

LONG COVID - SCIENCE & TECHNOLOGY

NEWS: A recent study, published in *Nature Genetics*, looked at the genetic information of many people from different parts of the world to see if **inherited differences play a role in Long COVID**.

- The study used a method **called Genome-Wide Association Study (GWAS)**.
- This method scans our DNA for tiny “**spelling mistakes**” (called **single-nucleotide polymorphisms or SNPs**) that are **more common in people with a certain condition**.

WHAT'S IN THE NEWS?

What is Long COVID?

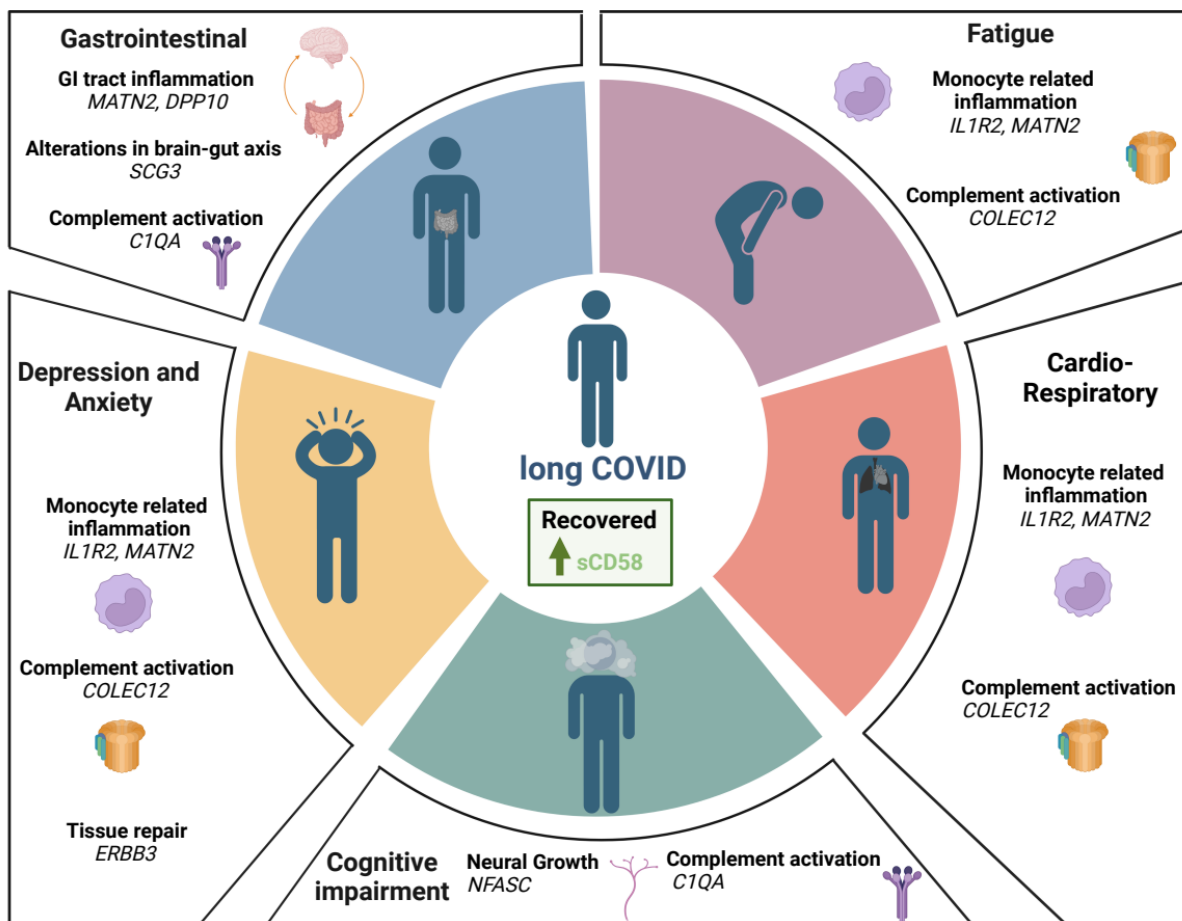
- **Persistent Post-COVID Condition:**
Long COVID refers to the **prolonged symptoms** experienced by individuals **weeks or even months** after recovering from the initial SARS-CoV-2 infection. These symptoms can occur **even in mild or asymptomatic cases**.
- **Recognized by WHO:**
The **World Health Organization (WHO)** officially recognizes Long COVID as a **multi-system post-viral condition**, affecting both physical and mental health.
- **Common Symptoms:**
The most frequently reported symptoms include:
 - **Chronic fatigue** and exhaustion
 - **Breathlessness or difficulty breathing**
 - **Cognitive issues**, such as poor concentration or memory loss (“brain fog”)
 - **Sleep disturbances, chest pain, palpitations, and joint or muscle aches** in some patients
- **Lack of Targeted Treatment:**
As of now, there is **no approved or specific drug therapy** for Long COVID. Management is mainly **symptom-based** and may involve **rehabilitation, mental health support, and respiratory therapy**.

