Why do different people react differently to the same virus infection?

New research maps epigenetic markers in immune cells, explaining why the same virus infection can have different disease severity levels and paving the way for personalized treatment.

Scientists have mapped how genetic material and life experiences leave lasting 'epigenetic imprints' on immune cells. This finding helps explain why people react so differently to the same virus and opens up the possibility of personalized treatment in the future.

The COVID-19 pandemic clearly demonstrated a fact: even with the same virus, some people experience only mild symptoms, while others develop severe, life-threatening conditions. This difference raises a major question: why do two people infected with the same pathogen have such different outcomes?

The answer largely lies in two factors: genetics (the genes you inherit) and life experiences (environment, disease history, vaccinations, etc.). These two factors shape our cells through subtle molecular changes called epigenetic modifications. These changes don't alter the DNA sequence, but rather control which genes are 'on' or 'off,' thereby determining how the cell functions.

Researchers at the Salk Institute have just built a comprehensive 'epigenetic map' that separates the impact of genetics and life experiences on various types of immune cells. This new database, published in *Nature Genetics* on January 27, 2026, provides a clearer understanding of why immune responses differ between individuals and could aid in the development of more precise treatments.

According to Professor Joseph Ecker, co-lead author of the study, immune cells carry within them a 'molecular profile' of both genes and life experiences. These two forces shape the immune system in very different ways. He said that infections and environmental factors leave long-lasting 'epigenetic fingerprints,' affecting how immune cells function. By analyzing at the cell type level, scientists can begin to link genetic and epigenetic risk factors to the very cells where disease originates.

What is epigenetics?

Every cell in the body contains the same set of DNA, but their functions are very different. This difference is partly explained by 'epigenetic markers' – small chemical groups attached to DNA that determine which genes are active and which are silenced. The collection of all these markers is called the epigenome.

Unlike DNA, which is fixed, epigenetics is flexible. Some changes are strongly influenced by genetic material, while others develop gradually over time due to environmental factors and life experiences. Immune cells are influenced by both of these factors, but until now, scientists did not know whether they acted in the same or different ways.

Researcher Wenliang Wang stated that the 'innate versus environmental' debate has a long history in biology. The team's question was: exactly how are these two factors expressed in immune cells and how do they affect health?

What kind of impact do infections and the environment have?

The research team analyzed blood samples from 110 individuals with diverse genetic backgrounds and exposure histories. Participants had been exposed to a variety of factors, including influenza, HIV-1, MRSA, MSSA, SARS-CoV-2, anthrax vaccination, or organophosphorus pesticides.

They focused on four main groups of immune cells. T and B cells are responsible for long-term immune memory, while monocytes and NK (natural killer) cells respond quickly and broadly to threats. By analyzing epigenetic patterns in each cell type, the team constructed a detailed catalog of distinct DNA methylation regions (DMRs).

According to researcher Wubin Ding, many disease-related gene variants actually function by altering DNA methylation levels in specific types of immune cells. By mapping these links, scientists can pinpoint exactly which cells and molecular pathways are affected, thereby opening up avenues for more targeted treatments.

Distinguishing between genetic markers and experiential markers.

A major achievement of the research is the distinction between genetically determined epigenetic modifications (gDMRs) and epigenetic modifications (eDMRs). These two groups are often concentrated in different regions of the epithelium.

gDMRs – which are influenced by genes – are typically found near stable gene regions, particularly in long-lived T and B cells. Meanwhile, eDMRs – which are linked to experience – are concentrated in flexible regulatory regions that control situational immune responses.

This suggests that genetics establishes a stable, long-term immune 'backdrop,' while life experiences fine-tune adaptive responses to context. However, further research is needed to fully understand how these two factors impact immune performance and disease risk.

Researcher Manoj Hariharan believes this atlas of human immune cells will be a valuable resource for future disease mechanism research, from infectious to genetic diseases, as well as supporting diagnosis and prognosis. When patients develop the disease, these 'epigenetic signatures' could act as maps to help classify and assess risk levels.

Predicting disease risk and providing personalized treatment.

The research findings show that both innate and environmental factors contribute to shaping immune cell identity and immune system behavior. This new catalog lays the foundation for future personalized prevention and treatment strategies.

Professor Ecker said that as the database expands with more patient samples, it could help predict individual responses to infectious diseases. For example, if there is enough data from COVID-19 patients, scientists could identify a common protective epigenetic marker in survivors. Doctors could then check if newly infected patients carry a similar marker, and if not, could intervene in the related regulatory mechanisms.

Wang emphasized that this research lays the foundation for precision prevention strategies in infectious diseases. In the future, with COVID-19, influenza, or many other diseases, we may be able to predict how a person will react to a virus even before they are exposed. Instead of waiting for the disease to occur, scientists could use genomes to predict how infection will affect epigenetics, thereby predicting the severity of symptoms.