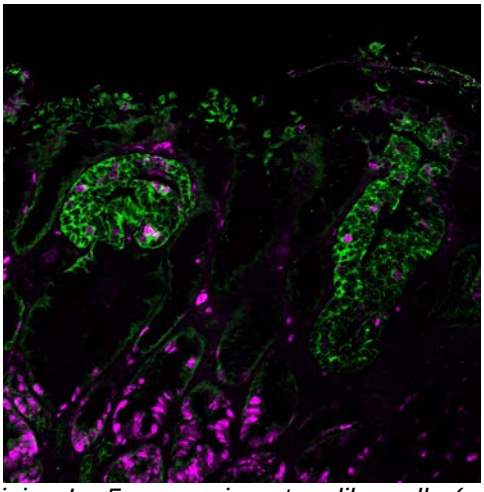
MEDIA FACT SHEET

6 DECEMBER 2021

NEW PRECLINICAL MODELS HELP IDENTIFY STEM CELLS THAT DRIVE GASTRIC CANCER GROWTH AND SPREAD

Singapore and Japan scientists have developed new, more accurate preclinical models to understand gastric cancer, one of the top 10 cancers in Singapore



An invasive gastric tumour containing Lgr5-expressing stem-like cells (green), some of which are actively proliferating (magenta). Elimination of these tumour-resident Lgr5-expressing populations greatly reduces tumour growth and spread in mice.
*Image credit: Sowmya Sagiraju and Grace Lim, Institute of Molecular and Cell Biology (IMCB), A*STAR*

SINGAPORE – Scientists from A*STAR's Institute of Molecular and Cell Biology (IMCB) have developed new, more accurate preclinical models of advanced human gastric cancer development and spread. Using these models, they have identified Lgr5-expressing tumour cells as the cancer stem cells responsible for driving gastric cancer growth and spread. These findings established Lgr5-expressing tumour cells as a potential therapeutic target, and could pave the way for developing more effective treatments against gastric cancer, one of the top 10 cancers in Singapore.[1]

The research was published in leading scientific journal *Nature Cell Biology* on 2 December 2021, led by IMCB in collaboration with researchers from A*STAR's Singapore Immunology

[1] Stomach Cancer (Gastric Cancer), The National University Cancer Institute: https://www.ncis.com.sg/Cancer-Information/About-Cancer/Pages/Stomach-Cancer-Gastric-Cancer.aspx

Network and Genome Institute of Singapore, as well as the Cancer Research Institute of Kanazawa University, Duke-NUS Medical School, National University Health System, and Cancer Science Institute of Singapore at the National University of Singpaore (NUS).

The research team identified a marker called Claudin18, that is only expressed on the epithelial lining of the stomach within the gut. Using this new marker, they generated mice producing a Cre enzyme exclusively in the stomach, which facilitated the introduction of cancer-causing mutations specifically within the stomach lining. In parallel, the team developed a transplantation model in which cultured gastric cancer cells are introduced into a healthy mouse stomach. They showed that the advanced cancers generated in these models accurately recapitulate the major disease stages from early tumour growth to invasion and metastasis to other organs including liver, lung and peritoneum, similar to human gastric cancers in their pathology and behaviour.

The team also found out that by selectively eliminating a specific subset of the gastric tumours expressing the stem cell marker Lgr5, it effectively reduces the growth and spread of the cancers. These new models will help to decipher gastric cancer progression, identify new disease biomarkers to aid in diagnosis, and evaluate new gastric cancer drugs for more targeted treatment.

“It's a breakthrough for us to apply our new models of advanced human gastric cancer to identify the specific cells – Lgr5-expressing tumour cells – involved in cancer progression. The discovery of these cells is invaluable for understanding the spread and development of gastric cancers, as well as informing the development of more effective treatments in future,” said Professor Nick Barker, Research Director at A*STAR’s IMCB and lead researcher of the study.

Building on this work, the team will continue to evaluate the Lgr5-expressing tumour cancer stem cells as a therapeutic target by performing detailed expression analyses in comparison to healthy stem cells. They will also work on identifying changes in gene expression occuring during the various stages of cancer progression, using the models to identify key mechanisms that can be potentially targeted, and novel disease biomarkers for diagnostic applications.

– END –

Enclosed:

ANNEX A – Notes to Editor on Research Findings

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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 Cell Biology* Journal, under the title, “A Tumour–Resident Lgr5+ Stem Cell – Like Pool Drives the Establishment and Progression of Advanced Gastric Cancers”.

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