MEDIA RELEASE

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SINGAPORE SCIENTISTS DEVELOP GENE-EDITING TECHNOLOGY THAT ELIMINATES EV-A71 RNA VIRUSES

Singapore scientists have developed a CRISPR-Cas13 therapeutic against EV-A71, the RNA virus that causes hand, foot, and mouth disease

SINGAPORE – A team of scientists from A*STAR's Genome Institute of Singapore (GIS) and the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) has made an important breakthrough in the fight against RNA viruses that cause human diseases and pandemics.

Their research shows that the CRISPR-Cas13 editor delivered by adeno-associated virus (AAV) can directly target and eliminate RNA viruses in laboratory models. AAV are delivery vehicles derived from small viruses that naturally infect humans. They are clinically approved for use in gene therapy drugs which are used to treat diseases such as spinal muscular atrophy, Duchenne muscular dystrophy, and haemophilia.

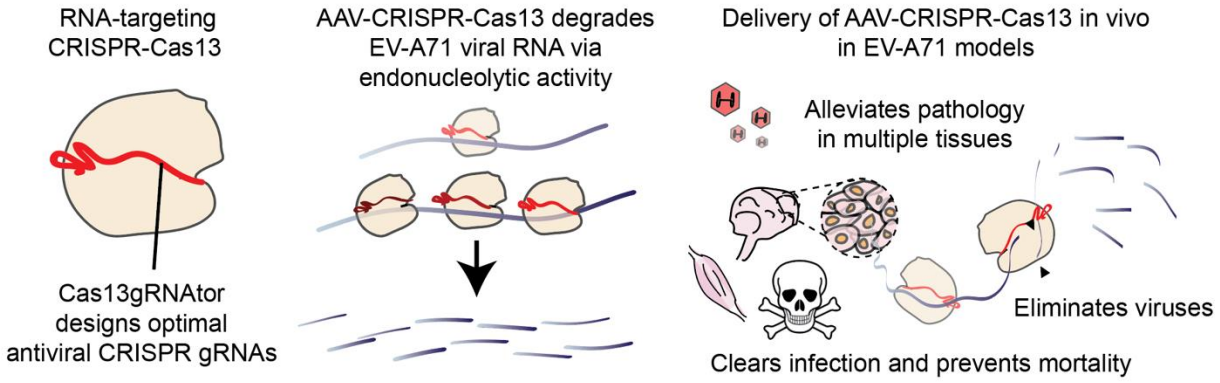
The EV-A71 virus is the cause of the hand, foot, and mouth disease, and in severe cases, can lead to nervous system disease and death. To treat the viral infection, the team turned to CRISPR-Cas13, an RNA-editing technology that alters RNA in a cell.

CRISPR-Cas13 edits RNA and opens therapeutic avenues to a wide range of diseases that are untreatable by the Nobel Prize-winning CRISPR-Cas9, which edits DNA.

CRISPR-Cas13 is programmed by guide RNAs (gRNAs) to target specific RNA sequences. Upon binding to these RNA sequences, the CRISPR-Cas13 cuts the RNA target into pieces, inactivating the RNA. CRISPR-Cas13 could also be utilised for RNA-editing, where a specific RNA sequence is changed to another sequence within the cell.

In this recent work, the team of scientists first developed the Cas13gRNAtor computational programme to design CRISPR gRNAs that cut viral RNA across different viral strains. They show that CRISPR-Cas13 treatment potently reduces viral burden, with less than 0.1% of the viruses remaining in previously infected cells.

Importantly, the research findings show that the AAV-CRISPR-Cas13 therapy clears the EV-A71 infection and prevents organ damage and mortality.



A newly developed antiviral CRISPR-Cas13 therapeutics

“This is a stunning demonstration that one dose of CRISPR-Cas13 can mean a difference between life and death. We are building on this research to develop further life-changing

nucleic acid therapeutics." said Dr Chew Wei Leong, Associate Director and Principal Scientist at A*STAR's GIS.

Associate Professor Justin Chu from NUS Medicine's Department of Microbiology and Immunology and Infectious Diseases Translational Research Programme added, "This amazing study has helped to unlock the new frontiers in antiviral strategies by using AAV-CRISPR-Cas13 to combat human enteroviruses, paving the way for potential therapeutics against viral diseases."

Professor Liu Jian Jun, Acting Executive Director of A*STAR's GIS said, "The CRISPR technology allows the rewriting of the genetic code in almost any organism. This joint research with NUS is an extremely important development which can potentially treat many diseases caused by RNA viruses, and open many avenues for further therapeutic solutions."

These findings demonstrate a therapeutic development pipeline for antiviral AAV-CRISPR-Cas13 against potentially deadly RNA virus infections. Further therapeutic development could bring this technology towards treating human RNA viruses in the clinic. This research was published on 28 June 2023, in eBioMedicine, part of The Lancet Discovery Science.

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About A*STAR's Genome Institute of Singapore (GIS)

The Genome Institute of Singapore (GIS) is an institute of the Agency for Science, Technology and Research (A*STAR). It has a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity. Established in 2000 as a centre for genomic discovery, the GIS pursues the integration of technology, genetics and biology towards academic, economic and societal impact, with a mission to "read, reveal and (ω)rite DNA for a better Singapore and world".

Key research areas at the GIS include Precision Medicine & Population Genomics, Genome Informatics, Spatial & Single Cell Systems, Epigenetic & Epitranscriptomic Regulation, Genome Architecture & Design, and Sequencing Platforms. The genomics infrastructure at the GIS is also utilised to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact.

For more information about GIS, please visit www.a-star.edu.sg/gis.

About the Agency for Science, Technology and Research (A*STAR)

A*STAR is Singapore's lead public sector R&D agency. Through open innovation, we collaborate with our partners in both the public and private sectors to benefit the economy and society. As a Science and Technology Organisation, A*STAR bridges the gap between academia and industry. Our research creates economic growth and jobs for Singapore, and enhances lives by improving societal outcomes in healthcare, urban living, and sustainability. A*STAR plays a key role in nurturing scientific talent and leaders for the wider research community and industry. A*STAR's R&D activities span biomedical sciences to physical sciences and engineering, with research entities primarily located in Biopolis and Fusionopolis. For ongoing news, visit www.a-star.edu.sg.

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About National University of Singapore (NUS)

The National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education, research and entrepreneurship, with a focus on Asian perspectives and expertise. We have 16 colleges, faculties and schools across three campuses in Singapore, with more than 40,000 students from 100 countries enriching our vibrant and diverse campus community. We have also established our NUS Overseas Colleges programme in more than 15 cities around the world.

Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, research centres of excellence, corporate labs and more than 30 university-level research institutes focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research and cybersecurity.

For more information on NUS, please visit https://nus.edu.sg.

About the NUS Yong Loo Lin School of Medicine (NUS Medicine)

The NUS Yong Loo Lin School of Medicine is Singapore's first and largest medical school. Our enduring mission centres on nurturing highly competent, values-driven and inspired healthcare professionals to transform the practice of medicine and improve health around the world.

Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,000 graduates have passed through our doors.
In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is one of the leading medical schools in Asia and ranks among the best in the world (Times Higher Education World University Rankings 2023 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2023).

For more information about NUS Medicine, please visit https://medicine.nus.edu.sg/.