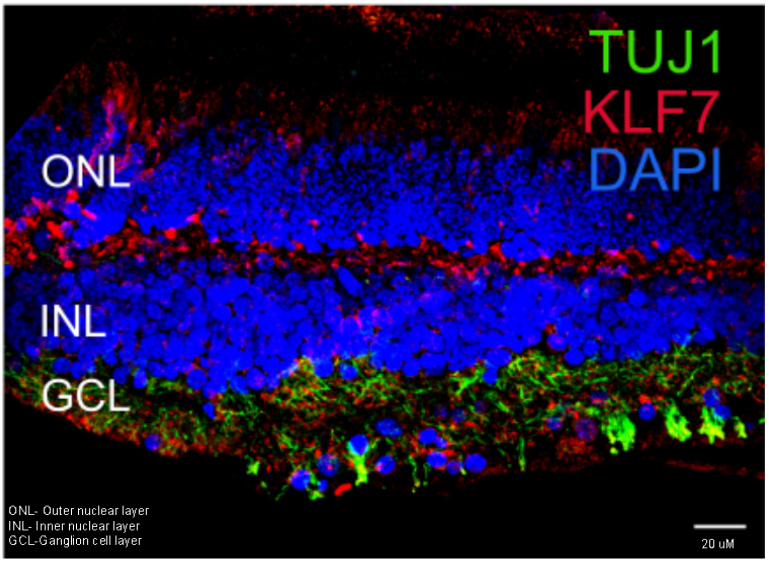
MEDIA FACT SHEET

6 DECEMBER 2021

FIRST SINGLE-CELL ATLAS OF HUMAN, PORCINE EYES MAPS GENES INVOLVED IN EYE DISORDERS

The cell-by-cell atlas will help in the study of eye disorders and development of cell therapy to replace damaged eye tissue.



KLF7(red),which could accelerate retinal ganglion cell (RGC) generation, is generally expressed in the RGC layer marked by TUJ1+ neurons (green) of retina. Lab grown RGCs could replace damaged RGCs as a potential therapy for eye disorders.
*Image credit: Pradeep Gautam, Institute of Molecular and Cell Biology (IMCB), A*STAR*

SINGAPORE – Scientists from the Agency for Science, Technology and Research (A*STAR)'s Institute of Molecular and Cell Biology (IMCB) have constructed the world's first single-cell atlas of the human and porcine eyes. This has allowed them to create a disease map of genes involved in eye disorders across the different cell types, as well as the key switches which control cell specialisation of individual ocular tissues. The work would help to provide new insights about human eye diseases and age-related eye disorders, and potentially pave the way for regenerative medicine and cell replacement therapies for eye

diseases. The research was published in leading scientific journal *Nature Communications* on 28 September 2021.

The research team, led by IMCB, consisted of researchers from the National University of Singapore (NUS), Nanyang Technological University (NTU), Singapore Eye Research Institute (SERI), Mayo Clinic, Icahn School of Medicine at Mount Sinai,University of Melbourne, and Shenzhen Eye Hospital.

The human eye comprises different cell types from different developmental origins and functional roles. In order to decipher this diversity of cellular functions using single cell RNA sequencing, the research team catalogued over 50,000 cells in human and porcine eyes, and developed a cell atlas of these eyes that distinguishes individual cells by the activity of their genes.

As certain eye disorders are associated with mutations in the human genes, the atlas which profiles disease-causing genes across all cell types of the eye, could aid understanding of how cell types are affected by such disorders. A map of cell surface proteins that can act as viral entry receptors in the human eye could shed light on how infections could travel through ocular route. The research showed that ACE2 and TMPRSS2, the primary cell surface proteins responsible for entry of SARS-CoV-2 into human, are expressed in the conjunctival cells of eye. Similar observations have been reported from different research groups, suggesting an infection from ocular route is likely.

“It is fascinating to observe the cross-talk of ocular cells through the interaction of signalling molecules with receptors. This will help us to understand how individual cell responds to external factors like injury,” said Mr Pradeep Gautam, PhD scholar at IMCB, A*STAR, who is the co-first author of the paper.

Eye diseases such as glaucoma, which is the leading cause of blindness globally, is caused by the degeneration of retinal ganglion cells (RGCs). Using embryonic stem cells as a platform for differentiation, the research team generated RGC progenitor cells in culture and validated that a switch KLF7 could accelerate RGC generation, opening up opportunities for the cultivation of lab grown RGCs to replace damaged RGCs as a potential therapy.

“This study paves the way to create mature retinal ganglion cells in the lab, which could be harnessed for the development of new approaches to reverse vision loss that results from optic nerve degeneration, including glaucoma,” said Dr Jonathan Loh Yuin-Han, Research Director at A*STAR’s IMCB and lead researcher of the study.

Moving forward, the research team hopes to use RGCs for cell therapies in patients and is working further to validate the KLF7-derived RGCs for preclinical studies. With the understanding of key molecular switches and ability to engineer cell types in culture, lab grown cells provide a key to therapy.

– END –

Enclosed:

ANNEX A – Notes to Editor on Research Findings

For media queries and clarifications, please contact:

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About A*STAR's 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.

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ANNEX A – NOTES TO EDITOR

The research findings described in this media release can be found in the *Nature Communications* Journal, under the title, "Multi-species single-cell transcriptomic analysis of ocular compartment regulons".

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