



PRESS RELEASE

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NUS researchers discover an essential protein controlling cerebral blood vessel development and brain functions

Singapore, 5 May 2020 - Brain blood vessels are critical networks to maintain brain functions. These blood vessels control the exchange of nutrients, gases, and wastes between neuronal cells and blood. Defects in these blood vessels result in life threatening diseases such as stroke and brain haemorrhages. How blood vessels absorb nutrients for their own functions and how they supply the brain with essential nutrients is yet to be fully understood.

On May 5, researchers from the Yong Loo Lin School of Medicine at the National University of Singapore reported online in the prestigious *Journal Clinical Investigation (JCI)* that they had discovered a protein named Mfsd7c in blood vessel cells that is critical for blood vessel development and brain growth. Their findings may pave the way for better understanding of the essential nutrients required for blood vessel health and brain growth.

Mfsd7c is an orphan protein transporter that has been linked with Fowler syndrome. Affected subjects with genetic variations in Mfsd7c exhibit signs of severe neurological defects. Typical hallmarks of this disease are congenital hydrocephalus, hydranencephaly, hypervasculation and thinning of cortices in the central nervous system (CNS). These developmental abnormalities are associated with high prenatal lethality. In this breakthrough study, the NUS researchers revealed the effects of *Mfsd7c* deficiency in mice and compare it to phenotypic findings in humans with bi-allelic Mfsd7c mutations. They found that MFSD7c is required for the normal growth of brain blood vessels and ablation of this gene results in microcephaly-associated vasculopathy in mice and humans.

In the study, led by Assistant Professor Long N. Nguyen from the Department of Biochemistry and his team (postdoctoral fellows Pazhanichamy Kalailingam and Toan Quoc Nguyen, and undergraduate students Xiu Ru Toh and Kai Qi Wang), the researchers discovered that Mfsd7c is not only essential for brain blood vessel development, but essential for brain growth. Loss of Mfsd7c causes severely reduced blood vessel density and functions that results in hypoxia and neuronal cell death. Deficiency of Mfsd7c also causes microcephaly (small brain) in mice and humans. Although detailed mechanisms by which Mfsd7c regulates these two seemingly related processes require further investigations, their study suggested that molecules transported to the brain by Mfsd7c are critical for the central nervous system (CNS).

The researchers noted that many protein transporters are expressed in brain blood vessels. However, what we know about the human brain is still limited. Nutrients that the brain needs during early development and in adulthood are yet to be fully uncovered. “Our study helped reveal that Mfsd7c is a critical gateway in blood vessels, likely by bringing in essential nutrients to the brain” said Dr Nguyen. “This study opens up new avenues of research aimed at identifying essential nutrients transported via CNS blood vessels for brain growth and functions”. “We are actively pursuing these scientific questions with hope that our research outcomes can be utilized for treatment of neuronal diseases via manipulating essentially nutritional molecules required by the brain”.

The study also involved researchers at the Genetics Institute, Rambam Health Care Center, Haifa, Israel and the Genetics and Rare Diseases Research Area, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy. The research was supported by the Singapore Ministry of Health's National Research Council NMRC/OF-IRG/0066/20, Ministry of Education MOE2018-T2-1-126, MOE-Tier-1, MOE PDF fellowship, NUS Young Investigator Award (NUSYIA_FY16_P19), NUHSRO/2017/066/BRIDGING/04, and NUSMED-FOS joint research programme healthy brain ageing grants.

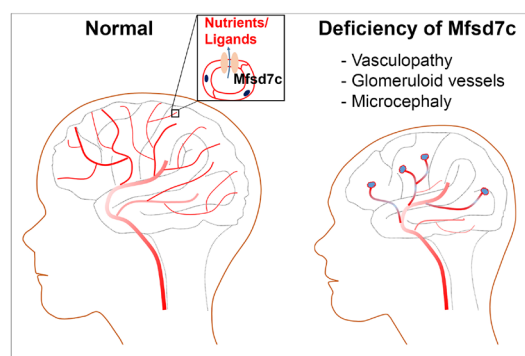


Image: This image illustrates that deficiency of Mfsd7c causes severe defects in blood vessel development and microcephaly, a form of small brain. Credit: Long N. Nguyen

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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 2019 by subject and Quacquarelli Symonds (QS) World University Rankings by Subject 2018 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>