Scientists identify cellular communicators for cancer virus

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A new discovery by UNC scientists describes how cells infected by the Epstein-Barr virus (EBV) produce small vesicles or sacs called exosomes, changing their cellular "cargo" of proteins and RNA. This altered exosome enters cells and can change the growth of recipient cells from benign to cancer-producing.

In this way, virus-infected cells can have wide-ranging effects and potentially manipulate other cells throughout the body. The findings are reported in the November 8, 2010 early online edition of the Proceedings of the National Academy of Sciences.

Nancy Raab-Traub, PhD, professor of microbiology and Immunology, said, "Exosomes may be the Trojan Horse through which EBV gains control of cells that are not even infected. Importantly, the production of exosomes may provide a new therapeutic target that can be blocked to reduce cancer growth." Raab-Traub is a Sarah Graham Kenan Professor and member of UNC Lineberger Comprehensive Cancer Center.

Epstein-Barr Virus (EBV) is perhaps the world's most successful virus as almost everyone is infected with it for life. EBV cannot be eliminated by the immune system and is constantly secreted into saliva where it is effectively transmitted. Infection with the virus rarely causes disease; however, EBV is found in several major cancers, including lymphoma and cancer of the nose and throat, where its proteins hijack the cell's growth regulatory mechanisms to induce uncontrolled cell growth characteristic of cancer.

Through exosomes, a protein called latent membrane protein 1, that is considered the EBV oncogene, can be delivered to uninfected cells. Significantly, EBV also changes the entire contents of the exosomes to deliver cellular proteins that are also activated in cancers. This surprising finding reveals that one infected cell can have wide-ranging effects and induce the unchecked growth of neighboring cells.

The immune system is constantly on guard to identify foreign viral proteins. Through exosomal uptake, cancer cells would be stimulated to grow without the expression of proteins that "announce" infection to the immune system, thus allowing unchecked growth. The study also showed that the cells that produce blood vessels, the process called angiogenesis, readily take in the altered exosomes and are potentially induced to grow.

"The next step," explains David Meckes, PhD, postdoctoral fellow in the Raab-Traub lab and first author of the paper, "is to determine how the virus controls which proteins are sorted into exosomes and how this process could be inhibited."

Provided by University of North Carolina School of Medicine

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