HERVCOV: new insights into the role of human endogenous retroviruses in Long COVID

The European project HERVCOV announces significant progress in the study of Long COVID disease, which frequently follows COVID-19 infection, offering new evidence on the role of human endogenous retroviruses (HERVs) — in particular, the HERV-W envelope (ENV) protein — in the persistence of symptoms following SARS-CoV-2 infection.

On September 10–11, 2025, researchers from the HERVCOV consortium will meet in Athens for the Third Annual Meeting, which will include an outreach event open to the general public to share the project's latest findings.

THE 2025 CONSORTIUM MEETING

This year, Greece will host the consortium's annual gathering. The event will be held at the National and Kapodistrian University of Athens, featuring two full days of presentations, discussions, and networking among project partners.

September 10 will be dedicated to internal meetings, during which partners will present the scientific progress achieved over the past year.

September 11 will focus on public engagement, offering an opportunity to present results to non-specialist audiences and raise awareness about Long COVID and ongoing research efforts.

PROJECT OBJECTIVES

The HERVCOV project investigates the role of HERVs in the immunopathogenesis of COVID-19 and Long COVID, with the goal of identifying and validating biomarkers

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essential for diagnosis, prognosis, clinical monitoring, and the development of personalized treatments.

A key objective is to understand how SARS-CoV-2 triggers HERV activation at the cellular and molecular levels. In its first year, the project demonstrated that in vitro exposure to the virus induces the expression of the HERV-W ENV pro-inflammatory envelope protein and the protein was frequently found in the serum of COVID-19 patients.

The project is also working to identify biomarkers capable of distinguishing between different bioclinical profiles of COVID-19 patients, with the aim of advancing personalized medicine. High-throughput sequencing is being carried out on well-characterized biological samples to map the HERV transcriptional signature in both acute and Long COVID patients.

In addition, HERVCOV aims to define a biomarker panel associated with HERV activation to support patient stratification, diagnostic criteria, and prognosis.

NEW RESULTS

Among the project's key findings is the persistent expression of HERV-W ENV in post-COVID patients' samples — even months after the acute infection phase. A clear correlation has been observed between protein levels and clinical severity, supporting its potential use as a prognostic biomarker.

While lymphocyte counts may return to normal after infection, their function remains impaired. These immune cells show an "exhausted" phenotype, contributing to long-term immune dysfunction — an effect closely linked to HERV activation.

Another scientific advance has been the identification of a ribosomal readthrough mechanism, which enables full expression of the HERV-W ENV protein despite the presence of a stop codon in its mRNA.
This finding may have significant implications for understanding the molecular

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mechanisms behind Long COVID and other inflammatory conditions involving this protein.

Further experiments have compared Long COVID patients with asymptomatic individuals, integrating clinical, cognitive, and biological data. The research has also led to the integration of immunological, biochemical, and cytokine markers, contributing to the definition of predictive bioprofiles useful for stratifying patients and guiding personalized treatment strategies.

THE PARTNERS

HERVCOV is funded by the European Commission through the Horizon Europe Framework Programme, under the call HORIZON-HLTH-2021-DISEASE.

With nearly €7 million in funding, the project brings together a multidisciplinary consortium of academic institutions, research centres, biotech companies, and science communication organizations from Croatia, France, Greece, Italy, and Spain.

Consortium Partners:

Inserm – Institut National de la Santé et de la Recherche Médicale (France)
Inserm Transfert (France)
GeNeuro Innovation SAS (France)
National and Kapodistrian University of Athens (Greece)
University of Rome “Tor Vergata” (Italy)
Frascati Scienza (Italy)
IACS – Instituto Aragonés de Ciencias de la Salud (Spain)
ARAID - Fundación Agencia Aragonesa para la Investigación y el Desarrollo (Spain)
Klinicki Bolnicki Centar Rijeka (Croatia)

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