

:: DEPARTMENT OF PHARMACY SUMMARY

The mission of the Department of Pharmacy at NUS is to translate innovative scientific studies into optimal health outcomes by discovering, developing, testing and managing medications that will be safe, efficacious and patient-friendly.

The NUS Pharmacy's research adopts a drug-product-patient tripartite approach with the goal of developing safe and effective treatments for cancer, immunological, cardiovascular, neurological and other disorders. Our prowess, spanning from biologics and chemical drugs to health product processing and quality to patient outcome and informatics to disease markers and management, is reflected in our educational and research programs, facilities and clinical services.

Translational research entails the participation of a multi-disciplinary team of pharmaceutical scientists and clinical pharmacists who are experts in pharmaceutical

chemistry, formulation science, pharmaceutical technology, biopharmaceutics, pharmacoinformatics, pharmacoconomics, clinical pharmacy or pharmacy practice in collaboration with other scientists, engineers and health professionals on campus, across Singapore and beyond.

We have put together the essential ingredients to recruit and train top undergraduate and graduate students from Asia to excel as tomorrow's pharmacists, pharmaceutical scientists and pharmaceutical engineers, finally becoming leaders impacting academia, government and industry. We strive to realize the promise of tomorrow's medicines and technologies today and to be the home where complex and controversial issues can be discussed, studied and addressed with a balance of science and compassion by students, alumni and friends. We invite you to join and support us on this exciting journey!

Research Breakthrough

PHARMACY

Bacteria Shed Light on Cancer Treatment

Associate Professor Victor Yu Chun Kong

What can bacteria teach us about fighting cancer? Scientists at the National University of Singapore (NUS) and A-STAR's Institute of Molecular and Cell Biology (IMCB) were the first to discover that the bacterial protein called FimA has a unique function in turning off the suicide program, known as apoptosis, of the host cells during infection. This finding is published on 26 March 2010 in the prestigious science journal, *Molecular Cell*.

On a daily basis, many cells in our body are infected by bacterial or viral pathogens and others may undergo mutations that may cause the affected cells to become cancerous. These infected or mutated cells would activate a cell suicide program, known as apoptosis, to permit the cells to be "self-destructed", thereby preventing the infection or other types of damages from spreading to neighbouring cells. This is the body's defense mechanism.

'Missing link found' in cancer fight

By VICTORIA VAUGHAN

A DISCOVERY made by the National University of Singapore (NUS) and A*Star's Institute of Molecular and Cell Biology may lead to a new way of treating cancer and reduce the use of radiation and chemotherapy.

Researchers have identified a link between bacterial infection such as salmonella and cancer.

Prof Yu found that once the invasive bacteria gets into a cell, it releases a molecule, FimA, which hijacks the command centre. FimA goes to the cell's mitochondria and locks together to a protein complex called VDAC-hexokinase, which needs to break apart for the cell to "commit suicide". This means the bacteria invades the cell and a person will fall sick.

Oncologists have long suspected that this protein complex in a cell might play a role in stopping cancer cells from activating the "suicide program" and forming tumours instead.

The fact that FimA is a molecule which affects cells in this way may be the missing link for cancer specialists who can now use this work to see if FimA is key in causing cancer and therefore target it with treatments.

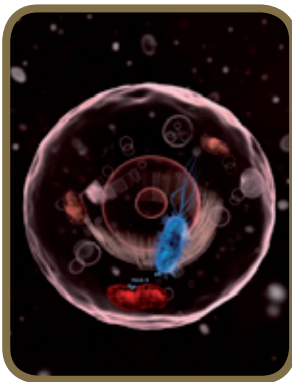
In fact, radiation and chemo therapies actually kill the cancer by getting the cells to initiate the "suicide program".

