Hypertrophy of Cerebral Arterioles in Mice Deficient in Expression of the Gene for CuZn Superoxide Dismutase

Gary L. Baumbach, MD; Sean P. Didion, PhD; Frank M. Faraci, PhD

**Background and Purpose**—Reactive oxygen species are believed to be an important determinant of vascular growth. We examined effects of genetic deficiency of copper-zinc superoxide dismutase (CuZnSOD; SOD1) on structure and function of cerebral arterioles.

**Methods**—Systemic arterial pressure (SAP) and cross-sectional area of the vessel wall (CSA) and superoxide (O2–) levels (relative fluorescence of ethidium [ETH]) were examined in maximally dilated cerebral arterioles in mice with targeted disruption of one (+/−) or both (−/−) genes encoding CuZnSOD. Wild-type littermates served as controls. Vasodilator responses were tested in separate groups of mice.

**Results**—CSA and ETH were significantly increased (P<0.05) in both CuZnSOD+/− and CuZnSOD−/− mice (CSA = 435±24 and 541±48 μm²; ETH = 18±1 and 34±2%) compared with wild-type mice (CSA = 327±28 μm²; ETH = 6%). Furthermore, the increases in CSA and ETH relative to wild-type mice were significantly greater (P<0.05) in CuZnSOD−/− mice than in CuZnSOD+/− mice (CSA = 108 versus 214 μm²; ETH = 12 versus 28%). In addition, dilatation of cerebral arterioles in response to acetylcholine, but not nitroprusside, was reduced by ∼25% in CuZnSOD+/− (P<0.075) and 50% in CuZnSOD−/− mice (P<0.05) compared with wild-type mice.

**Conclusions**—Cerebral arterioles in CuZnSOD+/− and CuZnSOD−/− mice undergo marked hypertrophy. These findings provide the first direct evidence in any blood vessel that CuZnSOD normally inhibits vascular hypertrophy suggesting that CuZnSOD plays a major role in regulation of cerebral vascular growth. The findings also suggest a gene dosing effect of CuZnSOD for increases in O2– induction of cerebral vascular hypertrophy and impaired endothelium-dependent dilatation. *(Stroke. 2006;37:1850-1855.)*

**Key Words:** cerebral arteries ■ hypertrophy ■ reactive oxygen species ■ superoxide dismutase

S
small resistance arteries and arterioles undergo hypertrophy in models of hypertension.1,2 Several determinants apparently contribute to vascular hypertrophy including increases in arterial pressure3,4 (including pulse pressure) and the renin-angiotensin system.5 Another determinant that may influence vascular hypertrophy is nitric oxide (NO). This suggestion is based on the observations that NO donors inhibit proliferation of vascular muscle in culture,6 and that cerebral arterioles undergo hypertrophy in endothelial NO synthase (eNOS)−deficient mice, even in the absence of increases in arteriolar pulse pressure.7

The bioactivity of NO depends, in part, on its interaction with reactive oxygen species (ROS), particularly superoxide (O2–).8 Many studies have suggested that inactivation of NO by O2– contributes to impaired vascular function.9,10 Local levels of O2– reflect both the rate of O2– formation and the rate of its removal by endogenous antioxidants (primarily superoxide dismutases [SODs]). Much attention has been focused on sources of O2– in relation to O2– levels and vascular dysfunction. However, much less is known regarding the functional importance of expression or activity of SODs within the vascular wall.

SODs exist as 3 isoforms localized within specific cellular compartments: copper-zinc SOD (CuZnSOD; SOD1) located predominately within the cytosol, manganese SOD (MnSOD; SOD2) targeted to the mitochondrial matrix, and extracellular SOD (EC-SOD; SOD3) found primarily bound to heparan sulfate proteoglycan on cell surfaces. Although it is known that the 3 isoforms of SOD are expressed within the vessel wall, the predominant isoform of SOD (when expressed as percent of total SOD activity) is CuZnSOD.12,13 The goal of this study was to examine the hypothesis that loss of CuZnSOD results in increased O2– levels and altered vascular growth. To test this hypothesis, we measured O2– levels and examined mechanics and structure, as well as vasodilator responses, of cerebral arterioles in wild-type and CuZnSOD-deficient mice.14

**Methods**

**Animals**

CuZnSOD-deficient mice were produced as described previously.13 We interbred heterozygous CuZnSOD-deficient mice to generate wild-type (WT; +/+), heterozygous CuZnSOD-deficient (+/−), and homozygous CuZnSOD-deficient (−/−) mice.

