

Research indicates new virus is culprit, not bystander, in deadly skin cancer

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University of Pittsburgh scientists are uncovering more evidence that a virus they recently discovered is the cause of Merkel cell carcinoma, an aggressive and deadly form of skin cancer.

The findings, published in this week's early online edition of the *Proceedings of the National Academy of Sciences*, put to rest the possibility that MCV infects tumors that already have formed. If that were the case, the virus would be a passenger rather than the driver of the disease.

Experiments in human tumors reveal that the cancer develops in two steps: during infection, the Merkel cell polyomavirus, or MCV, integrates into host cell DNA and produces viral proteins that promote cancer formation. Tumors occur when a mutation removes part of a viral protein needed for the virus to reproduce and infect other healthy cells, explained senior investigator, Patrick Moore, M.D., M.P.H, professor of microbiology and molecular genetics at the School of Medicine and director of the Molecular Virology Program at the University of Pittsburgh Cancer Institute. The virus then can spread only as the cancer cells themselves multiply.

Clearly, "MCV infects normal cells before they turn into cancer cells," Dr. Moore noted. "The virus could not have infected a tumor afterwards because it can no longer replicate. It looks very much like MCV is the culprit that causes the disease."

The researchers propose two possible reasons why these mutations develop: If viral replication continues, the immune system could recognize the intruder to eliminate diseased cells, or the viral replication itself will lead to the death of the cancer cells. Both of these possibilities provide promising leads to find better ways to kill Merkel cell cancer cells without harming healthy tissues.

Also, "this research shows evolution within tumors on a molecular level," Dr. Moore pointed out. "You can see the specific molecular steps." The team's current work could account for known risk factors for Merkel cell carcinoma such as UV exposure and ionizing radiation, which damage DNA and can lead to the viral mutations.

Merkel cell cancers are rare, occurring in about 1,500 Americans annually. Half of patients who have advanced disease die within nine months of diagnosis, and two-thirds die within two years. The elderly and people with compromised immune systems are at greater risk of developing the cancer, which arises in skin nerve cells that respond to touch or pressure.

In a paper published in *Science* in January, Dr. Moore and his wife, Dr. Yuan Chang, who co-directs their lab, reported their identification of the virus and that it could be found in 80 percent of Merkel cell tumors. They cautioned that although up to 16 percent of the population carries MCV, very few will develop cancer.

There is no treatment for MCV infection right now, but identifying the agent and understanding how it triggers disease could lead to targeted interventions, Dr. Moore said.

Source: University of Pittsburgh

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