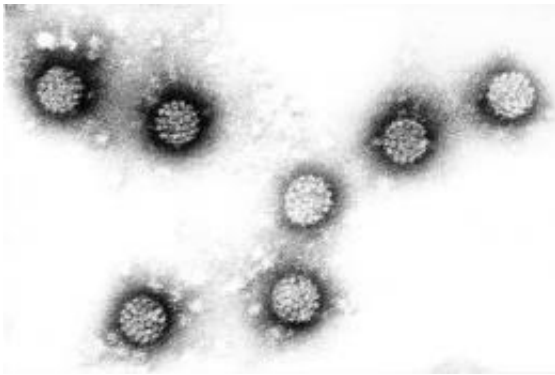


# Papillomavirus silences innate immune response

December 3 2009

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Electron micrograph of human papilloma viruses. Credit: Hanswalter Zentgraf, German Cancer Research Center

In the 1980s, Harald zur Hausen and his co-workers discovered that specific types of human papillomavirus (HPV) cause cervical cancer. Scientists soon found out how these pathogens cause cells to degenerate. It is known today that the main culprits are viral proteins E6 and E7. Both proteins switch off different cellular control functions, thus promoting cell growth.

Professor Dr. Frank Rösl and his co-workers at DKFZ have now discovered another mechanism by which the E6 oncoprotein of high-risk [HPV16](#) promotes carcinogenesis. The oncogene silences production of an immune protein called interferon-kappa. Interferons are proteins which are part of our immune system and are responsible primarily for

stimulating the immune response to viruses and tumors. Interferons are produced by white blood cells and other cell types. Interferon-kappa is relevant for HPV infections, because it is produced mainly in cells of the skin and mucosa (keratinocytes) which are the preferred hosts of the viruses. If interferon-kappa is not working in cells, other proteins involved in immune defense also cease to function properly.

Dr. Bladimiro Rincon-Orozco of Rösl's team has now shown for the first time that HPV16 switches off the interferon-kappa gene by biochemical modification of DNA. Such alterations of the genetic material are called epigenetic mutations. Studying HPV infected cells in a culture dish, the research team observed that interferon-kappa is epigenetically silenced. They were later able to confirm this result in [cervical cancer](#) tissue samples.

"Interferon-kappa is an important part of what is called innate immunity," Frank Rösl explains. Using this evolutionary old defense mechanism, the body can defend itself immediately after being infected with pathogenic agents, while formation of the specific "acquired" immune system may take some time. "By switching off the interferon production, the viruses prevent infected cells from being destroyed by this type of immune response," says Rösl, explaining the strategy of the virus that causes cancer. In the next step, the researchers are planning to investigate whether administering interferon-kappa can slow down the growth of cervical cancer cells and may thus support treatment of the disease.

More information: Bladimiro Rincon-Orozco, Gordana Halec, Simone Rosenberger, Dorothea Muschik, Ingo Nindl, Anastasia Bachmann, Tina Maria Ritter, Bolormaa Dondog, Regina Ly, Franz X. Bosch, Rainer Zawatzky und Frank Rösl: Epigenetic Silencing of Interferon- $\kappa$  in [Human Papillomavirus](#) Type 16-Positive [Cells](#). *Cancer Res* 2009; 69: (22) November 15, 2009

Source: Helmholtz Association of German Research Centres ([news](#) : [web](#)  
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Citation: Papillomavirus silences innate immune response (2009, December 3) retrieved 18 April 2024 from <https://medicalxpress.com/news/2009-12-papillomavirus-silences-innate-immune-response.html>

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