

# EXPANDING IMMUNE REACTIVITY AGAINST GLIADIN AND TTG EPITOPES LONG PRECEDES CELIAC DISEASE DIAGNOSIS

**AuthorBlock:** *Rok Seon Choung<sup>1</sup>, Vasanth Jayaraman<sup>2</sup>, Eric Marietta<sup>1</sup>, John J. Rajasekaran<sup>2</sup>, Tianhao Wang<sup>2</sup>, Kang Be<sup>2</sup>, Hari Krishnan Krishnanmurthy<sup>2</sup>, Joseph A. Murray<sup>1</sup>*

<sup>1</sup>Mayo Clinic, Rochester, Minnesota, United States; <sup>2</sup>Vibrant Science, San Carlos, California, United States;

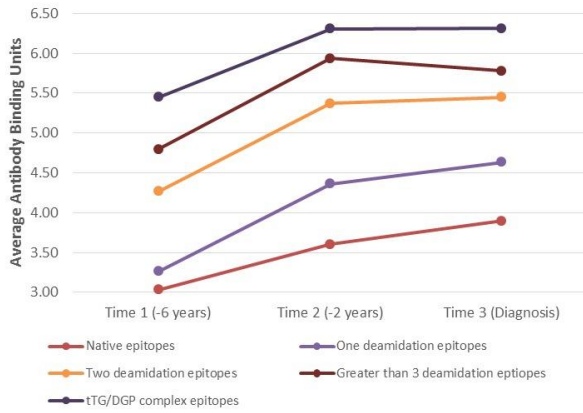
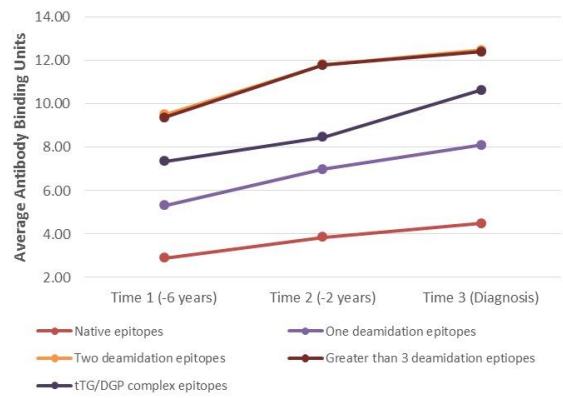
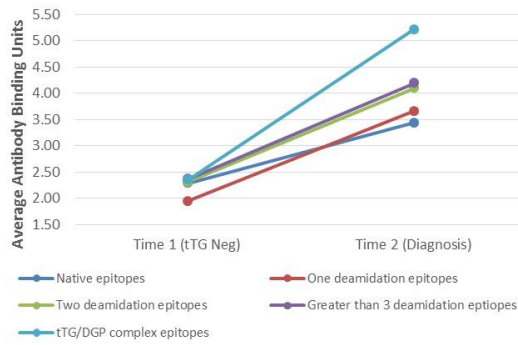
**Background:** Celiac disease (CD) is an autoimmune disease that can be diagnosed by the presence of antibodies. Moreover, it has been demonstrated that celiac associated antibodies are highly correlated with the severity of pathologic changes in CD, suggesting that the development of these antibodies must coincide or precede clinical disease. However, the development of CD associated antibodies before diagnosis of the disease has not been extensively explored.

**Aim:** The aim of this study was to explore the changes of immune recognition against gliadin peptides and tissue transglutaminase in serum samples of a young adult population subsequently diagnosed with CD.

**Methods:** Sera from 30 patients with incidental CD, who had at least two medical encounters with CD (based on ICD-9 code=579.0) were obtained from the Department of Defense Serum Repository. Three samples per subject were obtained: around diagnosis, approximately 2 years prior to diagnosis, and 6 years prior to diagnosis. With a novel peptide microarray that utilizes peptides derived from the (tTG)-DGP complex, we evaluated this sera for the presence of antibodies with specificity for such peptides. Also evaluated were peptides derived from native gliadin and deamidated gliadin, as well as anti tTG IgA.

**Results:** Among 30 patients with incidental CD, 15 patients were persistently positive to tTG-IgA in samples obtained prior to diagnosis, and 15 patients were sero-converters whose tTG-IgA results turned from negative to positive. We were able to detect antibodies against synthesized epitopes of native gliadin, deamidated gliadin, and tTG-DGP in both sero-converters and persistently positive group. The average antibody-binding intensity of synthesized epitopes gradually increased as approaching the diagnosis of disease in persistently positive group (Figure A & B). The increasing trend of immune reactivity was more prominent in sero-converters (Figure C & D), compared to persistently positive group. Interestingly, some sero-converters showed increased immune reactivity against gliadin epitopes in preclinical sera, to which tTG-IgA was negative. This is suggestive of antibody recognition to native and deamidated gliadin prior to tTG recognition.

**Conclusions:** Surprisingly, even 6 years before diagnosis, immune responses against gliadin peptides are already present in a subset of celiac patients. This immune reactivity was further augmented as disease progressed from silent to clinically obvious disease.

**A Persistent  $\gamma$ Positive Group: IgG Immune Reactivity****B Persistently Positive Group: IgA Immune Reactivity****C Sero-Converters: IgG Immune Reactivity****D Sero-Converters: IgA Immune Reactivity**