PRESS RELEASE

NUS researchers discover protein that causes neurological complications in Hand, Foot and Mouth Disease

The finding could aid in prevention of the severe consequences through drug development

Singapore, 20 April 2021 — Hand, Foot & Mouth Disease (HFMD) is a generally mild, contagious viral infection common in young children. In Singapore, HFMD is endemic and is most commonly caused by intestinal viruses known as coxsackieviruses and enteroviruses.

While most HFMD patients experience common symptoms such as sore throat, fever, ulcers inside the mouth and blisters and lesions on the palms and soles, infection with Enterovirus-A71 (EV-A71) may lead to serious neurological complications that can be potentially fatal or lead to long-term neurological deficits (cognitive and motor deficits). These complicated HFMD cases are mainly seen in young children.

Researchers from NUS Yong Loo Lin School of Medicine's Infectious Diseases Translational Research Programme have identified two new proteins that play a critical role in the ability of EV-A71 to invade the central nervous system. One of these proteins is a druggable target, which means that there are drugs available that target this protein and which could potentially be used to limit the neurological complications associated with this illness.

Since there are currently no antiviral treatments available for HFMD, only symptomatic relief is available to patients. This new discovery could allow for the development of more effective treatment of the disease, particularly for such severe cases. A number of compounds that have been developed to target this discovered protein have mainly been studied in the context of cancer. However, this finding is likely to change the course of the advancement of some of these compounds.

"This exciting finding will bring us one step closer to preventing EV-A71-infected HFMD patients from experiencing potential neurological complications. As this virus is considered to be endemic in Singapore, with cyclical epidemics every two to three years, our discovery is likely to have a significant impact on the country's public health," said Associate Professor Sylvie Alonso, Principal Investigator of the study and Co-Director of the Infectious Diseases TRP at NUS Medicine.

"The new data reported contributes to better understanding of the molecular mechanisms of EV-71 neuroinvasion that may lead to neurological complications of HFMD caused by EV-A71. This is a step towards identifying possible targets for interventions to reduce/prevent EV-A71 complications," shared Dr Chan Si Min, the Head and Senior Consultant of the Division of Paediatric Infectious Diseases at National University Hospital.

The Infectious Diseases TRP aims to provide a holistic, patient-centric approach to infectious diseases that are relevant to Singapore and the region. The Programme focuses on programmatic research areas including pathogen evolution and transmission, host-microbe interactions and vaccine and therapeutics development.

Lim Z.Q., Ng Q.Y., Oo Y., Chu J.J., Sze S.K. & Alonso S. (2021). Enterovirus-A71 exploits peripherin and Rac1 to invade the central nervous system. *EMBO Reports.* Retrieved from: https://www.embopress.org/doi/abs/10.15252/embr.202051777

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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, 30 university-level research institutes, research centres of excellence and corporate labs 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.

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

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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 Asia's leading medical school and ranks among the best in the world (Times Higher Education World University Rankings 2020 by subject and the Quacquarelli Symonds (QS) World University Rankings by Subject 2020).

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