

# Selective cfDNA/NETs apheresis with NucleoCapture® in a Prolonged Clinically Relevant Porcine Intensive Care Sepsis Model

A. Aswani<sup>1,2</sup>, D. Genkin<sup>1</sup>, K. Surkov<sup>1</sup>, P. Skorup<sup>4</sup>, R. Varsebroucq<sup>3</sup>, M. Wargnies<sup>3</sup>, J. Candiracci<sup>3</sup>, M. Herzog<sup>3</sup>, J. Micallef<sup>3</sup>, M. Lipcsey<sup>5</sup>

<sup>1</sup> Santerus AG, Zurich, Switzerland

<sup>2</sup> Guy's and St Thomas' NHS Foundation Trust, Department of Critical Care Medicine, London, United Kingdom

<sup>3</sup> Belgian Volition SRL, Isnes, Belgium

<sup>4</sup> Uppsala University, Department of Medical Sciences, Uppsala, Sweden

<sup>5</sup> Uppsala University, Department of Surgical Sciences, Uppsala, Sweden

## ABSTRACT

### Background

Cell-free DNA (cfDNA)/Neutrophil Extracellular Traps (NETs) are associated with sepsis. We previously demonstrated that NucleoCapture® selective cfDNA/NETs apheresis improved organ function and survival in a 7-hour model of porcine sepsis. We therefore investigated the use of NucleoCapture® in an extended 24-hour clinically relevant porcine intensive care model of sepsis.

### Methods

We induced sepsis in two pigs with a 2-hour intravenous infusion of *Pseudomonas aeruginosa*. Antibiotics were administered at either 6 hours or earlier if the norepinephrine requirement was greater than 0.1mg/kg/min. One pig was then subjected to NucleoCapture® apheresis using the Terumo Optia system with regional citrate anticoagulation for 8 hours, followed by a further dose of antibiotics. A second NucleoCapture® treatment was then applied for another 8 hours. The other pig was subjected to the same protocol with sham column apheresis. We measured cfDNA/NETs using the NuQ H3.1 nucleosome assay (Volition).

### Results

The baseline levels of circulating cfDNA/NETs measured in the NucleoCapture® and sham treated pigs were 2.52 ng/ml and 1.64 ng/ml, respectively. Infusion of *Pseudomonas aeruginosa* resulted in an increase in cfDNA/NETs to 82.6 ng/ml and 87.4 ng/ml, respectively.

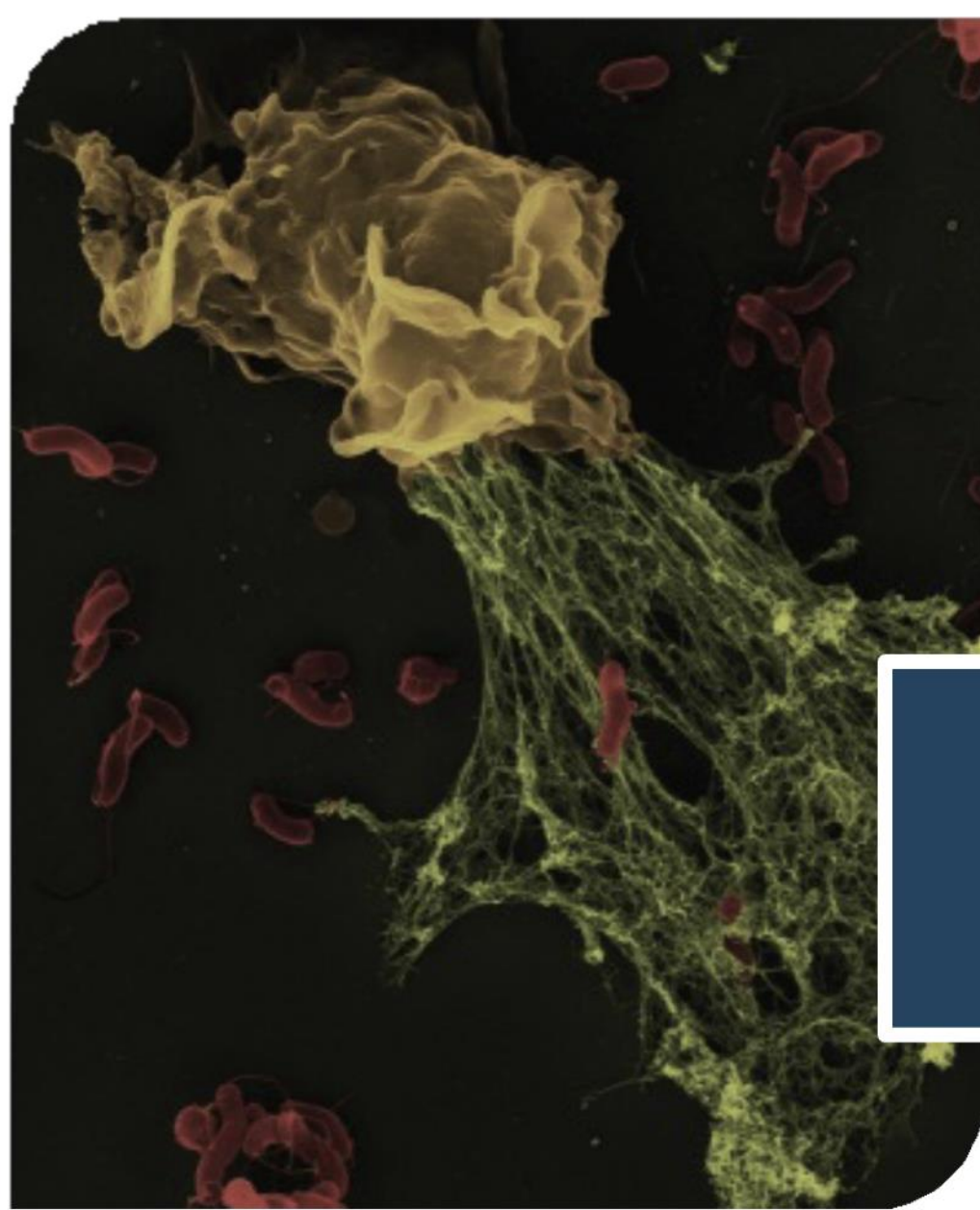
The level of cfDNA/NETs in the sham treated pigs rose continuously during the experiment reaching 508.9 ng/ml. In contrast, NucleoCapture® treatment caused a sustained decrease of cfDNA/NET levels to 20.9 ng/ml by the end of the experiment.

