Project Notes:

Inhibition of Gliadin-α2 Binding to HLA-DQ2.5 Using Novel Chemical Synthesis
Derek Desrosiers

Note Well: There are NO SHORT-cuts to reading journal articles and taking notes from them. Comprehension is paramount. You will most likely need to read it several times, so set aside enough time in your schedule.

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Knowledge Gaps:

This list provides a brief overview of the major knowledge gaps for this project, how they were resolved and where to find the information.

Knowledge Gap	Resolved By	Information is located	Date resolved
Pathology of CD	Youtube videos	Various videos found on youtube (did not put them in project notes) Link 1 Link 2 Link 3 Link 4	9/12/23
Proteins involved in TCR reception	Literature reading	Article 13	10/10/23
Why all foods don't cause an immune response	Prof. Stern	Didn't use any online information or papers, but answer is contained here	10/13/23
Peptide sequences bound to HLA-DQ2.5	Google search (below)	Articles 15 and 18	11/15/23

Literature Search Parameters:

These searches were performed between 08/29/2023 and 12/15/2023.
List of keywords and databases used during this project.

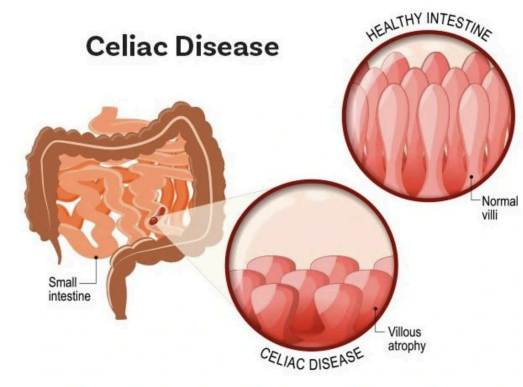
Database/search engine	Keywords	Summary of search
Scopus.org	TITLE-ABS-KEY (celiac AND disease AND nsaid) AND (LIMIT-TO (EXACTKEYWORD , "celiac disease") OR LIMIT-TO (EXACTKEYWORD , "nonsteroid antiinflammatory agent")) AND (LIMIT-TO (DOCTYPE , "ar"))	Found one article, otherwise did not come back to this search
Google.com	“Celiac disease pathology”	Founds lots of videos that proved helpful for basic information (what I was looking for)
Google.com	“tTG-modified gliadin peptides”	Used to find articles that contain peptide sequences both unmodified and modified by tTG
National Library of Medicine	“HLA-DQ2.5”	Used to find articles about the specific HLA I was using to study, also found some peptide sequences

Tags:

Tag Name	
#INTRODUCTION	#ABSTRACT
#PROCEDURE	#METHODOLOGY

#TCELL	#ENZYME
#NSAID	#CDTEST
#BRAINSTORMING	#CDTREATMENT

Article #1 Notes: What is Celiac Disease?

Source Title	Celiac Disease Foundation
Source citation (APA Format)	*What is Celiac Disease?	Celiac Disease Foundation*. (2014). Celiac Disease Foundation; Celiac. https://celiac.org/about-celiac-disease/what-is-celiac-disease/
Original URL	https://celiac.org/about-celiac-disease/what-is-celiac-disease/
Source type	General article
Keywords	Celiac disease, gluten, villi, autoimmune disorders
#Tags	#INTRODUCTION
Summary of key points + notes (include methodology)	Celiac disease is a serious autoimmune disease that occurs in genetically predisposed people where the ingestion of gluten leads to damage in the small intestine. Currently, the only treatment for celiac disease is strict adherence to a gluten-free diet. Celiac disease can also lead to iron deficiency anemia, small intestine cancer, vitamin and mineral deficiencies, and heart disease. What is Celiac Disease? [notes]
Research Question/Problem/ Need	What is celiac disease?
Important Figures	 Diagram depicting effect of CD on

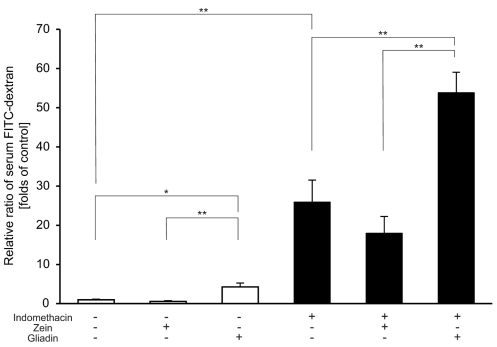
	the small intestine and the villi.
VOCAB: (w/definition)	Multiple sclerosis: an autoimmune disease that affects the Central Nervous system Lymphocytic colitis: inflammation of the large intestine
Cited references to follow up on	none
Follow up Questions	1. How is celiac disease related to multiple sclerosis? 2. What are the genes associated with celiac disease?

Article #2 Notes: Symptoms of Celiac Disease

Source Title	Celiac Disease Foundation
Source citation (APA Format)	*Symptoms of Celiac Disease | Celiac Disease Foundation*. (2019). Celiac Disease Foundation; Celiac. https://celiac.org/about-celiac-disease/symptoms-of-celiac-disease/
Original URL	https://celiac.org/about-celiac-disease/symptoms-of-celiac-disease/
Source type	General article
Keywords	Celiac disease, symptoms, malabsorption, iron-deficiency anemia,
#Tags	#INTRODUCTION
Summary of key points + notes (include methodology)	Celiac disease can be difficult to diagnose because it affects people differently. There are more than 200 known celiac disease symptoms which may occur in the digestive system or other parts of the body. Symptoms of celiac disease [notes]
Research Question/Problem/ Need	What are the symptoms of celiac disease?
Important Figures	none
VOCAB: (w/definition)	none
Cited references to follow up on	none
Follow up Questions	1. How do people develop celiac disease at different ages? 2. How does iron-deficiency anemia affect celiac disease or vice versa?

Article #3 Notes: Involvement of gliadin, a component of wheat gluten, in increased intestinal permeability leading to non-steroidal anti-inflammatory drug-induced small-intestinal damage

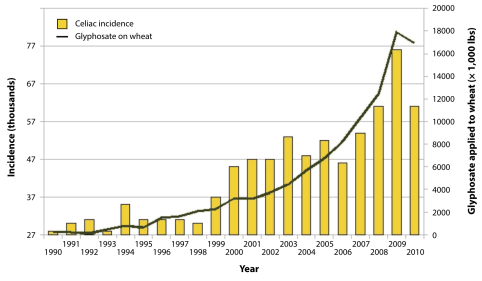
Source Title	PLoS One
Source citation (APA Format)	Shimada, S., Tanigawa, T., Watanabe, T., Nakata, A., Sugimura, N., Itani, S., Akihiro Higashimori, Yuji Nadatani, Otani, K., Taira, K., Shuhei Hosomi, Yasuaki Nagami, Tanaka, F., Kamata, N., Hirokazu Yamagami, Shiba, M., & Fujiwara, Y. (2019). Involvement of gliadin, a component of wheat gluten, in increased intestinal permeability leading to non-steroidal anti-inflammatory drug-induced small-intestinal damage. *PLOS ONE*, *14*(2), e0211436–e0211436. https://doi.org/10.1371/journal.pone.0211436
Original URL	https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0211436
Source type	Journal article
Keywords	Permeability, gastrointestinal tract, diet, phosphorylation, NSAIDs, small intestine, histology, gene expression
#Tags	#INTRODUCTION #PROCEDURE #NSAID
Summary of key points + notes (include methodology)	Gliadin, a component of wheat gluten known to be an important factor in the cause of celiac disease, was investigated with the significance of non-steroidal anti-inflammatory drug (NSAID)-induced small-intestinal damage in mice. It was shown that gliadin increased the intestinal paracellular permeability both with and without indomethacin administration. Gliadin induced phosphorylation of epidermal growth factor receptor (EGFR) in small-intestinal tissues caused the permeability exacerbated by gliadin. Involvement of gliadin, a component of wheat gluten, in increased intestinal…
Research Question/Problem/ Need	Does gliadin affect the permeability of NSAID-induced small-intestinal damage in mice?

