

**MEDIA RELEASE
FOR IMMEDIATE RELEASE**

23 JUNE 2016

**SCIENTISTS DISCOVER UNSUSPECTED BACTERIAL LINK TO BILE
DUCT CANCER**

Findings could open up possibilities for more targeted therapies for the disease

SINGAPORE – An international research collaboration has identified bacteria in the bile duct as a potential risk factor in the development of bile duct cancer, or Cholangiocarcinoma (CCA), a rare but aggressive form of cancer with symptoms that do not present themselves at the early stages.

CCA is associated with multiple risk factors that are geographically distinct – choledocal cysts and primary sclerosing cholangitis have been implicated in the development of CCA in Western populations, while infections by the liver fluke parasite have resulted in higher incidence of CCA in Southeast Asia. However, the role of bacteria in CCA development has not been previously established, despite their relatively well-characterised involvement in colon and gastric (GI tract) cancers.

To address this gap, the team of researchers profiled the tissue microbial community of liver fluke-infected and non-infected CCA based on the 16S ribosomal RNA (rRNA) gene, a highly conserved marker gene for studying different bacterial lineages.

Led by first author Dr Chng Kern Rei, Senior Research Fellow of Computational & Systems Biology at A*STAR's Genome Institute of Singapore (GIS), the team discovered that bile duct tissue harboured a community of diverse bacteria species. *Stenotrophomonas* species – previously implicated in bile duct infections – were found to be preferentially dwelling in tumour tissue (compared to normal tissue) of non-fluke-infected CCA patients, highlighting their potential role in development of CCA.

In comparison to non-fluke-infected CCA tissues, fluke-infected CCA tissues were found to contain enteric bacteria whose metabolic outputs (bile acids and ammonia) have been previously linked to carcinogenesis, or the formation of cancers. Taken together, the results suggest a role for bile duct tissue microbiome in development of CCA and which may accordingly be used as a target for therapy.

Besides main collaborator National Cancer Centre Singapore (NCCS), this multi-national, multi-institutional project also involved National University of

Singapore, Singapore General Hospital, and Duke-NUS Medical School from Singapore; Fundeni Clinical Institute from Romania; Khon Kaen University from Thailand; and Massachusetts General Hospital and Harvard Medical School from the United States. Published in scientific journal *EBioMedicine*'s June 2016 issue, the study was also featured on the cover.

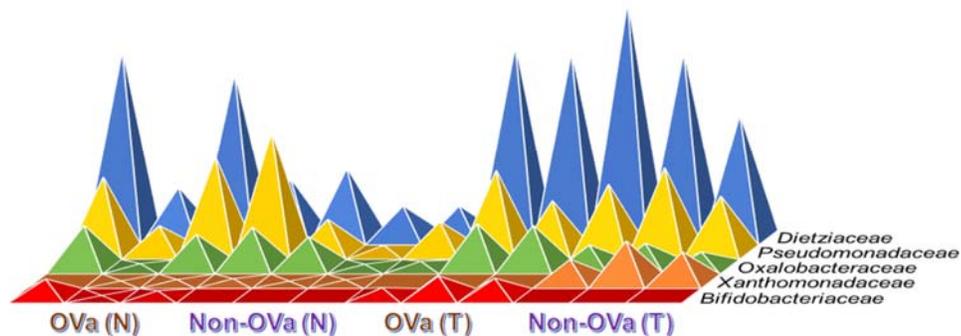
“Until recently, our understanding of bacterial communities resident in our body and their association with diseases has been limited. The associations detected in this study provide a smoking gun for the role of bacteria in bile duct cancer, and we hope that this discovery will accelerate our search for a cure for cholangiocarcinoma,” said Dr Nagarajan, the study’s joint corresponding author and Principal Investigator of Computational & Systems Biology at the GIS.

“Understanding how our cells interact with our environment and in this case our "microbial self" is increasingly recognized to be important for our understanding of health and disease. Such fundamental research while still in its early stages may pave the way for novel therapeutic strategies in time as the microbiome is far more manipulable than our genome. We are grateful to NMRC for their support in this study,” said Dr Joanne Ngeow, Co-Principal Investigator of this study and Senior Consultant Medical Oncologist, National Cancer Centre Singapore.

