PRESS RELEASE

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SINGAPORE RESEARCHERS FIND KEY GATEKEEPER GENE THAT PLAYS KEY ROLE IN COLON CANCER

Cancer is the leading cause of death in Singapore. Worldwide, the disease accounted for 7.9 million deaths in 2007, according to the World Health Organization figures.

The key to reducing deaths from colon cancer is by early detection and better therapy.

A team of researchers at the NUS Yong Loo Lin School of Medicine and Institute of Molecular and Cell Biology (IMCB), Agency for Science, Technology and Research (A*STAR) have discovered a new gatekeeper gene. A gatekeeper determines whether or not the disease begins in the human body - a crucial step in developing both an early diagnostic test as well as a therapeutic target. The absence of this gene paves the way for the growth and development of colon cancer.

In an earlier research breakthrough, the same team of researchers led by Professor Yoshiaki Ito, NUS Yong Loo Lin Professor in Medical Oncology and Principal Investigator of the Institute of Molecular and Cell Biology, A*STAR had reported that RUNX3 is a major tumor suppressor of gastric cancer. The research had also shown that RUNX3 plays a key role in breast cancer and bladder cancer, among others.

This latest finding is reported in the September issue of Cancer Cell, a top-tier biomedical research journal. In it, Professor Ito describes how he and his team found that inactivation of RUNX3 causes full-blown colon cancer to develop.

The body usually has a fail-safe mechanism to get rid of abnormal cells. However, this does not work when RUNX3 is not present. RUNX3 is a gene which acts as a gatekeeper and prevents the uncontrolled growth of cells that may result in cancerous tumor. Disruption of the RUNX3 gene can cause colon cancer as well as many other types of cancers, including those of the bladder, breast, colon and lung.

In most cases of human colon cancer, a tumor suppressor gene called APC is disrupted. This results in the activation of beta-catenin and TCF4, a protein complex which plays an important role in the development of cancer. For decades, this has been considered the molecular basis to induce colon cancer.

However, until Professor Ito’s latest discovery, it had not been recognized that the activity of beta-catenin/TCF4 is inhibited by RUNX3.
In his study, supported by A*STAR, Professor Ito and his team analyzed animal models as well as tissue samples from patients diagnosed with colon cancer, with prior ethical approval obtained from the Institutional Review Board, to examine how RUNX3 is involved in colon cancer. The team discovered for the first time that the inactivation of RUNX3 occurs at a very early stage of colon cancer.

This is a significant finding because the inactivation of RUNX3 is relatively easy to detect and it is possible that inactivated RUNX3 can be reactivated, said Professor Ito.

“My team and I have been working on our research for the past 6 years and we are extremely excited about how our research findings can be translated into practical clinical applications to help patients suffering from cancers such as bladder, breast, colon and lung. We certainly look forward to our continuous teamwork with our clinical colleagues in improving the lives of cancer patients,” said Professor Ito, who is the NUS Yong Loo Lin Professor in Medical Oncology and Principal Investigator at the Institute of Molecular and Cell Biology, A*STAR.

Said Professor John Wong, Dean, Yong Loo Lin School of Medicine, NUS and Director, National University Cancer Institute, Singapore, NUHS, “Professor Ito’s research offers exciting, fresh hope as it lays the groundwork for a diagnostic kit for early detection of colon cancer as well as a possible therapeutic target.”

Said Professor Lee Eng Hin, Executive Director of the Biomedical Research Council, A*STAR, “This is a wonderful example of world-class research being done here. As biomedical research efforts in Singapore begin to reap clinically significant outcomes, the working relationships between our scientists and hospital clinicians must be further strengthened. Not only does the success of Professor Ito’s work open new doors to colon cancer treatment, it also serves as a leading example for other scientists to follow.”

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About Professor Yoshiaki Ito
Professor Yoshiaki Ito studied animal virology and obtained his Doctor of Medical Sciences (MD PhD) from Tohoku University, Japan. After postdoctoral training in Duke University and Imperial Cancer Research Fund, London, he became a staff member of ICRF, where he discovered middle T antigen of Polyomavirus. Subsequently, he became chief of the cell transformation section at the National Cancer Institute in USA and then moved to the Institute for Virus Research, Kyoto University in 1984, where he contributed to the establishment of RUNX gene family as a new frontier of cancer research. He discovered that RUNX3 is a major tumor suppressor of gastric cancer. He served as director of the Institute for Virus Research, Kyoto University between 1995-2001. He joined NUS as director of the Oncology Research Institute as well as Principal Investigator at the Institute of Molecular and Cell Biology as a Professor in 2002.

About the National University Health System
Established in January 2008, the National University Health System (NUHS) groups the National University Hospital and the National University of Singapore’s Yong Loo Lin School of Medicine and Faculty of Dentistry under a common governance structure to create synergies to advance its tripartite mission of excellence in clinical care, translational clinical research and education. For more information, please visit www.nuhs.edu.sg

About the National University Hospital
The National University Hospital (NUH) is a specialist hospital that provides advanced, leading-edge medical care and services. Equipped with state-of-the-art facilities as well as dedicated and well-trained staff, the NUH is a major referral centre that delivers tertiary care for a wide range of medical specialties including Cardiology, Gastroenterology & Hepatology, Obstetrics & Gynaecology, Oncology, Ophthalmology, Paediatrics and Orthopaedic Surgery. Backed by substantive expertise and experience, the NUH has been chosen by the Ministry of Health to develop two new national specialist centres to meet the growing need for cardiac and cancer treatments.

