Groundbreaking Discovery of the Cellular Origin of Cervical Cancer

Singapore - (ACN Newswire) - A team of scientists from A*STAR's Institute of Medical Biology (IMB) and Genome Institute of Singapore (GIS) together with clinicians from Boston's Brigham and Women's Hospital (BWH) have identified a unique set of cells in the cervix that are the cause of human papillomaviruses (HPV) related cervical cancers. Significantly, the team also showed that these cells do not regenerate when excised. These findings have immense clinical implications in the diagnosis, prevention and treatment of cervical cancer. The study was published in the prestigious journal, Proceedings of the National Academy of Sciences (PNAS), this week.
Cervical cancer is the 7th most common female cancer in Singapore and about 200 cases are diagnosed every year.[1] Infection with HPV is the most common cause or risk factor for cervical cancer. HPV infection causes pre-invasive cancer, termed CIN (Cervical Intraepithelial Neoplasia), which are pre-cancerous lesions that can progress and potentially become invasive cancer if left untreated.

Dr Christopher P. Crum, Director of Women's and Perinatal Pathology in the Department of pathology at BWH, said, "It has been a decades-old mystery why cervical cancers caused by HPV arise only from a discrete region of the cervix, known as the 'squamocolumnar junction', despite the presence of the virus throughout the genital tract. The discovery of these cells finally resolves this mystery and will have wide-ranging impact from developing more meaningful animal models of early cervical carcinogenesis to clinical implications."

The team discovered that this discrete set of cells, located at the squamocolumnar junction of the cervix, uniquely express biomarkers that are seen in all forms of invasive cervical cancers linked to HPV. This means that the signature markers of this population of cells can provide a way of distinguishing potentially dangerous precancerous lesions from those with a benign prognosis.

Dr Wa Xian, Principal Investigator at IMB, said, "Our study also revealed that this exotic population of cells does not reappear after ablation[2] by cone biopsy. This finding helps to explain the low rate of new HPV infections in the cervix after excisional therapy and also raises the distinct possibility that preemptive removal of these cells in young women could reduce their risk of cervical cancer. This could be an alternative to current vaccines which only protect against HPV 16 and 18."

This study further validates previous work[3] by Dr Xian and Dr McKeon in collaboration with BWH and NUS, which showed for the first time that some cancers originate from just a small set of cells that are unique from the other cells that reside around them. (Refer to Background)

Dr Frank Mckeon, Senior Group Leader at GIS, said, "Our previous work on

esophageal cancer opened up the possibility of 'preventive therapy' to stamp out the disease by eliminating this small group of cells. This recent work in the cervix further validates this concept and raises important possibilities for early intervention to prevent malignancies linked to very small populations of these unusual, discrete population of cells."

Prof Birgitte Lane, Executive Director of IMB, said, "This compelling study lends further weight to the importance of specific target cell populations underlying cancer. It is a powerful example of what can be done by combining skilled pathology with modern molecular genetics to uncover important new information, even in such a well-studied disease as cervical cancer."

Prof Ng Huck Hui, Acting Executive Director of GIS, said, "This study is a fine example of how A*STAR research institutes can integrate our research capabilities to better collaborate with an international partner like the Brigham and Women's Hospital to carry out excellent research with strong clinical and translational applications."

Background
In a landmark paper published in Cell in June 2011, Dr Wa and Dr Mckeon identified a novel mechanism for the evolution of highly aggressive cancers in collaboration with BWH and NUS. They discovered that a discrete population of cells at the junction of the esophagus and stomach were linked to precursors of esophageal cancer (Barrett's metaplasia). It was the first time scientists realized that some cancers originate from just a small set of cells that are unique from the other cells that reside around them.

[1] www.singhealth.com.sg/PatientCare/ConditionsAndTreatments/Pages/home.aspx - "Cervical Cancer"

[2] Cervical ablation is the removal of some of the outer layers of the cervix. Gynecologists perform cervical ablation when there is evidence or suspicion of cervical cancer.

[3] This paper can be found in the 24 June, 2011 advance online issue of Cell entitled "Residual Embryonic Cells as Precursors of a Barrett's-Like Metaplasia".

About the 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 improve public health and public prosperity. Established in 2001 as a centre for genomic discovery, the GIS will pursue the integration of technology, genetics and biology towards the goal of individualized medicine. The key research areas at the GIS include Systems Biology, Stem Cell & Developmental Biology, Cancer Biology & Pharmacology, Human Genetics, Infectious Diseases, Genomic Technologies, and Computational & Mathematical Biology. The genomics infrastructure at the GIS is utilized to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact. www.gis.a-star.edu.sg [1]

About the Institute of Medical Biology (IMB)
IMB is one of the Biomedical Sciences Institutes of the Agency for Science, Technology and Research (A*STAR). It was formed in 2007, the 7th and youngest of the BMRC Research Institutes, with a mission to study mechanisms of human disease in order to discover new and effective therapeutic strategies for improved quality of life. From 2011, IMB also hosts the inter-research institute Skin Biology Cluster platform. IMB has 20 research teams of international excellence in stem cells, genetic diseases, cancer and skin and epithelial biology, and works closely with clinical collaborators to target the challenging interface between basic science and clinical medicine. Its growing portfolio of strategic research topics is targeted at 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 [2].

About A*STAR
The Agency for Science, Technology and Research (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 six consortia and centres, 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 universities, hospitals, research centres, and with other local and international partners. For more information about A*STAR, visit www.a-star.edu.sg [3].

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