Metabolite that promotes cancer cell transformation and colorectal cancer spread identified
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Osaka University researchers revealed that the metabolite D-2-hydroxyglutarate (D-2HG) promotes epithelial–mesenchymal transition of colorectal cancer cells, leading them to develop features of lower adherence to neighboring cells, increased invasiveness, and greater likelihood of metastatic spread. The finding highlights the value of targeting D-2HG to establish new therapeutic approaches against colorectal cancer.

A metabolite is found to make the colorectal cancer cells more invasive and increase likelihood of more tumors spreading to distant organs; this makes the metabolite a promising target for future cancer therapies.

Osaka, Japan – Cancer cells exhibit a range of properties that diverge from those of their normal healthy counterparts, including levels of various metabolites. However, it has been difficult to determine whether such altered levels is a cause or a consequence of the cancerous growth.

In a breakthrough that offers hope for improved treatment of colorectal cancer, Osaka University researchers have identified a metabolite that causes cancer cells to develop more dangerous properties and increases the likelihood that cancer will spread in colorectal cancer patients.

The team examined different varieties of cancer cells and cells from normal tissues and revealed high levels of D-2-hydroxyglutarate (D-2HG) in colorectal cancer cells. They then administered either D-2HG into cancer cells and found it induced the cells to undergo transformation. This transformation involved the cells adhering less strongly to each other and migrating more easily. These properties in the body are associated with cancer progression and spread.

"When we grew the cells with D-2HG on plates and measured their movement, they migrated further than untreated cells," lead author Hugh Colvin says. "Using a Matrigel assay that models the ability of cancer cells to enter local tissue, the D-2HG treated cells were also more invasive."

The researchers showed that D-2HG acts by increasing the expression of a gene called ZEB1, which promotes this cell transformation. They also obtained specimens from 28 human colorectal cancer patients and divided them into two groups with low or high levels of D-2HG. The patients' records showed that the high group had more often suffered cancer spread to distant organs, which suggested the importance of D-2HG in patient prognosis.
"When cancer cells initially emerge, it can be difficult for them to survive and multiply because of the local conditions," coauthor Hideshi Ishii says. "D-2HG makes cancer cell survival more likely by causing them to transform from epithelial to mesenchymal cells, meaning that they can invade local tissue, enter the blood, and be transported elsewhere to establish a new tumor."

With the importance of this molecule in cancer progression and prognosis revealed, it can be focused on as a promising target for colorectal cancer treatments.


Provided by Osaka University

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