

Insights into the genetic architecture of penicillin allergy

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Researchers announce the first robust evidence for the role of the major histocompatibility complex gene *HLA-B* in penicillin allergy. To identify genetic risk factors for penicillin allergy, the international team of researchers harnessed self-reported data and the electronic health records of more than 600,000 people, as well as replicating their findings in two independent research cohorts involving more than 1 million individuals. Kristi Krebs, Ph.D., of the University of Tartu in Estonia, presented the results of the study at the American Society of Human Genetics 2020 Virtual Meeting.

Penicillin is a life-saving antibiotic but also the most common cause of drug [allergy](#), with manifestations ranging from temporary skin reactions to life-threatening systemic syndromes. However, the role of genetic factors influencing the susceptibility to [penicillin allergy](#) remains largely unknown.

Dr. Krebs and her colleagues collected data from the [electronic health records](#) of more than 600,000 people of European ancestry from the UK, Estonian, and Vanderbilt University Medical Center's BioVU biobanks. They conducted a [genome-wide association study](#) in all three cohorts

and the results were further meta-analyzed.

The analyses revealed a significant signal coming from the human leukocyte antigen (HLA) region on chromosome 6. HLA is the human version of the major histocompatibility complex (MHC), a gene group that occurs in many species. This gene group is involved in the immune system's ability to distinguish the body's own proteins from proteins made by foreign invaders, such as viruses and bacteria.

Fine-mapping of the association narrowed the signal down to a specific version of the *HLA-B* gene, an allele called *HLA-B*55:01* with an average frequency of 2% in the European population.

"Overall, carriers of this allele were found to have a 33 percent higher relative odds of [penicillin](#) allergy," says Dr. Krebs.

As a final step, the researchers performed a replication of the association between this allele and penicillin allergy in two independent research cohorts totaling more than 1 million individuals.

Again, they detected a robust association between self-reported penicillin allergy and the *HLA-B*55:01* allele.

Dr. Krebs says that more research is needed to determine the precise immune processes involved in penicillin allergy and to gain more clinically actionable insights into [genetic risk factors](#) underlying [hypersensitivity reactions](#) to the drug.

"This discovered association between the *HLA-B*55:01* allele and penicillin allergy would need further in-depth research on the specific types of penicillin-induced hypersensitivity reactions," says Dr. Krebs.

"Studying both severe and milder types of hypersensitivity reactions could help reveal the

mechanism behind the role of the *HLA-B*55:01* allele in this condition and to determine the precise underlying immune processes."

This study illustrates the power of biobanks linked with electronic health records by demonstrating that leveraging data from large-scale cohorts, we have the necessary means for research on penicillin allergy and for also other adverse drug reactions in the future.

Provided by American Society of Human Genetics

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