

Einstein Cancer Center



Conquering Cervical Cancer

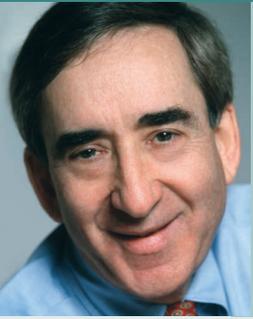
A century ago, cervical cancer was the leading cancer killer of American women, but today it's not even in the top 10. This great progress was due mainly to better prevention, screening and treatment—and Albert Einstein Cancer Center researchers have played active roles in all of these areas.

The Vaccines

Some 13 different types of human papillomavirus (HPV) cause cervical cancer, but just two are responsible for most cases: HPV16 (50 percent of cases) and HPV18 (10 percent). Today, two cervical cancer vaccines—Cervarix and Gardasil—protect against HPV16 and HPV18. How do they compare?

“The College of Medicine was the lead site in a postmarketing clinical trial of these vaccines and found stronger immunity with Cervarix,” says Mark Einstein, M.D., M.S. '05, associate professor of obstetrics & gynecology and women's health. But Gardasil has an added virtue: It not only prevents cervical cancer; it also protects against genital warts by targeting two other viruses, HPV6 and HPV11. His conclusion: Both vaccines work and can spare women from potentially debilitating disease.

MESSAGE FROM THE DIRECTOR



I. DAVID GOLDMAN, M.D.
Director, Albert Einstein
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Astounding breakthroughs have occurred in our understanding of the genetic abnormalities that trigger cancer. Based on those insights, researchers have developed powerful new drugs to target genetic defects in individual cancers. But these agents have had only limited impact in easing cancer's burden. Clearly, the best strategy against cancer is to prevent it!

One preventive-medicine success story is the decline in the incidence of cervical cancer and the deaths it causes. This issue of the newsletter describes the important role the Albert Einstein Cancer Center (AECC) has played in this achievement.

The clear relationship between specific types of human papillomavirus (HPV) and cervical cancer has been established after decades of research. Vaccines to prevent HPV infection have been developed and are widely available. AECC scientists are now studying the vaccines' effectiveness in settings where sexual activity occurs at an early age and where sexually transmitted diseases are prevalent.

HPV infections are relatively common: more than 40 percent of American women ages 14 to 59 are infected. Fortunately, the cervical lesions caused by such infections rarely progress to cervical cancer. AECC scientists are working to distinguish benign lesions from ones destined to become cancerous. Their approach: analyze the molecular characteristics of HPV, and the cervical cells it infects, to identify infections that warrant aggressive—and curative—local treatment.

AECC scientists are applying this research in treating women with HIV/AIDS and HPV infections of the cervix. Their goal is a long life free of cervical cancer for all women infected with HPV.

Conquering Cervical Cancer *(continued from page 1)*

"My daughters will be getting the vaccine when they come of age," says Dr. Einstein, also associate professor of epidemiology & population health and director of clinical research for women's health and gynecologic oncology at Montefiore, the University Hospital and academic medical center for Einstein.

Remaining Challenges

Much work remains to be done if we are to make cervical cancer a disease of the past. Getting more girls vaccinated should be a top priority.

The Centers for Disease Control and Prevention recommends the vaccine for all girls ages 11 and 12. Yet only half of all American girls are getting it, many not early enough. Einstein's Nicolas F. Schlecht, Ph.D., and colleagues detected HPV DNA in 59 percent of cervical samples from 97 sexually active, inner-city adolescent minority women who had not



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been vaccinated, meaning the adolescents had already been exposed and infected. By contrast, in another study that included 327 fully vaccinated adolescents, the number of cervical samples positive for HPV was as much as 80 percent lower, depending on the type of HPV. These studies illustrate the urgency of the need for early vaccination, says Dr. Schlecht.

Tackling the Problem of HIV and HPV

Kathryn Anastos, M.D., studies cervical cancer risk worldwide in women with HIV. In research conducted with Dr. Einstein, Robert D. Burk, M.D., and Howard D. Strickler, M.D., she

found that women infected with HIV—the human immunodeficiency virus, which causes AIDS—are more likely to have high-risk, and multiple types of, HPV infection and cervical precancer. An organization that she co-founded in 2004 in Rwanda, the Women's Equity in Access to Care



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and Treatment for HIV, brings antiretroviral drugs and cervical cancer screening to HIV-positive women.

Dr. Strickler heads HPV research in the Women's Interagency HIV Study (WIHS). This study followed more than 3,000 HIV-infected and 1,000 uninfected women for more than a decade. It is the most comprehensive prospective investigation of the natural history of HPV infection and precancer/cancer development in HIV-positive women. This study has played a major role in defining cancer screening guidelines. Dr. Strickler is also the Harold and Muriel Block Chair in Epidemiology & Population Health and co-leader of the AECC's Cancer Epidemiology Program.

