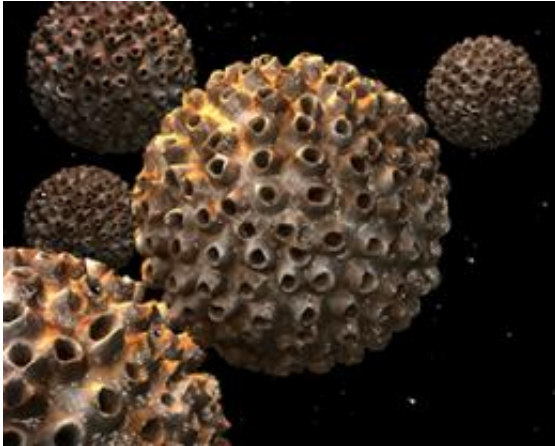


# Virology: A marker for a cancer-causing virus

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A digital representation of the human papillomavirus.  
Credit: iStockphoto/Thinkstock

(Phys.org)—Depending on the strain, or genotype, of the human papillomavirus (HPV) (see image), the lesions it causes can range from relatively benign to cancer-causing. Differentiating between lesions caused by low-risk and high-risk viral genotypes, however, is difficult. Françoise Thierry at the A\*STAR Institute of Medical Biology in Singapore and co-workers have now identified proteins that could be used as reliable, sensitive markers to diagnose infections with high-risk types of HPV.

Commonly known as an inducer of [genital warts](#), HPV is transmitted by sexual contact. Of the approximately 100 HPV genotypes known, a few, including HPV-18, have a high likelihood of leading to cervical or [anal cancer](#). If pre-[cancerous lesions](#) are identified in their early stages, they can usually be removed using simple surgical procedures, with a very good prognosis.

The marker proteins identified by Thierry and colleagues, called E2<sup>E4</sup>, are natural fusions between two known HPV proteins, E2 and E4. When Thierry and her co-workers discovered the

[fusion proteins](#), they were investigating the activity of the HPV-18 E2 protein, using cells engineered to express the E2 protein only. The results were repeatedly 'contaminated' by E4 protein.

Sequencing the HPV-18 E2 gene transcripts revealed the source of the E4 sequences: the gene includes triggers to make the E4 protein and attach it to the E2 protein. The DNA for the E4 gene is embedded within the DNA for the E2 gene, just 'shifted' over by one [DNA base](#)—akin to starting to read the word 'intermittent', and finding the word 'mitten' at the sixth letter. Thus, cells infected with HPV-18 automatically produce E2<sup>E4</sup> along with E2.

Knowing that a protein unique to HPV-18 could be clinically useful, the researchers checked the [DNA sequences](#) of other HPV types and found that they could not produce the fusion protein. "Since E2<sup>E4</sup> transcripts (and proteins) are specific to HPV-18, they could be used to unambiguously detect the presence and expression of this particular HPV genotype in early stage lesions," Thierry explains.

What makes the protein useful as a marker may have even broader clinical implications. Because the proteins are specifically expressed in only a few high-risk HPV types, the researchers suspect they may not only mark but also contribute to these genotypes' virulence. "We would like to find out whether or not they are involved in the oncogenic potential of HPV-18 compared to other high-risk HPV genotypes which do not express E2<sup>E4</sup>," says Thierry.

**More information:** Tan, C. L., Gunaratne, J., Lai, D., Carthagena, L., Wang, Q. et al. HPV-18 E2<sup>E4</sup> chimera: 2 new spliced transcripts and proteins induced by keratinocyte differentiation. *Virology* 429, 47–56 (2012).

[www.sciencedirect.com/science/.../ii/S0042682212001808](http://www.sciencedirect.com/science/.../ii/S0042682212001808)

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