PRESS RELEASE

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It's in the blood

NUS researchers unveil mystery behind workings of blood cells

Singapore, 13 November 2017 — Giving a literal expression to the idiom, researchers from National University of Singapore (NUS) have uncovered the secret behind how blood cells release a vital biological substance involved in essential processes like immune and blood vessel functions. This knowledge of the pathway by which blood cells release sphingosine-1-phosphate (S1P) carries broad implications for the treatment of various immune and vascular diseases.

S1P is a lipid that is released into the circulation system and directs the movement of immune cells (such as T and B cells) as part of the body's immune response. However, too much of these immune cells can cause conditions such as autoimmune and inflammatory diseases. Blocking the S1P signalling pathway with a drug called Fingolimod has been a successful approach in the treatment of multiple sclerosis, an autoimmune disease that affects nerve cells, the brain and spinal cord. On the other hand, too little S1P in the circulation is also harmful to blood vessels, often causing vascular complications such as cardiovascular diseases and stroke.

For a long time, researchers had suspected that red blood cells and platelets were the major suppliers of S1P to the blood. However, it was unclear how S1P was being transported into the body's circulation system. "Our study identified a critical molecular player for S1P production," said Dr Long Nguyen, who is an assistant professor from the Department of Biochemistry at the NUS Yong Loo Lin School of Medicine (NUS Medicine). "This opens up new avenues of investigation aimed at controlling the activity of S1P for the treatment of various diseases." This study was published in *Nature* on 18 October 2017.

In the landmark study, Dr Nguyen's team, including postdoctoral fellow Dr Thiet Vu, found that the absence of a transport protein namely Mfsd2b is related to low levels of S1P in the blood. This resulted in abnormally low numbers of T and B cells, and increased sensitivity to anaphylactic shock, a severe allergic reaction. Their breakthrough findings pave the way for the manipulation of S1P levels in the blood for the treatment of inflammatory and vascular diseases *(see Appendix).* The team also found that a lack of Mfsd2b is linked to low red blood cell counts, and chemotherapy and radiotherapy sensitivities. This suggests that increasing plasma S1P levels could be beneficial to cancer patients receiving chemotherapy and radiotherapy treatments.

The study also involved Professor Markus Wenk, Head of Department of Biochemistry, and researchers from NUS Centre for Life Sciences (CeLS), Cancer Science Institute (CSI),

Biomedical Institute for Global Health Research and Technology (BigHeart), the National University Hospital (NUH), Duke-NUS Medical School, and NUS Engineering, Department of Biomedical Engineering.

The research was mainly supported by a New Investigator Grant from the Singapore Ministry of Health's National Medical Research Council and an NUS Young Investigator Award.

Commenting on the finding, Associate Professor Mark Chan, Department of Medicine, NUS Medicine and Senior Consultant from the Department of Cardiology, National University Heart Centre Singapore, said, "S1P is a highly potent signal, known to regulate the vascular and immune functions. Finding a new protein that controls its transport inside and out of cells, opens up powerful therapeutic implications as this protein can now serve as a new target for drugs. This could pave the way for development of new therapeutics to prevent and treat vascular diseases."

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Appendix

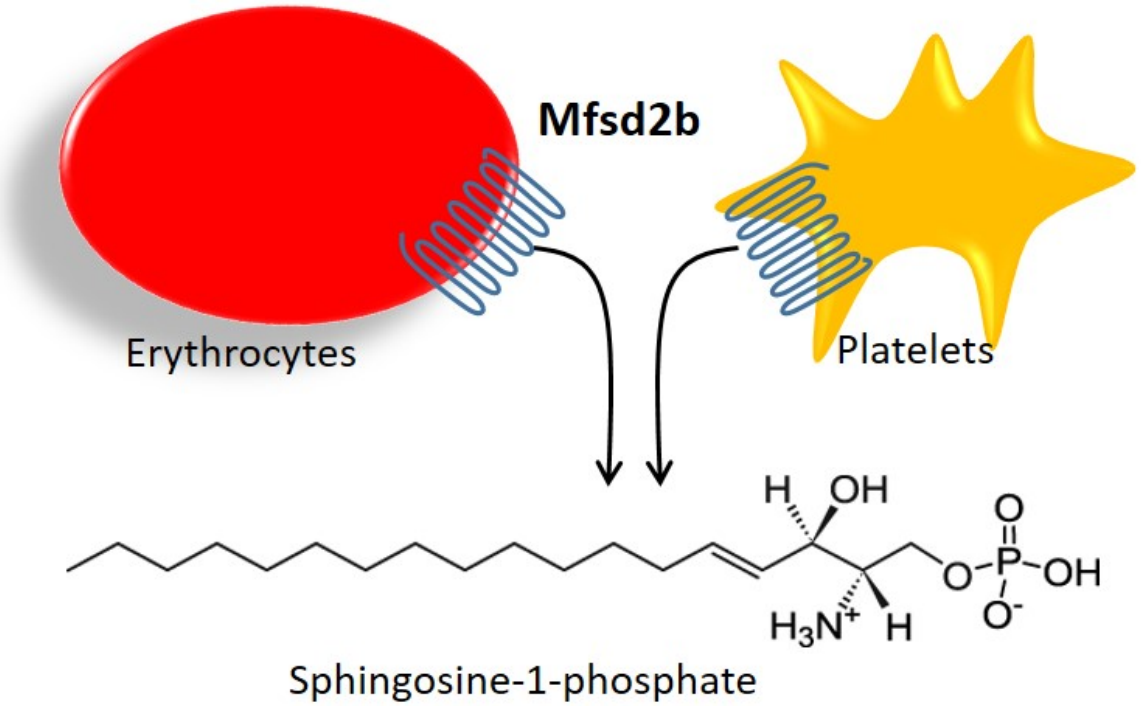

Figure: The lipid substance Sphingosine-1-phosphate (shown chemical structure) produced in erythrocytes and platelets is transported out of the cells into the blood by the Mfsd2b protein.

About the National University of Singapore (NUS)

A leading global university centred in Asia, the National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education and research, with a focus on Asian perspectives and expertise.

NUS has 17 faculties and schools across three campuses. Its transformative education includes a broad-based curriculum underscored by multidisciplinary courses and cross-faculty enrichment. Over 38,000 students from 100 countries enrich the community with their diverse social and cultural perspectives. NUS also strives to create a supportive and innovative environment to promote creative enterprise within its community.

NUS takes an integrated and multidisciplinary approach to research, working with partners from industry, government and academia, to address crucial and complex issues relevant to Asia and the world. Researchers in NUS' Schools and Faculties, 30 university-level research institutes and centres, and Research Centres of Excellence cover a wide range of themes including: energy, environmental and urban sustainability; treatment and prevention of diseases common among Asians; active ageing; advanced materials; risk management and resilience of financial systems. The University's latest research focus is to use data science, operations research and cybersecurity to support Singapore's Smart Nation initiative.

For more information on NUS, please visit www.nus.edu.sg.

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

Established in 1905, the NUS Yong Loo Lin School of Medicine is the first institution of higher learning in Singapore and the genesis of the National University of Singapore.

The School offers one of the finest undergraduate medical programmes in the Asia Pacific region and enjoys international recognition and respect. The Times Higher Education World University Rankings 2016 by subject and Quacquarelli Symonds (QS) World University Rankings by Subject 2017 list NUS Medicine as a leading medical school in Asia.

It admits 300 students to the MBBS degree programme annually and its principal missions are to educate and train the next generation of healthcare professionals, and foster research that will help to advance the practice of medicine.

The 18 NUS Medicine departments in the basic sciences and clinical specialties work closely with the Centre for Medical Education, the Centre for Biomedical Ethics, the Centre for Healthcare Simulation as well as the restructured public hospitals to ensure that teaching and research are aligned and relevant to Singapore's healthcare needs. The School is a founding institutional member of the National University Health System.

For more information about NUS Medicine, please visit http://nusmedicine.nus.edu.sg