Dr. Einstein is the principal investigator of a National Cancer Institute (NCI)-funded trial being carried out at four large African hospitals. Women with cervical cancer and HIV infection will be treated with a combination of radiation and chemotherapy. And through Dr. Anastos' NCI-funded education grant, African scientists and healthcare professionals come to Einstein for training in various aspects of clinical and epidemiological research.

CANCER Q&A

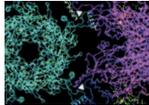
Q: Who should get vaccinated against HPV infection?

A: The vaccines are not just for preventing cervical cancer in girls and women ages 9 through 26. One of the two vaccines, Gardasil, also protects against genital warts and anal cancer in men as well as women, and the U.S. Centers for Disease Control recommends that males be vaccinated with Gardasil at age 11 or 12.

Screening and Treatment

Looking for changes in tumor cells.

So-called epigenetic changes are normal ways by which a cell's gene expression is controlled. The most common epigenetic changes involve molecules called methyl groups that attach to and silence genes. Cancer can develop if methyl groups silence tumor-suppressor genes that help keep cancerous cells in check. Dr. Einstein and his colleagues are studying patients at Montefiore and Jacobi



CERVICAL CANCER BY THE NUMBERS

Projected new U.S. cases in 2013: **12,340**

Projected U.S. deaths: **4,030**

Source: American Cancer Society

Medical Centers who have persistent HPV infection and early precancerous cervical lesions to see if methylation patterns in the cervical cells predict which lesions are likely to develop into cancer.

Looking for changes in viruses.

Dr. Burk and his colleagues examined methylation patterns in the genomes of HPV viral types that cause most cases of cervical cancer. In a 2012 study in the *Journal of the National Cancer Institute*, the researchers reported higher HPV DNA methylation in women with precancerous cervical lesions compared to women with the same HPV type but no detectable precancerous cells. The findings suggest that HPV viral methylation can be useful in identifying which HPV cervical infections may lead to cancer.

Dr. Burk is professor of pediatrics (genetics), of microbiology & immunology, of obstetrics & gynecology and women's health, and of epidemiology & population health. He is also vice chair for translational research in pediatrics at Einstein and attending physician in pediatrics at The Children's Hospital at Montefiore.

How viruses slip under the radar.

Einstein scientists led by Dr. Strickler found that HIV-positive women have a low immune-system response to HPV16, suggesting that the virus has

developed a way to avoid immune-system surveillance. The researchers are looking for genetic and epigenetic (gene-expression) factors that give the virus this "invisibility cloak."

Molecular methods for cervical cancer screening. A new four-year study led by Dr. Strickler and involving Drs. Burk, Einstein and Anastos will examine the use of molecular methods to identify HPV and cellular factors that can improve the accuracy of cervical cancer screening in HIV-positive women. The NCI-supported study follows a 2012 paper published in the *Journal of the American Medical Association* by the team suggesting that HPV DNA testing can help reduce the frequency of Pap testing in HIV-positive women.

HIV, aging and immune status.

Because antiretroviral therapy has been so successful, more HIV-positive women now live to the ages when cervical cancer rates peak. Dr. Strickler recently received an NIH grant to explore:

- how menopause and HIV affect HPV infection and development of early cervical lesions;
- what immune deficits drive the relationship of HIV with cervical cancer and thus can be targeted in prevention and treatment;
- which genes govern the interaction between the immune system and abnormal cervical cells.

A better treatment regimen.

Cisplatin is an effective cancer chemotherapy drug. But if cervical cancer recurs and cisplatin has already been used, only 13 percent of patients respond to the drug. Dr. Einstein and Dennis Y. S. Kuo, M.D., professor of clinical obstetrics & gynecology and women's health, found that the combination of paclitaxel and oxaliplatin—two other anticancer agents—is effective in treating patients with recurrent cervical cancer who have previously been exposed to cisplatin.



ON THE WEB

To learn more about the Albert Einstein Cancer Center, please visit www.einstein.yu.edu/cancer.

Einstein's Early Contributions

"I came to Einstein in 1984 to work on the hepatitis B virus and liver cancer," says Dr. Burk, "but I was intrigued by the emerging evidence that cervical cancer was also caused by a virus."

Dr. Burk and his Einstein colleagues went on to publish numerous papers on HPV. One of their most significant contributions involved the natural history of HPV infection and cervical disease in young women.

"We showed that HPV infections and the abnormal Pap smears that they cause are usually transient," says Dr. Burk. "Standard practice then was surgical removal of these lesions, on the assumption that they'd progress to cervical cancer. We found that 95 percent of these lesions disappear within two years on their own, which really changed the way physicians treat young women with early cervical disease."

