Institute of Molecular and Cell Biology
IMCB

**SCIENTIFIC RELEASE**

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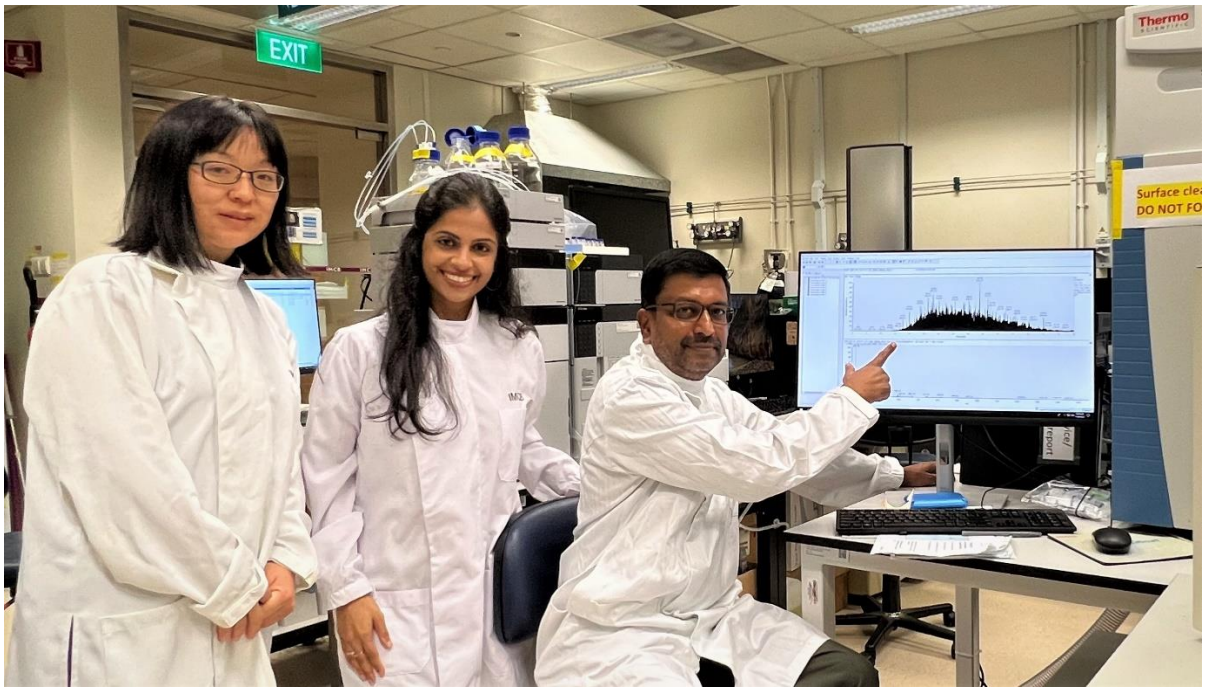
# SINGAPORE STUDY DISCOVERS NOVEL THERAPEUTIC TARGET TO ADVANCE THE TREATMENT OF DIABETIC EYE DISEASES




*Caption: The core scientific research team, (L-R) Associate Professor Wang Xiaomeng from the Cardiovascular and Metabolic Disorders Programme and Centre for Vision Research at Duke-NUS Medical School, Research Scientist Dr Asfa Alli Shaik and Senior Principal Investigator Dr Jayantha Gunaratne from IMCB, investigated disease-modified protein profiles in the eye to discover novel therapeutic targets for Diabetic Retinopathy, a condition which leads to blindness induced by prolonged diabetes.*

**SINGAPORE -** A local study discovered a novel therapeutic target named ADAM10 that could be used to treat patients with Diabetic Retinopathy (DR), a condition which leads to blindness induced by prolonged diabetes. Abnormal blood vessel formation in the eyes of diabetic patients is a common phenomenon for DR which could ultimately result in vision loss. The study, published in the journal *Theranostics*, demonstrated that by restoring the function of ADAM10, a major shedding protein, it was possible in preclinical models to control the abnormal formation of blood vessels, offering an attractive therapeutic target to treat DR.

A collaborative effort involving researchers and clinicians from A*STAR's Institute of Molecular and Cell Biology (IMCB), Duke-NUS Medical School, SingHealth, Singapore Eye Research Institute (SERI) and Singapore National Eye Centre (SNEC), the research team is exploring the potential of ADAM10 in various aspects of angiogenesis and how it may be translated into beneficial solutions for patients.