---

Received March 16, 2006; accepted April 6, 2006.
From the Department of Pathology (G.L.B.), University of Iowa College of Medicine & Cardiovascular Center, Iowa City, IA; and the Department of Internal Medicine (S.P.D., F.M.F.), University of Iowa College of Medicine & Cardiovascular Center, Iowa City, IA.
Correspondence to Gary L. Baumbach, MD, Department of Pathology, 5231-D RCP, 200 Hawkins Drive, University of Iowa College of Medicine, Iowa City, IA 52242. E-mail g-baumbach@uiowa.edu

© 2006 American Heart Association, Inc.

*Stroke* is available at [http://www.strokeaha.org](http://www.strokeaha.org)

DOI: 10.1161/01.STR.0000227236.84546.5a
within the same litter. This approach allowed us to use WT littersmates as controls. Genotyping of the animals was performed by polymerase chain reaction from tail biopsies. All mice were studied at about 7 months of age (WT= 7.6±0.4 months; CuZnSOD+/− = 7.3±0.2 months; CuZnSOD−/− = 7.4±0.4 months). Procedures followed in this study were in accordance with institutional guidelines for care and use of experimental animals at the University of Iowa.

In Vivo Preparation

Because anesthesia can lower arterial pressure in mice, we measured systemic arterial pressure in conscious mice before examination of cerebral arteriolar structure using a method we have described previously.15,16 Following measurement of conscious arterial pressure, animals were weighed and anesthetized with sodium pentobarbital (5 mg 100 g−1 body wt IP), intubated, and mechanically ventilated with room air and supplemental O2. Supplemental anesthetic was administered intravenously at a rate of 1.7 mg 100 g−1 body wt.

A catheter was inserted into a femoral vein for injection of drugs and fluids. A catheter was inserted into a femoral artery to record systemic arterial pressure and obtain blood samples for measurement of arterial blood gases, and a catheter was inserted into the other femoral artery to withdraw blood to produce hypotension (for studies of vascular mechanics).

Measurement of Cerebral Arteriolar Pressure and Diameter

We measured pressure and diameter in first-order arterioles on the cerebrum through an open skull preparation that we have described in detail.15,16 Cerebral arteriolar systolic, diastolic, mean and pulse pressures were measured continuously with a micropipette connected to a servo-null pressure-measuring device (model 5, Instrumentation for Physiology and Medicine, Inc). Arterioles were monitored through a microscope connected to a closed-circuit video system with a final magnification of x356. Arteriolar diameter was measured from digitized images of arterioles using image analysis software.

Experimental Protocol

About 20 to 30 minutes after completion of surgery, measurements of cerebral arterioles were obtained under baseline conditions. Arterioles were then suffused with artificial cerebral spinal fluid containing EDTA (67 mmol/L), which produces maximal dilatation of cerebral arterioles.18 Pressure-diameter relationships were obtained in maximally dilated cerebral arterioles between cerebral arteriolar pressures of 40 and 10 mm Hg. Arterioles were fixed at physiological pressure in vivo by suffusion of vessels with glutaraldehyde fixative (2.25% glutaraldehyde in 0.10 mol/L cacodylate buffer) while maintaining cerebral arteriolar pressure at baseline levels. After the anesthetized animal was killed using sodium pentobarbital, the arteriolar segment used for pressure-diameter measurements was removed, processed and embedded in Spurr’s low viscosity resin while maintaining cross-sectional orientation. Cross-sectional area of the arteriolar wall was determined histologically using a method we have described previously.4,18 Mechanical characteristics of cerebral arterioles (circumferential stress, circumferential strain and tangential elastic modulus) were calculated from measurements of cerebral arteriolar pressure, diameter and cross-