The NUH, together with the National University of Singapore’s Yong Loo Lin School of Medicine and Faculty of Dentistry, are under the common governance of the National University Health System (NUHS). Formed in January 2008, the NUHS provides a unified platform for these three entities to create greater synergies to achieve its tripartite mission of excellence in clinical care, translational clinical research and education. With combined capabilities and facilities (from the teaching hospital and medical faculty), the NUH will be able to meet the healthcare needs of patients, train future generations of doctors more effectively, and help develop solutions to our healthcare problems through research.

In 2004, the NUH became the first Singapore hospital to receive Joint Commission International (JCI) Accreditation, an international stamp for excellent clinical practices in patient care and safety. It was also the first hospital in Singapore to receive a triple ISO certification concurrently for Quality, Environmental, and Occupational Health & Safety Management Systems in 2002.

For more information, please visit www.nuh.com.sg

About the Yong Loo Lin School of Medicine
The Yong Loo Lin School of Medicine was established in 1905 as the first institution of higher learning in Singapore and the genesis of what would become the National University of Singapore. The School of Medicine strives to fulfill its tripartite mission of providing excellent clinical care, training the next generation of healthcare professionals, and fostering research that will transform the practice of medicine. It plays a pivotal role in producing future leaders in healthcare delivery, discovery, and public service as well as in Singapore's Biomedical Sciences Initiative and Singapore Medicine. The School's 17 departments in the basic sciences and clinical specialties work closely with the Alice Lee Centre for Nursing Studies, the Centre for Biomedical Ethics, and the Centre for Health Services Research to ensure that teaching and research are aligned and
relevant to Singapore's healthcare needs. In January 2008, the School of Medicine, the Faculty of Dentistry and the National University Hospital were unified under the common governance of the National University Health System, further enhancing quality clinical care, education, and research.

For more information, please visit [http://medicine.nus.edu.sg/corporate/](http://medicine.nus.edu.sg/corporate/)

**About the Faculty of Dentistry**

The Faculty of Dentistry began as a Department of Dentistry within the King Edward VII College of Medicine in 1929. It was the first dental school to be established in a British colony in the east. The three departments of the Faculty - Oral and Maxillofacial Surgery, Restorative Dentistry and Preventive Dentistry - together with the Division of Graduate Dental Studies strive to fulfill the Faculty's mission of excelling in clinical care, research and education. The Faculty works closely with the departments of the Yong Loo Lin School of Medicine and other teaching hospitals and institutions across Singapore in healthcare delivery and education and also partners departments in other Faculties of the University, public institutions and private enterprises in multi-disciplinary research activities. In January 2008, under the common governance of the National University Health System, the Faculty of Dentistry, Yong Loo Lin School of Medicine and the National University Hospital were unified to further enhance translational clinical research, quality clinical care and education.

For more information, please visit [http://www.dentistry.nus.edu.sg/](http://www.dentistry.nus.edu.sg/)

**About the Institute of Molecular and Cell Biology**

The Institute of Molecular and Cell Biology (IMCB) is a member of Singapore’s Agency for Science, Technology and Research (A*STAR) and is funded through A*STAR’s Biomedical Research Council (BMRC). It is a world-class research institute that focuses its activities on six major fields: Cell Biology, Developmental Biology, Structural Biology, Infectious Diseases, Cancer Biology and Translational Research, with core strengths in cell cycling, cell signalling, cell death, cell motility and protein trafficking. Its recent achievements include leading an international consortium that successfully sequenced the entire pufferfish (Fugu) genome. The IMCB was awarded the Nikkei Prize 2000 for Technological Innovation in recognition of its growth into a leading international research centre and its collaboration with industry and research institutes worldwide. Established in 1987, the Institute currently has 35 independent research groups with more than 400 staff members.

For more information, please visit [http://www.imcb.a-star.edu.sg](http://www.imcb.a-star.edu.sg)

**About the Agency for Science, Technology and Research**

The Agency for Science, Technology and Research, or A*STAR, is Singapore's lead agency for fostering world-class scientific research and talent for a vibrant knowledge-based Singapore. A*STAR actively nurtures public sector research and development in Biomedical Sciences, Physical Sciences and Engineering, with a particular focus on fields essential to Singapore's manufacturing industry and new growth industries. It oversees 14 research institutes and supports extramural research with the universities, hospital research centres and other local and international partners. At the heart of this knowledge-intensive work is human capital. Top local and international scientific talent drive knowledge creation at A*STAR research institutes. The Agency also sends scholars for undergraduate, graduate and post-doctoral training in the best universities, a reflection of the high priority A*STAR places on nurturing the next generation of scientific talent.

For more information, please visit [http://www.a-star.edu.sg](http://www.a-star.edu.sg)