Researchers Detect HERV-W ENV in COVID-19 Patients and Link Expression to Disease Severity

- Data published in the Lancet's EBioMedicine shows that the pathogenic envelope protein of the human endogenous retrovirus W (HERV-W ENV) is found on lymphocytes of hospitalized patients with COVID-19, and that its level of expression is associated with disease severity.

- HERV-W ENV's pro-inflammatory properties thought to act as an “accelerant” of the activation of the innate immune system, fueling the severity of COVID-19 evolution and impacting long-term recovery.

- Preliminary data available on Research Square also shows HERV-W ENV expression in lymphocytes following in vitro exposure to SARS-CoV-2 in about 20% of healthy blood donors, suggesting individual susceptibility.

- With HERVs as a possible aggravating agent of COVID-19, GeNeuro’s temelimab, an anti-HERV-W ENV monoclonal antibody already in Phase II clinical trials with an excellent tolerability and safety, could, without any prejudice to its existing programs, start tests against COVID-19 as early as this summer.

Geneva, Switzerland, April 15, 2021, 7:30am CEST – GeNeuro (Euronext Paris: CH0308403085 - GNRO), acknowledges data published today in the Lancet's EBioMedicine showing that HERV-W ENV expression was detected in the lymphocytes of all 30 studied hospitalized COVID-19 patients, versus none in healthy subjects, and that the level of HERV-W ENV was correlated with the severity of the evolution of the disease. The study, published under the title “Evidence of the pathogenic HERV-W envelope expression in T lymphocytes in association with the respiratory outcome of COVID-19 patients”, was conducted by a team led by Dr. Claudia Matteucci at University of Rome “Tor Vergata”, in collaboration with the International Center for Infectiology Research in Lyon, France (CIRI) and GeNeuro.

“Our findings on HERV-W ENV in the blood of hospitalized COVID-19 patients are truly novel, as this pro-inflammatory protein is usually found in specific disease situations, mostly in the brain, but has never before been observed circulating in the body at high levels and, in particular, was never seen expressed in T-lymphocytes” said Prof. Claudia Matteucci, Department of Experimental Medicine, University of Rome “Tor Vergata”. “The study shows a clear association between HERV-W ENV expression in lymphocytes and the severity of the respiratory evolution of COVID-19 in hospitalized patients. Understanding the mechanisms leading from SARS-CoV-2 infection to severe disease is critical for the development of effective treatments. The identification of the association between HERV-W ENV expression and inflammatory and immune dysfunction in COVID-19 opens an avenue for further investigation of its role as a trigger of detrimental immune response and potential target for therapy.”

In a parallel effort supported by the French National Research Agency (ANR), the CIRI in Lyon started research to understand why HERV-W ENV was found at high levels in the blood of hospitalized COVID-19 patients. Preliminary findings, available online on Research Square, show that when human peripheral blood mononuclear cells from healthy donors were cultured and exposed to SARS-CoV-2, about 20% of donors responded by expressing HERV-W ENV in lymphocytes, cells in which the virus did not replicate. This expression was triggered specifically by the spike protein of SARS-CoV-2, independently from cytokine release.
“Our research suggests a genetic and/or epigenetic susceptibility associated to the activation of HERV-W ENV in blood lymphoid cells, which could be important in understanding how SARS-CoV-2 infection may lead to severe forms of COVID-19 in some patients,” said Dr Branka Horvat, who heads the “Immunobiology of Viral infections” team at the International Center Infectiology Research-CIRI. “The findings made in Rome and Lyon, combined with the known pro-inflammatory properties of the HERV-W ENV protein, may shed a new light on the development of severe forms of COVID-19, and may also offer an unforeseen opportunity to stop this evolution through a novel therapeutic approach.”