Important Figures	 Graph showing effect of gliadin on small-intestinal permeability without and with indomethacin administration determined according to relative ratios of the concentration of serum fluorescein isothiocyanate (FITC)-dextran.
VOCAB: (w/definition)	Non-steroidal anti-inflammatory drugs: aspirin, ibuprofen Pathogenic: disease-causing Indomethacin: nonsteroidal anti-inflammatory drug (NSAID) used to treat mild to moderate acute pain and relieve symptoms of arthritis or gout, such as inflammation, swelling, stiffness, and joint pain Diclofenac: NSAID that can treat pain, migraines, and arthritis in its oral form. It can also treat actinic keratoses in its topical form Prophylactically: guarding from or preventing the spread or occurrence of disease or infection
Cited references to follow up on	Luciani A, Villella VR, Vasaturo A, Giardino I, Pettoello-Mantovani M, Guido S, et al. Lysosomal accumulation of gliadin p31-43 peptide induces oxidative stress and tissue transglutaminase-mediated PPARgamma downregulation in intestinal epithelial cells and coeliac mucosa. Gut. 2010; 59(3):311–9. Epub 2009/12/03. https://doi.org/10.1136/gut.2009.183608 PMID: 19951908 Guo S, Nighot M, Al-Sadi R, Alhmoud T, Nighot P, Ma TY. Lipopolysaccharide Regulation of Intestinal Tight Junction Permeability Is Mediated by TLR4 Signal Transduction Pathway Activation of FAK and MyD88. Journal of immunology (Baltimore, Md: 1950). 2015; 195(10):4999–5010. Epub 2015/10/16. https://doi.org/10.4049/jimmunol.1402598 PMID: 26466961; PubMed Central PMCID: PMCPMC4637237.
Follow up Questions	1. What is the effect of lipopolysaccharides and bile on intestinal permeability? 2. What is the effect of gliadin on type 1 diabetes? 3. How does EGFR phosphorylation affect other diseases? 4. How do bile acids, enterobacteria, LPS, and alarmins affect gluten digestion? 5. How does oxidative stress affect EGFR phosphorylation?

Article #4 Notes: Can Genetically Modified Foods Trigger Gluten Sensitivity?

Source Title	Earth Island Journal
Source citation (APA Format)	Spector, K. (2018). *Can Genetically Modified Foods Trigger Gluten Sensitivity?* Earth Island Journal. https://www.earthisland.org/journal/index.php/articles/entry/can_genetically_modified_foods_trigger_gluten_sensitivity/
Original URL	https://www.earthisland.org/journal/index.php/articles/entry/can_genetically_modified_foods_trigger_gluten_sensitivity/
Source type	General article
Keywords	Celiac disease, gluten, genetically modified organisms, glyphosate
#Tags	#INTRODUCTION
Summary of key points + notes (include methodology)	A recent report highlights a potential link between genetically modified organisms (GMOs) and gluten sensitivity, impacting an estimated 18 million Americans. The report suggests GMOs might contribute to conditions such as imbalanced gut bacteria, immune activation, impaired digestion, and damage to the intestinal wall. Glyphosate, a commonly used herbicide in GMO farming, is also implicated due to its potential to harm beneficial gut bacteria, which is associated with gluten-related disorders. Can genetically modified foods trigger gluten sensitivity? [notes]
Research Question/Problem/ Need	Can genetically modified foods trigger gluten sensitivity?
Important Figures	none
VOCAB: (w/definition)	Glyphosate: patented antibiotic that destroys beneficial gut bacteria; used as a weed killer
Cited references to follow up on	none
Follow up Questions	1. Can hybridized wheat trigger or exacerbate celiac disease? 2. How does glyphosate affect celiac disease?

Article #5 Notes: Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance

Source Title	Interdisciplinary Toxicology
Source citation (APA Format)	Samsel, A., & Seneff, S. (2013). Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance. *Interdisciplinary Toxicology*, *6*(4), 159–184. https://doi.org/10.2478/intox-2013-0026
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3945755/
Source type	Journal article
Keywords	Celiac disease, gluten, glyphosate, food, cytochrome P450, deficiency
#Tags	#INTRODUCTION #METHODOLOGY
Summary of key points + notes (include methodology)	This study serves to show how glyphosate affects celiac disease. This include (1) disrupting the shikimate pathway, (2) altering the balance between pathogens and beneficial biota in the gut, (3) chelating transition metals, as well as sulfur and selenium, and (4) inhibiting cytochrome P450 enzymes. Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intoler…
Research Question/Problem/ Need	How does glyphosate affect celiac disease?
Important Figures	 Graph depicting hospital discharge diagnosis (any) of celiac disease ICD-9 579 and glyphosate applications to wheat.

<table>
<tr>
<td></td>
<td>

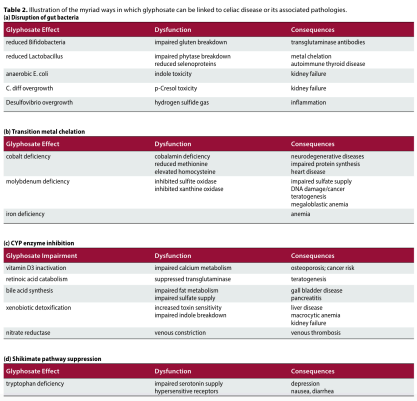
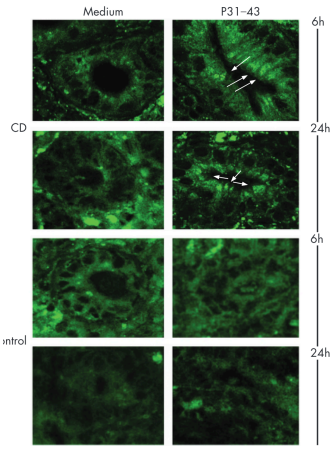



Table 2. Illustration of the myriad ways in which glyphosate can be linked to celiac disease or its associated pathologies.
(a) Disruption of gut bacteria
<table>
<tr><th>Glyphosate Effect</th><th>Dysfunction</th><th>Consequences</th></tr>
<tr><td>reduced Bifidobacteria</td><td>impaired gluten breakdown</td><td>transglutaminase antibodies</td></tr>
<tr><td>reduced Lactobacillus</td><td>impaired phytase breakdown
reduced selenoproteins</td><td>metal chelation
autoimmune thyroid disease</td></tr>
<tr><td>anaerobic E. coli</td><td>indole toxicity</td><td>kidney failure</td></tr>
<tr><td>C. diff overgrowth</td><td>p-Cresol toxicity</td><td>kidney failure</td></tr>
<tr><td>Desulfovibrio overgrowth</td><td>hydrogen sulfide gas</td><td>inflammation</td></tr>
</table>
(b) Transition metal chelation
<table>
<tr><th>Glyphosate Effect</th><th>Dysfunction</th><th>Consequences</th></tr>
<tr><td>cobalt deficiency</td><td>cobalamin deficiency
reduced methionine
elevated homocysteine</td><td>neurodegenerative diseases
impaired protein synthesis
heart disease</td></tr>
<tr><td>molybdenum deficiency</td><td>inhibited sulfite oxidase
inhibited xanthine oxidase</td><td>impaired sulfate supply
DNA damage/cancer
teratogenesis
megaloblastic anemia</td></tr>
<tr><td>iron deficiency</td><td></td><td>anemia</td></tr>
</table>
(c) CYP enzyme inhibition
<table>
<tr><th>Glyphosate Impairment</th><th>Dysfunction</th><th>Consequences</th></tr>
<tr><td>vitamin D3 inactivation</td><td>impaired calcium metabolism</td><td>osteoporosis; cancer risk</td></tr>
<tr><td>retinoic acid catabolism</td><td>suppressed transglutaminase</td><td>teratogenesis</td></tr>
<tr><td>bile acid synthesis</td><td>impaired fat metabolism
impaired sulfate supply</td><td>gall bladder disease
pancreatitis</td></tr>
<tr><td>xenobiotic detoxification</td><td>increased toxin sensitivity
impaired indole breakdown</td><td>liver disease
macrocytic anemia
kidney failure</td></tr>
<tr><td>nitrate reductase</td><td>venous constriction</td><td>venous thrombosis</td></tr>
</table>
(d) Shikimate pathway suppression
<table>
<tr><th>Glyphosate Effect</th><th>Dysfunction</th><th>Consequences</th></tr>
<tr><td>tryptophan deficiency</td><td>impaired serotonin supply
hypersensitive receptors</td><td>depression
nausea, diarrhea</td></tr>
</table>
Illustration of the myriad ways in which glyphosate can be linked to celiac disease or its associated pathologies.
</td>
</tr>
<tr>
<td>VOCAB: (w/definition)</td>
<td>Vasculature - the vascular system of a part of the body and its arrangement
Nephrosis - kidney disease, especially when characterized by edema and the loss of protein from the plasma into the urine due to increased glomerular permeability
Malignancy - the state or presence of a malignant tumor; cancer</td>
</tr>
<tr>
<td>Cited references to follow up on</td>
<td>Gobbetti M, Giuseppe Rizzello C, Di Cagno R, De Angelis M.(2007). Sourdough lactobacilli and celiac disease. Food Microbiol 24(2): 187–96.
Bode R, Melo C, Birnbaum D. (1984). Mode of action of glyphosate in Candida maltosa. Arch Microbiol 140(1): 83–5.</td>
</tr>
<tr>
<td>Follow up Questions</td>
<td>1. How does celiac disease affect serotonin synthesis?
2. How does serotonin synthesis cause depression? (functional dyspepsia)
3. How does celiac disease result in Shikimate pathway suppression and what are the direct relations/probabilities of depression?</td>
</tr>
</table>