Headline: 'Missing link found' in cancer fight

Source: *The Straits Times*, Science, pD10

Date: 10 April 2010

When a talented postdoctoral fellow, Dr. Sunil Sukumaran, with extensive experience in working with bacterial pathogens in the human gut joined the laboratory six years ago, it inspired the research team to address the question of whether bacterial pathogens in the gut inhibit the suicide response of the infected cells, by directly manipulating the command center of apoptosis in mitochondria. They found that once the bacteria enter the cell, the FimA released by the bacteria rapidly target host cell mitochondria and turn off the cell suicide program, by binding to the VDAC-hexokinase protein complex to prevent them from separation which is a necessary step for activating the cell suicide program. This



Headline: NUS Researchers Discover Bacteria May Help Cancer Develop
Source: *Lianhe Zaobao*, Section 1, p9
Date: 26 March 2010

is remarkable because the same protein complex is already thought to be involved in shutting down the suicide program in cancer cells.

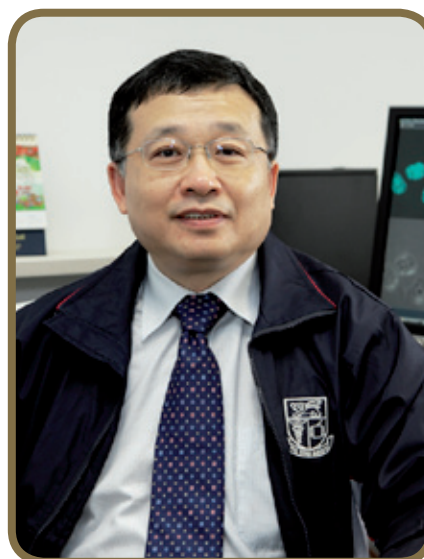
The discovery of the connection between bacterial infection and cancer will have far reaching implications and may even lead to new treatment for these two seemingly unrelated diseases. In future chemicals capable of binding to the protein complex could potentially be exploited as drug candidates for treating cancers as well as infectious diseases caused by the gut bacteria.

INTERVIEW with Associate Professor Victor Yu Chun Kong

<http://www.pharmacy.nus.edu.sg/staff/phayuv/index.html>

'The results are uncertain but the risk is worth taking'

Assoc Prof Victor Yu Chun-Kong graduated from University of Houston, Texas with a B.Sc. (Magnum cum Laude) Pharmacy in 1982. He obtained his Ph.D. (Pharmaceutical Chemistry) from University of California, San Francisco in 1987 and appointed a postdoctoral fellow of Howard Hughes Medical Institute, University of California, San Diego. From 2001 - 2009, he was an Associate Professor at the Institute of Molecular and Cell Biology, Singapore and concurrently Adjunct Associate Professor in Department of Pharmacology, NUS. Currently he is an Associate Professor in the Department of Pharmacy.



The groundbreaking research on 'Molecular Mechanism of Apoptosis Signalling in Mitochondria' in the field of cancer cell biology bears good news for cancer treatment in the future. In this interview, Principal Investigator Associate Professor Yu sheds some light on the research and the hope it brings.

Can you describe your research and its link to cancer?

Apoptosis is a physiological process engaged by all multi-cellular organisms (i.e. from worm to man). It is a highly effective way to keep the organism in healthy state by getting rid of the damaged and infected cells.

In chemotherapy, drugs work by taking advantage of the vulnerability of rapidly dividing cancer cells due to DNA damages induced by the drugs. DNA damages, in turn, trigger potent signals for apoptosis and in principle will bring death to cancer cells. But cancer cells suffer from a reduced sensitivity to respond to apoptosis signals, causing

the treatment to fail. It is known that mitochondria are the key organelles that regulate sensitivity of cells to apoptosis signals. Our research finding has brought us a further step towards understanding the mechanism of apoptosis signaling at the level of the mitochondria. This has important implications for cancer treatment.

What is the next phase of this research?

The long term goal of my work is to identify ways to regulate the core apoptotic mechanism in mitochondria to support the drug development effort. I hope that suitable cellular targets and compounds that would be useful for supporting drug development effort in combating human cancers will be identified.

According to Assoc Prof Yu, there will likely be expansion into using animal models to study clinical course of infectious diseases or cancer. The results are uncertain but the risk is worth taking when it is healthcare at stake.