Towards Improved Pandemic Preparedness: Launch of New EU Project COMBINE

International research team seeks to examine the virus-host interaction of Marburg virus (MARV) and establish a blueprint for the targeted development of antiviral strategies for newly emerging viruses.

Braunschweig, Germany, 21 January 2025 – With viral disease emergence expected to accelerate, preparing for possible future pandemics is paramount. Beyond saving lives during outbreaks, robust pandemic preparedness safeguards economies, sustains societal functioning, and reinforces the resilience of global systems. The new EU project COMBINE ("Comparative Signature of Marburg Virus Cell Activation as a Blueprint for the Identification of Antiviral Targets against Newly Emerging Viruses") acknowledges that understanding how viruses infiltrate host cells is crucial to combating emerging infectious diseases. The project sets out to advance our understanding of how viruses enter cells, using the Marburg Virus (MARV) as a model, and to create a blueprint for identifying new targets for antiviral strategies – a critical cornerstone of pandemic preparedness. Coordinated by the German Helmholtz Centre for Infection Research (HZI), COMBINE brings together seven partners from five European countries and will receive a total funding of 7.2 million EURO over the next five years through the European Union's "Horizon Europe" Framework Programme for Research and Innovation.

The COMBINE Approach: Identification, Characterisation & Inhibition of the Virus-Cell Binding Step

Any viral infection begins with the attachment of the virus to host cells and subsequent activation of cellular receptors, making it essential to identify the factors and mechanisms involved. Therefore, COMBINE focuses on the critical virus-cell binding step, aiming to identify key factors and potential therapeutic targets involved early in viral infections. "We will apply a combination of pioneering approaches designed to identify the signature of virus-cell activation, characterise the mechanisms of virus binding and entry, and develop novel inhibitors and vaccine candidates. Using the Marburg virus as a highly-pathogenic BSL-4 model virus, this novel approach provides a comprehensive view of the virus entry process, differentiating between initial attachment and subsequent cellular activation and internalisation," explains project coordinator Professor Christian Sieben, leading the group Nanoscale Infection Biology at HZI.

Marburg virus, like Ebola virus, a member of the filovirus family, is a highly infectious and lethal pathogen with substantial epidemic potential. The virus occurs in fruit bats, widely distributed across Africa, and may also be transmitted between humans. Additionally, the virus' incubation period, ranging from 2 to 21 days, allows for potential silent transmission by individuals who are not yet symptomatic, further complicating outbreak control efforts. The recent recurrent outbreaks of the Marburg virus, including in previously unaffected countries, coupled with the lack of a licensed vaccine or specific antiviral treatment and the virus's high lethality, underscore the ongoing threat posed by the virus as well as the significant clinical and societal interest in developing suitable antivirals.

Using the COMBINE approach, the team aims to establish the fundamental pre-clinical basis for the continued development of specific anti-MARV drugs and optimised MARV vaccines. "With COMBINE, we aim to make a lasting impact by reducing premature mortality and the healthcare burden of the Marburg virus through novel treatments and optimised vaccines. However, our work will not only strengthen the global virology community with new tools and knowledge, but also increase pandemic

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preparedness by addressing the health threats posed by the Marburg virus and other emerging viral diseases," emphasises Sieben.

A Blueprint for the Identification of Antiviral Targets against Newly Emerging Viruses

Beyond unveiling crucial insights into MARV cell entry, the project will break new ground and develop an innovative experimental pipeline for identifying and targeting proteins involved in the virus attachment process, a critical factor in combating viral outbreaks. COMBINE seeks to create a versatile, adaptable blueprint that facilitates cross-country collaborations to develop novel drugs and vaccines against emerging viruses. The research conducted in the scope of the project will, therefore, not only expand the knowledge of the Marburg virus cell entry and therapeutic options but also establish a technology pipeline that can be rapidly applied to other emerging viruses, strengthening global health security and readiness for future pandemics.

Project Key Facts

Title:	Comparative Signature of Marburg Virus Cell Activation as a Blueprint for the Identification of Antiviral Targets against Newly Emerging Viruses (COMBINE)
Start:	1 January 2025
Duration:	60 months
Budget:	7.2 Mil €
Coordinator:	Helmholtz Centre for Infection Research (HZI)
Website:	www.combine-MARV.eu
Social Media:	https://www.linkedin.com/showcase/combine-marv-project/

Project Partners

Belgium

- Vlaams Instituut voor Biotechnologie (VIB)

Germany

- European Research and Project Office GmbH (EURICE)
- Helmholtz Centre for Infection Research (HZI)
- University of Marburg (UMR)

Norway

- University of Oslo (UiO)

Romania

- Institute of Biochemistry of the Romanian Academy (IBRA)

Sweden

- Karolinska Institutet (KI)

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Group Picture

COMBINE consortium at Kick-Off Meeting in Braunschweig.

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