GIS Executive Director Prof Ng Huck Hui said, “Microbiome studies are an increasingly important area of research, evident in the National Microbiome Initiative launched by the Obama administration recently¹. Enabled by cutting-edge technologies at GIS, I look forward to more studies in this area with a view to understanding the role of microbial communities in diseases, and eventually leading to better health outcomes for patients.”

¹<https://www.whitehouse.gov/the-press-office/2016/05/12/fact-sheet-announcing-national-microbiome-initiative>

IMAGE



(Image source: A*STAR's Genome Institute of Singapore)

Major bacterial families in fluke-associated (Ova) versus non-associated (non-Ova) tumor (T) and normal (N) bile duct tissues.

Notes to Editor:

The research findings described in this media release can be found in the scientific journal *EBioMedicine*, under the title, "Tissue Microbiome Profiling Identifies An Enrichment of Specific Enteric Bacteria In Opisthorchis Viverrini Associated Cholangiocarcinoma" by Kern Rei Chng¹, Sock Hoai Chan², Amanda Hui Qi Ng¹, Chenhao Li¹, Apinya Jusakul³, Denis Bertrand¹, Andreas Wilm¹, Su Pin Choo², Damien Meng Yew Tan⁴, Kiat Hon Lim⁵, Roy Soetinko⁴, Choon Kiat Ong³, Dan G Duda⁷, Simona Dima⁸, Irinel Popescu⁸, Chaisiri Wongkham⁹, Zhu Feng¹⁰, Khay Guan Yeoh^{10,11}, Bin Tean Teh^{3,6}, Puangrat Yongvanit⁹, Sopit Wongkham⁹, Vajaraphongsa Bhudhisawasdi⁹, Narong Khuntikeo⁹, Patrick Tan^{1,6}, Chawalit Pairojkul^{9#}, Joanne Ngeow^{2,12#}, Niranjan Nagarajan^{1#}

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Full text of the *EBioMedicine* paper can be accessed online from: [http://www.ebiomedicine.com/article/S2352-3964\(16\)30177-3/fulltext](http://www.ebiomedicine.com/article/S2352-3964(16)30177-3/fulltext)

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About A*STAR's Genome Institute of Singapore (GIS)

The Genome Institute of Singapore (GIS) is an institute of the Agency for Science, Technology and Research (A*STAR). It has a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity. Established in 2000 as a centre for genomic discovery, the GIS will pursue the integration of technology, genetics and biology towards academic, economic and societal impact.

The key research areas at the GIS include Human Genetics, Infectious Diseases, Cancer Therapeutics and Stratified Oncology, Stem Cell and Regenerative Biology, Cancer Stem Cell Biology, Computational and Systems Biology, and Translational Research.

The genomics infrastructure at the GIS is utilised to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact.

For more information about GIS, please visit www.gis.a-star.edu.sg

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 agency that spearheads economic oriented research to advance scientific discovery and develop innovative technology. Through open innovation, we collaborate with our partners in both the public and private sectors to benefit 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 contributing to societal benefits such as improving outcomes in healthcare, urban living, and sustainability.

We play a key role in nurturing and developing a diversity of talent and leaders in our Agency and Research Institutes, the wider research community and industry. A*STAR oversees 18 biomedical sciences and physical sciences and engineering research entities primarily located in Biopolis and Fusionopolis.

For more information on A*STAR, please visit www.a-star.edu.sg

About National Cancer Centre Singapore

National Cancer Centre Singapore (NCCS) provides a holistic and multi-disciplinary approach to cancer treatment and patient care. We treat almost 70 per cent of the public sector oncology cases, and they are benefiting from the sub-specialisation of our clinical oncologists. NCCS is also accredited by the US-based Joint Commission International for its quality patient care and safety.

To deliver among the best in cancer treatment and care, our clinicians work closely with our scientists who conduct robust cutting-edge clinical and

translational research programmes which are internationally recognised. NCCS strives to be a global leading cancer centre, and shares its expertise and knowledge by offering training to local and overseas medical professionals.
www.nccs.com.sg