Researchers uncover population of cells that are targeted by cancer-causing human papillomaviruses

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Virtually all cervical cancers are caused by HPV infections, with just two HPV types, 16 and 18, responsible for about 70 percent of all cases, according to the National Cancer Institute. Scientists have presumed for decades that the cervical cancers that develop from HPV infection arise in a specific location in the cervix.

Now, new research from Brigham and Women's Hospital (BWH) in close collaboration with Harvard Medical School and the Agency for Science Technology and Research in Singapore finds that a specific population of cells that are found only in the region of the cervix called the 'squamo-columnar junction' can become cancerous when infected with HPV while other cells in the cervix apparently do not. This research is published online the week of June 11 in the Proceedings of the National Academy of Sciences (*PNAS*).

"We have discovered a discrete population of cells that are located in a specific area of the cervix that could be responsible for most, if not all, of HPV-associated cervical cancers," said Christopher Crum, MD, director, Women's and Perinatal Pathology at BWH and a senior author on the paper.

Xian Wa, PhD, Assistant Professor of Medicine at the National University of Singapore and Frank McKeon, PhD, Professor of Cell Biology at Harvard Medical School are also senior authors of the *PNAS*

research paper. A prior discovery published in 2011 by the Xian/McKeon group on the origins of cancer in the esophagus set the stage for the current study.

Dr. Crum and Michael Herfs, PhD, a research fellow from the University of Liège and the lead author in the study, collaborated with the Xian/Mckeon laboratory to show that these cells have a unique gene expression that is also found in the cells of aggressive tumors of the cervix. This knowledge could potentially allow clinicians to differentiate benign from potentially dangerous precancerous lesions in the cervix and guide therapy.

Additionally, the investigators noted that when the cells are removed from the cervix, which typically happens when treating precancers, they do not regenerate. They believe this opens up intriguing prospects for cancer prevention.

"The removal of these cells in young women before they are subject to HPV infection or precancerous changes could potentially reduce the risk of cervical cancer, but further research is needed to evaluate the benefits and risks of this potential therapy," said the authors. Additionally, Crum noted that the discovery of these cells could promote more meaningful cell models to further study cervical cancer.

Provided by Brigham and Women's Hospital