

PRESS RELEASE

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A*STAR SCIENTISTS SCORE “HAT-TRICK” AGAINST CANCER

A*STAR scientists made three separate groundbreaking discoveries in fight against cancer

1. Scientists from Singapore’s Agency of Science, Technology and Research (A*STAR) have made three successive breakthroughs in key areas of cancer research. Their work, published in top scientific journals *Cancer Cell*, *Nature Cell Biology*, and *Cancer Research*, sheds light on the mechanism behind cancer metastasis, suggest why breast cancer cells live as long as they do, and show a better way to detect and fight cervical cancer.

Stopping the spread of cancer

2. A team of scientists led by Dr Zeng Qi^{1,2} from A*STAR’s Institute of Molecular and Cell Biology (IMCB) has made a discovery about how PRL-3, a protein that plays a key role in tumorigenesis and cancer metastasis, is regulated in the body by PCBP1. Together with her collaborator Dr. Leah Vardy from A*STAR’s Institute of Molecular Biology (IMB), the scientists found that PCBP1 impedes the translation of PRL-3 mRNA. Their discovery, published today in the leading journal *Cancer Cell*, sheds light on the role of PRL-3 in cancer and suggests possible ways to prevent metastasis, arguably the most pernicious and harmful aspect of the disease.

3. PRL-3³ was first identified by Dr Zeng in 1998. However, the mechanism controlling the expression of PRL-3 is poorly understood. While trying to understand how PRL-3 expression is regulated in the body, the scientist discovered that PCBP1 was responsible for suppressing the expression of PRL-3. Using their mouse model, the scientists found that inducing over-expression of PCBP1 significantly reduced tumour size, suggesting that controlling levels of PCBP1 may be a means of suppressing the growth and spread of tumours in the body.

4. Said Dr Zeng, “The finding of PCBP1 as a potential tumor suppressor is highly significant as a similar mechanism may be regulating other cancer genes. Since PRL-3 plays multiple tasks in contributing to cancer metastasis, we are extremely excited to discover the mechanism underlying PRL-3’s expression control as it

¹ Dr Zeng Qi was awarded an ETPL Flagship grant worth S\$3.1 million in 2009.

² Dr Zeng is also an adjunct Associate Professor at the Department of Biochemistry of the National University of Singapore.

³ PRL-3 was first found to be upregulated in colorectal cancer metastasis (Saha et al., 2001). Subsequently, many other groups demonstrated that the PRL-3 transcript or protein is often overexpressed in various types of human cancer. Cancers which express PRL-3 are associated with poor prognoses. Two recent reviews summarise the work on PRL-3 (Bessette and Pallen, 2008; Stephens et al., 2005).

uncovers another piece of the puzzle surrounding one of the most important proteins involved in cancer.”

5. Their findings were praised by Prof Neal Copeland, Executive Director of IMCB, who said, “This study by Drs Zeng and Vardy is a fine example of how basic research contributes to understanding processes that lead to metastasis, perhaps the most devastating aspect of cancer. There are many facets of the disease which still remain obscure at the cellular and molecular level, and this sort of painstaking research is needed in the fight against cancer.”

6. Dr Zeng aims to undertake more research to elucidate the regulatory mechanisms surrounding PRL-3. “PRL-3’s association with diverse human cancers makes it an excellent therapeutic target. An increased understanding of PRL-3 will definitely help us develop strategies to block PRL-3 expression or inhibit its activity and thus prevent it from promoting cancer metastasis, allowing us to deal a heavy blow to this most dreaded human disease,” added Dr Zeng.

Shortening the life of breast cancer

7. Another team of scientists from IMCB led by Dr Vinay Tergaonkar have discovered a protein, Rap1, which plays an important role in breast cancer. Their work, published in *Nature Cell Biology* showed that the presence and abundance of Rap1 could serve as biomarkers of various human illnesses including breast cancer. They also found that Rap1 could protect cancer cells from self-programmed cell death and that Rap1 levels in breast tumours might be responsible for cancer cell metastasis, making the protein an excellent target for cancer therapies.

A more sensitive test for cervical cancer

8. The third team of scientists led by Dr Françoise Thierry of IMB discovered that the human papillomavirus (HPV) E2 protein could be used for the early detection of HPV⁴. Their work, published in *Cancer Research*, is a step forward in the fight against cervical cancer, the second cause of death by cancer in women worldwide. Dr Thierry, together with Drs Jeffrey Low and Diana Lim of the National University Health System, Singapore, showed that HPV detection methods based on HPV E2 were more sensitive than methods based on detection of the HPV DNA. Furthermore, the presence of HPV E2 was intimately linked to the progression of cervical cancer, and could therefore help to control the progression of the disease.

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⁴ More than 99% of cervical cancer cases are associated with infection by human papillomaviruses (HPV)

About the Institute of Medical Biology (IMB)

The Institute of Medical Biology is a member of the Agency for Science, Technology and Research (A*STAR). It was formed in 2007, with a mission to study mechanisms of human disease in order to discover new and effective therapeutic strategies for improved quality of life. Its research focus areas are in stem cells, genetic diseases, epithelial and neurobiology, cancer, and control of differentiation. IMB is developing internationally excellent research programmes working closely with clinical collaborators, targeting the challenging interface between basic science and clinical medicine, and aiming to promote increased and effective throughput of research from bench to bedside. Its growing portfolio of strategic research topics aims to promote translational research on the mechanisms of human diseases with a cell to tissue emphasis that can help identify new therapeutic strategies for disease amelioration, cure and eradication.

For more information about IMB, please visit www.imb.a-star.edu.sg.

About the Institute of Molecular and Cell Biology (IMCB)

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, Genomics, 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 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 about IMCB, please visit www.imcb.a-star.edu.sg

About the Agency for Science, Technology and Research (A*STAR)

A*STAR is the lead agency for fostering world-class scientific research and talent for a vibrant knowledge-based and innovation-driven Singapore. A*STAR oversees 14 biomedical sciences, and physical sciences and engineering research institutes, and nine consortia & centres, which are located in Biopolis and Fusionopolis, as well as their immediate vicinity.

A*STAR supports Singapore's key economic clusters by providing intellectual, human and industrial capital to its partners in industry. It also supports extramural research in the universities, hospitals, research centres, and with other local and international partners.

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