Baseline Values in CuZnSOD-Deficient Mice

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CuZnSOD Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WT (+/+)</td>
</tr>
<tr>
<td></td>
<td>Male</td>
</tr>
<tr>
<td><strong>Before Maximal Dilatation</strong></td>
<td></td>
</tr>
<tr>
<td>Systemic Arterial Mean Pressure, mm Hg</td>
<td></td>
</tr>
<tr>
<td>Unanesthetized</td>
<td>127±7</td>
</tr>
<tr>
<td>Anesthetized</td>
<td>75±6</td>
</tr>
<tr>
<td>Cerebral Arteriolar Pressure, mm Hg</td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>38±2</td>
</tr>
<tr>
<td>Diastolic</td>
<td>28±2</td>
</tr>
<tr>
<td>Mean</td>
<td>31±2</td>
</tr>
<tr>
<td>Pulse</td>
<td>10±1</td>
</tr>
<tr>
<td>Arterial Blood Gases</td>
<td></td>
</tr>
<tr>
<td>$P_{CO_2}$</td>
<td>39±4</td>
</tr>
<tr>
<td>pH</td>
<td>7.32±0.04</td>
</tr>
<tr>
<td>$P_{O_2}$</td>
<td>94±7</td>
</tr>
<tr>
<td>Internal Cerebral Arteriolar Diameter, μm</td>
<td>35±2</td>
</tr>
<tr>
<td><strong>After Maximal Dilatation</strong></td>
<td></td>
</tr>
<tr>
<td>Cerebral Arteriolar Diameter, μm</td>
<td></td>
</tr>
<tr>
<td>Internal</td>
<td>58±2</td>
</tr>
<tr>
<td>External</td>
<td>61±2</td>
</tr>
<tr>
<td>Wall Thickness, μm</td>
<td>1.7±0.1</td>
</tr>
<tr>
<td>$E_t$ vs Stress</td>
<td>6.16±0.49</td>
</tr>
<tr>
<td>N</td>
<td>5</td>
</tr>
</tbody>
</table>

Measurements of internal diameter before maximal dilatation of cerebral arterioles were obtained at prevailing levels of arterial pressure. Measurements of internal diameter after maximal dilatation were made at an arteriolar mean pressure of 40 mm Hg. Values of external diameter after maximal dilatation were calculated from measurements of internal diameter at 40 mm Hg arteriolar pressure and histological measurements of cross-sectional area of the vessel wall. $E_t$ vs Stress: slope of tangential elastic modulus ($E_t$) vs stress. Values are mean±SEM.

*P<0.05 vs male WT mice; †P<0.05 vs female WT mice; ‡P<0.05 vs male heterozygous SOD-deficient mice; §P<0.05 vs female homozygous SOD-deficient mice.
sectional area using an approach we have described in detail previously.\(^1,8\)

**Measurement of Superoxide**

O\(_2\) levels were evaluated in vitro in 6 to 8 \(\mu\)m thick frozen sections of unfixed cerebral arterioles using hydroethidine-based (2 \(\mu\)mol/L hydroethidine) confocal microscopy as described previously.\(^9,19\) Laser settings were identical for acquisition of images, and vessels from WT, CuZnSOD\(^{+/+}\) and CuZnSOD\(^{+-}\) mice were processed and imaged in parallel. Relative increases in ethidium fluorescence were determined and normalized to the cross-sectional area of the vessel wall.

**Evaluation of Endothelium-Dependent Responses in Cerebral Arterioles**

Endothelium-dependent and independent responses were examined in cerebral arterioles using separate groups of WT, CuZnSOD\(^{+/+}\) and CuZnSOD\(^{+-}\) mice and a method we have described previously.\(^13\) The diameter of 1 arteriole per animal was measured under control conditions and during topical application of acetylcholine (1 and 10 \(\mu\)mol/L) and nitroprusside (0.1 and 1 \(\mu\)mol/L). Arterial blood gases were monitored and were similar in the 3 groups: WT \(P_{CO_2}=33\pm2\), \(P_{O_2}=191\pm24\), \(pH=7.35\pm0.03\); CuZnSOD\(^{+/+}\) \(P_{CO_2}=35\pm2\), \(P_{O_2}=163\pm17\), \(pH=7.35\pm0.02\); CuZnSOD\(^{+-}\) \(P_{CO_2}=35\pm3\), \(P_{O_2}=167\pm20\), \(pH=7.33\pm0.01\) (mean±SE).

**Statistical Analysis**

Analysis of variance was used to compare systemic mean pressure and arteriolar pressures, diameters, cross-sectional area of the vessel wall, slope of tangential elastic modulus versus stress, relative density of ethidium fluorescence and dilator responses. Probability values were calculated using a Student \(t\) test. Statistics were determined using JMP statistics software (SAS Institute Inc).

