The core mission of the University of Chicago Celiac Disease Center is to develop therapeutic strategies to prevent and cure celiac disease.

To tackle celiac disease, Dr. Jabri has developed a multifaceted and multidisciplinary approach in close collaboration with her clinical colleagues Drs. Stefano Guandalini, Carol Semrad, Sonia Kupfer and Hilary Jericho, as well as with prominent research groups in the United States and across the world. Dr. Jabri is also dedicated to training and fostering the next generation of young scientists and clinicians working on celiac disease. Dr. Jabri, along with her team and her collaborators at other institutions, is determined to dramatically improve the lives of celiac disease patients and their families.

RESEARCH IN PROGRESS...

1. Evidence that viral infections play a role in celiac disease. The prevalence of celiac disease continues to rise, suggesting that environmental factors must trigger and precipitate the disease. For a long time, it was suspected that viruses might play a role in celiac disease, and more generally in autoimmunity. Thanks to generous donations, we were able to initiate studies and obtain preliminary data that were critical for receiving NIH funding to study the role of intestinal viruses in celiac disease pathogenesis in collaboration with Drs. Terrence Dermody (University of Pittsburgh) and Ramnik Xavier (Massachusetts General Hospital and Broad Institute). We now have a manuscript under revision showing that viruses can disrupt tolerance to gluten and promote inflammatory immune responses and transglutaminase activation. Furthermore, our study defines the mechanistic basis for how viruses can disrupt tolerance to gluten and initiate celiac disease. This study will help define vaccine strategies targeting viruses that have the potential to trigger celiac disease, and hence may help prevent disease in at-risk children with a family history of celiac disease.

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2. Initiation of a clinical trial testing the ability of Montelukast, an FDA-approved drug for asthma that blocks cysteinyl leukotrienes, to prevent tissue damage in celiac disease patients eating gluten. Our publication in the high impact *Journal of Experimental Medicine,* with News & Views, reveals that the lipid signaling molecules cysteinyl leukotrienes are highly increased in celiac disease and are involved in tissue destruction. Based on this publication, Dr. Sonia Kupfer was able to obtain approval for and launch a clinical trial at the University of Chicago aimed at assessing the therapeutic potential of Montelukast in adult celiac disease patients.

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3. Completion of a clinical trial in celiac disease patients who do not respond to a gluten-free diet. There is currently no effective treatment for refractory celiac disease. Based on encouraging results, we are finalizing the enrollment of patients with refractory celiac disease in a clinical trial testing the efficacy of a drug blocking the cytokine IL-15, which we have identified as playing a critical role in celiac disease. This trial is sponsored by the NIH and conducted in collaboration with Professor Thomas Waldmann (NIH/NCI) and Professor Joseph Murray (Mayo Clinic). Our goal is to complete the trial by the end of 2017 and analyze and publish the results in 2018.

WE HAVE MADE PROGRESS,
BUT WE NEED TO CONTINUE OUR JOURNEY OF DISCOVERY AND HARD WORK.

4. Discovery of an important mechanism underlying the development of a disease-promoting microbiota in celiac disease. Our body harbors more than 40 trillion microbial cells. These microbes play an important role in our health. However, under certain circumstances, deleterious microbes outgrow good microbes and prevent them from exerting their beneficial effects. We unexpectedly found that IL-15, the stress-induced cytokine overexpressed in celiac disease patients, alters the microbiota and prevents expression of butyrate, a health-promoting short chain fatty acid. This result was published this year in *ISME Journal*, a highly regarded multidisciplinary journal of microbial ecology. We are further analyzing the impact of these microbial alterations and are assessing ways to revert the deleterious effect of IL-15 on the microbiota.

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5. Generating relevant mouse models for celiac disease. The lack of a relevant mouse model of celiac disease has been a major limitation in the field of celiac disease. Such preclinical models are essential to test new therapeutic avenues. We now have developed the first relevant mouse model of celiac disease where mice expressing the human celiac disease-predisposing HLA molecule develop anti-gluten antibodies, anti-tissue transglutaminase 2 antibodies and villous atrophy upon eating gluten. We are currently using this preclinical mouse model to determine whether inhibitors of tissue transglutaminase-2 developed by our collaborator Dr. Chaitan Khosla (an internationally renowned chemist at Stanford University) can prevent celiac disease. If successful, this study will provide strong support for initiating clinical trials testing inhibitors of tissue transglutaminase-2 in celiac disease patients.

We cannot express how grateful we are for the support we have received over the years from celiac disease patients and their families.

This funding has allowed our team to make groundbreaking discoveries and develop the scientific basis for new therapeutic strategies and personalized treatments in celiac disease. Today, the University of Chicago Celiac Disease Center is a premier research center for celiac disease in the United States and the world. This would not have been possible without the trust and ongoing support we have had the privilege to receive from celiac disease patients and their families. This support was particularly central to the development of transformative, high impact research programs. We have made progress, but we need to continue our journey of discovery and hard work. These are exciting times, and now, more than ever before, we are closer to achieving our dreams of developing cures and improving the life of celiac disease patients and their families.

2001
- Celiac Center Founded
- First Annual Free Blood Screening

2003
- Initiated research program to develop a mouse model with villious atrophy

2004
- Successfully developed mouse model with loss of oral tolarance

2005
- Preceptorship Program established

2008
- Breakthrough discovery regarding anti-gluten T-Cell response in celiac published in *Nature*

2009
- Medical Center kitchens accredited by GFCO.org

2010
- Dr. Jabri awarded Warren Prize for Excellence in Celiac Research

2011
- Dr. Guandalini founds The North American Society for the Study of Celiac Disease (NASSCD)
- Discovery of relationship of retinoic acid and IL-15 to intestinal inflamation published in *Nature*

2013
- 15th International Celiac Disease Symposium Host
- FDA Gluten-Free standard established

2014
- Friends of the Celiac Disease Center established

2015
- Identification of role of cysteinyl leukotrines in the pathogenesis of celiac disease published in *The Journal of Experimental Medicine*
- Discovery of Role of IL-15; Important contributions of epithelial stress to active celiac disease and potential abnormalities in family members (published in *Gastroenterology)*
- Leadership of FDA GREAT Workshop

2016
- Feasibility clinical trial of Montelukast

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