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Researchers find promising therapeutic target for deadliest brain cancer

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(Medical Xpress)—A multicenter team of researchers has identified an enzyme key to the survival and spread of glioblastoma cancer cells that is not present in healthy brain cells, making the enzyme a promising therapeutic target.

"With this enzyme, we may have found a way to make sure that these cancer cells that are very invasive do not become as aggressive," says Alfredo Quinones-Hinojosa, M.D., professor of neurological surgery and oncology at the Johns Hopkins University School of Medicine. Glioblastoma is considered the most devastating human cancer, with median survival at only 14 months after diagnosis. "Our latest findings provide an inroad to possibly stopping cancer cells from having enough energy to grow."

These findings are described in the November issue of *Molecular Cancer Research*.

Previous research had shown that the enzyme, glucose-6-phosphatase (G6PC), is present in cells from other cancers, enabling them to use glucose at a rate up to 200 times higher than normal, healthy cells. In searching the literature, however, the team found nothing to suggest that G6PC was present in glioblastoma. Quinones-Hinojosa was certain it was in his patients' tumors, however, so the team set out to study glioblastoma cells from patients.

"Essentially all cells, including cancer cells, need energy to grow and

spread," says Sara Abbadi, Ph.D, a research fellow on the team. And cancer cells have the ability to survive in situations where normal, healthy cells cannot, which has been an important factor for why glioblastoma is so difficult to treat, says Abbadi.

By inhibiting G6PC production, the team found that the cancer was less viable, including less able to move. The team also challenged glioblastoma cells—some with G6PC production inhibited, some not—with the glucose analog 2-deoxy-D-glucose (2DG), which previously had been shown to transform glioblastoma cells into a less malignant form, making them sensitive to other treatments. With G6PC expression unchecked, some of the glioblastoma cells could recover their malignancy after being challenged with 2DG and, in the lab, could move even faster than they had before. Dual treatment with 2DG and blocking G6PC expression, however, not only prevented those cells from recovering their malignancy but also killed them.

"Part of the problem in treating cancer is that it's going to be virtually impossible to find one magic bullet," says Quinones-Hinojosa, "but at least we're beginning to dismantle the different mechanisms that these cells use."

The next step in turning this discovery into a treatment is to find a pharmaceutical method to inhibit G6PC expression in the brain. G6PC is naturally produced elsewhere in the body—including in the liver, kidney and pancreas—so while further studies are underway, any human trials are still years away. Because G6PC expression is shared by many cancers, however, the team's discovery "is worth exploring in other cancers," the authors write in their paper.

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