

New alternate cell growth pathway could lead to better treatments for metastatic cancers

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Cancer cell during cell division. Credit: National Institutes of Health

While researchers have a basic understanding of how primary cancer cells grow, less is known about metastasis, the deadly process by which cancers spread. A team led by Dr. Paul Krebsbach, dean of UCLA's

School of Dentistry and professor of periodontics, has found that mEAK-7, a gene they discovered last year, may play a significant role in cancer metastasis, at least in lung cancers.

Building on that earlier gene discovery in [human cells](#), the team compared mEAK-7 expression levels in normal and [cancer cells](#) using tumor cell genetic information from several databases as well as tissue samples from [cancer patients](#).

"By focusing on non-[small cell lung cancer](#), we found that mEAK-7, which is important for cell proliferation and migration, was highly expressed in metastatic non-small cell lung cancer," said Dr. Joe Nguyen, first author and postdoctoral scholar at the National Cancer Institute. "We also discovered that mEAK-7 was expressed in primary cancer cells but not expressed in non-cancerous cells, which shows that the protein could be a key culprit in [cancer metastasis](#)."

The research was published in the journal *iScience*.

The researchers also found that mEAK-7, when combined with a large molecule called DNA-PKcs (which helps regulate DNA repair and controls or enhances cancer growth), created an alternative mTOR signaling pathway used by cancer cells for their growth and proliferation. In [normal cells](#), two well-studied pathways are controlled by a gene called mTOR, which regulates normal cell growth, proliferation and survival.

"This third complex or pathway is very important for cancer stem cells, which begin the process of colony formation and [cell proliferation](#), and lead to metastasis that is the leading cause of death in most cancers," Krebsbach said. "We determined that there are high mEAK-7 protein levels in the tumors and lymph nodes of metastatic cancer patients. Development of mEAK-7 inhibitors may benefit patients with metastatic

cancers that demonstrate aberrant mTOR signaling associated with high levels of mEAK-7."

The researchers, who also looked at these signaling molecules in cancer stem cells, determined that the novel, "third" mTOR complex in cancer cells was made up of mTOR, mEAK-7 and DNA-PKcs.

"Understanding the molecular interactions of metastatic cancer is crucial to determining treatments for cancer at these later stages," said Jin Koo Kim, co-author and a UCLA Dentistry project scientist. "Currently, treatments for solid tumors include surgery and radiation therapies. However, many patients relapse, as the target tumors develop resistance to radiation and other treatments. This study found that this resistance is correlated to higher mEAK-7 expression in cancer cells."

More information: Joe Truong Nguyen et al. mEAK-7 Forms an Alternative mTOR Complex with DNA-PKcs in Human Cancer, *iScience* (2019). [DOI: 10.1016/j.isci.2019.06.029](https://doi.org/10.1016/j.isci.2019.06.029)

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