Article #6 Notes: Effects of Nonsteroidal Anti-Inflammatory Drugs at the Molecular Level

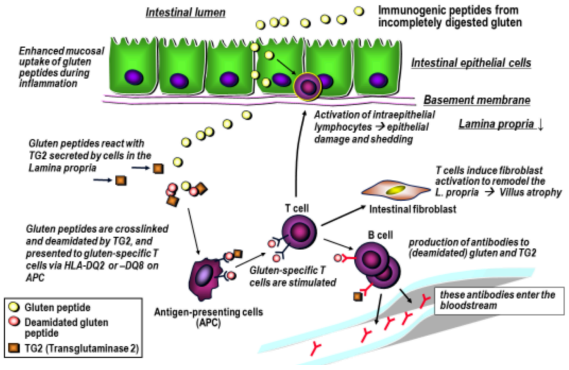
Source Title	The Eurasian Journal of Medicine
Source citation (APA Format)	Gunaydin, C., & Sirri Bilge. (2018). *Effects of Nonsteroidal Anti-Inflammatory Drugs at the Molecular Level*. Eajm.org. https://www.eajm.org//en/effects-of-nonsteroidal-anti-inflammatory-drugs-at-the-molecular-level-133048%5C
Original URL	https://www.eajm.org//en/effects-of-nonsteroidal-anti-inflammatory-drugs-at-the-molecular-level-133048%5C
Source type	Journal article
Keywords	Nonsteroidal anti-inflammatory drugs, mechanism, cyclooxygenase, molecular
#Tags	#INTRODUCTION #NSAID
Summary of key points + notes (include methodology)	This article explores the molecular effects of NSAIDs on different systems in the body. In the gastrointestinal system, NSAIDs block the production of prostaglandins through the inhibition of two cyclooxygenase enzymes. The inhibition of COX-1 enzymes cause gastric hypermotility and can lead to restricted blood flow. Effects of Nonsteroidal Anti-Inflammatory Drugs at the Molecular Level [notes]
Research Question/Problem/ Need	How do NSAIDs affect different systems of the body?
Important Figures	N/A (none in the article)
VOCAB: (w/definition)	Gastric hypermotility - inherited or acquired changes that come with decreased contractile forces or slower transit Tissue hypoxia - oxygen is not available in sufficient amounts at the tissue level to maintain adequate homeostasis
Cited references to follow up on	Matsui, H., Shimokawa, O., Kaneko, T., Nagano, Y., Rai, K., & Ichinosuke Hyodo. (2011). The pathophysiology of non-steroidal anti-inflammatory drug (NSAID)-induced mucosal injuries in stomach and small intestine. *Journal of Clinical Biochemistry and Nutrition*, 48(2), 107–111. https://doi.org/10.3164/jcbn.10-79
Follow up Questions	1. What is the relationship between angiogenesis and angiotensin? 2. What mechanism causes gastric hypermotility from COX-1-inhibition?

Article #7 Notes: Growth factor-like activity of gliadin, an alimentary protein: implications for coeliac disease

Source Title	Gut
Source citation (APA Format)	Maria Vittoria Barone, Gimigliano, A., Castoria, G., Paolella, G., Maurano, F., Paparo, F., Maglio, M., Mineo, A., Miele, E., Nanayakkara, M., Troncone, R., & Auricchio, S. (2007). Growth factor-like activity of gliadin, an alimentary protein: implications for coeliac disease. *Gut*, *56*(4), 480–488. https://doi.org/10.1136/gut.2005.086637
Original URL	https://gut.bmj.com/content/56/4/480
Source type	Journal article
Keywords	Gliadin, celiac disease, EGFR, vesicle, signal transduction
#Tags	#INTRODUCTION #METHODOLOGY
Summary of key points + notes (include methodology)	Gliadin effects were tested on a number of cell lines and on cultured mucosa samples, and standard biochemical methods were used to assess prolonged epidermal growth factor receptor activation. This work shows that gliadin peptides interfere with EGFR endocytosis, amplifying the effects of epidermal growth factor. Growth factor-like activity of gliadin, an alimentary protein: implications for …
Research Question/Problem/ Need	What mechanisms drive gliadin-induced effects in CD?
Important Figures	 Persistence of endocytic vesicles containing epidermal growth factor (EGF)-Alexa488 after P31–43 treatment in cultured biopsies from coeliac disease

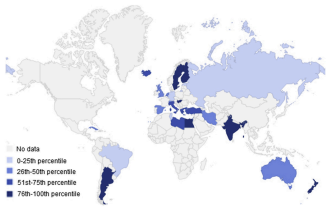
	(CD) patients.
VOCAB: (w/definition)	Epithelial - relating to or denoting the thin tissue forming the outer layer of a body's surface and lining the alimentary canal and other hollow structures Enteropathy - ongoing damage or irritation and swelling to the small intestine
Cited references to follow up on	Clemente MG, De Virgiliis S, Kang JS, et al. Early effects of gliadin on enterocyte intracellular signalling involved in intestinal barrier function. *Gut* 2003;2:218–23.
Follow up Questions	1. How does gliadin elicit its EGF-like effects? 2. What is the viability of gliadin peptides?

Article #8 Notes: Gluten Degrading Enzymes for Treatment of Celiac Disease

Source Title	MDPI Nutrients
Source citation (APA Format)	Wei, G., Helmerhorst, E. J., Darwish, G., Blumenkranz, G., & Schuppan, D. (2020). Gluten Degrading Enzymes for Treatment of Celiac Disease. *Nutrients*, *12*(7), 2095–2095. https://doi.org/10.3390/nu12072095
Original URL	https://www.mdpi.com/2072-6643/12/7/2095
Source type	Journal article
Keywords	celiac disease, gluten, enzyme therapy, treatment, autoimmunity, endopeptidase, glutenase, wheat, enteric coating
#Tags	#INTRODUCTION #METHODOLOGY #ENZYME
Summary of key points + notes (include methodology)	Many bacterial, fungal and plant derived glutenases are considered promising candidates for an (adjunctive) oral enzyme therapy. However, a major challenge for enzyme therapy remains to secure rapid and complete enzymatic digestion of immunogenic gluten peptides that are embedded in a complex food matrix. Gluten Degrading Enzymes for Treatment of Celiac Disease [notes]
Research Question/Problem/ Need	What enzymes have been shown to reduce gluten levels in the small intestine?
Important Figures	 Figure depicting the pathomechanism of CD
VOCAB: (w/definition)	Concomitant - naturally accompanying or associated Ameliorate - make (something bad or unsatisfactory) better
Cited references to follow up on	Hausch, F.; Shan, L.; Santiago, N.A.; Gray, G.M.; Khosla, C. Intestinal digestive