HERV-W ENV is found in specific disease situations, and its presence is always tied to negative disease outcomes for the patient. The pro-inflammatory effects of HERV-W ENV are mediated through the activation of the TLR4 innate immune receptor, a pathway closely associated with some of the key features of COVID-19, such as hyper-activation of immune functions, endothelial cell activation, vasculitis as well as coagulopathy. To date, HERV-W ENV has mostly been studied in neurodegenerative diseases, with widely observed pathogenic effects on peripheral and central nervous system cells.

“The presence of HERV-W ENV in COVID-19 patients may have a double effect. In the short-term, when activated in genetically susceptible individuals, HERV-W ENV can act as an accelerant to the innate immune response, fueling complications and leading to the need for ventilation. But even after the primary infection is over, if HERV-W ENV has reached a self-fueling expression level, it may cause persistent damage to endothelial cells in blood vessels and also to cells from the peripheral and central nervous system, which could explain many of the long-term neurological symptoms experienced by patients long after SARS-CoV-2 infection,” said Dr. Hervé Perron, Chief Scientific Officer of GeNeuro, who has been working on HERVs for over 30 years.

The link between viral infection and HERV activation in specific diseases has already been well documented. But until now, HERV expression had been observed in limited amounts and mainly found in an affected organ, predominantly in the brain in neurodegenerative disorders. GeNeuro was founded in 2006 as a spin-off of Institut Mérieux to leverage HERV biology into novel treatments by neutralizing pathogenic HERV proteins. Its most advanced drug candidate, temelimab, has shown very promising results in Phase II trials against Multiple Sclerosis (MS), and is presently in a trial against disability progression at the Karolinska Institute’s Academic Specialist Center (ASC) in Stockholm, Sweden. Temelimab is an anti-HERV-W ENV monoclonal antibody, with demonstrated excellent tolerability and safety in over 400 patient-years of treatment, and is immediately available to study the effects of neutralizing HERV-W ENV in COVID-19 patients.

“GeNeuro is focused on developing treatments to neutralize the pathogenic effects of HERVs for the benefit of patients. Our main focus is on autoimmune and neurodegenerative diseases, such as MS, where the link between HERVs and disease is best established,” said Jesús Martin-Garcia, CEO of GeNeuro. “We are intrigued by these very novel findings, which show once again the importance of HERV biology to understand and tackle severe conditions. As the leaders in the HERV field and with HERV-W ENV as a possible aggravating agent of COVID-19, we have started working with leading medical centers in Europe and the USA to evaluate temelimab as a therapeutic treatment, both to prevent immune system hyper-activation in recently infected patients, as well as to tackle severe neurological and psychiatric syndromes in long-COVID patients. Without any prejudice to our existing programs, we have enough temelimab to start both tracks of clinical trials, as early as this summer.”

About GeNeuro

GeNeuro’s mission is to leverage HERV biology to develop safe and effective treatments for the benefit of patients, by neutralizing causal factors encoded by HERVs that represent 8% of human DNA.

GeNeuro is based in Geneva, Switzerland and has R&D facilities in Lyon, France. It has rights to 17 patent families protecting its technology.

For more information, visit: www.geneuro.com
About University of Rome “Tor Vergata”
The University of Rome “Tor Vergata” was established in 1982. Designed on the model of Anglo-Saxon campuses, it hosts important research institutions, such as the National Research Council – CNR and the Italian Space Agency – ASI. Tor Vergata’s School of Medicine and Surgery is ranked among the top academic medical centers in Italy and its Department of Experimental Medicine works closely with the “Policlinic Tor Vergata” university hospital. For more information, visit https://en.uniroma2.it/.

About the International Center for Infectiology Research (CIRI)
The International Center for Infectiology Research (CIRI) is a joint research unit of the Lyon 1 University, Inserm, CNRS and the ENS de Lyon in partnership with VetAgro Sup, the Institut Pasteur and the Hospices Civils de Lyon. The CIRI gathers the scientific and medical research communities with complementary disciplinary backgrounds grouped in 3 specialties working together with the objective to understand host-microbe interactions to better fight infectious diseases. For more information, visit https://ciri.ens-lyon.fr

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