Single HLA-DQ2.2 haplotype, without HLA-DQ8 or DQ2.5 heterozygosity, demonstrates an association with Celiac Disease

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Introduction

- **Overview of Celiac Disease:** Celiac disease (CD) is an autoimmune disorder triggered by gluten, leading to an immune attack on the intestinal mucosa and impaired nutrient absorption.
- **Genetic Factors:** The Human Leukocyte Antigen (HLA) plays a crucial role in CD, with HLA-DQA1 and HLA-DQB1 being the primary genes that increase susceptibility.
- **Haplotype Prevalence:** Most celiac patients carry the DQ2.5 (DQA1*05:01-DQB1*02) heterodimer, while others without DQ2 often have DQ8 (DQA1*03:01-DQB1*03:02), indicating a strong genetic predisposition to the disease.
- **Immune Response Mechanism:** When gluten is consumed, gliadin peptides are modified by tissue transglutaminase 2 (TG2), which allows them to bind to HLA-DQ2.5 and DQ8, activating CD4+ T cells and initiating an immune response.
- **Consequences of Inflammation :** The immune response leads to further intestinal damage, with heat shock proteins and the release of TG2 contributing to the inflammatory cycle and promoting the production of IgA anti-TG2 antibodies, worsening the condition.

Figure 1: HLA typing and associated celiac disease risk. This table presents detected HLA alleles, along with their respective risk levels for developing celiac disease

HLA Type	Alleles Detected	Celiac Disease Risk
DQ2.5	DQB1*02, DQA1*05	High risk
DQ8	DQB1*03, DQA1*03	Moderate risk
DQ2.2	DQB1*02, DQA1*02	Increased risk
DQ2.1	DQB1*02, DQA1*01	Moderate risk

Case Report

12-year-old female with a history of abdominal pain, poor appetite and lethargy is presented to the lab with Celiac Investigation.

Materials & Methods

- **Sample Collection:** Blood was collected in EDTA tube and stored at 4 degrees.
- **DNA Extraction:** DNA extraction was done using the buffy coat method on Qiagen EZ2 connect.
- **HLA Typing:** HLA-DQA1 and -DQB1 typing was performed using Luminex® LABScan3D and analyzed using HLA Fusion.

Results

HLA-DQ Typing:
- Negative for DQ8 and DQ2.5
- Detected alleles: DQB1*02; DQB1*05; DQA1*01; DQA1*02

Duodenum Histopathology Results:
- Presence of intraepithelial lymphocytosis
- Severe villous blunting observed

Tissue TG2 IgA Test:
- Elevated antibody levels (>40): Strong indication of celiac disease (CD)

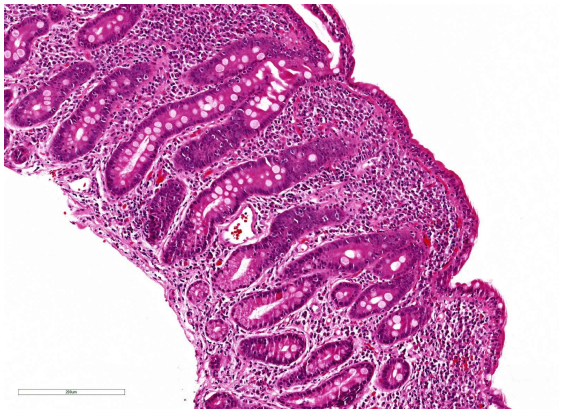

Figure 1. Microscopic view of a Duodenum section stained with hematoxylin and eosin (H&E): This image showcases the crypt architecture and cellular detail, showing the presence of intraepithelial lymphocytosis indicating an immune response within the epithelial layer, highly suggestive of celiac disease

Conclusion

- Our laboratory previously excluded DQ2.2 from the reporting criteria due to a lack of sufficient documentation linking the DQ2.2 haplotype to celiac disease, especially in cases without HLA-DQ8 and DQ2.5 heterozygosity. However, after reviewing this case, we have updated our celiac disease investigation policy to include DQ2.2 in the final report.
- HLA-DQ2 and HLA-DQ8 heterodimers are significant contributors to celiac disease heritability, while the remaining heritability is thought to involve various non-HLA genes. Recent genome-wide association studies have identified many non-HLA genes that may play a role in the risk of developing celiac disease.

References

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