The suppressed cfDNA/NETs level in the NucleoCapture® treated pig was consistent with the attenuation of septic shock as evidenced by a marked 4-fold reduction in the total norepinephrine requirement: 3,725 µg vs 13,841 µg. The NucleoCapture® treated pig also produced more urine: 3,260ml vs 2,531ml.

### Conclusions

In this extended 24 hour clinically relevant model of porcine sepsis, which included the use of antibiotics and intensive care support, prolonged selective cfDNA/NETs apheresis with NucleoCapture® effectively removed cfDNA/NETs from the circulation of a septic pig and resulted in improved physiological indicators. We aim to progress the investigation of NucleoCapture® to clinical trials in sepsis and other indications.

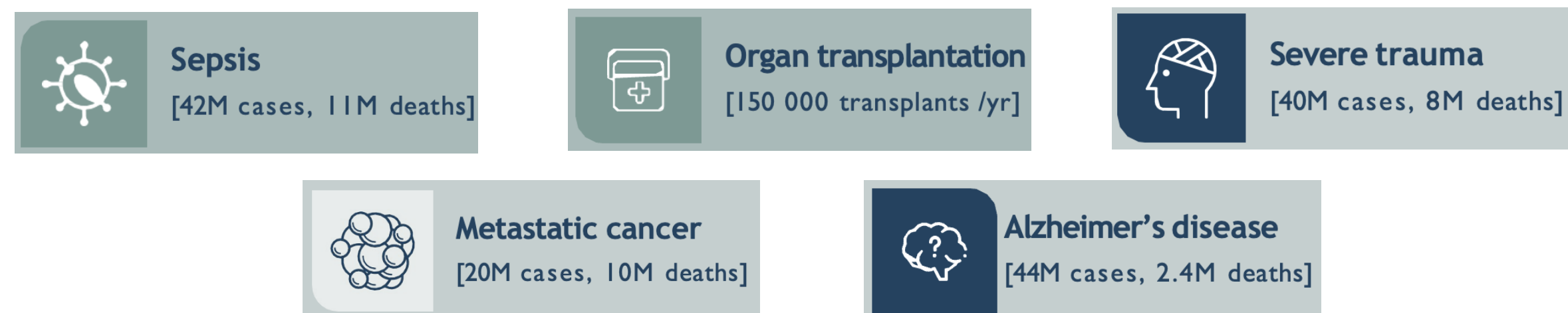
## Neutrophil Extracellular Traps (NETs) are a leading cause of serious diseases with unmet medical need



NETosis is a unique form of neutrophil cell death that is characterized by the release of NETs composed of DNA web-like structures decorated with highly cytotoxic protein components.

