Fasting insulin [Time Frame: Baseline and 6 weeks].

B). Study Title: Age associated arterial dysfunction, western diet and the gut microbiome.
Clinicaltrials.gov identifier: NCT03334201
Sponsor: University of Colarado, Boulder
Collaborator: University of California, San Diego
Primary Outcome: Change in gut microbiome, endothelial function and arterial stiffness [Time Frame: 7 days]

C). Study Title:. Fabulous Fibre Study; effect of wheat bran extract on gut and general health in healthy aging subjects.
Clinicaltrials.gov identifier: NCT02693782
Sponsor: University of Aberdeen
Collaborator: Cargill
Primary Outcomes: Changes in the gut microbiota metabolites [Time Frame: Samples collected on test visit 1, 3, 4, 6 (day 5, 15, 20, 30) over an expected period of 35 days]
Secondary Outcomes: Changes in the gut microbiota, blood glucose, HDL, LDL, triglycerides, cholesterol, gastro-intestinal tolerance. [Time Frame: Samples collected on test visit 1, 3, 4, 6 (day 5, 15, 20, 30) over an expected period of 35 days].

D). Study Title:.European Project on Nutrition in Elderly People
Clinicaltrials.gov identifier: NCT01754012
Sponsor: University of Bologna
Collaborator: European Commission
Primary Outcomes: Inflammatory Response Reduction of inflammatory markers after one year of Nu-AGE dietary intervention in elderly [Time Frame: 1 year] Measures of inflammatory status and immune health will be evaluated on plasma: C-reactive protein (hsCRP) IL-1Beta, IL-12, INF gamma, IL-6, sIL-6R, IL-1RA, TNFalpha, IL-17, IL-8, IL-10, TGF-beta1, positivity for HCMV.
Secondary Outcomes: Cognitive status, cardiovascular health, insulin sensitivity, liver function, hormonal status, nutritional status, digestive health, bone health, physical functioning at 1 year. A subgroup of 120 individuals will be characterised for changes in epigenome, transcriptome, metagenome, proteasome and immunoproteasome, metabolome, at one year.