Key Genetic Discovery: FOXP4 Gene and Long COVID Risk

- **Chromosome 6 Linkage:**
A large genetic study has identified a **significant association** between Long COVID and a **specific region on chromosome 6**, near a gene known as **FOXP4** (Forkhead Box P4).
- **Variant rs9367106 Identified:**
Researchers pinpointed a **particular genetic variant**, named **rs9367106**.
 - Individuals carrying the “**C**” **version** of this variant were found to be about **63% more likely** to develop Long COVID symptoms compared to those without it.
- **Independent of Disease Severity:**
The increased risk associated with this variant was observed **even among individuals who were not hospitalized** or had only mild COVID.

- This suggests that **genetic susceptibility plays a role**, separate from how severe the original infection was.
- **Population-Based Variation:**
The **frequency of the “C” variant** of rs9367106 varies significantly between ethnic populations:
 - Present in only **1.6% of non-Finnish Europeans**
 - But seen in **up to 36% of East Asians**, indicating **unequal genetic risk distribution** across global populations.

Distinct proteome of long COVID subtypes



What Does FOXP4 Do? — Function and Relevance

- **Role in Lung Tissue:**
The FOXP4 gene is **highly active in the lungs**, particularly in **type 2 alveolar cells**, which are:
 - Essential for **gas exchange, fluid clearance, and repair of damaged lung tissue**
 - Responsible for **secreting surfactants** to keep alveoli (air sacs) from collapsing
- **Immune Response Regulation:**
FOXP4 is also involved in **regulating immune responses**, including how **lung cells react to respiratory viruses** such as **SARS-CoV-2**.

Its overactivity could result in **persistent inflammation** or **impaired healing**, contributing to Long COVID.

- **Elevated FOXP4 Linked to Higher Risk:**

Individuals with **moderately elevated levels** of FOXP4 in the blood — even after recovery from acute infection — were found to be **twice as likely** to report lingering Long COVID symptoms.

Long COVID in the Indian Context: Emerging Concerns

- **Multiple COVID-19 Waves with Lingering Impact:**

India has faced **several waves of COVID-19 infections**, including Delta and Omicron, with **millions affected**.

Despite this, there is still **limited awareness, insufficient surveillance, and lack of long-term follow-up** mechanisms to track **Long COVID cases** systematically.

- **High Prevalence of Long COVID Symptoms:**

Several Indian clinical studies and post-COVID patient surveys report a **high incidence of Long COVID symptoms**:

- Between **45% to 80% of patients** (depending on the study and population) experienced symptoms **lasting weeks or months** after testing negative.
- In one study, **16.5% of hospitalized COVID-19 patients** still reported symptoms like **fatigue, breathlessness, and reduced physical endurance** even **one year after recovery**.

Data Gaps in Global Research and Their Implications

- **Underrepresentation of South Asians in Global Studies:**

Many large-scale international genetic studies on Long COVID, including the FOXP4 gene variant analysis, had **limited participation from South Asia**.

This creates a **major research gap**, as findings may not fully apply to Indian populations without further validation.

- **Unique Indian Health Landscape Not Captured:**

India has **distinct public health challenges** that can influence Long COVID outcomes:

- **High levels of air pollution**, especially in urban and industrial zones, which worsen pre-existing respiratory conditions.
- A large burden of **underdiagnosed lung diseases** such as **asthma, COPD, and tuberculosis scars**, which can complicate COVID recovery.
- **Uneven healthcare access** across socio-economic groups and rural–urban divides, often delaying diagnosis and follow-up care.

Unclear Role of FOXP4 Gene Variant in Indian Population

- **No Current Data on FOXP4 Variant Frequency in Indians:**

The specific Long COVID-linked genetic variant **rs9367106 near the FOXP4 gene** has been studied primarily in European and East Asian populations.

Its **frequency, expression pattern, and clinical impact in Indian ethnic groups** remain largely unknown.

- **Need for Population-Specific Genetic Studies:**

Since **genetic diversity within India is vast**, understanding the **prevalence and influence** of this gene in Indian communities is essential for **accurate risk assessment** and **personalized healthcare** strategies.

India's Genomic Progress: The GenomeIndia Project

- **Nationwide Genetic Sequencing Initiative:**

The **GenomeIndia Project**, launched by the Department of Biotechnology (DBT), aims to **sequence the whole genomes of 10,000 Indian individuals** from diverse geographic, linguistic, and ethnic backgrounds.

- **Foundation for Precision Medicine in India:**

Although not disease-focused, the project will build an **open-access genetic reference database** that can:

- Serve as a baseline for studying **disease susceptibility**, including emerging conditions like **Long COVID**.
- Help identify **population-specific genetic markers**, such as FOXP4 variants or others influencing **immune response, inflammation, or lung repair**.

- **Support for Future Research and Tailored Healthcare:**

As this genomic dataset matures, it can:

- Guide **Indian researchers and clinicians** in designing **locally relevant studies** on Long COVID and post-viral syndromes.
- Contribute to the development of **customized treatments, screening tools, and preventive care protocols** for different Indian sub-populations.

Conclusion

- The findings around the **FOXP4 gene** offer a crucial **biological insight** into why certain individuals develop **Long COVID**, even without severe illness.
- This knowledge could eventually lead to the development of **targeted therapies, predictive genetic tests, and personalized treatment strategies** for those at greater risk of Long COVID.
- Further research is needed to **validate these results** across more populations and to explore **interventions that could modulate FOXP4 expression** as a preventive or therapeutic approach.

Source: <https://www.newsweek.com/why-are-so-many-children-getting-long-covid-2080950>