Studies have pointed to the massive release of cfDNA/NETs into the bloodstream as playing a pivotal role in the progression of certain acute, chronic debilitating and fatal conditions which cost healthcare systems around the world billions every year.

Neutrophil releasing a NET (green)  
Why Immune Cells Extrude Webs of DNA and Protein. The Scientist, Oct 1, 2019



## NucleoCapture® for selective removal of cfDNA/NETs

NucleoCapture® blood purification technology is based on biocompatible polymer beads conjugated with proprietary human recombinant histone H1.3 protein, the basis of our patents.

NucleoCapture® easily integrates to existing extracorporeal treatment modalities creating an add-on product to standard critical care therapies

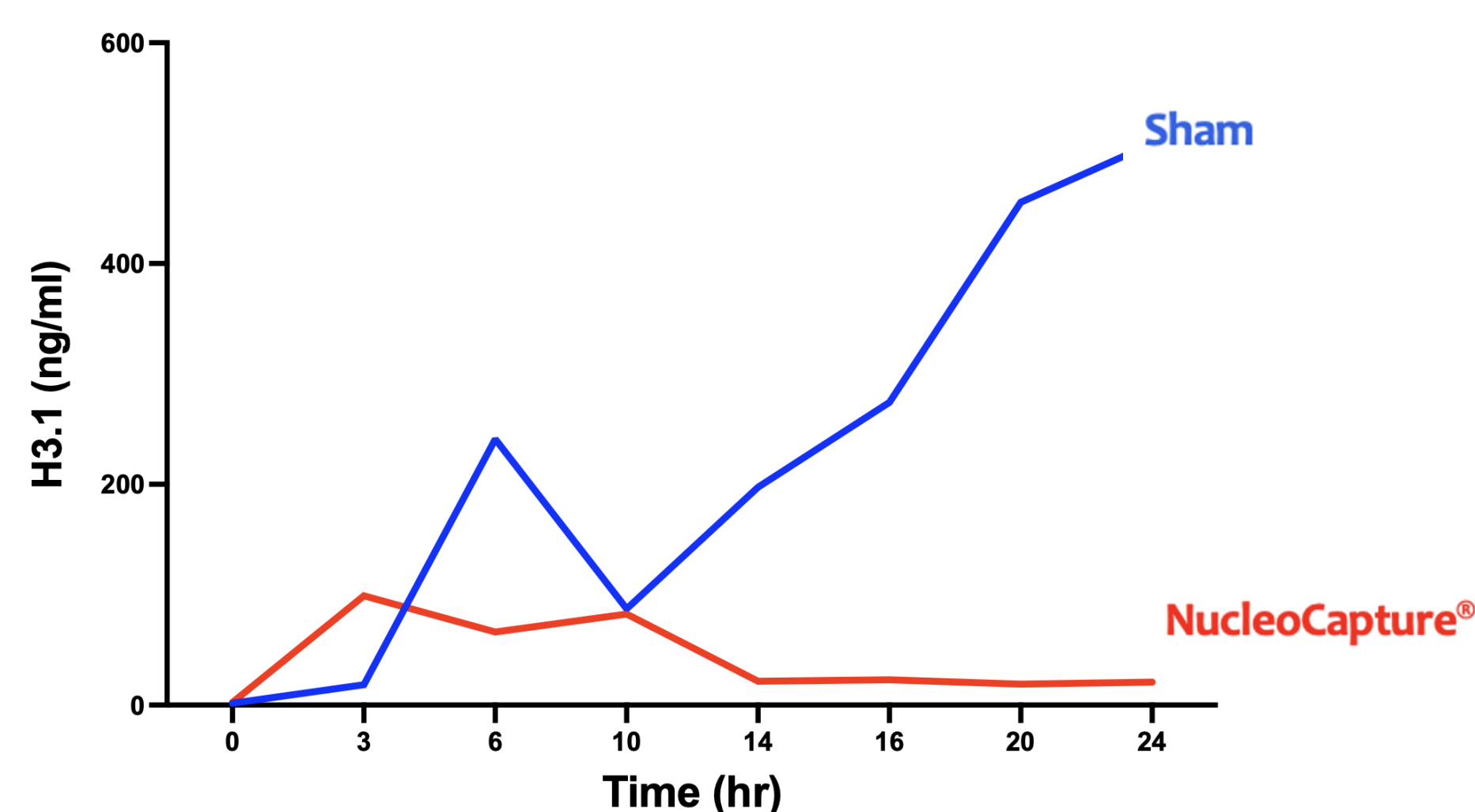
As a result, single pass of contaminated plasma through NucleoCapture® results in over 95% clearance of NETs from plasma.

