Dietary intervention yielding high colonic levels of short chain fatty acid metabolites (principally acetate and butyrate) as a potential preventative or treatment approach for Type 1 diabetes (T1D) and other autoimmune diseases.

- Proof of concept efficacy data for dietary combination in T1D in vivo
- Potential as medical food or dietary intervention
- Potential to be autoimmune therapy

THE CHALLENGE

Type 1 diabetes (T1D) is one of the most common chronic diseases in children. There is currently no cure for T1D. 1.25M Americans are living with T1D including about 200,000 youth (less than 20 years old) and over a million adults (20 years old and older). 5 million people in the U.S. are expected to have T1D by 2050, including nearly 600,000 youth. In the U.S alone T1D-associated healthcare expenditures and lost income is 14 billion annually.

T1D has a strong genetic basis, particularly in the MHC; however the environment is a significant contributor to the rising incidence of the disease. Diet may be partially responsible for the increased incidence of T1D and other immune-inflammatory diseases in affluent western countries over the past 40 years.

Compared to other societies, the modern western diet is dominated by energy dense, highly refined foods that are generally low in fiber and high in fat.

Increased fiber consumption is recognised for its potential to protect against chronic disease, particularly consumption of resistant starches that are fermented by the colonic microbiota. This fermentation produces short chain fatty acids (SCFAs) principally acetate, propionate and butyrate.

It is likely that SCFAs mediate many of the effects ascribed to fiber, and their supply is critical for optimal gut function.

THE TECHNOLOGY

The Monash University research team, together with CSIRO, has made a surprising discovery that SCFAs play an important role in protection against autoimmune disease.

A combination diet yielding very high amounts of acetate and butyrate (HAMSA and HAMSB respectively) which was restricted to the colon inhibited progression to autoimmune diabetes in the NOD mouse. The protective effects of acetate and butyrate were only partially overlapping, indicative of different mechanisms. These included:
- changes in gut bacterial ecology towards acetate-producing strains
- improved gut integrity through increased IL-22 and decreased pro-inflammatory cytokines
- increased function of Treg cells, and
- decreased frequencies of auto-reactive T cells.

Dietary interventions to alter metabolite levels represents a highly promising alternative to pharmaceutical approaches to prevent or treat T1D and other autoimmune diseases.

THE OPPORTUNITY

Monash is now seeking a commercial partner to further develop and translate this opportunity.

Intellectual property: An international patent application (PCT/AU2017/050845) has been filed on the method of combination and delivery of metabolite compounds for the treatment and prevention of autoimmune diseases.

Figure 1: SCFAs delivered via diets protect against diabetes. Incidence of T1D in female NOD mice fed the non-purified (NP) diet (n = 25 mice), High-amylose maize starch (HAMSA) diet (n = 17 mice), High-amylose maize starch butyrylated (HAMSB) diet (n = 11 mice), or combined (HAMSA plus HAMSB) diet (n = 11 mice) for 10 weeks (HAMSA plus HAMSB; orange arrows) or 5 weeks (all other diets; blue arrows), starting at 5 weeks of age. NS (NP vs HAMS, HAMSB vs HAMS, HAMSP vs HAMS, and HAMSP vs NP); *P = 0.0482 (HAMSB vs NP), #P = 0.0490 (HAMSA vs HAMS), **P = 0.0069 (HAMSA vs NP), ***P = 0.0025 (HAMSA+HAMSB vs HAMS) and ****P = 0.0008 (HAMSA+HAMSB vs NP) (Mantel-Cox log-rank test).

Reference