Study offers first clinical evidence of anti-cancer drug triggering viral infection

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Important advances in the fight against cancer have come as researchers proved that viruses and cancers interact in ways that were previously unknown to scientists.

A new study led by UNC scientists shows that a common cancer drug can activate a viral infection that, paradoxically, can help anti-viral medications eradicate virus-associated cancer.

The cooperative study, conducted by a team of UNC School of Medicine scientists and the UNC Project in Malawi, demonstrated for the first time in humans that a common drug used to treat Burkitt lymphoma can activate infection by the Epstein-Barr virus (EBV), a virus which typically lies latent inside the tumor cells of affected patients. The finding paves the way for a future study using both a cancer drug and an antiviral agent to eradicate both the active virus infection and the tumor. The findings are reported in the April 1 issue of the journal *Clinical Cancer Research*.

Margaret Gulley, MD, professor of pathology and laboratory medicine, said, "What we have learned from this work is a potential means of capitalizing on presence of viral genomes within tumor cells to alter those tumor cells in a way that makes them more susceptible to treatment. Our findings have implications for other EBV- related malignancies that, overall, are among the most common cancers worldwide." Gulley is a member of UNC Lineberger Comprehensive Cancer Center.

EBV infects more than 90 percent of the world's population and is associated with diseases ranging from infectious mononucleosis to lymphomas, gastric cancer and cancer of the nose and throat.

Burkitt lymphoma, which is associated with EBV, is rare in most parts of the world, but is endemic in sub-Saharan Africa. Burkitt lymphoma is an aggressive, fast-growing type of non-Hodgkin lymphoma that often occurs in children. The disease may affect the jaw, bowel, lymph nodes, or other organs

The study demonstrated that initiating treatment with the anti-cancer drug cyclophosphamide in children with Burkitt lymphoma simultaneously triggered an active EBV infection. The increased replication of EBV in cancer tissue makes these cells more susceptible to the antiviral drugs that kill cells containing replicating virus. Antiviral agents such as ganciclovir and valacyclovir are already in routine clinical use for treating active viral infections.

Researchers enrolled 21 patients with a confirmed diagnosis of EBV-related Burkitt lymphoma. The patients ranged in age from 5-15 and were under treatment with cyclophosphamide for their cancer. Through laboratory analysis of biopsy samples, researchers found that cyclophosphamide seems to induce the phase of viral infection most susceptible to antiviral therapy.

"The next step," explains Gulley," is to design a clinical trial using both cytoxan and an antiviral agent simultaneously." Plans for such a trial are already underway under the leadership of Carol Shores, MD, PhD, associate professor of surgery in UNC's Department of Otolaryngology/Head and Neck Surgery and senior author of the study.

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