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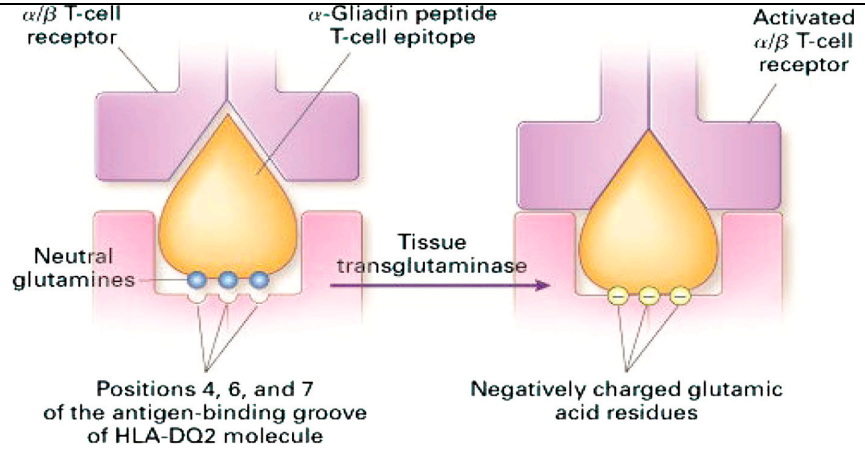
SNP SUMMARY: HUMAN LEUKOCYTE ANTIGEN (HLA) GENE HAPLOTYPE

Overview	Celiac disease (CD) is characterized by a permanent intolerance for gluten proteins present in dietary wheat, rye, and barley. Gluten initiates a wide array of disorders. Recently, the increasing number of patients worldwide who are sensitive to dietary gluten without evidence of celiac disease or wheat allergy has contributed to the identification of a new gluten-related syndrome defined as non-celiac gluten sensitivity (NCGS). The human leukocyte antigen (HLA) genes produce a group of proteins called the HLA complex, which is responsible for how the immune system distinguishes between the body proteins and foreign proteins. Six gene variations in the HLA gene region determine the risk level for celiac disease, which is the most severe form of gluten intolerance. A negative result can exclude the likelihood of symptoms being caused by celiac disease.
Name of gene	Human Leukocyte Antigen gene
Symbol of gene	HLA
rs numbers	rs2395182 rs4639334 rs7775228 rs7454108 rs2187668 rs4713586

Haplotype	Combinations of the six genetic variants are used to determine the presence or absence of the HLA haplotypes, and consequently the risk of developing celiac disease. Studies have shown that certain DQ genotypes are associated with a greater risk than other DQ genotypes The risk genotypes are DQ2 or DQ8.
Haplotype nomenclature	DQ2 and DQ8
Impact of SNPs on biological pathway/s	Wolters and Wijmenga (2008) describe the genotype/phenotype impact as follows: Gluten proteins provoke the disease, as the high proline content of gluten is relatively resistant to proteolytic digestion in the intestinal tract. The undigested gluten peptides are deamidated by tissue transglutaminase, which results in a better binding capacity to the pocket of HLA-DQ2 or HLA-DQ8 molecules on antigen-presenting cells. This complex is presented to CD4+ T-cells and the ensuing immune response causes inflammation and intestinal tissue damage.
Biochemical pathway	This figure is from Wolters, V. M., & Wijmenga, C. (2008). Pathogenesis of celiac disease: Gliadin is absorbed into the lamina propria and presented in conjunction with HLA-DQ2 or HLADQ8 cell-surface antigens by antigen-presenting cells, to sensitized T-cells expressing the α/β-cell receptor. Tissue transglutaminase deamidates gliadin peptides, generating acidic, negatively charged residues of glutamic acid from neutral glutamines. Because negatively charged residues are preferred in positions 4, 6, and 7 of the antigen-binding groove of HLA-DQ2, deamidated gliadin elicits a stronger T-cell response.

	
Nutrient interaction	All foods containing gluten
Established diet-gene interactions	• Approximately 99% of people with celiac disease and 60% of those with NCGS have the DQ2 or DQ8 risk version of HLA, compared to only 30% of the general population. • The most important genetic factors identified are HLA-DQ2 and DQ8, which are necessary but not sufficient, by themselves, to predispose an individual to CD. • A positive test result for DQ2 or DQ8 is not a diagnosis of celiac disease, and further investigation will be recommended. However, having a negative result for DQ2 and DQ8 rules out celiac disease. • Since only about 60% of individuals with NCGS possess DQ2 or DQ8, a negative test result cannot be used to rule out NCGS.
Potential dietary recommendations	• As little as 50 mg/day of gluten ingested can be enough to cause adverse effects in individuals with celiac disease. • A definitive celiac disease diagnosis requires a gluten-free diet, however as a practitioner if you suspect NCGS, you may wish to trial the removal of gluten.

<table>
<tr><td></td><td colspan="2">The gluten-free diet includes the removal of gluten containing foods listed in the table below from the diet.
Common gluten-containing foods include pasta, couscous, bread, flour tortillas, biscuits, cakes, muffins, pastries, cereal, crackers, beer, dressings, sauces etc.
Hidden gluten sources include thickening agents, instant coffee, malt drinks, ready-made coffee or cocoa (from machines), battered/crumbed e.g. battered fish or crumbed chicken, processed meats and sausages, some cheeses. Read the labels for margarine and butters to make sure the product is gluten free.
Gluten-free foods that are permitted in the gluten-free diet are also listed in the table below. In addition all foods labeled gluten-free are permitted in the diet.
Other foods permitted in the gluten-free diet include: All “unprocessed” vegetables and fruits, meat, fish, poultry, dairy products and oils. These foods are naturally gluten-free.
It is important that the individual reads the nutritional information and labels regarding the contents of gluten. Most products indicate whether the product is gluten-free or contains gluten.
In addition it is important for the individual to know that “wheat-free” does not necessarily mean “gluten-free”.
It is also important to know that ‘gluten free’ is not the same as healthy. Many gluten-free products are processed foods that contain refined carbohydrates and added sugars, and should be used as little as possible.
This web page from the Coeliac Support Association is an excellent resource. www.csaceliacs.org/grains_and_flours_glossary.jsp</td></tr>
<tr><td>Various foods and their gluten content</td><td>Gluten Containing Foods
(Storage protein not permitted)</td><td>Gluten free foods
(Storage protein permitted)</td></tr>
</table>

	Wheat Whole wheat flour White flour Durum wheat Semolina Kamut Rye Barley Triticale Oats* Some thickening agents e.g. in gravy	Amaranth Arrowroot Buckwheat Corn/maize Indian Rice Grass Legumes Mesquite Millet Nuts Potato Quinoa Rice Sorghum/Milo Soy Tapioca Polenta Sweet potato Wild Rice
	*Oats consumption is controversial for individuals with gluten sensitivity because it appears to be contaminated in the commercial industry. However it has been demonstrated that some individuals are able to eat non-contaminated oats without experiencing symptoms. The healthcare provider should assist the individual regarding the dietary intake thereof.	
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