

# HLA-DQA1 Gene

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## 1. Introduction

The *HLA-DQA1* gene provides instructions for making a protein that plays a critical role in the immune system. The *HLA-DQA1* gene is part of a family of genes called the human leukocyte antigen (HLA) complex. The HLA complex helps the immune system distinguish the body's own proteins from proteins made by foreign invaders such as viruses and bacteria.

The HLA complex is the human version of the major histocompatibility complex (MHC), a gene family that occurs in many species. The *HLA-DQA1* gene belongs to a group of MHC genes called MHC class II. MHC class II genes provide instructions for making proteins that are present on the surface of certain immune system cells. These proteins attach to protein fragments (peptides) outside the cell. MHC class II proteins display these peptides to the immune system. If the immune system recognizes the peptides as foreign (such as viral or bacterial peptides), it triggers a response to attack the invading viruses or bacteria.

The protein produced from the *HLA-DQA1* gene attaches (binds) to the protein produced from another MHC class II gene, *HLA-DQB1*. Together, they form a functional protein complex called an antigen-binding DQαβ heterodimer. This complex displays foreign peptides to the immune system to trigger the body's immune response.

Each MHC class II gene has many possible variations, allowing the immune system to react to a wide range of foreign invaders. Researchers have identified hundreds of different versions (alleles) of the *HLA-DQA1* gene, each of which is given a particular number (such as *HLA-DQA1\*05:01*).

## 2. Health Conditions Related to Genetic Changes

### 2.1. Celiac Disease

At least two specific combinations of HLA gene variants (HLA haplotypes) have been found to increase the risk of developing celiac disease, a disorder in which inflammation damages the intestinal tract and other organs and tissues. One of these haplotypes, known as DQ2, is composed of the protein produced from *HLA-DQA1* gene variants known as *HLA-DQA1\*05:01* or *HLA-DQA1\*05:05* bound to the protein produced from *HLA-DQB1* gene variants known as *HLA-DQB1\*02:01* or *HLA-DQB1\*02:02*. The other haplotype, known as DQ8, is composed of the protein produced from *HLA-DQA1* gene variants known as *HLA-DQA1\*03:01* or *HLA-DQA1\*03:02* bound to the protein produced from the *HLA-DQB1* gene variant known as *HLA-DQB1\*03:02*.

The DQ2 and DQ8 haplotypes, which may occur separately or together, seem to increase the risk of an inappropriate immune response to the protein gluten, which is found in wheat, rye, and barley. This immune system malfunction results in the damage to the body's organs and tissues that occurs in celiac disease. However, the DQ2 and DQ8 haplotypes are also found in 30 percent of the general population, and only 3 percent of individuals with these haplotypes develop celiac disease.

### 2.2. Type 1 Diabetes

Combinations of variations in the *HLA-DQA1* gene and other HLA genes affect the risk of type 1 diabetes. Type 1 diabetes is characterized by high blood sugar levels resulting from a shortage of the hormone insulin and is caused by autoimmune damage to insulin-producing cells in the pancreas.

Type 1 diabetes risk is most increased by two HLA haplotypes involving variations of the *HLA-DQA1* and *HLA-DQB1* genes and another HLA gene called *HLA-DRB1*. One haplotype, written as *DRB1\*03:01-DQA1\*05:01-DQB1\*02*, is called DR3. The other haplotype, written as *DRB1\*04:01/02/04/05/08-DQA1\*03:01-DQB1\*02*, is called DR4. People at highest risk of developing type 1 diabetes have one copy of the DR3 haplotype and one copy of the DR4 haplotype in each cell. Other HLA haplotypes only mildly increase the risk of type 1 diabetes, while some haplotypes seem to protect against developing this condition. Variations in other genes and environmental factors are also thought to affect the risk of this complex disorder.

### 2.3. Autoimmune Disorders

Certain normal variations of the *HLA-DQA1* gene have been associated with increased risk of autoimmune disorders, which occur when the immune system malfunctions and attacks the body's own tissues and organs. It is unclear how different versions of the *HLA-DQA1* gene influence the risk of developing autoimmune disorders. These conditions are thought to result from a combination of multiple environmental and genetic factors. Changes in other HLA and non-HLA genes, some of which remain unknown, also likely contribute to the risk of developing these complex conditions.

