The European mitochondrial lineage may protect against severe forms of COVID-19

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An international study led by Spanish research teams has identified how genetic factors can influence the severity of disease caused by SARS-CoV-2

A study published in the journal *Communications Biology* shows that specific genetic variants in the mitochondrial DNA of Europeans may protect them against the more severe forms of COVID-19. The results of the study provide new clues to the origin of individual differences in the response to infection. The research was led by Dr. José Antonio Enríquez, head of the GENOXPHOS group at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) and a member of the Spanish research network on frailty and healthy aging (CIBERFES).

The study identified patterns suggesting a possible relationship between certain mitochondrial haplogroups (genetic variants shared by individuals with a common ancestor) and susceptibility to more severe forms of COVID-19. "The study demonstrates the **importance of the mitochondrial HV lineage as a protective factor against the severe consequences of infection with SARS-COV2**, supporting the idea that mitochondria play a key role in the response to infectious disease," explained José Antonio Enríquez.

Dr. José Luis Cabrera, first author on the study, added that "these results **advance our understanding of the variability in the response to SARS-CoV-2 and may help to improve the personalized care of patients with COVID-19.**"

The study analyzed data from more than 14300 patients in the SCOURGE registry (Spanish Coalition to Unlock Research on Host Genetics on COVID-19) and confirmed that **individuals with genetic variants found in the HV lineage—the most common mitochondrial lineage among Europeans, accounting for 37%–58% of the European population–had a lower risk of developing severe forms of COVID-19.** Mitochondrial DNA is the only part of the human genome that is inherited exclusively through the maternal line and plays **a key role in the cellular generation of energy and the inflammatory response**

In addition to the CNIC and CIBERFES, acclaimed Spanish and international institutions participating in the study included the University of Santiago de Compostela (USC), *Marqués de Valdecilla* University Hospital–IDIVAL, *Nuestra Señora de Candelaria* University Hospital, *La Paz* University Hospital, and the Autonomous University of Nuevo León (México).

The study used advanced genetic analysis models to identify data patterns, revealing how **previous pandemics may have influenced the current distribution of these genetic variants in Europe** through the process of natural selection.

Ángel Carracedo, who heads the Spanish research network on rare diseases (CIBERER) at USC and CIMUS (*Centro Singular de Investigación en Medicina Molecular y Enfermedades Crónicas*), and who also participated in the study, added, "the results not only contribute to the understanding of COVID-19, but could also have **implications for the study of other infectious diseases and their relation to mitochondrial genetics."**

- *Cabrera-Alarcon JL, Cruz R, Rosa-Moreno M, Latorre-Pellicer A, de Almeida SD; Scourge Cohort Group; Riancho JA, Rojas-Martinez A, Flores C, Lapunzina P, Sánchez-Cabo F, Carracedo Á, Enriquez JA. Shaping current European mitochondrial haplogroup frequency in response to infection: the case of SARS-CoV-2 severity***. Commun Biol.** *2025 Jan 9;8(1):33. doi: 10.1038/s42003-024-07314-y. PMID: 39789223; PMCID: PMC11718132*

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