**Results**

**Blood Pressure and Baseline Characteristics**

In the unanesthetized state, systemic mean arterial pressure was similar in male and female CuZnSOD\(^{+/+}\) and WT mice (Table). In contrast, unanesthetized systemic mean arterial pressure in male and female CuZnSOD\(^{+-}\) mice was significantly lower than in male and female WT CuZnSOD\(^{+/+}\) mice (Table). Anesthesia substantially reduced arterial pressure in all groups of mice (Table). During anesthesia, systemic mean arterial pressure and cerebral arteriolar mean and pulse pressure were not significantly different in any of the groups of mice (Table).

**Superoxide Levels**

Basal \(O_2\) levels appeared to be higher in cerebral arterioles of CuZnSOD\(^{+/+}\) mice than in WT mice (Figure 1). Quantification of ethidium signal revealed significantly higher fluorescence in cerebral arterioles of both CuZnSOD\(^{+/+}\) and CuZnSOD\(^{+-}\) mice compared with WT (Figure 1). In addition, relative fluorescent intensity was significantly greater in cerebral arterioles of CuZnSOD\(^{+/+}\) than CuZnSOD\(^{+-}\) mice (Figure 1). No gender differences in relative fluorescence were noted in any of the groups of mice.

**Vascular Mechanics**

Diameter before EDTA was similar in cerebral arterioles of male and female WT, CuZnSOD\(^{+/+}\) and CuZnSOD\(^{+-}\) mice (Table). After maximal dilatation with EDTA, internal and external diameters in male and female CuZnSOD\(^{+/+}\) and CuZnSOD\(^{+-}\) mice were not significantly different than in male and female WT mice (Table). Wall thickness and cross-sectional area of the vessel wall were significantly greater in cerebral arterioles in male and female CuZnSOD\(^{+/+}\) and CuZnSOD\(^{+-}\) mice than in male and female WT mice (Figure 2). Furthermore, wall thickness and cross-sectional area of the vessel wall in male and female CuZnSOD\(^{+-}\) mice were intermediate between male and female WT and CuZnSOD\(^{+/+}\) mice (Figure 2). Thus, cerebral arterioles in both CuZnSOD\(^{+/+}\) and CuZnSOD\(^{+-}\) mice underwent hypertrophy of the vessel wall regardless of gender.

During maximal dilatation, internal diameter in cerebral arterioles in male and female CuZnSOD\(^{+/+}\) and CuZnSOD\(^{+-}\) mice were similar to diameter in male and female WT mice at all levels of arteriolar pressure between 10 and 40 mm Hg (Figure 3). The stress-strain curve in cerebral arterioles in male CuZnSOD\(^{+/+}\) mice was comparable to the curve in cerebral arterioles in male WT mice (Figure 4, left panel). In contrast, the stress-strain curves in male CuZnSOD\(^{+-}\) mice and male and female CuZnSOD\(^{+/+}\) mice were shifted to the right of the curves in male and female WT mice (Figure 4). The slope of tangential elastic modulus versus stress was significantly reduced in female CuZnSOD\(^{+/+}\) mice and male and female CuZnSOD\(^{+-}\) mice but not in male CuZnSOD\(^{+-}\) mice (Table). These findings suggest that a deficiency of CuZnSOD may result in increased distensibility of cerebral arterioles.

**Vasodilator Responses**

Baseline diameter of cerebral arterioles was similar \((P>0.05)\) in WT mice (33±4 \(\mu\)m; \(n=7\)), CuZnSOD\(^{+/+}\) mice
There are several major new findings in this study. First, basal O$_2$ levels in cerebral arterioles, as measured using hydroethidium, were significantly increased in CuZnSOD-deficient mice. Increases in cerebral arteriolar O$_2$ levels occurred in both CuZnSOD$^{+/+}$ and CuZnSOD$^{+/−}$ mice, but were greater in the CuZnSOD$^{−/−}$ group. Second, mean and pulse pressures in cerebral arterioles of CuZnSOD$^{+/+}$ and CuZnSOD$^{+/−}$ mice were similar to cerebral arteriolar pressures in WT mice. Third, cerebral arterioles in CuZnSOD-deficient mice underwent hypertrophy of the vessel wall with the degree of hypertrophy being greater in CuZnSOD$^{−/−}$ than CuZnSOD$^{+/−}$ mice. Cerebral arteriolar hypertrophy in CuZnSOD$^{−/−}$ mice was associated with an increase in arteriolar distensibility. Fourth, we confirmed that endothelium-dependent dilatation of cerebral arterioles was impaired in CuZnSOD$^{−/−}$ mice, and we also found that this response was reduced in CuZnSOD$^{−/−}$ mice, though to a lesser degree. Finally, external diameter was not reduced in arterioles of CuZnSOD-deficient mice. Thus, deficiency of CuZnSOD did not result in inward or outward remodeling of cerebral arterioles. Taken together, these findings suggest that increases in basal O$_2$ in cerebral blood vessels attributable to deficiency of CuZnSOD produce cerebral vascular hypertrophy, even in the absence of increases in arteriolar pressure. Furthermore, the findings indicate that the loss of a single copy of the CuZnSOD gene is sufficient to induce hypertrophy and impair endothelium-dependent dilatation of cerebral arterioles.

