PRESS RELEASE

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Scientists reveal how blood cells release key signalling lipid

Singapore, 8 September 2026 — Scientists from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), and St. Jude Children's Research Hospital in the United States have discovered how blood cells release an important signalling fat called sphingosine-1-phosphate, or S1P, into the bloodstream.

S1P plays an important role in keeping blood vessels healthy, helping immune cells move around the body, and supporting normal cell function. To carry out these roles, S1P must first leave the cells in which it is produced. However, it cannot pass through the cell membrane freely and on its own. Instead, it relies on specialised proteins that act like gateways. One such gateway is MFSD2B, a protein found mainly in red blood cells and platelets.

In the new study, published in *Nature Communications*, researchers used cryo-electron microscopy (cryo-EM), computer simulations, and protein engineering to capture a detailed view of MFSD2B while S1P was sitting inside it. The study was led by Associate Professor Nguyen Nam Long from the Department of Biochemistry and Immunology Translational Research Programme (TRP) at NUS Medicine.

Assoc Prof Nguyen said, "About 10 years ago, we discovered MFSD2B and knew that it helps release S1P from blood cells[1], but we did not know exactly how it worked. For the first time, we were able to see how S1P sits inside this transporter and identify the parts of the protein that help move it through the cell membrane. This gives us a much clearer picture of how S1P enters the bloodstream to carry out its signalling functions."

Using cryo-EM, the researchers were able to view MFSD2B at close to the atomic level. They found that S1P fits deep inside the transporter. Its long fatty tail sits inside a pocket within the protein, while its charged head interacts with specific parts of MFSD2B that help hold and guide it. The team also identified an opening in MFSD2B that is likely to serve as the main route through which S1P moves in and out of the transporter. Two amino acids of the protein, K88 and K423, appear to act like a series of handholds, briefly interacting with S1P and helping guide it along the transport pathway.

Dr Min Huang, former postdoctoral fellow, Department of Biochemistry, NUS Medicine, and co-first author of the study said, "Capturing S1P inside MFSD2B gave us an important snapshot of the transport process. We then combined this structural information with computer

[1] Vu, T., Ishizu, AN., Foo, J. *et al.* Mfsd2b is essential for the sphingosine-1-phosphate export in erythrocytes and platelets. *Nature* **550**, 524–528 (2017). https://doi.org/10.1038/nature24053

simulations and laboratory experiments to see how S1P could move through the protein. Together, these approaches helped us understand the steps involved in transporting S1P across the cell membrane."

The researchers also found that MFSD2B moves S1P in a relatively simple and energy-efficient way. Instead of relying on sodium or other sources of energy to push S1P across the cell membrane, MFSD2B allows the lipid to move from an area where it is abundant to an area where it is less abundant. Red blood cells naturally contain higher levels of S1P than the surrounding blood plasma. This difference in concentration can therefore help drive S1P out of the cells and into the bloodstream.

The researchers also found that a change involving just one building block of the MFSD2B protein could alter the way the transporter works. Changing one amino acid made the transporter dependent on acidic conditions, showing how a small change in the protein can affect the way it moves S1P.

Understanding how MFSD2B controls S1P levels may also be useful for future research into diseases where S1P levels become disrupted. Previous studies have linked low levels of S1P in the bloodstream with problems involving blood-pressure regulation, blood vessel damage, swelling, and increased vulnerability to septic shock[2,3]. In these situations, increasing the amount of S1P circulating in the blood may potentially be beneficial. At the same time, having more S1P inside red blood cells has been linked in previous research to protection during low-oxygen conditions and kidney injury[4,5]. As such, for some conditions, researchers may instead want to reduce MFSD2B activity so that more S1P remains inside red blood cells.

These possibilities require further research, but scientists are already working on compounds that can block MFSD2B. The researchers said further studies will be needed to understand the full transport process and how S1P is passed on to carrier proteins once it enters the bloodstream.

Assoc Prof Nguyen added, "Our main aim is to understand how S1P is released from blood cells so that it can carry out its important signalling roles in the body. We hope that this detailed picture of MFSD2B will also provide a foundation for future studies looking at whether the transporter can be safely targeted in disease."

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[2] Del Gaudio *et al.* Blood-borne sphingosine 1-phosphate maintains vascular resistance, blood pressure, and cardiac function in mice. Proc Natl Acad Sci U S A. 2026 Jan 13;123(2):e2512853123. doi: 10.1073/pnas.2512853123. Epub 2026 Jan 9. PMID: 41512042; PMCID: PMC12799142.
[3] Winkler, M.S., Nierhaus, A., Holzmann, M. *et al.* Decreased serum concentrations of sphingosine-1-phosphate in sepsis. *Crit Care* 19, 372 (2015). https://doi.org/10.1186/s13054-015-1089-0
[4] Sun, K., Zhang, Y., D'Alessandro, A. *et al.* Sphingosine-1-phosphate promotes erythrocyte glycolysis and oxygen release for adaptation to high-altitude hypoxia. *Nat Commun* 7, 12086 (2016). https://doi.org/10.1038/ncomms12086
[5] Xie T *et al.* Erythrocyte Metabolic Reprogramming by Sphingosine 1-Phosphate in Chronic Kidney Disease and Therapies. Circ Res. 2020 Jul 17;127(3):360-375. doi: 10.1161/CIRCRESAHA.119.316298. Epub 2020 Apr 14. PMID: 32284030.

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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 15 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 around 15 NUS Overseas Colleges entrepreneurial hubs 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, 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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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 in 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 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 2026 by subject and the Quacquarelli Symonds (QS) World University Rankings by Subject 2026).

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