A Bait-and-Fish Approach to Netting Deadly Brain Tumor Trigger?

Neuroimmunologists ID tiny protein fragments in quest for better glioblastoma detection, treatment in this informative Q&A

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All cells in the human body secrete extracellular vesicles (EVs), tiny membrane-enclosed sacs that deliver important cargo – including RNA, proteins, lipids and DNA – to other cells. Cancer cells, notorious for rapid growth, are prolific EV creators.

Neuroimmunology researchers at the University of Colorado Anschutz Medical Campus studied the EVs from two types of brain cancer – glioblastoma, the deadliest brain tumor, and meningioma, a more common benign central nervous system tumor that has significant recurrence rates. In a recent study published in the International Journal of Molecular Sciences, they identified peptides that bind to specific subpopulations of EVs from glioblastoma tumors.

“Our hypothesis was that those EVs from cancer cells may be important in terms of triggering the cancer’s growth,” said Xiaoli Yu, PhD, an associate research professor in the Department of Neurosurgery at the University of Colorado School of Medicine. She collaborated on the National Institutes of Health-funded study with Michael Graner, PhD, a research professor in neurosurgery and University of Colorado Cancer Center member.

Here, Yu explains the CU Anschutz resources that aided their research as well as the implications their findings have for brain tumor patients.

This interview has been edited and condensed.

Why is this research important?

Glioblastoma, referred to as a grade IV astrocytoma, is the deadliest brain cancer. It’s the type of cancer that claimed the lives, for example, of President Joe Biden’s son Beau and U.S. Sen. John McCain. Once diagnosed, patients often only have months to live. If we can find ways to detect the disease early, as well as delay the tumor growth, it would be significant.

What is a peptide?

A peptide is a small fragment of a protein, the building block of cells. Basically, it's like a little bait. The EV is the fish, and the peptide is the bait. Through our data, we show that we can identify this peptide on the surface of the EV, which can identify those EVs for glioblastoma. Furthermore, we showed that these peptides can inhibit EV-induced neuronal cytotoxicity (loss of neurons).

How did you identify the peptides?

We used phage display peptide libraries, which is a technology used to identify novel targets that may reside on the surfaces of EVs in patients with brain tumors. As far as we know, no other researchers have used this technology – which has been around since the 1980s – to identify surface features of brain tumor EVs. I believe phage display technology could be universally applied to EV research in other fields, such as heart and lung disease as well as other cancers. They all secrete EVs.

So, this is a very first step. We showed there is a specific target we can identify using the phage technology. We think this could potentially lead to a biomarker study as well as potential therapeutic designs.

How are these tumors typically discovered?

Most of the time, these tumors are discovered when patients show symptoms such as headaches or even seizures. We're hopeful we can find a common signature of EVs across a large population of brain tumor patients. Other cancers, such as breast cancer, have biomarkers that can be identified through tests. Hopefully, glioblastoma could have some sort of marker that gives an early indication for the disease. So far, that marker hasn't been detected.

We're always interested in collaborations and looking to expand the use of our brain tumor sample bank to solve the mystery of brain tumors.

You were able to access samples for your study from a tumor bank. Why is this important?

We have the Nervous System Biorepository in the Department of Neurosurgery which provides vital resource for researchers. There are over 1,500 brain tumor samples as well as 50 tumor cell lines in the bank. Also, each tumor sample is paired with blood samples. This is thanks to our department chair, Kevin Lillehei, MD, who had the vision to create the brain tumor bank, which has provided resources for important studies and collaborations.

Do you plan to continue research into EVs and the role they play in brain cancer?

Yes. Healthy people have EVs in their body. And even for cancer patients, not all of their EVs are unhealthy. We've identified unique subpopulations of brain tumor EVs which could be special – a

unique indicator for what will hopefully lead us to an early detection of cancer or prediction of a possible recurrence of tumors.

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