First in human clinical data in sepsis were submitted to FDA (The United States Food and Drug Administration) and in Q1 2022 Santerus AG was granted a Breakthrough Device designation



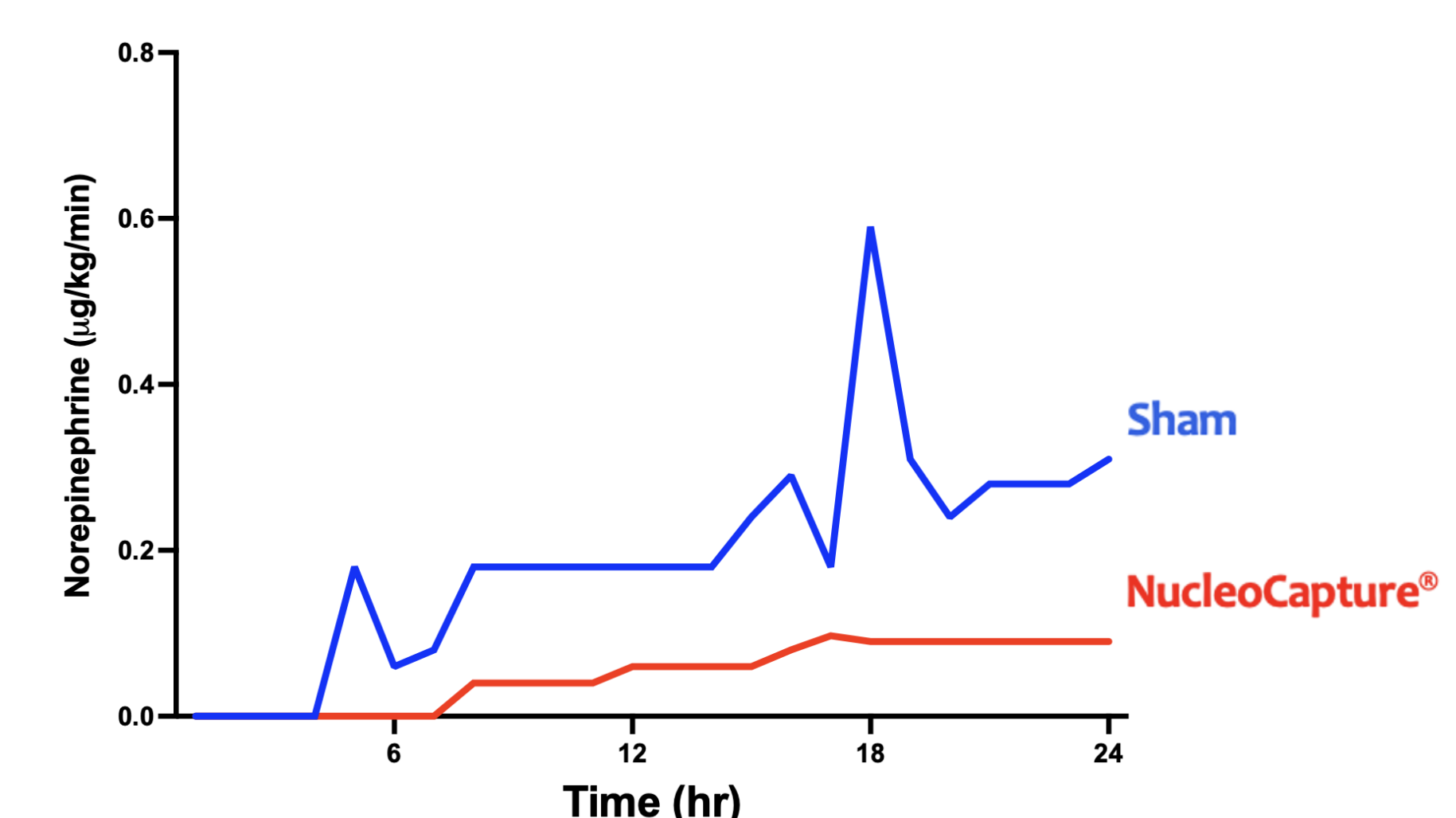
## NucleoCapture® cfDNA/NETs apheresis in a large animal prolonged model of sepsis

95% reduction in circulating cfDNA/NETs



## NucleoCapture® cfDNA/NETs apheresis attenuates shock and multiple organ dysfunction

Vasopressor use reduced 4-fold



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