

Is immune tolerance abnormal in coeliac disease?

Although most of the population regularly consume gluten, and approximately 1 in 3 people carry the essential susceptibility genes, only 1 in 100 actually develop coeliac disease. The reason for this is unknown, however environmental factors are likely to be very important by influencing the balance between a destructive pro-inflammatory and a tolerant immune response to gluten. In this proposal we will address for the first time the functional basis for the immune response to gluten by directly measuring two major immune cell (T cell) subsets in patients with coeliac disease: one is pro-inflammatory and responsible for tissue damage and the other is regulatory (“tolerogenic”) and capable of preventing or suppressing the damaging immune response to gluten. Here we utilise a method that allows study of these T cell subsets from blood after volunteers participate in an oral gluten challenge. These immune responses will be correlated by symptoms and intestinal damage in volunteers with coeliac disease and healthy non-coeliac but genetically matched controls after gluten exposure. The question of immune tolerance to gluten is now perhaps the most pressing scientific question in the field of coeliac disease immunology. This proposal outlines a simple experiment plan that will open up this area for the first time.

The effect of plant enzyme supplementation on duodenal histology in coeliac patients maintaining a gluten free diet

This is Proof-in-Principle double blind, parallel design randomized trial evaluating plant enzyme therapy for management of coeliac disease, monitored by small bowel histology, level of antibodies in blood against tissue trans-glutaminase (tTG) and recording of disease symptoms. Ten coeliac volunteers with medically proven coeliac disease on a gluten-free diet but who still have high levels of tTG antibodies and abnormal histology (implying gluten damage of the small bowel) will participate. Six participants will receive tablets containing enzyme supplement derived from papaya fruit (caricain) and four placebos for six weeks. Biopsies and bloods (tTGs) will be taken before start and end of six weeks therapy.

Primary evaluation of treatment efficacy by histopathology before and after the course of treatment, graded according to Marsh scale 1 to 4. The secondary evaluation of treatment is comparison of symptoms and anti-tTG antibody levels before and after the treatment.

An evaluation of cognitive changes in response to gluten challenge in patients with coeliac disease on a strict gluten free diet

Coeliac disease is a common autoimmune condition resulting from an abnormal immune response to ingested gluten. The immune response results in inflammation in the small bowel and the mainstay of treatment remains a lifelong gluten free diet (GFD). The impacts of coeliac disease beyond the small bowel are being increasingly recognized and include osteoporosis as well as skin, liver and thyroid disease. Coeliac disease can also have effects on the nervous system. Some aspects of the nervous system have been well researched and conditions such as 'gluten ataxia' are well characterized. Coeliac disease can also cause more subtle neurological problems such as fatigue, difficulty concentrating, poor memory and in coordination. These subtle deficits have not been well studied. In this trial we aim to explore these subtle neurological (or cognitive) effects of gluten exposure in people with coeliac disease already on a GFD. We will enroll otherwise healthy people with coeliac disease who have been on a strict GFD for more than 2 years and expose them to biscuits or muffin which contain either gluten or a placebo ('dummy' gluten). Before and after ingestion of the study food, participants will undergo a sequence of testes examining sublet aspects of memory, concentration, coordination and fatigue. In conducting this research we hope to gain insights into the effects of gluten exposure beyond the gut in patients with coeliac disease. Finding an association between these subtle neurological deficits and gluten exposure will have significant implications for the quality of life in patients with coeliac disease before and after diagnosis.