Oxidative response gene polymorphisms and risk of adult brain tumors  -- Rajaraman ...

Preetha Rajaraman 1*, Amy Hutchinson 2, Nathaniel Rothman 1, Peter M. Black 3, Howard A. Fine 4, Jay S. Loeffler 5, Robert G. Selker 6, William R. Shapiro 7, Martha S. Linet 1, Peter D. Inskip 1

1 Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, MD, USA
2 Core Genotyping Facility, Division of Cancer Epidemiology and Genetics, Advanced Technology Program, SAIC Frederick, Inc., National Cancer Institute, Frederick, MD, USA
3 Department of Neurosurgery, Brigham and Women’s Hospital, Boston, MA, USA
4 Division of Neuro-oncology Branch, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, MD, USA
5 Department of Radiation Oncology, Massachusetts General Hospital Cancer Center, Boston, MA, USA
6 Division of Neurosurgery, Western Pennsylvania Hospital, Pittsburgh, PA, USA
7 Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, AZ, USA

* To whom correspondence should be addressed. E-mail: rajarama@mail.nih.gov

Abstract

Oxidative stress is believed to play a key role in tumor formation. Although this mechanism could be especially pertinent for brain tumors given the high oxygen consumption of the brain, very little has been published regarding brain tumor risk with respect to genes mediating oxidative stress. Using data from non-Hispanic whites in a hospital-based case-control study conducted by the National Cancer Institute between 1994 and 1998, we
evaluated risk of glioma ($n = 362$), meningioma ($n = 134$), and acoustic neuroma ($n = 69$) compared to noncancer controls ($n = 494$) with respect to nine single nucleotide polymorphisms from seven genes involved in oxidative stress response (\textit{CAT}, \textit{GPX1}, \textit{NOS3}, \textit{PON1}, \textit{SOD1}, \textit{SOD2}, and \textit{SOD3}). We observed increased risk of glioma (odds ratio [OR]$_{CT/CC} = 1.3$; 95% confidence interval [95% CI], 1.0-1.7) and meningioma (OR$_{CT/CC} = 1.7$; 95% CI, 1.1-2.7) with the C variant of SOD3 rs699473. There was also indication of increased acoustic neuroma risk with the SOD2 rs4880 Ala variant (OR$_{CT/CC} = 2.0$; 95% CI, 1.0-4.2) and decreased acoustic neuroma risk with the CAT rs1001179 T allele variant (OR$_{CT/TT} = 0.6$; 95% CI, 0.3-1.0). These relationships persisted when major groups of disease controls were excluded from the analysis. Our results suggest that common variants in the SOD2, SOD3, and CAT genes may influence brain tumor risk.

**Key Words:** acoustic neuroma, brain, case-control, glioma, meningioma, neoplasm, oxidative response, polymorphism, tumor