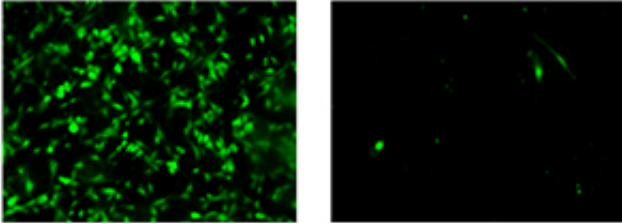


Team discovers mechanism responsible for tumor invasion in brain cancer

9 April 2015



Invasion assays using Glioblastoma (GBM) cells on the left lacking Id4, in comparison to the same cells being genetically engineered to express Id4 on the right. Every invaded cell in this assay is colored green and the assay showed that the cells on the left, lacking Id4, invaded much more than the cells on the right in which there was forced expression of Id4.

A neuro-oncology research team at Dartmouth's Norris Cotton Cancer Center, led by the Director Mark A. Israel, MD with first author Gilbert J. Rahme, PhD, recently identified the transcription factor Id4 as a suppressor of tumor cell invasion in glioblastoma. Their paper, "Id4 suppresses MMP2-mediated invasion of glioblastoma-derived cells by direct inactivation of Twist1 function," was recently published in *Oncogene*. A key finding was the mechanism by which Id4 silences matrix metalloproteinase 2 (MMP2), determined to be inhibition of the protein Twist1 that is required for MMP2 expression.

"This finding suggests a novel therapeutic target to decrease invasion of [tumor cells](#) in patients and may also provide a novel biomarker that could help predict survival of patients with glioblastoma," explained Israel.

Glioblastoma is the most lethal form of [primary brain tumor](#) and leads to death in patients by invading the brain tissue in a process that allows single cells to move through normal brain tissue,

which makes complete surgical removal of the tumor impossible. Israel and his team sought to understand the mechanisms that drive tumor invasion of normal tissue in glioblastoma.

Using data from The Cancer Genome Atlas (TCGA), the Dartmouth team demonstrated that Id4 expression correlates with survival of glioblastoma patients and inversely correlates with MMP2 expression. The data suggests that the upregulation of MMP2 resulting from decreased Id4 expression in [glioblastoma](#) multiforme (GBM) may contribute to the morbidity and mortality of GBM patients.

This study used Dartmouth's Shared Resources including Microscopy and Molecular Biology. "Using the core facilities greatly facilitated the conduct of the work saving time and reducing cost," Rahme said. All 14 of Dartmouth's Shared Resources are available to outside investigators by arrangement.

"Conventional drugs targeting the enzymes encoded by MMP genes have not been successful in the clinic due to adverse side effects," said Rahme. "We believe that proteins in the pathway that controls the expression of MMP2 are likely to be better therapeutic targets. Targeting Twist1 might silence MMP2 and decrease tumor invasion, which will help patients with GBM. Furthermore, the [expression](#) of Id4 may serve as a tumor biomarker that can predict the degree of tumor infiltration."

Looking forward, the therapeutic targets revealed in this study to be actors in tumor invasion need to be further characterized as drug targets and, if possible, therapeutically inhibited. Their pursuit of Id4 as a biomarker for [patients](#) with GBM continues in hopes of making useful predictions of [tumor invasion](#) and survival.

Provided by Dartmouth-Hitchcock Norris Cotton Cancer Center

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