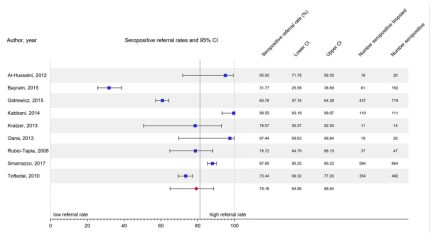
	resistance of immunodominant gliadin peptides. Am. J. Physiol. Gastrointest. Liver Physiol. 2002, 283, G996–G1003. Ehren, J.; Moron, B.; Martin, E.; Bethune, M.T.; Gray, G.M.; Khosla, C. A food-grade enzyme preparation with modest gluten detoxification properties. PLoS ONE 2009, 4, e6313. Darwish, G.; Helmerhorst, E.J.; Schuppan, D.; Oppenheim, F.G.; Wei, G. Pharmaceutically modified subtilisins withstand acidic conditions and effectively degrade gluten in vivo. Sci Rep. 2019, 9, 7505. Wolf, C.; Siegel, J.B.; Tinberg, C.; Camarca, A.; Gianfrani, C.; Paski, S.; Guan, R.; Montelione, G.; Baker, D.; Pultz, I.S. Engineering of Kuma030: A Gliadin Peptidase that rapidly degrades immunogenic gliadin peptides in gastric conditions. J. Am. Chem. Soc. 2015, 137, 13106–13113. Shan, L.; Molberg, O.; Parrot, I.; Hausch, F.; Filiz, F.; Gray, G.M.; Sollid, L.M.; Khosla, C. Structural basis for gluten intolerance in celiac sprue. Science 2002, 297, 2275–2279. [CrossRef] Shan, L.; Qiao, S.W.; Arentz-Hansen, H.; Molberg, O.; Gray, G.M.; Sollid, L.M.; Khosla, C. Identification and analysis of multivalent proteolytically resistant peptides from gluten: Implications for celiac sprue. J. Proteome Res. 2005, 4, 1732–1741. [CrossRef]
Follow up Questions	1. What other enzymes have been tested to reduce gluten? 2. What enzymes could theoretically reduce gluten but haven't been tested? 3. What enzymes could stop the signaling pathways that result in CD? 4. Could you compete out 33mer and 26mer to prevent it from binding to the T cells?

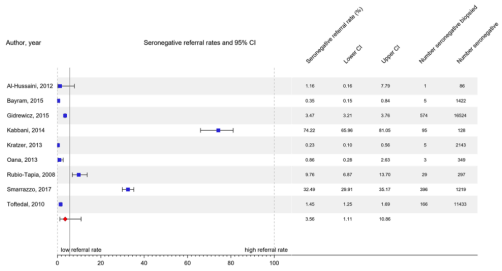
Article #9 Notes: Global Prevalence of Celiac Disease: Systematic Review and Meta-analysis

Source Title	Clinical Gastroenterology and Hepatology
Source citation (APA Format)	Singh, P., Arora, A., Strand, T. A., Leffler, D. A., Catassi, C., Green, P. H., Kelly, C. P., Ahuja, V., & Govind Makharia. (2018). Global Prevalence of Celiac Disease: Systematic Review and Meta-analysis. *Clinical Gastroenterology and Hepatology*, *16*(6), 823-836.e2. https://doi.org/10.1016/j.cgh.2017.06.037
Original URL	https://www.cghjournal.org/article/S1542-3565(17)30783-8/fulltext
Source type	Journal article
Keywords	Epidemiology, gluten, diet, autoimmune disorder
#Tags	#INTRODUCTION
Summary of key points + notes (include methodology)	This study shows that the prevalence values for celiac disease were 0.4% in South America, 0.5% in Africa and North America, 0.6% in Asia, and 0.8% in Europe and Oceania; the prevalence was higher in female vs male individuals, and greater in children vs adults. Global Prevalence of Celiac Disease: Systematic Review and Meta-analysis [n…
Research Question/Problem/ Need	What is the global prevalence of celiac disease?
Important Figures	 Figure depicting the global prevalence of CD
VOCAB: (w/definition)	Seroprevalence - number of persons in a population who test positive for a specific disease based on serology specimens Biopsy - procedure to remove a piece of tissue or a sample of cells from your body so that it can be tested in a laboratory
Cited references to follow up on	Fabiani E, Peruzzi E, Mandolesi A, et al. Anti-human versus antiguinea pig tissue transglutaminase antibodies as the first-level serological screening test for coeliac disease in the general population. *Dig Liver Dis* 2004;36:671–676.

Follow up Questions	none

Article #10 Notes: Estimating the Impact of Verification Bias on Celiac Disease Testing

Source Title	Journal of Clinical Gastroenterology
Source citation (APA Format)	Hujoel, I. A., Jansson-Knodell, C., Hujoel, P. P., Margaux L.A. Hujoel, Rok Seon Choung, Murray, J. A., & Rubio–Tapia, A. (2020). Estimating the Impact of Verification Bias on Celiac Disease Testing. *Journal of Clinical Gastroenterology*, *55*(4), 327–334. https://doi.org/10.1097/mcg.0000000000001361
Original URL	https://journals.lww.com/jcge/Citation/2021/04000/Estimating_the_Impact_of_Verification_Bias_on.8.aspx
Source type	Journal article
Keywords	Diagnostic accuracy; verification bias; serology; celiac disease
#Tags	#CDTEST
Summary of key points + notes (include methodology)	A large number of studies estimating the accuracy of IgA tTG are at high risk for verification bias and that adjusting for this bias led to a substantial decrease in the sensitivity estimate. Continued use of IgA tTG as an initial diagnostic test may lead to underdiagnosis of CD. Estimating the Impact of Verification Bias on Celiac Disease Testing [notes]
Research Question/Problem/ Need	What is the impact of verification bias on the diagnostic accuracy of immunoglobulin A tissue transglutaminase (IgA tTG) in detecting celiac disease?
Important Figures	

	 Figure 1: referral rates to upper endoscopy and duodenal biopsy after an abnormal IgA tissue transglutaminase antibody test from the 9 studies identified in the systematic review, as well as a pooled referral rate. Figure 2: referral rates to upper endoscopy and duodenal biopsy after a normal IgA tissue transglutaminase antibody test from the 9 studies identified in the systematic review, as well as a pooled referral rate.
VOCAB: (w/definition)	Kappa statistic - The kappa statistic compares observed accuracy with expected accuracy (random chance) Begg and Greenes method - uses observed proportions of those who have and do not have the target condition among the verified participants to calculate the expected number of those who have and do not have the target condition among those participants who did not undergo condition verification
Cited references to follow up on	Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, Murray JA, American College of G. ACG clinical guidelines: diagnosis and management of celiac disease. American Journal of Gastroenterology. 2013;108(5):656–676; quiz 677. Reitsma J, Glas A, Rutjes A, Scholten R, Bossuyt P, Zwinderman A. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. J Clin Epidemiol. 2005;58(10):982–990. [PubMed: 16168343]
Follow up Questions	1. How could you improve the accuracy of the test? 2. Could you design another test that tests for antigens instead of TTG-IgA?

Article #11 Notes: Celiac Disease Tests

Source Title	National Institute of Diabetes and Digestive and Kidney Diseases
Source citation (APA Format)	Murray, J. (2023, October 25). *Celiac Disease Tests*. National Institute of Diabetes and Digestive and Kidney Diseases; NIDDK - National Institute of Diabetes and Digestive and Kidney Diseases. https://www.niddk.nih.gov/health-information/professionals/clinical-tools-patient-management/digestive-diseases/celiac-disease-health-care-professionals
Original URL	https://www.niddk.nih.gov/health-information/professionals/clinical-tools-patient-management/digestive-diseases/celiac-disease-health-care-professionals
Source type	General article
Keywords	Celiac disease test, biopsy, serologic test, tTG-IgA test, EMA-IgA test, genetic test
#Tags	#CDTEST
Summary of key points + notes (include methodology)	Many tests for celiac disease begin with blood tests. However, these blood tests all have restrictions and are not always accurate, so a biopsy is the only true way to determine if a patient has CD. Celiac Disease Tests [notes]
Research Question/Problem/ Need	What tests are used to diagnose celiac disease?
Important Figures	none
VOCAB: (w/definition)	none
Cited references to follow up on	Husby S, Murray JA, Katzka DA. AGA clinical practice update on diagnosis and monitoring of celiac disease—changing utility of serology and histologic measures: expert review. Gastroenterology. 2019;156(4):885–889. doi:10.1053/j.gastro.2018.12.010
Follow up Questions	1. Could you design a blood test that tests patients with mild CD? 2. Can you test for the presence of gliadin-a2 remaining in the system?

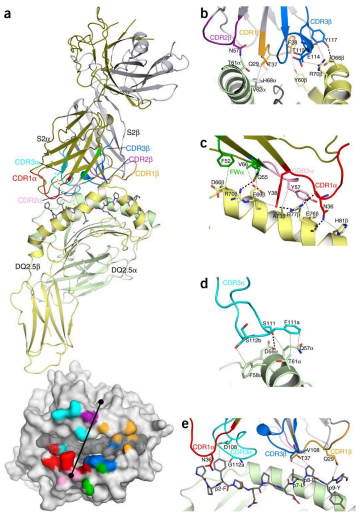
Article #12 Notes: The Intestinal T Cell Response to α-Gliadin in Adult Celiac Disease Is Focused on a Single Deamidated Glutamine Targeted by Tissue Transglutaminase

Source Title	Journal of Experimental Medicine
Source citation (APA Format)	Arentz-Hansen, H., Körner, R., Øyvind Molberg, Hanne Quarsten, Vader, W., Kooy, Y., Knut E.A. Lundin, Koning, F., Roepstorff, P., Sollid, L. M., & McAdam, S. N. (2000). The Intestinal T Cell Response to α-Gliadin in Adult Celiac Disease Is Focused on a Single Deamidated Glutamine Targeted by Tissue Transglutaminase. *Journal of Experimental Medicine*, *191*(4), 603–612. https://doi.org/10.1084/jem.191.4.603
Original URL	https://rupress.org/jem/article/191/4/603/30043/The-Intestinal-T-Cell-Response-to-Gliadin-in-Adult
Source type	Journal article
Keywords	HLA-DQ2, modification, gluten, oral tolerance, mucosal immunity
#Tags	#METHODOLOGY #INTRODUCTION
Summary of key points + notes (include methodology)	This study demonstrates that intestinal T cell response to α-gliadin in adult CD is focused on two immunodominant, DQ2-restricted peptides that overlap by a seven-residue fragment of gliadin. tTG converts a glutamine residue within this fragment into glutamic acid and this process is critical for T cell recognition. STEM Meeting #4
Research Question/Problem/ Need	How does the intestinal system respond to varied gliadin peptides?
Important Figures	stem update meeting #4
VOCAB: (w/definition)	Motif - a short conserved sequence pattern associated with distinct functions of a protein or DNA Deamidation - a chemical reaction in which an amide functional group in the side chain of the amino acids asparagine or glutamine is removed or converted to another functional group Chymotrypsin - another serine protease produced by the pancreas that hydrolyzes

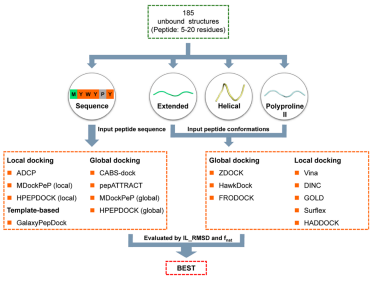
	the peptide bonds of tryptophan, leucine, tyrosine, and phenylalanine Polyclonal - produced by, involving, or being cells derived from two or more cells of different ancestry or genetic constitution In situ - latin phrase meaning “in the original/same place”
Cited references to follow up on	Johansen, B.H., F. Vartdal, J.A. Eriksen, E. Thorsby, and L.M. Sollid. 1996. Identification of a putative motif for binding of peptides to HLA-DQ2. Int. Immunol. 8:177–182. Vartdal, F., B.H. Johansen, T. Friede, C.J. Thorpe, S. Stevanovic, J.E. Eriksen, K. Sletten, E. Thorsby, H.G. Rammensee, and L.M. Sollid. 1996. The peptide binding motif of the disease associated HLA-DQ (a1*0501, b1*0201) molecule. Eur. J. Immunol. 26:2764–2772. Arentz-Hansen, E.H., S.N. McAdam, Ø. Molberg, C. Kristiansen, and L.M. Sollid. 2000. Production of a panel of recombinant gliadins for the characterisation of T cell reactivity in coeliac disease. Gut. 46:46–51.
Follow up Questions	1. How can you inhibit cytokine IFN-γ? 2. Can you inhibit tTG modification of gliadin-a2?

Article #13 Notes: T-cell receptor recognition of HLA-DQ2–gliadin complexes associated with celiac disease

Source Title	Nature Structural & Molecular Biology
Source citation (APA Format)	Petersen, J., Verónica Montserrat, Mujico, J. R., Khai Lee Loh, Beringer, D. X., Mennno van Lummel, Thompson, A., M. Luisa Mearin, Schweizer, J. J., Kooy–Winkelaar, Y., Jeroen van Bergen, Drijfhout, J. W., Kan, W.-T., La, N. L., Anderson, R. P., Reid, H. H., Koning, F., & Rossjohn, J. (2014). T-cell receptor recognition of HLA-DQ2–gliadin complexes associated with celiac disease. *Nature Structural & Molecular Biology*, *21*(5), 480–488. https://doi.org/10.1038/nsmb.2817
Original URL	https://www.nature.com/articles/nsmb.2817
Source type	Journal article
Keywords	T-cell receptor, gliadin-a2, HLA-DQ2.5, epitope, gliadin, peptide, celiac disease
#Tags	#INTRODUCTION #BRAINSTORMING
Summary of key points + notes (include methodology)	This study identifies 3 unique TCRs specific for DQ2.5-glia-α2. Their interactions with the gliadin determinants differ significantly, providing a basis for epitope specificity. CamScanner 10-23-2023 17.50.pdf
Research Question/Problem/ Need	How does HLA-DQ2.5 bind to T-cells and how are they recognized?

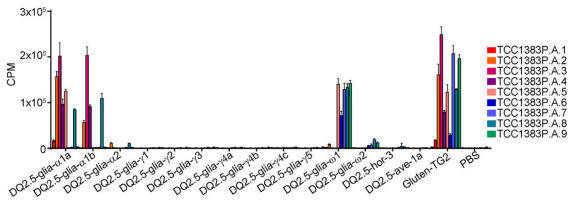
Important Figures	 (a) Overview of the S2–HLA-DQ2.5-glia-α1a complex with the peptide shown as gray sticks. (b) Interactions between the S2 β-chain and HLA-DQ2.5. (c) Interactions between the S2 CDR1α loop and the HLA-DQ2.5 β-chain. (d) Largely apolar interactions between the S2 CDR3α loop and the HLA-DQ2.5 β-chain. (e) Interactions between the S2 TCR and the DQ2.5-glia-α1a peptide.
VOCAB: (w/definition)	Lamina propria - loose connective tissue in a mucosa BSA - serum albumin protein derived from cows. It is often used as a protein concentration standard in lab experiments beta/alpha loops - patternless regions which connect two regular secondary structures
Cited references to follow up on	Abadie, V., Sollid, L.M., Barreiro, L.B. & Jabri, B. Integration of genetic and immunological insights into a model of celiac disease pathogenesis. Annu. Rev. Immunol. 29, 493–525 (2011). Qiao, S.W. et al. Tissue transglutaminase-mediated formation and cleavage of histamine-gliadin complexes: biological effects and implications for celiac disease. J. Immunol. 174, 1657–1663 (2005). Yin, Y., Li, Y. & Mariuzza, R.A. Structural basis for self-recognition by autoimmune T-cell receptors. Immunol. Rev. 250, 32–48 (2012).
Follow up Questions	1. Can you inhibit the recognition of TCRs to gliadin? 2. How likely is each gliadin epitope likely to bind to a TCR?

