Astrocyte-specific expression of survivin mediates reactive gliosis after intracerebral hemorrhage

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Introduction

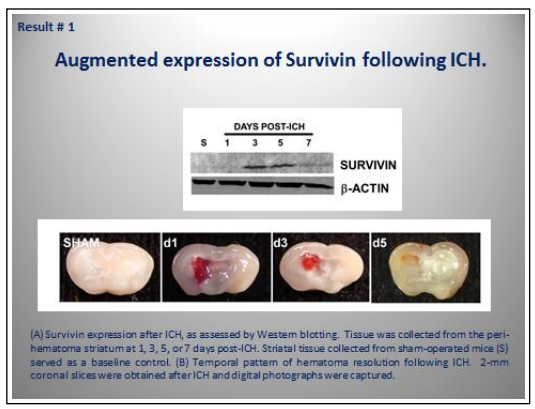
Intracerebral hemorrhage (ICH), the most common form of hemorrhagic stroke, accounts for up to 15% of all strokes. Despite maximal surgical intervention and supportive care, ICH is associated with significant morbidity and mortality, in part, due to a lack of viable treatment options. Astrogliosis, an enigmatic and poorly-defined process, is a key feature of secondary injury characterized by glial proliferation. As astrogliosis is associated with both beneficial and detrimental outcomes after brain injury, an improved understanding of the underlying cellular and molecular mechanisms may aid in the design of novel therapeutics.

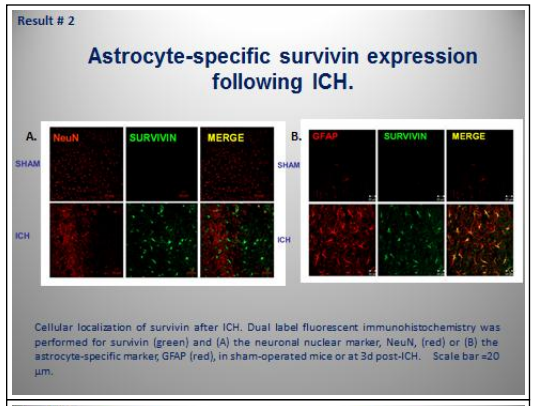
Methods

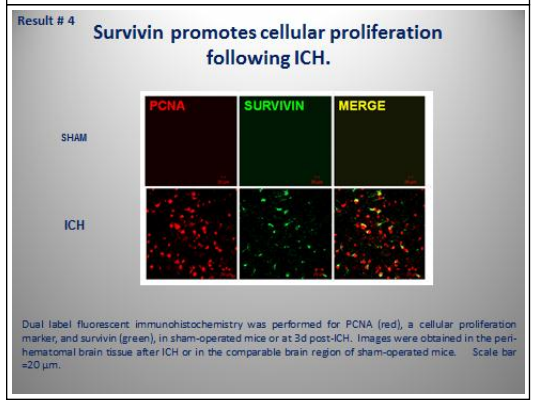
ICH was induced using an established pre-clinical murine model of collagenase-induced ICH. Endpoints were quantified using Western blotting and immunohistochemistry.

Results

We observed a delayed upregulation of survivin, a key molecule involved in tumor cell proliferation and survival, by 72h post-ICH. Notably, this increase in survivin expression was prominent in glial fibrillary acidic protein (GFAP)- positive astrocytes, but absent from both neurons and microglia. Similarly, survivin expression was below the level of detection in both the contralateral hemisphere and in the brain of sham-operated mice. Finally, survivin co-localized with proliferating cell nuclear antigen (PCNA), an established marker of cellular proliferation, and temporally correlated with development of reactive gliosis after ICH.







Conclusions

These data suggest a novel role for survivin in functionally promoting astrocytic proliferation after ICH.

Learning Objectives

By the conclusion of this session, participants should be able to identify a novel cellular mechanism of gliosis and describe the potential therapeutic role of survivin following ICH.

References

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