Liquid Biopsy to Improve Colorectal Cancer Care

Singapore, 4 March 2015 – Choosing the right cancer treatment may soon be easier with a new liquid biopsy method developed by researchers from the Institute of Bioengineering and Nanotechnology (IBN) of A*STAR. This technology could improve the care of colorectal cancer patients to realize the promise of personalized medicine.

Professor Jackie Y. Ying, IBN Executive Director, said, “IBN is interested in developing medical technologies that can make a difference to healthcare. We are excited about our liquid biopsy approach, which could make it easier for doctors to check and administer the appropriate drug treatment for cancer patients. Our technologies have been validated by Fortis Surgical Hospital and have been successfully licensed for clinical applications.”

Doctors currently use genetic testing on tissue to determine the treatment and survival outcome of colorectal cancer patients. The standard approach is to test biopsies or resected tissue for genetic mutations (genotyping). This involves the initial removal of a piece of tissue from the affected part of the patient’s body. More tissue samples would need to be removed if the cancer has spread to other parts of the body. Tissue biopsy is a surgical procedure, which may be associated with pain and discomfort.

IBN’s liquid biopsy, in contrast, offers an alternative, less invasive method to analyze cancer cells through blood testing. This invention comprises two families of patented technologies:

- **Microsieve to Capture Circulating Tumor Cells**

  Circulating tumor cells are cells that detach from a primary tumor and travel in the bloodstream to other locations, leading to metastasis or the spread of tumor in the body. These cells are a valuable early indicator of cancer metastasis, but are extremely rare compared to the large number of blood cells in the body. IBN has fabricated a silicon microsieve to rapidly capture the circulating tumor cells from blood. Measuring 7.5 mm in diameter and with pores finer than a strand of hair, the microsieve utilizes a densely packed array of 90,000 pores to separate tumor cells from a blood sample within five minutes. Cancer cells are generally larger and stiffer, so the microsieve has been designed to trap the cancer cells, while allowing normal blood cells to pass through it. IBN’s microsieve can be used for rapid detection and analysis of circulating tumor cells, and cancer metastasis research.
Non-Invasive Genetic Test for Colorectal Cancer Treatment

Colorectal cancer is known to have two key mutated genes, KRAS and BRAF. Doctors use tissue biopsy to check for the presence of these gene mutations in order to determine the most appropriate treatment. IBN has developed ultrasensitive molecular assays to identify matching gene mutations using the captured circulating tumor cells from the microsieve. The assays were tested on 44 colorectal cancer patients who underwent surgery at Fortis Surgical Hospital, and the results revealed that the liquid biopsy was highly accurate in detecting KRAS and BRAF mutations in blood. Recently published in the journal *Molecular Oncology*, this finding represents a major milestone of the Fortis-IBN TissueBank, which was established by IBN and Fortis Surgical Hospital in July 2012 to advance translational research in colorectal care.

Dr Min-Han Tan, IBN Team Leader and Principal Research Scientist, said: “As an oncologist and researcher, I believe care for our cancer patients can be improved through real-world innovation. Our work shows matching genetic mutations in the tumor tissue and corresponding circulating tumor cells of patients with colorectal cancer. This opens up an avenue for liquid biopsies, or the testing of cancer cells through blood, which we hope can reduce the need for invasive biopsies.”

Dr Poh-Koon Koh, Senior Consultant and Director, Colorectal Surgical Oncology & Cancer Genetics Service, Fortis Surgical Hospital, and Adjunct Clinician Scientist at IBN, shared, “In partnering IBN to set up the Fortis-IBN TissueBank, our aim was to create a resource that will allow cutting-edge research to benefit patients clinically. This liquid biopsy invention is an invaluable tool in our fight against colorectal cancer at the molecular level. The technique also allows a non-invasive means to obtain DNA material in tumors that are not easily or safely accessible through conventional biopsy techniques.”

IBN’s liquid biopsy invention can be targeted for colorectal cancer as well as other types of cancer. The microsieve technology was licensed to CellSieve Pte Ltd, a spin-off company from IBN, in August 2011 for commercialization. The latest non-invasive genetic test was licensed to AITbiotech Pte Ltd, a Singapore-based biotechnology company, in January this year for development into a ready-to-use test kit. AITbiotech provides molecular diagnostics and genomic services to hospitals and research laboratories.

AITbiotech CEO Alex Thian said, “We are pleased to be IBN’s commercialization partner for these test kits. This is a good example of a win-win public-private partnership, whereby a local SME like us is able to leverage on IBN’s expertise to introduce innovative products to the local and global markets.”

Colorectal cancer is the number 1 cancer in Singapore, especially among those aged 50 and above. It is the most commonly diagnosed cancer in men (17%) and the second most commonly diagnosed cancer in women (13%), according to the Singapore Cancer Society. This disease can be managed if detected and treated early.

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References:

1. Microsieve to Capture Circulating Tumor Cells

2. Non-Invasive Genetic Test for Colorectal Cancer Treatment

Images Available on Request:

Image 1: (From left) The research team: Ms Nur-Afidah Mohd Suhaime, Prof Jackie Y. Ying, Dr Min-Han Tan from IBN with Dr Poh-Koon Koh from Fortis Surgical Hospital.

Image 2: IBN’s silicon microsieve with a densely packed array of pores to rapidly capture circulating tumor cells from blood within five minutes.
Image 3: A microscopic image of the circulating tumor cells captured by IBN’s microsieve.

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Established in 2003, the Institute of Bioengineering and Nanotechnology (IBN) is the world’s first bioengineering and nanotechnology research institute. IBN’s mission is to conduct multidisciplinary research across science, engineering, and medicine for breakthroughs to improve healthcare and quality of life.

IBN’s research activities are focused in the following areas:

- **Nanomedicine**, where functionalized polymers, hydrogels and biologics are developed as therapeutics and carriers for the controlled release and targeted delivery of therapeutics to diseased cells and organs.

- **Cell and Tissue Engineering**, where biomimicking materials, stem cell technology, microfluidic systems and bioimaging tools are combined to develop novel approaches to regenerative medicine and artificial organs.

- **Biodevices and Diagnostics**, which involve nanotechnology and microfabricated platforms for high-throughput biomarker and drug screening, automated biologics synthesis, and rapid disease diagnosis.

- **Green Chemistry and Energy**, which encompass the green synthesis of chemicals and pharmaceuticals, catalytic conversion of biomass, utilization of carbon dioxide, and new nanocomposite materials for energy applications.

Scientific Impact

- More than 1,000 papers published in leading scientific journals
- Over 1,100 seminars and presentations at international conferences, including over 700 invited, keynote and plenary lectures
Organized premier scientific meetings such as the International Conference on Bioengineering and Nanotechnology, Nano Today Conference, and the IBN International Symposium

Technological and Commercialization Impact
- 500 active patents and patent applications
- 86 licensed patents and patent applications
- 7 spin-off companies
- 140 active research collaborations with industrial, clinical and academic partners

Nurturing Future Research Talents
- Trained 106 PhD students
- More than 77,700 students and teachers from 290 local and overseas schools/universities have participated in IBN’s Youth Research Program
- Over 2,000 students and teachers have completed research attachments at IBN

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