**Discussion**

There are several major new findings in this study. First, basal O$_2$ levels in cerebral arterioles, as measured using hydroethidium, were significantly increased in 

---

**Figure 2.** Representative histological sections and cross-sectional area of the vessel wall in cerebral arterioles of WT (CuZnSOD$^{+/+}$), CuZnSOD$^{+/−}$, and CuZnSOD$^{−/−}$ mice. Values are means±SE in 5 male and 6 female WT, 8 male and 10 female CuZnSOD$^{+/−}$, and 5 male and 5 female CuZnSOD$^{−/−}$ mice. *P<0.05 versus male WT; †P<0.05 versus female WT; ‡P<0.05 versus CuZnSOD$^{+/−}$; §P<0.05 versus female CuZnSOD$^{−/−}$. Scale bar=20 μm.

(29±1 μm; n=9) and CuZnSOD$^{−/−}$ mice (34±2 μm; n=7). Dilatation of cerebral arterioles to acetylcholine tended to be reduced (P<0.075) in CuZnSOD$^{−/−}$ mice and was significantly reduced by about 50% (P<0.05) in CuZnSOD$^{−/−}$ mice compared with WT (Figure 4). In contrast, dilatation of cerebral arterioles in response to nitroprusside was similar (P>0.05) in all groups of mice (Figure 5).

**Hypertrophy of Cerebral Arterioles**

The finding in this study of cerebral arteriolar hypertension in CuZnSOD-deficient mice suggests that oxidative stress, and in particular O$_2$ levels, may be another factor that contributes to vascular hypertrophy in chronic hypertension. At least 2 other lines of evidence support this possibility. First, oxidative stress is a prominent component of chronic hypertension. O$_2$ levels are increased in mesenteric arterioles of spontaneously hypertensive rats, in aortic wall of Sprague-Dawley rats, and mice with angiotensin II–mediated hypertension, and in neutrophils of humans with essential hypertension. Second, oxidative stress may influence other factors that impact growth of vascular muscle, such as NO, epidermal growth factor–receptors, p38 mitogen-activated protein kinase, and Akt.

---

**Figure 3.** Pressure-internal diameter relationships in cerebral arterioles during maximal dilatation with EDTA in WT (+/+), CuZnSOD$^{+/−}$ (+/−) and CuZnSOD$^{−/−}$ (−/−) mice. Values are means±SE in 5 male and 6 female WT, 8 male and 10 female CuZnSOD$^{+/−}$, and 5 male and 5 female CuZnSOD$^{−/−}$. 

---

**Figure 4.** Representative histological sections and cross-sectional area of the vessel wall in cerebral arterioles of WT (CuZnSOD$^{+/+}$), CuZnSOD$^{+/−}$, and CuZnSOD$^{−/−}$ mice. Values are means±SE in 5 male and 6 female WT, 8 male and 10 female CuZnSOD$^{+/−}$, and 5 male and 5 female CuZnSOD$^{−/−}$ mice. *P<0.05 versus male WT; †P<0.05 versus female WT; ‡P<0.05 versus male CuZnSOD$^{+/−}$; §P<0.05 versus female CuZnSOD$^{−/−}$. Scale bar=20 μm.

