Dietary Proanthocyanidins Alter Energy Metabolism and the Microbiome in the Colon of Helminth-Infected Mice

A Vedsted-jakobsen[1], A Majgaard Jensen[1], M Tønsberg Limborg[1], S Milan Thamsborg[1], A Richard Williams[1].
[1] University of Copenhagen, Denmark

Background: Helminth infections affect approximately one-quarter of the global population, leading to malnutrition and increased morbidity. The establishment of protective immunity against helminths depends on a robust type-2 immunity. The precise regulatory mechanisms governing this response remain unresolved. Recent attention has turned toward the roles of microbiome and diet, both of which are recognised as modulators of inflammation regulation. Evidence suggests that high-fat diets facilitate the expulsion of *Trichuris muris* in mice, whereas diets rich in soluble plant fibres or plant metabolites lead to chronic infection. Host- and microbiome-derived metabolites appear to influence the host's type 1/type 2 immune balance. Nevertheless, the fundamental mechanisms driving these effects remain unexplored.

Aim: Our objective is to elucidate how diets through the metabolome and microbiome influence shifts in immunity against *T. muris*. We seek to identify metabolites responsible for the altered immunity arising from distinct diets and their associated changes in infection.

Methods: We conducted a mouse study involving dietary interventions with soluble fibres or polyphenols before and during *T. muris* infection. Comprehensive metabolomic analysis and 16SrRNA sequencing were performed to discern differences in the effects of various diets. The infection state and immune response were assessed through worm burden and serum antibody responses.

Results: Preliminary findings indicate substantial influence from both diet and infection on the metabolome and microbiome. It seems that there is a shift in energy metabolism once infected and on a diet consisting of 1% proanthocyanidins.

Conclusion: The identification of host- and microbiota-derived metabolites linked to type-2 immunity offers the possibility for interventions to promote immunity against helminth infection as well as therapeutics for type-2 driven inflammation.