confirm that successful recanalization is associated with better clinical outcome. This study also shed some light on the effect of intubation, procedure duration, and time to treatment on clinical outcome. However, this analysis was based on nonrandomized, self-reported data in the absence of a control. Therefore, efficacy of this treatment approach compared with standard medical therapy was not addressed by this study, and further randomized controlled studies are warranted.

Perlecan Domain V is a Novel Stroke Treatment

Perlecan domain V (DV) may improve functional stroke outcome. Boyeon Lee, PhD, Texas A&M College of Medicine, College Station, TX, presented findings from a study that investigated the effect of the extracellular matrix (ECM) fragment perlecan domain V on angiogenesis and neurogenesis in poststroke rats and mice.

Neurovascular coupling of angiogenesis and neurogenesis has been shown to involve ECM remodeling and ECM fragment initiation [Ohab JJ et al. *J Neuroscience* 2006]. Additionally, DV has been shown to interact with the ECM and promote angiogenesis [Segev A et al. *Cardiovasc Res* 2004; Mongiat M et al. *J Biol Chem* 2003]. In this study by Lee and colleagues, sham surgery control was performed or transient middle cerebral artery occlusive stroke was induced by using sterotactic injection of endothelin-1 in rats or tandem ipsilateral common carotid artery and middle cerebral artery occlusion in mice. All subjects received either intraperitoneal injections of human recombinant DV 0.5-1 mg/kg or phosphate-buffered saline control at Days 1, 3, 5, and 7 poststroke (n=15 for each group). Functional use of the affected limb was determined by the vibrissae-elicited paw placement reflex in mice and the cylinder test in rats. Concurrent brain microvascular endothelial cell *in vitro* studies were also performed to evaluate the effect of DV on angiogenesis.

Brain immunohistochemistry (von Willebrand factor) demonstrated that perlecan DV homed to the stroke and peri-infarct vasculature. DV was significantly higher in the stroked cerebral hemisphere at Days 1, 3, 5, and 7 poststroke compared with corresponding contralateral hemisphere levels (Day 1 p=0.0001; Day 3 p=0.0007; Day 5 p=0.007; Day 7 p=0.005). Additionally, subjects that were treated with DV had more neurons with normal morphology and lower incidence of TUNEL-positive cells or shrunken and misshapen cells, suggesting a neuroprotective component that was associated with DV. DV treatment was associated with increased poststroke neurogenesis and poststroke angiogenesis. Significant increases were observed in stroke peri-infarct vasculature in subjects that were treated with DV on poststroke Days 3, 5, and 7 versus control (p=0.001; p<0.00001; p<0.00001 for Days 3, 5, and 7, respectively). DV treatment also resulted in significantly more doublecortin-positive pixels on poststroke Days 3, 5, and 7 versus control (Day 3, p=0.00001; Day 5, p<0.00001; Day 7, p<0.00001, resulting in enhanced poststroke neurogenesis.

Functional stroke outcome was significantly better in stroked subjects that were treated with DV versus control, and improvement in contralateral paw use was observed at Days 3 (p=0.03) and 7 (p=0.009) poststroke. While significant contralateral forelimb improvement was noted in those that were treated with DV, PBS control subjects remained significantly impaired at poststroke Days 3 (p=0.008), 5 (p=0.006), and 7 (p=0.005).

The *in vitro* analysis that was included in this study revealed possible mechanisms by which DV affects angiogenesis. At 3 days poststroke, an increase in α5β1 levels was noted in those that were treated with DV. DV enhances brain endothelial cell formation, which may be inhibited via α5β1. In α5β1 and DV coimmunohistochemistry of brain endothelial cells, colocalization of DV and α5β1 was identified. DV also induces brain endothelial cell VEGF synthesis and release via the α5β1 integrin. A DV dose-dependent VEGF response was noted *in vitro*.

Dr. Lee concluded that DV is neuroprotective and promotes poststroke angiogenesis and neurogenesis, thus, contributing to improved functional stroke outcome. DV-induced VEGF release via the α5β1 integrin pathway plays a role in the DV angiogenesis and neurogenesis. However, the extent of their involvement remains unclear. Results from this study are promising and suggest that perlecan DV may provide a viable treatment option for stroke in the future.

Failure to Validate Association Between Variants on 12p13 and Ischemic Stroke

A meta-analysis of genomewide association studies (GWAS) did not validate findings that associated the single-nucleotide polymorphisms rs12425791 and rs11833579 with stroke. Representing the members of the International Stroke Genetics Consortium, Jonathan Rosand, MD, MSc, Massachusetts General Hospital, Boston, MA, detailed findings from this meta-analysis.

A previous GWAS found that two intergenic single-nucleotide polymorphisms (SNPs), rs12425791 and