(29±1 μm; n=9) and CuZnSOD$^{−/−}$ mice (34±2 μm; n=7). Dilatation of cerebral arterioles to acetylcholine tended to be reduced (P<0.075) in CuZnSOD$^{−/−}$ mice and was significantly reduced by about 50% (P<0.05) in CuZnSOD$^{−/−}$ mice compared with WT (Figure 4). In contrast, dilatation of cerebral arterioles in response to nitroprusside was similar (P>0.05) in all groups of mice (Figure 5).
Potential Mechanisms of Cerebral Arteriolar Hypertrophy

Interactions with NO

One mechanism by which oxidative stress may influence growth is by reducing availability of NO to the vessel wall. Previous findings suggest that reduced availability of NO in the vessel wall may contribute to the development of cerebral vascular hypertrophy as a consequence of reduced inhibition of smooth muscle growth. The bioactivity of NO depends, in part, on its interaction with reactive O₂ species, particularly O₂⁻. Thus, increased levels of O₂⁻ in CuZnSOD-deficient mice may lead to cerebral arteriolar hypertrophy by inactivating NO in the arteriolar wall, and thus diminishing NO’s inhibitory influence on vascular growth.

Even if interactions of O₂⁻ with NO play a role, however, it is unlikely that such interactions account entirely for O₂⁻’s trophic effects on cerebral arterioles. If these interactions were entirely responsible for trophic effects, we would anticipate that deficiency of eNOS would result in levels of arteriolar hypertrophy similar to those produced by deficiency of CuZnSOD. Instead, the degree of cerebral arteriolar hypertrophy that we found previously in homozygous eNOS-deficient mice was about half that found in this study in CuZnSOD⁻/⁻ mice. These findings suggest that other factors, in addition to an interaction with NO, may contribute to cerebral arteriolar hypertrophy in CuZnSOD deficiency.

Mediation by Hydrogen Peroxide

H₂O₂ is derived primarily from O₂⁻ and is considered to be one of the most important ROS by virtue of its interactions with multiple signaling systems. H₂O₂ is a good candidate to play a second messenger role in signaling processes that lead to vascular growth by virtue of its being uncharged, relatively long-lasting and freely diffusible. Because levels of O₂⁻ are typically increased in many conditions that stimulate vascular growth, such as hypertension and atherosclerosis, and because in most circumstances O₂⁻ is quickly converted to H₂O₂ by SOD, it is possible the contribution of O₂⁻ to vascular growth under conditions of oxidative stress is mediated at least in part by H₂O₂.

We think it is less likely that H₂O₂ contributed to the observation in this study of cerebral arteriolar hypertrophy in CuZnSOD-deficient mice. Because rapid conversion of O₂⁻ to H₂O₂ requires an enzyme such as the SODs, one might expect in the absence of CuZnSOD a shift in the O₂⁻:H₂O₂ balance...
that favors O$_2^-$ This expectation is borne out by the finding that O$_2$ levels are increased and levels of H$_2$O$_2$ are significantly reduced in CuZnSOD$^{+/−}$ mice. Furthermore, if H$_2$O$_2$ is an important stimulus of cellular growth in response to oxidative stress, we would anticipate that overexpression of CuZnSOD would increase levels of H$_2$O$_2$ and accelerate cellular growth. At least with fibroblasts, however, overexpression of CuZnSOD suppresses growth and induces features of cell senescence, despite elevated levels of H$_2$O$_2$. Thus, our findings in this intact system support the concept that ROS influence vascular growth, but provide new evidence to suggest O$_2$ may be a key mediator of vascular hypertrophy in vivo.

Conclusion

We found in this study that (1) cerebral arterioles in both CuZnSOD$^{+/−}$ and CuZnSOD$^{−/−}$ mice undergo hypertrophy and (2) the degree of hypertrophy is greater in CuZnSOD$^{−/−}$ mice than previously observed in homozygous eNOS-deficient mice. Based on these findings we conclude that interactions of O$_2$ with NO cannot account entirely for the degree of cerebral arteriolar hypertrophy found in CuZnSOD$^{−/−}$ mice. Our study provides genetic support for the concept that ROS influence vascular growth and CuZnSOD may play an important role in the regulation of vascular growth.

Acknowledgments

We thank Tom Gerhold, Shams Ghoneim and Cynthia Lynch for technical assistance, and Norma Sinclair and the University of Iowa Transgenic Facility for genotyping services.

Sources of Funding

This work was supported by National Institutes of Health Grants HL-22149, NS-62461, HL-38901 and HL-62984, and an American Heart Association grant (0230327N).

Disclosures

None.

References


Hypertrophy of Cerebral Arterioles in Mice Deficient in Expression of the Gene for CuZn Superoxide Dismutase
Gary L. Baumbach, Sean P. Didion and Frank M. Faraci

Stroke. 2006;37:1850-1855; originally published online June 8, 2006;
doi: 10.1161/01.STR.0000227236.84546.5a

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2006 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/37/7/1850