Article #14 Notes: Comprehensive Evaluation of Fourteen Docking Programs on Protein-Peptide Complexes

Source Title	Journal of Chemical Theory and Computation
Source citation (APA Format)	Weng, G., Gao, J., Wang, Z., Wang, E., Hu, X., Yao, X., Cao, D., & Hou, T. (2020). *Comprehensive Evaluation of Fourteen Docking Programs on Protein–Peptide Complexes*. J. Chem. Theory Comput. 2020, 16, 6, 3959–3969. https://pubs.acs.org/doi/10.1021/acs.jctc.9b01208
Original URL	https://pubmed.ncbi.nlm.nih.gov/32324992/
Source type	Journal article
Keywords	Peptide-peptide binding, software, simulation
#Tags	#METHODOLOGY
Summary of key points + notes (include methodology)	In this study, a large benchmark made of 185 protein−peptide complexes was constructed and tested in various protein-peptide docking programs. It concluded that in global docking, HPEPDOCK shows the best performance and in local docking, ADCP shows the best performance, both over the entire benchmark set. Comprehensive Evaluation of Fourteen Docking Programs on Protein-Peptid…
Research Question/Problem/ Need	What program best performs protein-peptide interaction prediction?
Important Figures	 Overview of this study - for docking programs requiring the peptide structures as the input, three initial peptide conformations and unbound proteins were used for docking. For the other docking programs, only the peptide sequence and unbound proteins were employed for docking.
VOCAB: (w/definition)	Empirical - based on, concerned with, or verifiable by observation or experience rather than theory or pure logic.
Cited references to follow up on	Petsalaki, E.; Russell, R. B. Peptide-mediated interactions in biological systems:

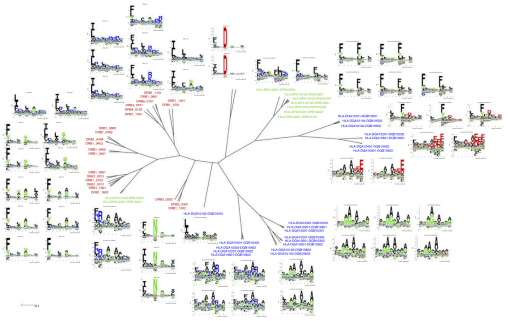
	new discoveries and applications. Curr. Opin. Biotechnol. 2008, 19, 344−350. Porter, K. A.; Xia, B.; Beglov, D.; Bohnuud, T.; Alam, N.; SchuelerFurman, O.; Kozakov, D. ClusPro PeptiDock: efficient global docking of peptide recognition motifs using FFT. Bioinformatics 2017, 33, 3299−3301. Wen, Z.; He, J.; Tao, H.; Huang, S. Y. PepBDB: a comprehensive structural database of biological peptide-protein interactions. Bioinformatics 2019, 35, 175−177.
Follow up Questions	1. Does my project involve global or local binding? 2. Are there any other softwares not tested that could work more efficiently? 3. What calculations do each of these programs do differently?

Article #15 Notes: Discriminative T-cell receptor recognition of highly homologous HLA-DQ2–bound gluten epitopes

Source Title	Journal of Biological Chemistry
Source citation (APA Format)	Dahal-Koirala, S., Ciacchi, L., Petersen, J., Louise Fremgaard Risnes, Ralf Stefan Neumann, Christophersen, A., Knut E.A. Lundin, Hugh Harrington Reid, Qiao, S., Rossjohn, J., & Sollid, L. M. (2019). Discriminative T-cell receptor recognition of highly homologous HLA-DQ2–bound gluten epitopes. *Journal of Biological Chemistry*, *294*(3), 941–952. https://doi.org/10.1074/jbc.ra118.005736
Original URL	https://www.jbc.org/article/S0021-9258(20)40029-8/fulltext
Source type	Journal article
Keywords	T-cell receptor, major histocompatibility complex, crystal structure, surface plasmon resonance, gluten intolerance, immune response, immunodominant epitope
#Tags	#METHODOLOGY
Summary of key points + notes (include methodology)	This study shows the ability of TCRs to recognize differences in the HLA-bound peptides in a human disease setting. It analyzes proliferation of 2 immunodominant peptides and modifications that affect binding. Discriminative T-cell receptor recognition of highly homologous HLA-DQ2–b…
Research Question/Problem/ Need	How do TCCs differ for DQ2.5-glia-1a and DQ2.5glia-1 differ in structure and binding?
Important Figures	 Graph depicting cell proliferation in various TCCs of different peptide-presenting antigens
VOCAB: (w/definition)	Phylogenetically - in a way that relates to the evolutionary development and diversification of a species or group of organisms Cleft - the space between domains of a protein, often the binding or catalytic site

	of an enzyme Chimera - an organism or tissue that contains at least two different sets of DNA, most often originating from the fusion of as many different zygotes (fertilized eggs)
Cited references to follow up on	Petersen, J., Montserrat, V., Mujico, J. R., Loh, K. L., Beringer, D. X., van, L. M., Thompson, A., Mearin, M. L., Schweizer, J., Kooy-Winkelaar, Y., van, B. J., Drijfhout, J. W., Kan, W. T., La Gruta, N. L., Anderson, R. P., Reid, H. H., Koning, F., and Rossjohn, J. (2014) T-cell receptor recognition of HLA-DQ2-gliadin complexes associated with celiac disease. Nat. Struct. Mol. Biol. 21, 480 – 488 Kim, C. Y., Quarsten, H., Bergseng, E., Khosla, C., and Sollid, L. M. (2004) Structural basis for HLA-DQ2-mediated presentation of gluten epitopes in celiac disease. Proc. Natl. Acad. Sci. U.S.A. 101, 4175– 4179 Christophersen, A., Raki, M., Bergseng, E., Lundin, K. E., Jahnsen, J., Sollid, L. M., and Qiao, S. W. (2014) Tetramer-visualized gluten-specific CD4 T cells in blood as a potential diagnostic marker for coeliac disease without oral gluten challenge. United European Gastroenterol J 2, 268 –278
Follow up Questions	1. Are there any other peptide positions that have a significant effect on binding strength/probability? 2. What specific part of the peptide is presented to the TCR?

Article #16 Notes: Improved methods for predicting peptide binding affinity to MHC class II molecules

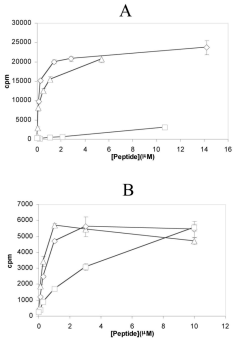
Source Title	Immunology
Source citation (APA Format)	Jensen, K. K., Andreatta, M., Paolo Marcatili, Buus, S., Greenbaum, J. A., Zhen, Y., Sette, A., Peters, B., & Nielsen, M. (2018). Improved methods for predicting peptide binding affinity to MHC class II molecules. *Immunology*, *154*(3), 394–406. https://onlinelibrary.wiley.com/doi/10.1111/imm.12889
Original URL	https://onlinelibrary.wiley.com/doi/10.1111/imm.12889
Source type	Journal article
Keywords	affinity predictions, immunogenic peptides, MHC binding specificity, peptide–MHC binding, T-cell epitope
#Tags	#METHODOLOGY
Summary of key points + notes (include methodology)	Two pieces of software were improved upon, designed to predict Binding Affinity and Eluted Ligand mass spectrometry for peptide binding to MHC-II molecules. They show that training with an extended data set improved the performance for peptide binding predictions for both methods. Improved methods for predicting peptide binding affinity to MHC class II mo…
Research Question/Problem/ Need	How accurately can you predict which peptides will be presented by the MHC-II molecule?
Important Figures	 Distance tree for all HLA molecules found in the data set generated using the MHC CLUSTER method. Sequence logos show the motif of the predicted binding core for each HLA and were generated using Seq2Logo.
VOCAB: (w/definition)	Immunogenicity - the ability of cells/tissues to provoke an immune response and is

	generally considered to be an undesirable physiological response Polymorphic - occurring in several different forms, in particular with reference to species or genetic variation
Cited references to follow up on	Brown JH, Jardetzky TS, Gorga JC, Stern LJ, Urban RG, Strominger JL et al. Threedimensional structure of the human Class II histocompatibility antigen HLA-DR1. J Immunol 2015; 194:5–11. Nielsen M, Lundegaard C, Blicher T, Peters B, Sette A, Justesen S et al. Quantitative predictions of peptide binding to any HLA-DR molecule of known sequence: NetMHCIIpan. PLoS Comput Biol 2008; 4:e1000107.
Follow up Questions	What other softwares exists? Is it possible to compare software accuracy?

