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Dental researcher finds switch that turns on the spread of cancer

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Reporting in *Nature Cell Biology,* researchers describe the discovery of a specific protein called disabled-2 (Dab2) that switches on the process that releases cancer cells from the original tumor and allows the cells to spread and develop into new tumors in other parts of the body.

The process called epithelial-mesenchymal transdifferientiation (EMT) has been known to play a role in releasing cells (epithelial cells) on the surface of the solid tumor and transforming them into transient mesenchymal cell: cells with the ability to start to grow a new tumor.

This is often the fatal process in breast, ovarian, pancreatic and colon-rectal cancers.

Searching to understand how the EMT process begins, Ge Jin, who has joint appointments at the Case Western Reserve University School of Dental Medicine and the Lerner Research Institute at the Cleveland Clinic, began by working backwards from EMT to find its trigger.

The researchers found that a compound called transforming growth factor-ß (TGF-ß) triggers the formation of the Dab2 protein. It was this protein, Dab2, that activated the EMT process.

He discovered that when the researchers knocked out Dab2, EMT was not triggered.

"This is the major piece in cancer research that has been missing," Jin

said.

Most tumors are epithelial in origin and have epithelial markers on their surface. The EMT process takes place when some of those cells dislodge from the surface and undergo a transformation into a fibrous mesenchymal cell maker with the ability to migrate.

"EMT is the most important step in this process," said Jin. He was part of a six-member research team, led by Philip Howe from the Department of Cancer Biology at the Lerner Research Institute in a National Cancer Institute-funded study.

The research group studied the biological processes that initiated the cancer spread by using cancer cells in animal models.

"It's a complicated cascade process," Jin said.

"If we can understand the signaling pathway for modulating EMT, then we can design drugs to delay or halt EMT cells and control tumor progression," Jin said.

Beyond cancer, Jin said. "The process we discovered may lead to understanding how other diseases progress."

More information: TGF-ß-mediated phosphorylation of hnRNP E1 induces EMT via transcript-selective translational induction of Dab2 and ILEI, Arindam Chaudhury and George S. Hussey, *Nature Cell Biology.*

Provided by Case Western Reserve University