CLONES

Construction of a Liver-on-a-chip for an Early diagnosis of Sepsis

Sepsis represents a major global public health challenge, with approximately 160 million cases per year, including 21 million deaths, and an incidence expected to double by 2050.

The liver plays a central role in the early innate immune response, being constantly exposed to circulating micro-organisms, antigens, and pathogen-associated and damage-associated molecular patterns. Its response relies on complex and finely tuned interactions between the different hepatic cell types, organised within a distinctive microarchitecture. Analysing the earliest cellular events of sepsis is essential in order to obtain biomarkers of interest, which are currently lacking.

Organ-on-a-chip technology offers a novel perspective, integrating microfluidics, 3D tissue architecture and real-time monitoring — particularly valuable for modelling a range of pathologies such as sepsis.

The main objective of the CLONES project is to develop a functional liver-on-a-chip model, a genuine "clinical twin of hepatic sepsis", combining hepatic cells derived from induced pluripotent stem cells with human non-parenchymal liver cells of immune and vascular origin. Once validated, this model will be configured for high-throughput use in order to elucidate the early molecular signalling pathways of sepsis. Identifying early predictive biomarkers will be a key asset in bringing this technology to the patient's bedside.

The project will be carried out by a consortium drawn from the IHU Sepsis, bringing together researchers with expertise in cell biology (INSERM UMR-1193), host–pathogen interactions (INRAE), sepsis (INSERM UMR-1173) and microfluidic technology (ENS Paris-Saclay), together with clinicians from the Henri Bismuth Hepatobiliary Centre and from the intensive care department of Raymond Poincaré Hospital.

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