Currently, DR affects about 103 million people worldwide[1]. According to a study done by the Centers for Disease Control and Prevention (CDC), DR is most common among diabetic patients, with almost one in three developing the condition. It is the leading cause of visual impairment and blindness in the working-age population globally[2]. DR usually presents without any symptoms in the early phase and is often diagnosed when the disease has advanced, requiring immediate treatment intervention. The current available form of treatment for DR is anti-VEGF (Vascular endothelial growth factor) injections, however only around half of DR patients respond to the treatment.

The research team, led by Dr Jayantha Gunaratne, Senior Principal Investigator at IMCB, conducted a comprehensive analysis of the eye fluid samples from a well-defined cohort of proliferative DR patients against the control cohort to deduce impaired mechanistic aspects within the eye. The findings show that eye fluids from DR patients displayed distinct protein patterns compared to the control cohort, implying that the molecular composition of eye fluids is reflective of the health status of the eye. By interrogating these altered profiles from DR patients, the team discovered impaired protein shedding by ADAM10 as a prominent disease feature of DR.

Working with the research team from Duke-NUS, these results were further validated using well-established cell-line and preclinical models with eye diseases through molecular, cell biological and functional assays to confirm the efficacy of the new target ADAM10 in controlling abnormal growth of blood vessels in the eye. With ADAM10 regulating various functional processes including neural and vascular aspects, it presents itself as an attractive therapeutic option for retinal angiogenic diseases.

This discovery provides key insights to the cause of DR and opens up a new path for developing effective therapeutics for DR patients, including patients who do not respond well to anti-VEGF treatments. Researchers also uncovered the involvement of other unknown potential molecular players in DR and the importance of understanding their mechanistic roles to effectively control or stop abnormal blood vessel formation in the eyes of DR patients.

Professor Hong Wanjin, Executive Director at A*STAR's IMCB, said, "Through our collaborations with the local healthcare ecosystem, we have made significant progress with the discovery of therapeutic target ADAM10 – This is a breakthrough for the scientific community and will help advance the development of targeted therapeutics leading to better healthcare outcomes."

Dr Jayantha Gunaratne, Senior Principal Investigator at A*STAR's IMCB and lead author of the study, said, "This proteomics-centric discovery is a paradigm shift from conventional to non-conventional drug target identification, focusing on protein shedding activities of cell membrane proteins. It is a novel direction with immense potential for investigating effective therapeutics for several other diseases as well."

Professor Gemmy Cheung from the SingHealth Duke-NUS Ophthalmology and Visual Sciences Academic Clinical Programme and Head and Senior Consultant, Medical Retina Department at SNEC, said, "This collaboration between IMCB and SERI provided our researchers and clinicians an immensely valuable platform to combine our expertise towards the discovery of new treatments targeting DR. The combination of eye fluid samples from patients and their clinical information provides our researchers with a very powerful dataset from which the sophisticated analytical methods was able to discover the new findings. We are confident that these discoveries will lead to improved understanding and treatment of DR."

**- END -**

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[1] Global Prevalence of Diabetic Retinopathy and Projection of Burden through 2045: Systematic Review and Meta-analysis, Ophthalmology, Volume 128, Issue 11, November 2021
[2] International Diabetes Federation

**Enclosed:**

**Annex A** – Notes to Editor on Research Findings

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**About the Institute of Molecular and Cell Biology (IMCB)**

The vision of Institute of Molecular and Cell Biology (IMCB) is to be a premier cell and molecular biology institute which addresses the mechanistic basis of human diseases and its mission is to conduct cutting-edge discovery research in disease pathways; to groom early career researchers to be future leaders in research; and to collaborate with the public sector, medical and industry communities for research impact. IMCB plays an important role training and recruiting scientific talents, and has contributed to the development of other research entities in Singapore. Its success in fostering a biomedical research culture in Singapore has catalysed Singapore's transformation into an international hub for biomedical research, development and innovation.

Funded by A*STAR, IMCB's use-inspired research comprises 4 major programmes: Neurometabolism in Health and Diseases; Cancer Signalling and Therapies; Cell Biology and Therapies; and Innovative Technologies. IMCB also has two semi-autonomous programmes, the Disease Intervention Technology Laboratory (DITL), and the Molecular Engineering Laboratory (MEL). IMCB's technologies and platforms focus on Mouse Models of Diseases, Molecular Histopathology, Cellular Microscopy, and Proteomics & Metabolomics. For more information about IMCB, please visit www.a-star.edu.sg/imcb.

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

The Agency for Science, Technology and Research (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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**ANNEX A – NOTES TO EDITOR**

Paper published in Theranostics

**System-wide vitreous proteome dissection reveals impaired sheddase activity in diabetic retinopathy**
https://www.thno.org/v12p6682

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