Article #17 Notes: HLA-DQ2: The Primary Celiac Disease Gene

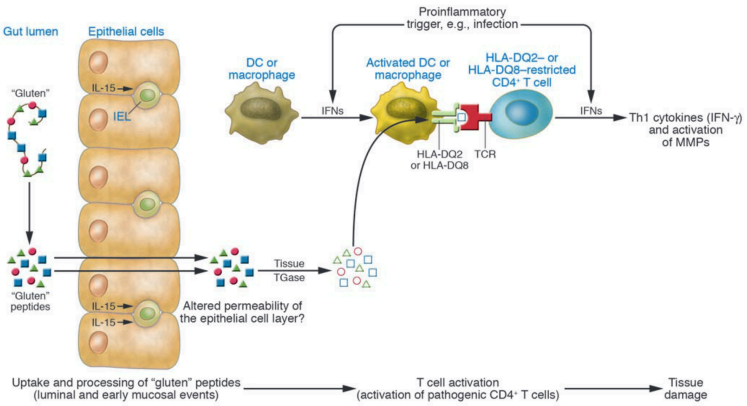
Source Title	Verywell Health
Source citation (APA Format)	Anderson, J. (2022). *HLA-DQ2: The Primary Celiac Disease Gene*. Verywell Health. https://www.verywellhealth.com/hla-dq2-the-primary-celiac-disease-gene-562569
Original URL	https://www.verywellhealth.com/hla-dq2-the-primary-celiac-disease-gene-562569
Source type	General article
Keywords	HLA-DQ2.5, CeD, genes, inheritance
#Tags	#INTRODUCTION
Summary of key points + notes (include methodology)	HLA-DQ2 is one of two main genes involved in celiac disease, and it is the most common out of the 2 main genes. Most doctors believe you need at least one copy of either HLA-DQ2 or HLA-DQ8 to develop celiac disease. HLA-DQ2: The Primary Celiac Disease Gene [notes]
Research Question/Problem/ Need	n/a
Important Figures	n/a
VOCAB: (w/definition)	none
Cited references to follow up on	Petersen J, Montserrat V, Mujico JR, et al. T-cell receptor recognition of HLA-DQ2-gliadin complexes associated with celiac disease. Nat Struct Mol Biol. 2014;21(5):480-8. doi:10.1038/nsmb.2817
Follow up Questions	How does a c-section influence risk of CeD? How does one's time of year of birth affect their risk of CeD?

Article #18 Notes: Inhibition of HLA-DQ2-Mediated Antigen Presentation by Analogues of a High Affinity 33-Residue Peptide from α2-Gliadin

Source Title	American Chemical Society
Source citation (APA Format)	Xia, J., Siegel, M., Bergseng, E., Sollid, L. M., & Khosla, C. (2021). *Inhibition of HLA-DQ2-Mediated Antigen Presentation by Analogues of a High Affinity 33-Residue Peptide from α2-Gliadin*. J. Am. Chem. Soc. 2006, 128, 6, 1859–1867. https://pubs.acs.org/doi/10.1021/ja056423o
Original URL	https://pubs.acs.org/doi/10.1021/ja056423o
Source type	Journal article
Keywords	Celiac Sprue, HLA-DQ2, gluten, gliadin, 33-mer, antigen presentation, inhibition
#Tags	#METHODOLOGY
Summary of key points + notes (include methodology)	Based on the gliadin-α2-33 mer, two ligands were able to cause the proliferation of disease-specific T cell lines in response to gluten antigens, and therefore represent examples of pharmacologically suitable DQ2 blocking agents for the potential treatment of CeD. Inhibition of HLA-DQ2-Mediated Antigen Presentation by Analogues of a Hig…
Research Question/Problem/ Need	What is the relationship between peptide structure and DQ2 affinity?
Important Figures	 T cell proliferation induced by three peptides, the 33-mer 1 (△), peptide 3 ( ), and the 20-mer 5 (◊). Paraformaldehyde-fixed DQ2 cells were used as antigen presenting cells. (A) Proliferation of a polyclonal T cell line (TCL P28 33mer) that is responsive to the DQ2-αI, DQ2-αII, and DQ2-αIII epitopes. (B) Proliferation of a T

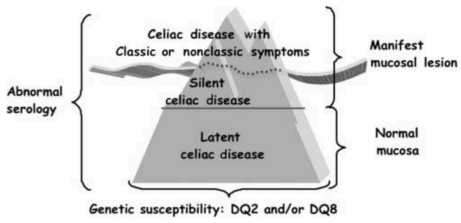
	cell clone (TCC P26c αII) that recognizes the DQ2-αII epitope (peptide 3).
VOCAB: (w/definition)	Encephalomyelitis - neurological disorder characterized by brief but widespread attacks of inflammation (swelling) in the brain and spinal cord that damages myelin Brush-border enzymes - enzymes that digest the products of luminal digestion to produce monosaccharides
Cited references to follow up on	Martin F. Kagnoff. Celiac disease: pathogenesis of a model immunogenetic disease. Journal of Clinical Investigation 2007, 117 (1) , 41-49. https://doi.org/10.1172/JCI30253 Elena Lionetti, Carlo Catassi. New Clues in Celiac Disease Epidemiology, Pathogenesis, Clinical Manifestations, and Treatment. International Reviews of Immunology 2011, 30 (4) , 219-231. https://doi.org/10.3109/08830185.2011.602443
Follow up Questions	Is it possible to do this using a software program instead of all in vitro? What other methods are there for analyzing the data?

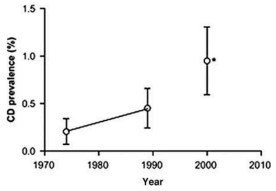
Article #19 Notes: Celiac disease: pathogenesis of a model immunogenetic disease

Source Title	The Journal of Clinical Investigation
Source citation (APA Format)	Kagnoff, M. F. (2007). Celiac disease: pathogenesis of a model immunogenetic disease. *Journal of Clinical Investigation*, *117*(1), 41–49. https://doi.org/10.1172/jci30253
Original URL	https://www.jci.org/articles/view/30253
Source type	Journal article
Keywords	celiac disease, enteropathy-associated T cell lymphoma, “gluten”-free diet, intraepithelial lymphocyte
#Tags	#INTRODUCTION
Summary of key points + notes (include methodology)	It is essential to develop animal models to model the key events in the pathogenesis of this disease. Discovery and understanding of the missing links in this process can lead to new approaches for the prevention, diagnosis, and treatment of CeD. Celiac disease: pathogenesis of a model immunogenetic disease [notes]
Research Question/Problem/ Need	What is the role of adaptive and innate immune mechanisms in the pathogenesis of CeD?
Important Figures	 Pathogenesis of CD. This schematic divides the pathogenesis of CD into 3 major series of events: luminal and early mucosal events; the activation of pathogenic CD4+ T cells; and the subsequent events leading to tissue damage.
VOCAB: (w/definition)	Squamoid - scaly

	Crypt hypertrophy - when the grooves are elongated compared to a normal intestinal lining which has short crypts Hexaploid genome - six copies of each chromosome
Cited references to follow up on	Khosla, C., Gray, G.M., and Sollid, L.M. 2005. Putative efficacy and dosage of prolyl endopeptidase for digesting and detoxifying gliadin peptides. Gastroenterology. 129:1362–1363; author reply 1363. Mention, J.J., et al. 2003. Interleukin 15: a key to disrupted intraepithelial lymphocyte homeostasis and lymphomagenesis in celiac disease. Gastroenterology. 125:730–745. Johansen, B.H., et al. 1996. Both alpha and beta chain polymorphisms determine the specific ity of the disease-associated HLA-DQ2 molecules, with beta chain residues being most influential. Immunogenetics. 45:142–150.
Follow up Questions	Are there any other potential therapeutics for CeD? What other important peptides to inhibit CeD are there? Why does barley and rye have less of an impact on CeD pathology?

