Press Release

ABIONYX Pharma Announces Landmark Validation: A Study published in NATURE Confirms Genetic Causality of Apolipoprotein A-I (ApoA-I) in Sepsis

A Global Turning Point for Critical Care Medicine

Toulouse, FRANCE, Fullerton, CA, USA, October 21, 2025, 6:00 p.m. CEST - **ABIONYX Pharma**, (**FR0012616852 - ABNX - PEA PME eligible**), a new generation biotech company dedicated to the discovery and development of innovative therapies based on the world's only recombinant apoA-I, today announced the publication of a ground breaking study in *Scientific Reports* in Nature Portfolio titled *"Plasma apolipoprotein A-I is a causal protective factor in sepsis."*

This landmark publication provides, for the first time, genetic proof of a causal linkage between higher plasma ApoA-I levels and a lower incidence of sepsis and lower mortality in patients who do develop sepsis — a breakthrough that reshapes the scientific and therapeutic landscape of one of medicine's deadliest conditions. At the same time, the publication provides genetic validation of the well-studied mechanism of apoA-I's beneficial impact on sepsis – the sequestration of the bacterial lipid toxin, LPS, which is responsible for the manifestations of sepsis. The report provides evidence that apoA-I is also effective in reducing mortality in Gram positive sepsis driven by the bacterial toxin lipoteichoic acid. Importantly, the findings were replicated across three independent data sets, including both Caucasian and Asian sepsis sufferers. This publication adds to the evidence from a previous publication by Trinder et al which provided genetic validation of similar benefits of higher HDL on sepsis incidence and mortality. The structural protein which defines HDL is apoA-I.

First Genetic Evidence of Causality

The study analyzed 442,601 participants from the UK Biobank, including 11,643 sepsis cases, and validated the findings across two large international cohorts, Europe (The Vasopressin and Septic Shock Trial VASST) and Japan (Chiba Cohort). Results demonstrate that each standard deviation increase in plasma apoA-I levels reduces the incidence of sepsis by 13% (OR = 0.87, 95% CI [0.86–0.89], $P = 7.4 \times 10^{-44}$) and 28-day mortality by 27% (OR = 0.73, 95% CI [0.71–0.76], $P = 8.2 \times 10^{-40}$).
Using *Mendelian randomization*, the researchers confirmed that this protective effect is **causal and independent** of other lipid fractions (HDL-C, LDL-C, triglycerides) (adjusted OR = 0.71, 95% CI [0.65–0.77], $P = 2.4 \times 10^{-20}$).
Mechanistically, higher apoA-I levels were linked to a **reduction in circulating endotoxin (LPS)** levels (logOR = -0.23, $P = 9.1 \times 10^{-81}$), reinforcing apoA-I's role as a central modulator of inflammatory response and innate immunity in sepsis.

A Paradigm Shift in Sepsis Therapeutics

Sepsis — a life-threatening dysregulated immune response responsible for over **11 million deaths each year worldwide** and the **third leading cause of in-hospital death** in the US — has long lacked any genetically validated therapeutic target or any specific therapy.
This study positions **apoA-I** as the **first proven causal protective factor** in sepsis, transforming the scientific foundation for drug development in critical care.
For **ABIONYX Pharma**, whose proprietary technology enables scalable GMP production of recombinant apoA-I and next-generation HDL mimetics, this discovery represents a new **scientific validation and strategic inflection point** after the recently published phase IIa study RACERS where CER-001 improved clinical outcomes in sepsis patients.

"This publication is a game-changer," said Dr. Rob SCOTT, MD, Head of R&D and CMO of ABIONYX Pharma. *" For decades, the field of sepsis has searched for a causal target. The mechanistic effect of apoA-I and HDL has been well documented over the last 40 years but now, this new genetic validation provides proof that apoA-I is a major factor determining whether patients develop sepsis and whether they survive it.*

This major publication in *Nature* is a significant milestone that reinforces the scientific and strategic value of the company in ongoing discussions with a leading partner in sepsis.

Reference

Campbell KR et al. (2025) Plasma apolipoprotein A-I is a causal protective factor in sepsis. Scientific Reports 15, Article 33625. DOI: 10.1038/s41598-025-19204-2
https://www.nature.com/articles/s41598-025-19204-2#auth-Keith_R_-Walley-Aff1

Additional resources on genetic causality and sepsis in general

Trinder, M., Walley, K. R., Boyd, J. H. & Brunham, L. R. Causal inference for genetically determined levels of high-density lipoprotein cholesterol and risk of infectious disease. *Arterioscler. Thromb. Vasc Biol.* **40**, 267–278 (2020).
https://pubmed.ncbi.nlm.nih.gov/31694394/

Sepsis information guides
https://www.sepsis.org/education/resources/sepsis-information-guides/

About ABIONYX Pharma

ABIONYX Pharma is a new generation biotech company that aims to contribute to health through innovative therapies in indications where there is no effective or existing treatment, even the rarest ones. Thanks to its partners in research, medicine, biopharmaceuticals and shareholding, the company innovates on a daily basis to propose drugs for the treatment of renal and ophthalmological diseases, or new HDL vectors used for targeted drug delivery.

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