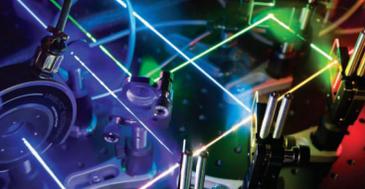
Gloria Ho, Ph.D., joined Einstein's department of epidemiology & population health in 1990 and, with Dr. Burk, published important findings on the transmission of HPV and the viral types that pose the greatest risk of cervical cancer.

Dr. Einstein Honored



Mark H. Einstein, M.D., M.S. '05, right, with Kathy Weinberg, president, National Women's Division, and Willie Geist of NBC's *Today* and MSNBC, Spirit Luncheon emcee.

Dr. Einstein was honored at the 58th annual "Spirit of Achievement" Luncheon, hosted by the New York chapter of Einstein's National Women's Division in May 2012 at the Plaza Hotel. The luncheon benefited the Women's Division's current initiative to support cutting-edge basic and translational research studies at the Albert Einstein Cancer Center targeting breast, ovarian, cervical and uterine cancers. This year's Spirit luncheon, held in April, also supported research on women's cancers.



our supporters

The Albert Einstein Cancer Center gratefully acknowledges the generosity of the following individuals and organizations whose support is critical to advancing its mission.

NOTABLE GIFTS AND GRANTS

Two research teams at Einstein and Montefiore have been awarded special grants from the National Cancer Institute (NCI). The grants, two of only 57 given nationwide and only five in New York City, total more than \$3 million.

The first, a grant of \$1.7 million over five years as part of the NCI's "provocative questions" program, was awarded to Steven K. Libutti, M.D., and Richard N. Kitsis, M.D. Using a model called multiple endocrine neoplasia type 1 (MEN1), the researchers will investigate why certain mutations promote cancer in some tissues of the body but not in others. The preliminary work for this grant was funded by a generous gift from **Linda and Earle Altman**. Dr. Libutti is associate director of clinical services at the Albert

Einstein Cancer Center, director of the Montefiore Einstein Center for Cancer Care, professor of surgery and of genetics at Einstein and vice chair of surgery at Einstein and Montefiore. Dr. Kitsis holds the Dr. Gerald and Myra Dorros Chair in Cardiovascular Disease, and is professor of medicine (cardiology) and of cell biology and director of the Wilf Family Cardiovascular Research Institute at Einstein.

The second team, consisting of Maja H. Oktay, M.D., Ph.D., Sumanta Goswami, Ph.D., and John S. Condeelis, Ph.D., has been awarded \$1.4 million over four years to explore a novel approach to studying metastasis. The scientists will focus on the crucial step in metastasis in which breast cancer cells

invade blood vessels and are then carried to distant sites. This award is the direct result of a pilot study that was funded, in part, by a generous gift from **Jane A. and Myles P. Dempsey**. Dr. Condeelis is leader of the Albert Einstein Cancer Center Tumor Microenvironment and Metastasis Program, the Judith and Burton P. Resnick Chair in Translational Research, professor and co-chair of anatomy and structural biology and co-director of the Gruss Lipper Biophotonics Center; Dr. Oktay is associate professor of pathology; and Dr. Goswami is assistant professor of anatomy and structural biology.

EVENTS: Lunch & Learn



Gloria S. Huang, M.D.; Paul R. Marantz, M.D., M.P.H.; Overseer Marilyn Katz, chair of the AECC's Cancer Research Advisory Board; and Overseer Stanley M. Katz.

Gloria S. Huang, M.D., and Paul R. Marantz, M.D., M.P.H., were the guest speakers at a "Lunch & Learn" program for Einstein supporters and friends in June 2012 at Brae Burn Country Club in Purchase, NY. Dr. Huang is a gynecologic oncologist and a member of the Albert Einstein Cancer Center's

Experimental Therapeutics Program; Dr. Marantz is associate dean for clinical research education, associate director of the Harold and Muriel Block Institute for Clinical and Translational Research at Einstein and Montefiore and director of Einstein's Center for Public Health Sciences. They updated guests on

new approaches to research on the prevention, screening and treatment of gynecologic cancers. Overseers **Marilyn and Stanley M. Katz** generously hosted the event. Overseers **Linda Altman, Rita and Philip Rosen, Roslyn Goldstein** and **Sue-ann Friedman** were among those who attended this most informative program.

To learn more about supporting the work of the AECC, please contact:

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ALBERT EINSTEIN CANCER CENTER

Our mission: to promote and conduct research that will elucidate the origins of cancer and lead to effective new approaches for the prevention, diagnosis and treatment of malignant diseases

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