Comments on Plasmalemmal Vesicle Associated Protein-1 as a Novel Marker Implicated in Brain Tumor Angiogenesis

To the Editor: We have read with great interest the November 1, 2005 article by Carson-Walter et al. (1) on plasmalemmal vesicle–associated protein 1 (PV-1; also called PLVAP) expression in malignant brain. The authors have shown that PLVAP is expressed in a subset of malignant and diseased brain tissue, is up-regulated by vascular endothelial growth factor (VEGF) and hepatocyte growth factor, and is required for tube formation and cell migration in an in vitro model. From these data, they conclude that PLVAP could be a suitable target for central nervous system–specific antiangiogenic therapy to treat brain malignancies and edema. The authors state that intratumoral administration would allow for site-specific delivery of the therapy, whereas the presence of the blood-brain barrier would prevent a systemic antiangiogenic threat.

We would like to add our own observations to this report. In an article published earlier this year (2), we present both a comprehensive study on the association between VEGF stimulation and an increase in PLVAP expression and a survey of PLVAP RNA and protein expression in normal and neoplastic human tissues. Specifically, we show the VEGF-dependent increase in PLVAP in human umbilical vein endothelial cells using VEGF inhibitory antibodies, receptor-selective engineered forms of VEGF, and inhibitors of downstream signaling pathways. We also compare the stimulatory ability of VEGF, in terms of PLVAP expression, to other mitogens including hepatocyte growth factor, basic fibroblast growth factor, and platelet-derived growth factor. Further, in our survey of PLVAP expression in benign and malignant human tissues, we show expression of PLVAP RNA and protein in vasculature associated with lymphoid malignancies and carcinomas of the pancreas, colon, liver, lung, kidney, ovary, prostate, breast, and skin. Expression of PLVAP in vasculature of brain neoplasms is not a site-specific phenomenon. Moreover, PLVAP expression in vasculature of numerous essential normal tissues is also shown. For example, we found uniform expression of PLVAP in small capillary vessels of the normal mucosa throughout the gastrointestinal tract.

Based on these findings, we would like to express our concern about the putative utility of PLVAP as an antiangiogenic target for central nervous system–specific malignancies. Carson-Walter et al. (1) show that PLVAP expression in central nervous system is confined to irregularities associated with disruptions in the blood-brain barrier. Therefore, it is possible that despite site-specific delivery of the therapy, the blood-brain barrier could be breached, resulting in exposure of the systemic vasculature to the antiangiogenic agent. Systemic expression of PLVAP in the vasculature of both vital and nonvital organs should preclude the use of this protein as an antiangiogenic therapeutic target in the clinic.

References
# Clinical Cancer Research

## Comments on Plasmalemmal Vesicle Associated Protein-1 as a Novel Marker Implicated in Brain Tumor Angiogenesis

Laura A. Sanders (Strickland) and Hartmut Koeppen


**Updated version**
Access the most recent version of this article at:
[http://clincancerres.aacrjournals.org/content/12/8/2649.1](http://clincancerres.aacrjournals.org/content/12/8/2649.1)

**Cited articles**
This article cites 2 articles, 1 of which you can access for free at:
[http://clincancerres.aacrjournals.org/content/12/8/2649.1.full.html#ref-list-1](http://clincancerres.aacrjournals.org/content/12/8/2649.1.full.html#ref-list-1)

**E-mail alerts**
Sign up to receive free email-alerts related to this article or journal.

**Reprints and Subscriptions**
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

**Permissions**
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.