New cancer 'vaccine' shows future promise in treating and preventing metastatic cancers

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Preclinical, laboratory studies suggest a novel immunotherapy could potentially work like a vaccine against metastatic cancers, according to scientists at Virginia Commonwealth University Massey Cancer Center. Results from a recent study show the therapy could treat metastatic cancers and be used in combination with current cancer therapies while helping to prevent the development of new metastatic tumors and train specialized immune system cells to guard against cancer relapse.

Recently published in the journal *Cancer Research*, the study detailed the effects of a molecule engineered by lead author Xiang-Yang Wang, Ph.D., on animal and cell models of melanoma, prostate and colon tumors. The molecule called Flagrp-170 consists of two distinct proteins, glucose-regulated protein 170 (Grp170), known as a "molecular chaperone," and a "danger signal" derived from flagellin, a protein commonly found in bacteria. The researchers used modified viruses, or adenoviruses, that can no longer replicate to transport Flagrp-170 directly to the tumor site to achieve localized vaccination. The novel therapy caused a profound immune response that significantly prolonged survival in animal models.

"Successfully promoting antitumor immunity will help eradicate tumor cells, control cancer progression and help prevent tumor relapse," says Wang, Harrison Scholar, member of the Cancer Molecular Genetics research program at VCU Massey Cancer Center and associate professor of Human and Molecular Genetics at VCU School of Medicine. "This immunotherapy has the potential to be used alone or in combination with conventional cancer treatments to develop and establish immune protection against cancer and its metastases."

Grp170 is currently being explored for its potential as a "cancer vaccine" because it has been shown to help the immune system recognize cancer antigens. Antigens are molecules from foreign objects such as bacteria, viruses or cancer that, when detected, provoke an immune response aimed at attacking them. However, because cancer cells can alter the microenvironment surrounding a tumor, they are able to suppress immune responses and continue replicating without being attacked by the body's natural defenses.

The chimeric chaperone Flagrp-170, created by strategically fusing a fragment of flagellin to Grp170, not only enhances antigen presentation, it also stimulates additional immune signals essential for functional activation of specialized immune cells, including dendritic cells, CD8+ T lymphocytes and natural killer (NK) cells. Dendritic cells act as messengers between the innate and adaptive immune systems. Once activated in response to a stimulus such as Flagrp-170, dendritic cells migrate to lymph nodes where they interact with other immune cells such as T lymphocytes to shape the body's immune response. CD8+ T lymphocytes and NK cells are known to respond to tumor formation and kill cancer cells by triggering apoptosis, a form of cell suicide.

"Overcoming cancer's ability to suppress the body's natural immune responses and restore or develop immunity for tumor eradication is the goal of cancer immunotherapy," says Wang. "More experiments are needed, but we are hoping Flagrp-170 may one day be used in formulating more effective therapeutic cancer vaccines."

Moving forward, Wang and his team are working to better understand the molecular mechanisms responsible for Flagrp-170's therapeutic effects. Additional studies are underway to more efficiently

target and deliver Flagrp-170 to tumor sites in order to provoke a more robust and durable immune response.

More information:
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