

CD97 gene expression and function correlate with WT1 protein expression and glioma invasiveness

February 7 2012

Researchers at Virginia Commonwealth University Medical Center's VCU Massey Cancer Center and Harold F. Young Neurosurgical Center (Richmond, VA) and Old Dominion University (Norfolk, VA) have discovered that suppression of Wilms tumor 1 protein (WT1) results in downregulation of CD97 gene expression in three glioblastoma cell lines and reduces the characteristic invasiveness exhibited by glial tumor cells. This finding is announced in the article, "Novel report of expression and function of CD97 in malignant gliomas: correlation with Wilms tumor 1 expression and glioma cell invasiveness," by Archana Chidambaram, Ph.D., and colleagues, published online ahead of print today in the [Journal of Neurosurgery](#). Although further studies must be performed, the authors propose that CD97 may prove to be a new target for anti-glioma therapies.

According to William C. Broaddus, M.D., Ph.D., neurosurgeon and leader of the research team, "the invasive behavior of glioma [cells](#) is a key feature of their malignancy in the first place, and more recently there is evidence that treatment of gliomas with anti-angiogenic approaches such as bevacizumab ([Avastin](#)) may stimulate the invasive behavior of some gliomas. This may even serve as the mechanism by which these tumors fail to respond to [bevacizumab](#) treatment. That means that treatments to attack the invasiveness of gliomas by attacking CD97 expression may have special promise as a new [treatment strategy](#)."

WT1 is a transcription factor involved in the normal development of several tissue types. Usually expression of this protein is switched off when tissue reaches the normal adult stage. However, WT1 expression has been identified in numerous malignant diseases—leukemia, lung and breast cancers, sarcomas, reproductive organ tumors, and gliomas to name a few. In fact, the same team of researchers previously documented WT1 expression in 80% of glioma cells and tumor specimens. Because WT1 expression in tumor cells has been shown to play a role in resistance to radiation and chemotherapy as well as promotion of cell proliferation, invasion, and/or angiogenesis, Dr. Broaddus brought together the team to investigate what genes present in malignant gliomas could be mediated by WT1 to confer the virulence displayed by this particular tumor. According to the authors, "given its structural identity...and functional history, it seemed logical that WT1 might regulate the transcription (or posttranscriptional expression) of other genes."

To this end, the research team set out to silence WT1 [gene expression](#) in malignant glioma cells and observe the effects of this silencing on other genes in these cells. The researchers did this by using short interfering RNA (siRNA) directed against WT1 in three glioblastoma [cell lines](#): U251-MG, U1242-MG, and GBM-6.

Application of siRNA consistently suppressed WT1 gene expression levels, which in turn produced a significant reduction in cellular invasiveness. A microarray analysis identified other genes that were affected by WT1 silencing. These included 27 genes that were significantly downregulated and 11 that were significantly upregulated. The authors point out that nine of the 27 downregulated genes have putative or established roles in oncogenesis, and seven of the 11 upregulated genes have putative or established roles in tumor suppression. All but one gene demonstrating dysregulation during WT1 silencing have at least one potential binding site for WT1 in their

promoter regions; the other gene (PDGF-D) has binding sites for Egr1, which recognizes and binds consensus binding sequences shared by WT1.

Prior to this study, there were no reports of CD97 overexpression in glioma cells. It was therefore surprising to the research team that the CD97 gene consistently displayed a direct correlation with WT1 in all three glioblastoma cell lines. Given CD97's putative role in aiding cell invasiveness and neoangiogenesis in other non-brain tumors, the decision was made to examine this cell-surface receptor specifically.

CD97 belongs to the adhesion G-protein-coupled receptor family. Western blot analysis demonstrated overexpression of CD97 protein in the three cell lines. Quantitative reverse transcriptase-polymerase chain reaction showed a six- to 21-fold increase in CD97 expression in the tumor cells over that found in normal human astrocytes, which displayed minimal CD97 expression. After siRNA transfection methods were applied to silence the CD97 gene, CD97 mRNA levels lowered significantly: approximately 50% in U251-MG cells, nearly 80% in GBM-6 cells, and 20% in U1242-MG cells. To examine whether these results would impact the glioblastoma cells' invasive capabilities, the researchers plated cells on Matrigel-coated filters of Transwell plates to see whether the cells would invade the Matrigel. In each cell type the cellular invasiveness potential decreased: to 54% of control ([tumor cells](#)) in U251-MG cells, approximately 50% of control in GBM-6 cells, and 26% of control in U1242-MG cells.

Perhaps the greatest challenge faced in treating malignant gliomas is their strong invasive capacity. The authors believe their data indicate that upregulation of CD97 mediated by WT1 possibly promotes this invasiveness. The findings of this study show a definite relationship between CD97 overexpression and the invasive quality of malignant glioma cells, which is correlated to the relationship between WT1

expression and the invasive characteristic of glioma cells—relationships that in the future may be exploited in a therapeutic setting.

More information: Chidambaram A, Fillmore HL, Van Meter TE, Dumur CI, Broaddus WC. Novel report of expression and function of CD97 in malignant gliomas: correlation with Wilms tumor 1 expression and glioma cell invasiveness. Laboratory investigation. *Journal of Neurosurgery*, published ahead of print February 7, 2012; [DOI: 10.3171/2011.11.JNS111455](https://doi.org/10.3171/2011.11.JNS111455)

Provided by Journal of Neurosurgery

Citation: CD97 gene expression and function correlate with WT1 protein expression and glioma invasiveness (2012, February 7) retrieved 25 April 2024 from <https://medicalxpress.com/news/2012-02-cd97-gene-function-wt1-protein.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--