

Brain

- [Oxford Journals](#)
- [Medicine](#)
- [Brain](#)
- [Brain Advance Access](#)
- [10.1093/brain/awn182](https://doi.org/10.1093/brain/awn182)

Brain Advance Access published online on August 9, 2008

Brain, doi:10.1093/brain/awn182

© The Author (2008). Published by Oxford University Press on behalf of the Guarantors of Brain. All rights reserved. For Permissions, please email: journals.permissions@oxfordjournals.org

VEGF-dependent induction of CD62E on endothelial cells mediates glioma tropism of adult haematopoietic progenitor cells

Ghazaleh Tabatabai¹, Caroline Herrmann¹, Gabriele von Kürthy¹, Michel Mittelbronn^{2,3}, Stefan Grau⁴, Brigitte Frank¹, Robert Möhle⁵, Michael Weller^{1,6} and Wolfgang Wick^{1,7}

¹Department of General Neurology, Laboratory of Molecular Neurooncology, Hertie Institute for Clinical Brain Research, ²Institute of Brain Research, University of Tübingen, Tübingen, Germany, ³Institute of Neuropathology, University of Zurich, Switzerland, ⁴Department of Neurosurgery, Klinikum Großhadern, Ludwig-Maximilians University of Munich, Munich, ⁵Department of Internal Medicine II (Hematology), University of Tübingen, Tübingen, Germany, ⁶Department of Neurology, University of Zurich, Switzerland and ⁷Clinical Cooperation Unit Neurooncology, German Cancer Research Center, Heidelberg, Germany

Correspondence to: Ghazaleh Tabatabai, MD, Department of General Neurology, Laboratory of Molecular Neurooncology, Hertie Institute for Clinical Brain Research, University of Tübingen, Hoppe-Seyler-Strasse 3, 72076 Tübingen, Germany E-mail: ghazaleh.tabatabai@uni-tuebingen.de

Haematopoietic progenitor cells (HPC) are attracted by experimental gliomas *in vivo*. This attraction is further enhanced by irradiation or hypoxic preconditioning of the glioma cells. Adhesive interactions might be critical to the preferential accumulation of HPC within the glioma tissue. Here, we studied the interactions of HPC with endothelial cells. Exposure of human cerebral endothelial cells (SV-HCEC), human microvascular endothelial cells (HMEC) and brain tumour endothelial cells derived from human glioblastomas (BTEC) to supernatants of glioma cells and primary glioma cells (SN-G) induced the expression of E-selectin (CD62E). CD62E expression was further enhanced when the glioma cells had been exposed to irradiation or hypoxia prior to the collection of

This Article

- ▶ [Full Text](#)
- ▶ [Full Text \(PDF\)](#)
- ▶ [Alert me when this article is cited](#)
- ▶ [Alert me if a correction is posted](#)

Services

- ▶ [Email this article to a friend](#)
- ▶ [Similar articles in this journal](#)
- ▶ [Similar articles in PubMed](#)
- ▶ [Alert me to new issues of the journal](#)
- ▶ [Add to My Personal Archive](#)
- ▶ [Download to citation manager](#)
- ▶ [Request Permissions](#)
- ▶ [Disclaimer](#)

Google Scholar

- ▶ [Articles by Tabatabai, G.](#)
- ▶ [Articles by Wick, W.](#)

PubMed

- ▶ [PubMed Citation](#)
- ▶ [Articles by Tabatabai, G.](#)
- ▶ [Articles by Wick, W.](#)

Social Bookmarking



[What's this?](#)

supernatants, as well as by irradiation or exposure to hypoxia of the endothelial cells. Vascular cell adhesion molecule 1 (VCAM-1) was constitutively expressed on SV-HCEC, HMEC and BTEC, but was not modulated by SN-G, irradiation or hypoxia. Transendothelial HPC migration was enhanced after CD62E induction *in vitro*. Neutralizing antibodies to CD62E strongly reduced the homing of $\text{lin}^{-}\text{Sca-1}^{+}\text{c-kit}^{+}$ cells to orthotopic SMA-560 gliomas *in vivo*. Tissue microarray sampling normal brain tissue and astrocytomas of WHO grades II–IV revealed a selective expression of CD62E on endothelial cells of tumour vessels. SN-G-induced CD62E expression on endothelial cells *in vitro* required transforming growth factor (TGF)- β signalling in glioma cells and vascular endothelial growth factor (VEGF)/VEGF receptor 2 (VEGF-R2) signalling in endothelial cells. Further, we observed a nuclear factor kappa B-dependent activation of the CD62E promoter peaking at 12 h after VEGF-R2 activation by glioma-derived VEGF. Taken together, we identify glioma cell-induced CD62E expression on endothelial cells as one mediator of the glioma tropism of HPC.

Key Words: brain tumour; haematopoietic progenitor cells; hypoxia; irradiation; vascular endothelial growth factor, CD62E

Abbreviations: BTEC, brain tumour endothelial cells isolated from human glioblastoma tissue; CD, cluster of differentiation; CD62E, E-selectin; CD62P, platelet selectin; CXCL12, CXC chemokine ligand 12; DAPI, 4',6-diamidino-2-phenylindole; ELISA, Enzyme-linked immunosorbent assay; FCS, foetal calf serum; G-CSF, granulocyte colony stimulating factor; HIF, hypoxia-inducible factor; HMEC, human microvascular endothelial cells; HPC, haematopoietic progenitor and stem cells; IL, interleukin; LSK, $\text{lin}^{-}\text{Sca-1}^{+}\text{c-kit}^{+}$; NF κ B, nuclear factor kappa B; NT, no treatment; pVEGF-R2, phosphorylated VEGF-R2; sKitL, soluble Kit ligand; sCD62E, soluble E-selectin; SCF, stem cell factor; SDF, stromal cell-derived factor; SN-G, supernatant of glioma cell lines LNT-229, LN-308 and primary glioma cultures T113, T132, T159; SN-Gp, supernatant of LNT-229 puro cells; SN-GpSD-208, supernatant of SD-208-treated LNT-229 puro cells; SN-G-siTGF- β , supernatant of LNT-229 siTGF- $\beta_{1,2}$ cells stably expressing shRNAs targeting TGF- β_1 and TGF- β_2 ; SN-FHAS, supernatant of SV-FHAS cells; SN-GRT, supernatant of irradiated glioma cells; SN-GHO, supernatant of hypoxic glioma cells; SFM, serum-free medium; SFI, specific fluorescence index; SV-HCEC, human cerebral endothelial cells; SV-FHAS, human astrocytic cell line; TGF- β , transforming growth factor- β ; TNF- α , tumour necrosis factor- α ; VCAM, vascular cell adhesion molecule; VEGF, vascular endothelial growth factor; VEGF-R, VEGF receptor

Received December 18, 2007. Revised July 11, 2008. Accepted July 17, 2008.

 CiteULike  Connotea  Del.icio.us [What's this?](#)

Disclaimer:

Please note that abstracts for content published before 1996 were created through digital scanning and may therefore not exactly replicate the text of the original print issues. All efforts have been made to ensure accuracy, but the Publisher will not be held responsible for any remaining inaccuracies. If you require any further clarification, please contact our [Customer Services Department](#).

Online ISSN 1460-2156 - Print ISSN 0006-8950

[Copyright © 2007](#) Guarantors of Brain

Oxford Journals *Oxford University Press*

- [Site Map](#)
- [Privacy Policy](#)
- [Frequently Asked Questions](#)

Other Oxford University Press sites:

