Press release, 18 March 2021

COVID-19: Institut *Imagine* and Cerba HealthCare are partnering to test for patients likely to develop severe symptoms

In 2020, researchers at Inserm, Université de Paris, and Assistance Publique–Hôpitaux de Paris (AP-HP), in collaboration with the university hospital organisation Institut *Imagine* (Hôpital Necker-Enfants malades AP-HP), which has been granted "Institut Carnot" certification through The Rockefeller University and the Howard Hughes Medical Institute in New York, identified the leading genetic and immunological causes responsible for at least 15% of serious forms of Covid-19. Today, this same French and American team, jointly lead by Jean-Laurent Casanova and Laurent Abel* at the Institut *Imagine* and The Rockefeller University, is joining forces with Cerba HealthCare, a leading stakeholder in medical diagnostics, to transform these discoveries into clinical applications and screen individuals who are more likely to develop a severe form of the disease and tailor their treatment accordingly.

A commonality among 15% of severe cases: impaired type-I interferon activity

At the start of the Covid-19 pandemic, Dr.Jean-Laurent Casanova and his team created an international consortium, Covid Human Genetic Effort, to identify the genetic and immunological factors responsible for the reason some patients experience serious forms of the disease. They focused their research on patients who were hospitalised with severe Covid throughout the world. These patients all had a quantitative or activity-related type-I interferon (type-I IFN) impairment. Type-I interferons are immune system molecules that normally serve a powerful anti-viral function.

In two articles published in the journal *Science*[1,2], researchers discovered changes in genes that were already understood to regulate the immune responses controlled by type-1 IFN, especially in reaction to the flu virus, in 3-4% of patients with a severe form of the disease. These mutations decreased the production of these interferons. In an even more surprising development, they identified an auto-immune reaction in 10-11% of other patients with serious Covid symptoms. These individuals produced autoantibodies that specifically targeted type-1 IFNs. In a recent article published in *Journal of Experimental Medicine*, these same anti-interferon autoantibodies were also identified as the cause of severe reactions to yellow fever live vaccine in around one-third of patients from an international cohort[3], confirming the discoveries of the *Imagine* teams.

From ground-breaking research to a screening test

"*These studies have revealed the crucial role of type-I interferons in the immune response against SARS-Cov-2 and the development of serious forms of the disease. The genetic variants that decrease their production or the auto-antibodies that neutralise their effect are present before the virus infects the body and play a critical role in the outcome of the disease. Some serious forms of Covid-19 could therefore be prevented by testing the general population to detect any auto-antibodies and by administering interferons at the onset of infection for certain patients*", Jean-Laurent Casanova and Laurent Abel explain.

Against this backdrop, Institut *Imagine* decided to form a partnership and sign its first collaboration agreement with Cerba HealthCare, a leading stakeholder in the fields of medical diagnostics and specialized biology.

"*Cerba HealthCare's expertise; knowledge of specialised medical biology, from prevention to screening and diagnostics; and its international network are all major assets. This collaboration will help us reach the next level by transforming our improved understanding of the disease into a concrete application designed to help patients. In reality, we are talking about adapting precision genetic medicine to the context of a pandemic*", says Dr. Stanislas Lyonnet, Director of Institut *Imagine*.

Jérome Sallette, Scientific Director of Cerba HealthCare, adds, "*Our partnership with Institut Imagine perfectly embodies our shared vision of the need to discover diagnostic tools and new treatments at a faster pace, particularly by building more bridges between different ecosystems. The reputation, expertise, and commitment*

of the teams at Institut Imagine are clearly a driver of success in this project, for which we have mobilised all of our areas of expertise. While the epidemic does lead to a race to innovate, it also underscores more than ever the importance of cooperation between public and private stakeholders."

For additional information, click here.

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*Jean-Laurent Casanova oversees genetics and experimental immunology in both branches, while Laurent Abel directs genetics and mathematical epidemiology in both branches.

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Sources

[1] **Inborn errors of type I IFN immunity in patients with life-threatening COVID-19**
Qian Zhang et al.
Science, 24 September 2020

[2] **Auto-antibodies against type I IFNs in patients with life-threatening COVID-19**
Paul Bastard et al.
Science, 24 September 2020

[3] **Auto-antibodies to type I IFNs can underlie adverse reactions to yellow fever live attenuated vaccine.**
Paul Bastard et al.
Journal of Experimental Medicine, 2021

About AP-HP

Europe's leading hospital and university center, the AP-HP and its 39 hospitals are organized into six university hospital groups (AP-HP.Center-University of Paris ; AP-HP.Sorbonne University ; AP-HP.Nord-University of Paris ; AP-HP.Université Paris Saclay ; AP-HP.Henri Mondor and AP-HP University Hospitals.Paris Seine-Saint-Denis University Hospitals) and are organized around five universities in the Ile-de-France region. Closely linked to major research organizations, the AP-HP has three world-class hospital-university institutes (ICM, ICAN, Imagine) and the largest French healthdata warehouse (EDS). A major player in applied research and innovation in health, AP-HP holds a portfolio of 650 active patents, its clinician-researchers sign nearly 9,000 scientific publications each year and more than 4,000 research projects are currently under development, all promoters combined. In 2020, AP-HP obtained the Institut Carnot label, which rewards the quality of partnership research : the Carnot@AP-HP offers industrial players solutions in applied and clinical research in the health sector. The AP-HP also created in 2015 the AP-HP Foundation for Research to support biomedical and health research carried out in all of its hospitals. https://www.aphp.fr

About Cerba HealthCare

Cerba HealthCare, a leading player in medical diagnosis, aims to support the evolution of health systems towards more prevention. It draws on more than 50 years of expertise in clinical pathology to better assess the risk of diseases development, detect and diagnose diseases earlier, and optimize the effectiveness of personalized medicine.

Every day, the Group's 8 500 employees through its subsidiaries on 5 continents sustain the transformation of medicine, driven by one deep conviction: to advance diagnosis is to advance health.

Cerba HealthCare, enlightening health.

About Inserm

Inserm is a public scientific and technological establishment, under the dual supervision of the Ministry of Health and the Ministry of Research. Dedicated to medical biological research and human health, it is positioned along the entire path from the research laboratory to the patient's bed. On the international scene, it is the partner of the largest institutions involved in the challenges and scientific progress of these fields.

About Institut *Imagine*

In an architecture designed by Bernard Valéro and Jean Nouvel on the campus of Hôpital Necker-Enfants malades (AP-HP), Institut *Imagine*, which has been labelled Institut Carnot, is the leading center for research, care and teaching on genetic diseases. With the mission of understanding and curing these diseases, the Institute brings together 1,000 of the best doctors, researchers and healthcare personnel in an architecture that creates synergies. This unprecedented continuum of expertise, combined with proximity to patients, enables *Imagine* to make discoveries for the benefit of patients. The 7,000 or so genetic diseases identified affect 35 million patients in Europe, and nearly 3 million in France, where there are 30,000 new cases each year. Nearly 60% of the children seen in consultations leave without a genetic diagnosis and 90% of genetic diseases do not yet have a cure. Faced with this major public health problem, the challenge is twofold: to diagnose and to cure.
www.institutimagine.org/fr

About Université de Paris

As a research-intensive, multidisciplinary university, the University of Paris ranks among the most prestigious French and international institutions thanks to its high-level research, its excellent higher education programs, its support for innovation and its active participation in the construction of the European research and education area.
The University of Paris has 61,000 students, 4,500 professors and researchers, 22 doctoral schools and 142 research laboratories. Visit u-paris.fr.