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Perlecan domain V promotes neuronal regeneration of stroked brain tissue

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Stroke is a significant world-wide cause of mortality and profound morbidity. Despite this sobering fact, little progress has been made in developing new therapies. Indeed, promising neuroprotective therapies have consistently failed to translate from animals to human patients. With this in mind, we hypothesized that better stroke therapies might be identified from a better understanding of the brain's self-repairing stroke response. To this end, we have recently demonstrated that perlecan domain V (DV), a proteolytic fragment of the vascular basement membrane, is persistently generated after stroke and when administered via intraperitoneal injection 24 hours post-stroke is neuroprotective, enhances angiogenic brain repair, and inhibits chronic glial scar formation (a potential barrier to brain repair). Protection was observed in two distinct models of transient focal ischemia in mice and rats. DV treatment resulted in rapid functional recovery to pre-stroke levels in two days. We now investigated whether DV could also be therapeutic in a permanent focal ischemia model in both young and aged (an important clinical factor) as mice and whether it might enhance neurorepair. We now report that DV treatment in a motor cortex photothrombotic stroke model was also neuroprotective in both young and aged mice. Furthermore, these animals had significantly improved post-stroke motor function. Additionally, DV enhanced several aspects of post-stroke neuronal regeneration including neurogenesis, migration, and neuronal repopulation in the peri-infarct region and ischemic core. Collectively, these results suggest that DV may be a promising neuroregenerative stroke therapy.

Biography

Gregory Bix completed his M.D. and Ph.D. degrees from Baylor College of Medicine and postdoctoral studies at Thomas Jefferson University. He is currently the Paul G. Blazer, Jr. endowed Stroke Research Associate Professor at Sanders-Brown Center on Aging at the University of Kentucky. He has published more than 20 papers in reputed journals and has won several research awards.

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