

# Genetic differences help distinguish type 1 diabetes in children from 'type 1.5' in adults

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A multi-center team of researchers led by Children's Hospital of Philadelphia (CHOP) has discovered a genetic signature that could help distinguish an adult-onset form of diabetes sharing many type 1 diabetes

(T1D) characteristics from pediatric-onset T1D, opening the door to potentially more straightforward diagnostic tests for the adult condition and improving responses by ensuring patients receive the most appropriate treatment.

"This is our first insight into [genetic differences](#) between latent autoimmune diabetes in adults and T1D in children that may be diagnostically useful," said study leader Struan Grant, Ph.D., Co-Director of the Center for Spatial and Functional Genomics at CHOP and the Daniel B. Burke Endowed Chair for Diabetes Research. "We have found a genetic means of discriminating between the two conditions without expensive and cumbersome anti-autobody screening."

The study was published online December 16, 2019 in *Diabetes Care*.

Latent autoimmune diabetes in adults (LADA) is sometimes referred to as "type 1.5 diabetes" because it shares characteristics of both T1D and type 2 diabetes (T2D). Like T1D, LADA produces autoantibodies that attack the body's insulin-producing beta cells in the pancreas. However, like those with T2D, patients with LADA are diagnosed in adulthood and do not require insulin at the time of diagnosis. For this reason, LADA is often misdiagnosed as T2D; studies have shown that up to 10% of T2D diagnoses are, in fact, LADA, and as a result patients do not respond to the commonly inappropriate treatments prescribed to them.

An earlier genome-wide association study led by CHOP found that, from a genetic perspective, LADA has more in common with T1D than with T2D. Researchers wanted to take a deeper dive and look for genetic differences that could help discriminate between LADA and T1D, meaning the diagnosis of LADA could potentially begin with a simple genotype array, rather than with a more complex and expensive autoantibody screening.

To do so, the team decided to look at the major histocompatibility complex (MHC), a highly variable region of the genome that helps drive the immune system and is implicated in T1D. Earlier studies have shown that when researchers control for T1D genetic variants in one part of the MHC, other variants associated with T1D appear in another part of the MHC.

The study team applied that methodology to both a set of T1D data as well as a cohort of LADA patients. They found that when it came to the T1D group, the results from the earlier studies held: controlling for genetic variants in one part of the MHC revealed variants in another part of the MHC.

However, researchers did not find the same effect with LADA patients. When controlling for genetic variants in the MHC in those patients, the additional association was not observed within this key region—an important genetic distinction between the two conditions. When a sensitivity test was applied to the two cohorts, researchers still saw the effect only in T1D patients, not in those with LADA.

"This suggests that these MHC class associations may be a genetic discriminator between LADA and childhood-onset T1D," said Diana Cousminer, Ph.D., a geneticist at CHOP and a joint-first author of the study. "The next step is to look at this association in different ethnicities, particularly African ancestry, where the prevalence of adult-onset [diabetes](#) can be significantly higher in certain parts of the world."

**More information:** Rajashree Mishra et al, Genetic Discrimination Between LADA and Childhood-Onset Type 1 Diabetes Within the MHC, *Diabetes Care* (2019). [DOI: 10.2337/dc19-0986](https://doi.org/10.2337/dc19-0986)

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