THE UNIVERSITY OF CHICAGO
CELIAC
DISEASE CENTER

IMPROVING LIVES THROUGH AWARENESS,
EDUCATION, AND RESEARCH

773-702-7593 www.CeliacDisease.net

At The University of Chicago Celiac Disease Center, our predominant research vision is to unlock the mystery of the damage caused by gluten in people with celiac disease and gluten sensitivity as a way to develop a permanent cure for these conditions.

In our quest for the cure, we hope to develop an alternative to the gluten-free diet for medical treatment of celiac disease. We are also concerned with improving the diagnosis of celiac disease and gluten sensitivity, as well as treating patients that respond poorly to a gluten free diet. In addition, we are working to identify treatments to prevent the development of celiac disease in at-risk children.

RESEARCH AT THE UNIVERSITY OF CHICAGO CELIAC DISEASE CENTER

OCTOBER 1ST, 2010

We benefit from a unique infrastructure combining pediatric and adult gastroenterologists dedicated to improving the life of patients with celiac disease, our Celiac Disease Center that supports forefront patient care and research, and an outstanding research group, which is the first in North America to have received the international Wm. K. Warren prize for outstanding celiac disease research. Our group has published on celiac disease in the most high impact journals such as *Nature*, *Immunity*, and the *Journal of Experimental Medicine*. Our approach is unique because we combine human research with the development of mouse models, which gives us an exceptional depth, power of analysis, and ability to make groundbreaking discoveries. Obtaining an endowment for celiac disease research would provide a unique opportunity to continue and expand pioneering work on celiac disease with the goal to treat and prevent celiac disease.

1. DEVELOPING CURATIVE AND PREVENTIVE THERAPIES FOR CELIAC DISEASE

a. *Mouse models of celiac disease.* In order to test new therapeutic strategies, it is critical to have mouse models of celiac disease that actually reproduce the human disease in a relevant manner. In addition, mouse models allow us to create a direct cause-effect relationship and hence allow us to identify the critical targets for therapies.

b. From human basic research to clinical trials. Our research has identified a killer pathway responsible for the destruction of the intestinal layer. We can target these pathways with appropriate pharmacological compounds. Such examples exist for Crohn's disease and rheumatoid arthritis, where development of anti-TNF therapies has changed the lives of patients touched by these diseases. We have identified such an effector molecule implicated in celiac disease and are working in collaboration with a pharmaceutical group to set up clinical trials.

c. We are creating a comprehensive research program with chemists to develop a treatment that can prevent and cure celiac disease. The idea is that celiac disease results from a bad destructive response to gluten and that if we could reorient this response to a good, tolerogenic, and beneficial response, we could prevent and cure celiac disease. To do this, it is necessary to have a comprehensive analysis of the intestinal immune system and a strong understanding of how it is deregulated in celiac disease. A mouse model is also necessary to test and adjust therapeutic avenues. Our background, past work, and mouse models put us in the position to achieve this.

d. Efficacy of a probiotic treatment in celiac patients with partial response to the gluten-free diet. A small portion of patients with celiac disease continue to present symptoms of gastrointestinal distress even after beginning the diet, as a result of an ongoing mild degree of inflammation. In addition, the microflora of celiac patients has been shown to be different from that of healthy individuals. Probiotics are known to beneficially affect intestinal inflammation and may normalize abnormal microflora. Thus, this study aims to assess the efficacy of a scientifically validated probiotic treatment in normalizing the microbial composition and ameliorating symptoms in celiac patients on the gluten-free diet.

2. IMPROVING THE DIAGNOSIS OF CELIAC DISEASE AND GLUTEN SENSITIVITY

a. Gluten Sensitivity: myth or reality? People suffer from gluten sensitivity, i.e. gluten-related symptoms, and yet do not have the classical markers of celiac disease. Because they may lack both anti-transglutaminase antibodies and the right genetic make-up (HLA-DQ2 or HLA-DQ8), their suffering is dismissed as being psychological. We have evidence that gluten sensitivity is a real disease. In gluten sensitive patients, gluten is viewed as a danger signal and virus by the body. Consequently, the body mounts an inappropriate stress response that results in alterations of the intestinal linings, abdominal pain, and diarrhea. Our goal is to develop diagnostic markers and understand how gluten can induce such a stress response, and to improve the diagnosis and treatment of patients suffering from gluten sensitivity.

b. Celiac disease and autoimmune diseases. Celiac disease is associated with an increase in autoimmune disorders such as type-1 diabetes. It is also known that the longer patients have untreated celiac disease, the higher their risk of developing an autoimmune disorder. Our group is working to identify the cause of this increased risk of developing autoimmunity in celiac disease. We have identified a factor in the blood that we believe can help identify at-risk patients and creates the possibility of developing therapeutic tools to prevent the development of autoimmune diseases in celiac disease patients.

c. Associating genetic studies with patient phenotyping. We know now that celiac disease is a complex genetic disorder and that there are different forms of celiac disease. Some patients suffer from destruction of their intestinal lining (they have villous atrophy), some have a skin disease or neurological symptoms, while others have general fatigue. Understanding how the genetic make-up and environmental factors such as viral infections and gluten lead to different forms of celiac disease is critical to advance the diagnosis and treatment of celiac disease.

d. Efficacy of rapid finger-prick test in diagnosing celiac disease. This trial will test the accuracy of a finger-prick test for celiac disease. The product is currently sold in Europe, and gives a tissue transglutaminase antibody reading in under ten minutes.

e. Timing of gluten intake in infant nutrition and risk of celiac disease autoimmunity. Studies have shown that breast feeding at-risk infants at the time of gluten introduction may delay or prevent the development of celiac disease. The risk of developing celiac disease is reduced by prolonged breast-feeding, introduction of gluten during breast-feeding, introduction of gluten in the right "time window," and introduction of gluten in small amounts. The University of Chicago Celiac Disease Center is partnering with the University of Maryland Center for Celiac Research on an international, multi-center study (25 centers in all) to further investigate the effects of early versus late gluten introduction in at-risk infants on the development of celiac disease.

In conclusion, we have a unique infrastructure, an extraordinary expertise, distinguished clinical and research programs, and exceptional tools that allow us the possibility to make a notable difference in the life of celiac disease patients and their families. Given the right resources, we believe that we can find a cure for celiac disease in the coming 10-15 years.