Inner workings of virus responsible for rare skin cancer

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Scientists at the University of Pittsburgh Cancer Institute have begun to uncover how the virus that causes most Merkel cell carcinoma – a rare and aggressive skin cancer – operates, meaning that a rational chemotherapeutic target for this cancer could be developed in the near future.

Patrick Moore, M.D., M.P.H., an American Cancer Society professor in the laboratory of Yuan Chang and Patrick Moore at the University of Pittsburgh Cancer Institute in Pittsburgh, Pa., presented these study results at the Second AACR International Conference on Frontiers in Basic Cancer Research, held here Sept. 14-18, 2011.

Merkel cell carcinoma is a rare and highly aggressive cancer, the incidence of which has increased fourfold during the last 20 years, particularly in immunosuppressed populations, according to Moore.

"Unfortunately, Merkel cell carcinoma is difficult to treat and clinical trials of chemotherapeutics have been disappointing in affecting clinical course and survival," he said. "Discovery of the molecular cause for this cancer provides opportunities to directly target the cellular pathways that are perturbed by the virus."

In 2008, Moore and colleagues discovered Merkel cell polyomavirus (MCV), the virus that causes most Merkel cell carcinoma. Polyoma refers to the ability of some members of this family to produce multiple tumors in animal models. Their laboratory previously discovered the

herpes virus that causes Kaposi's sarcoma, cancer that commonly occurs in patients with AIDS.

"MCV is the first polyomavirus to be consistently associated with human cancer, and is believed to cause 80 percent of Merkel cell carcinoma," Moore said.

MCV is a natural component of the human skin and is usually harmless, according to Moore. In fact, most adults carry the virus in some part of their skin cells. However, if someone becomes immunodeficient and the virus undergoes specific mutations, then it can generate Merkel cell carcinoma.

In the three years since they discovered MCV, this group has also discovered several of the unique characteristics of the virus. Most recently, their studies showed that MCV small T antigen protein is a new oncogene that can contribute to abnormal cell growth in both rodent and human cells. In addition, MCV does not act the same as other polyomaviruses that have served as classic models of cancer. These other polyomaviruses depend on viral interaction with the enzyme PP2A and heat-shock proteins; MCV interacts with them, but does not depend on them.

Moore and colleagues found that MCV could still cause the abnormal cell growth even after abolishing PP2A and heat-shock protein binding sites. The researchers hope to develop treatments that will directly target the cellular pathways affected by this virus.

"We are making headway on this approach now and have tested more than 1,350 drugs to identify better methods to treat this virus-caused cancer," Moore said.

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