

PRESS RELEASE

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The first global centre for Sepsis research, education and care: the PROMETHEUS University Hospital Institute (IHU) wins the IHU 3 Call for Proposals

As part of the France 2030 investment plan, the President of the French Republic has just announced the twelve University Hospital Institutes (IHU) which have won the national IHU 3 call for proposals. The PROMETHEUS IHU project is one of the laureates. Coordinated by Université Paris-Saclay, Université de Versailles Saint-Quentin-en-Yvelines (UVSQ), the French Alternative Energies and Atomic Energy Commission (CEA), Public Assistance - Hospitals of Paris (AP-HP), the National Institute of Health and Medical Research (Inserm) and their academic, non-profit and industrial partners,¹ this future global centre for research, education and care aims to reduce the number of deaths and sequelae caused by sepsis by half within the next ten years.

Sepsis is the most serious complication of an infection. It is characterised by uncontrolled inflammation - the physiological process by which the body eliminates pathogens, resulting in the impairment of vital functions. According to the World Health Organisation, each year sepsis affects 50 million children (mainly under the age of one) and adults (over the age of 75). The majority of cases occur at home. Sepsis is responsible for one in four deaths worldwide and for mental and motor disabilities in one in two survivors.² In France, the number of sepsis cases increased from 357 per 100,000 people in 2015 to 403 in 2019 and the hospitalisation cost for sepsis is on average €16,000³. While only half of patients return home after being treated for sepsis in hospital, 25% die in hospital and 15% are referred to a long-term care facility.

Despite decades of extensive research, the mechanisms by which the host response to pathogens is disrupted remain poorly understood, and no treatment has been found. The compartmentalisation of research and limited funding provide a likely explanation for this, as well as the low level of patient involvement in sepsis research. The involvement of patients is needed to improve the prevention of recurring sepsis, adapt care to the constraints of daily life, and identify how to support patients in the sometimes long and difficult stages of convalescence.

The creation of the world's first institute incorporating researchers, medical professionals and patients places France in a unique position in the development of new diagnostic tests and drugs, to halve the health, social and economic burden of sepsis within the next ten years.

In 2002, Djillali Annane provided hope that sepsis could be cured for the first time. A Professor at UVSQ, Head of the intensive care medicine department at the Raymond-Poincaré Hospital (AP-HP), and Head of the LARENES team at the Inflammation and Infection Laboratory (UVSQ/UPSaclay/Inserm), the researcher and his team showed that administering moderate doses of corticosteroids in the first 24 hours of a septic shock for seven days significantly reduced the

¹ Université Paris-Est-Créteil (UPEC), Université Paris Sciences & Lettres (PSL), Institut Pierre-Gilles De Gennes (IPGG), ENS Paris-Saclay, CNRS, INRAE, Université Paris Cité (UPC), University of Evry (UEVE), Université Sorbonne Paris Nord (UPSN), Paris School of Business, CONSTANCES, CRICS-TRIGERSEP (the national sepsis network), FHU SEPSIS, IDMIT, CNRGRH, Pfizer, Biomerieux, Volition, Sphingoteck, Primadiag, Biothelis, Arkhn) and the France Sepsis Association

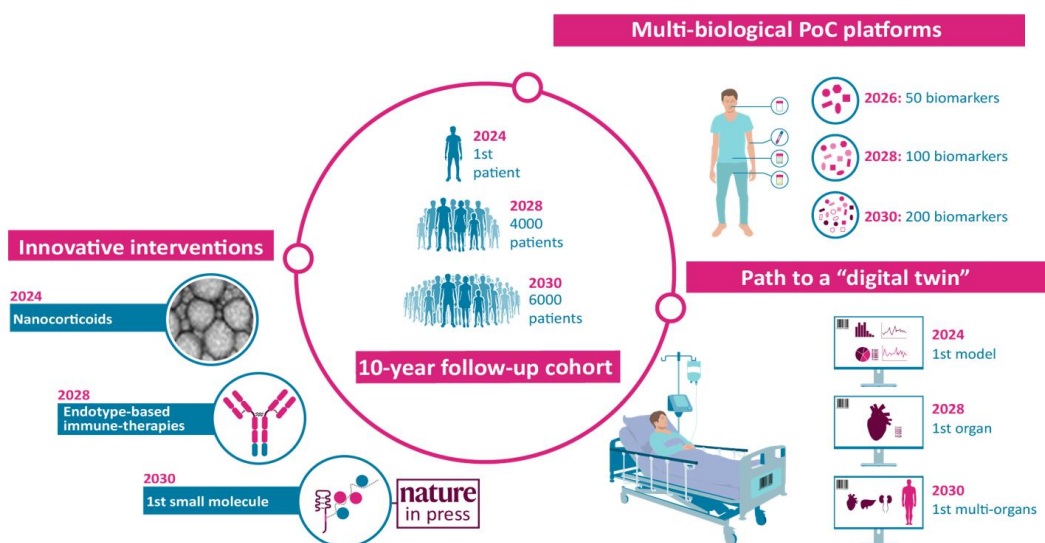
² Global report on the epidemiology and burden of sepsis: current evidence, identifying gaps and future directions. <https://as.who.int/iris/handle/10665/334216>

³ F. Pandolfi .2022. BMJ Open, 12, no. 5, p. e058205.

number of deaths and sequelae caused by sepsis. "This is to compensate for the body's abnormal response of producing insufficient cortisol to counteract the inflammation caused by an infection," he explains.

Today, Djillali Annane, Olivier Lambotte, Professor of Clinical Immunology at Université Paris-Saclay, and Roger Le Grand, Director of IDMIT⁴ at the CEA, have brought together 60 research teams in chemistry, physics, mathematics, engineering sciences, biology, medicine, social and human sciences and economics. The 275 researchers and 94 clinical doctors of this unique institute for care, research and education can count on leading industrial partners: Arkhn, Baxter, Biomérieux, Biothelis, Pfizer, Primadiag, Sphingoteck and Volition. The ambitious project also involves patients through the participation of patient associations in France (France Sepsis Association) and from around the world (European Sepsis Alliance, Global Sepsis Alliance and Sepsis Canada).

The PROMETHEUS IHU shares a threefold scientific objective



Firstly, the project aims to improve our understanding of the host-pathogen interactions that lead to the progression of an uncomplicated infection to sepsis. This will allow for the identification of signatures characterising the trajectory of each individual affected by an infection (endotype), and their response to a given treatment (treatable traits). The setting up of a prospective cohort will be a major support for characterising these individual sepsis profiles.

Secondly, the project aims to develop, validate and commercialise a rapid testing platform (allowing over 200 tests of treatable endotypes and traits to be performed in two hours), which will lead to the creation of a digital twin of organs and systems to help decide treatment regimens without delay. Early decision making in under six hours after the onset of symptoms, is critical to the success of treatment.

The project's third goal aims to develop customised medicine with innovative small molecules such as nanomedicines, biotherapies (monoclonal antibodies and vaccines targeting pathogens and the immune system), and strategies modulating microbiota.

The PROMETHEUS IHU: unprecedented socio-economic impact

The changes in how children and adults with sepsis are cared for will save many lives and prevent numerous disabilities. The cost of patient care will be halved in ten years, from an average of €16,000 per hospitalisation today to approximately €8,000 in 2033, not to mention the reduction of indirect

⁴ Infectious Disease Models and Innovative Therapies

costs related to the prevention of disabilities caused by sepsis and the preservation of patients' autonomy and socio-professional lives. Finally, the development of scientific and technological discoveries generated by the IHU will be a source of employment and creation for new companies.

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