### 2.4. Other Disorders

Normal variations in the *HLA-DQA1* gene can affect the body's ability to recognize and react to foreign invaders (pathogens). For example, variations of this gene have been shown to increase or decrease a person's chance of getting infections such as hepatitis B and leprosy or may affect the severity of illness if infection occurs.

A particular variant of the *HLA-DQA1* gene known as *HLA-DQA1\*02:01* increases the risk of liver damage in women with advanced breast cancer treated with a drug called lapatinib. Researchers suggest that the variant may increase immune system sensitivity to the drug, resulting in inflammation that damages the liver.

## 3. Other Names for This Gene

- DC-1 alpha chain
- DC-alpha
- DQ-A1
- FLJ27088
- FLJ27328
- GSE
- HLA class II histocompatibility antigen, DQ alpha 1 chain
- HLA class II histocompatibility antigen, DQ alpha 1 chain precursor
- HLA class II histocompatibility antigen, DQ(W3) alpha chain
- HLA-DCA
- HLA-DQA
- leucocyte antigen DQA1
- leukocyte antigen alpha chain
- MGC149527
- MHC class II antigen
- MHC class II DQA1
- MHC class II HLA-D alpha glycoprotein
- MHC class II HLA-DQ-alpha-1
- MHC class II surface glycoprotein

- MHC HLA-DQ alpha

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## References

1. Abadie V, Sollid LM, Barreiro LB, Jabri B. Integration of genetic and immunological insights into a model of celiac disease pathogenesis. *Annu Rev Immunol*. 2011;29:493-525. doi: 10.1146/annurev-immunol-040210-092915. Review.
  2. da Silva SA, Mazini PS, Reis PG, Sell AM, Tsuneto LT, Peixoto PR, Visentainer JE. HLA-DR and HLA-DQ alleles in patients from the south of Brazil: markers for leprosy susceptibility and resistance. *BMC Infect Dis*. 2009 Aug 22;9:134. doi:10.1186/1471-2334-9-134.
  3. Lipton RB, Drum M, Greeley SA, Danielson KK, Bell GI, Hagopian WA. HLA-DQ haplotypes differ by ethnicity in patients with childhood-onset diabetes. *Pediatr Diabetes*. 2011 Jun;12(4 Pt 2):388-95. doi: 10.1111/j.1399-5448.2010.00712.x.
  4. Noble JA, Valdes AM. Genetics of the HLA region in the prediction of type 1 diabetes. *Curr Diab Rep*. 2011 Dec;11(6):533-42. doi: 10.1007/s11892-011-0223-x. Review.
  5. Spraggs CF, Budde LR, Briley LP, Bing N, Cox CJ, King KS, Whittaker JC, Mooser VE, Preston AJ, Stein SH, Cardon LR. HLA-DQA1\*02:01 is a major risk factor for lapatinib-induced hepatotoxicity in women with advanced breast cancer. *J Clin Oncol*. 2011 Feb 20;29(6):667-73. doi: 10.1200/JCO.2010.31.3197.
  6. Taylor AK, Lebowitz B, Snyder CL, Green PHR. Celiac Disease. 2008 Jul 3 [updated 2019 Jan 31]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. *GeneReviews®* [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1727/>
  7. Tjon JM, van Bergen J, Koning F. Celiac disease: how complicated can it get? *Immunogenetics*. 2010 Oct;62(10):641-51. doi: 10.1007/s00251-010-0465-9.
  8. Uibo R, Tian Z, Gershwin ME. Celiac disease: a model disease for gene-environment interaction. *Cell Mol Immunol*. 2011 Mar;8(2):93-5. doi:10.1038/cmi.2010.62.
  9. Xun YH, Guo JC, Shi WZ, Shi JP, Liu CL. [Association between HLA-DQA1 gene polymorphism and the outcomes of hepatitis B virus infection]. *Zhonghua Shi Yan He Lin Chuang Bing Du Xue Za Zhi*. 2009 Dec;23(6):430-3. Chinese.
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