Article #20 Notes: New Clues in Celiac Disease Epidemiology, Pathogenesis, Clinical Manifestations, and Treatment

Source Title	International Reviews of Immunology
Source citation (APA Format)	Lionetti, E. & Catassi, C. New Clues in Celiac Disease Epidemiology, Pathogenesis, Clinical Manifestations, and Treatment. (2011). *International Reviews of Immunology*. Vol. 30, Issue 4. https://www.tandfonline.com/doi/full/10.3109/08830185.2011.602443
Original URL	https://www.tandfonline.com/doi/full/10.3109/08830185.2011.602443
Source type	Journal article
Keywords	celiac disease, epidemiology, pathogenesis, clinical manifestations, therapy
#Tags	#INTRODUCTION
Summary of key points + notes (include methodology)	CeD is the result of an abnormal immune reaction, the clinical spectrum of which is large, including cases with either typical intestinal or atypical extraintestinal features as well as silent forms. New pharmacological treatments are few and far between and are under heavy clinical testing. New Clues in Celiac Disease Epidemiology, Pathogenesis, Clinical Manifestati…
Research Question/Problem/ Need	n/a (review of topics)
Important Figures	 Iceberg model of CeD (above) and prevalence of CeD over multiple decades (below)

	
VOCAB: (w/definition)	Heterodimers - a protein composed of two polypeptide chains differing in composition in the order, number, or kind of their amino acid residues Hypotonia - decreased muscle tone
Cited references to follow up on	Mustalahti K, Catassi C, Reunanen A, et al. The prevalence of CD in Europe: results of a centralized, international mass screening project. Ann Med. 2010;42:587–595. Bach JF. The effect of infections on susceptibility to autoimmune and allergic diseases. N Engl J Med. 2002;347:911–920. Jabri B, Sollid LM. Tissue-mediated control of immunopathology in coeliac disease. Nat Rev Immunol. 2009;9:858–870.
Follow up Questions	Is the increased % of people with CeD a result of the disease becoming more prevalent or a greater improvement in testing accuracy? Why is CeD rising in developed countries more commonly than undeveloped countries? How can zonulin be modified to lessen the risk of gluten proteins entering the small intestine? Can other diseases in early childhood effect prevalence of CeD later in life (microbiome)?

Patent #1 Notes: Methods of Treating Celiac Disease Using SMAD7 Inhibition

Source Title	Google Patents
Source citation (APA Format)	Monteleone, G. (2021). *Methods of Treating Celiac Disease Using SMAD7 Inhibition* (U.S. Patent No. 20210207143). U.S. Patent and Trademark Office. https://patents.google.com/patent/US20210207143A1/en
URL	https://patents.google.com/patent/US20210207143A1/en?q=(celiac+disease+drug)&oq=celiac+disease+drug
Keywords	Inhibitor, CeD, treatment, oligonucleotide, growth factor signaling, villous atrophy
#Tags	#INTRODUCTION #CDTREATMENT
Summary of key points + notes	The invention consists of techniques for controlling the administration of the SMAD7 antisense oligonucleotide therapy for celiac disease, as well as ways to measure its efficacy based on examination of Transforming Growth Factor-β (TGF-β) signaling activity. Methods of Treating Celiac Disease Using SMAD7 Inhibition [notes]
VOCAB: (w/definition)	Growth factor - naturally occurring substance that can stimulate cell growth, wound healing, and tissue repair Oligonucleotide - short, single- or double-stranded DNA or RNA molecules Antisense - a non-coding DNA strand of a gene, used as a template for mRNA Clinical amelioration - relating to the direct medical treatment or testing of patients Enteric coating - polymer barrier applied to oral medication that prevents its dissolution or disintegration in the gastric environment
Follow up Questions	Was there any data analysis done? What methods were used? What is the relationship between SMAD7 and HLA? Does the inhibitor affect any other systems in the digestive tract or immune system?

Patent #2 Notes: Treatment of celiac disease

Source Title	Google Patents
Source citation (APA Format)	Bonnafous, C., Sicard, H., Buffet, R., Hermine, O. (2016). *Title of patent* (Fr. Patent No. 2016030488). Institut national de la propriété industrielle. https://patents.google.com/patent/WO2016030488A1/en
URL	https://patents.google.com/patent/WO2016030488A1/en?q=(celiac+disease+treatment)&oq=celiac+disease+treatment
Keywords	Inhibition, antibody, peptide, HLA, cell proliferation
#Tags	#INTRODUCTION #CDTREATMENT
Summary of key points + notes	It has been shown that KIR3DL2-positive persons can also have celiac disease. Treatment options for KIR3DL2-negative patients include employing an antigen binding agent that binds to a KIR3DL2 polypeptide to treat or prevent celiac disease in a single person. Treatment of celiac disease [notes]
VOCAB: (w/definition)	IEL - lymphocytes associated with the intestinal tract, respiratory tract, genitourinary tract epithelium, and the skin and are the first immune system cells to encounter pathogens that have invaded an epithelial surface Polyclonal - produced by, involving, or being cells derived from two or more cells of different ancestry or genetic constitution Ex vivo - takes place outside an orgnism Moiety - a specific group of atoms within a molecule that is responsible for characteristic chemical reactions of that molecule
Follow up Questions	Does KIR3DL2 interact with HLA-DQ2? Does tTG modification affect KIR3DL2 interaction with its peptides? What is LQYDELPYT (peptide sequence) derived from?

Patent #3 Notes: Peptide microarrays and novel biomarkers for celiac disease

Source Title	Google Patents
Source citation (APA Format)	Bei, K., Jayaraman, K., Krishna, K., Krishnamurthy, K., Rajasekaran, J., Wang, T. (2015). *Peptide microarrays and novel biomarkers for celiac disease* (Au. Patent No. 2019200921). IP Australia. https://patents.google.com/patent/AU2019200921B2/en
URL	https://patents.google.com/patent/AU2019200921B2/en?q=(celiac+disease+treatment)&oq=celiac+disease+treatment
Keywords	Automated robotics, chemoselectivity, antigens, peptides, inhibition
#Tags	#INTRODUCTION #CDTREATMENT
Summary of key points + notes	The invention is broadly related to peptide arrays and biomarkers, and specifically to a technique of identifying biomarkers for autoimmune diseases such as celiac disease utilizing a peptide array. A collection of highly sensitive and specific novel biomarkers for celiac disease are revealed, along with treatment strategies based on the novel biomarkers. Peptide microarrays and novel biomarkers for celiac disease [notes]
VOCAB: (w/definition)	Chemoselectivity - the tendency for a specific reaction pathway to occur among a set of potential alternatives in chemical reactions Endogenous antigens - antigens that exist on cells inside your body Th1 and Th2 cells - Th1 cells mainly develop following infections by intracellular bacteria and some viruses, whereas Th2 cells predominate in response to infestations by gastrointestinal nematodes Heat maps - 2-dimensional data visualization technique that represents the magnitude of individual values within a dataset as a color Linker molecule - cleavable or noncleavable molecules that connect a functional (bio)molecule with a molecular tag to form a conjugate
Follow up Questions	Why is the specific peptide length 12 amino acids long? Can these biomarkers be applied to other antigens or diseases with similar pathology?