



University of Pittsburgh

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September 7, 2018

Dr. Melvin Limson, PhD
Director of Programs & Development
Association of Pathology Chairs (APC)
100 West 10th Street, Suite 603
Wilmington, DE 19801

Dear Dr. Limson,

We are writing this letter to announce our intention to apply for the Society of '67 pathology trainee project grant in healthcare innovation for our research study entitled "The Neuropathologic Correlates of Sepsis-Associated Cognitive Dysfunction."

There is increasing awareness that the brain is also affected in the widespread organ dysfunction seen in sepsis. While sepsis is commonly associated with acute altered mental status at the time of illness, recent studies have shown that sepsis is also associated with long-term cognitive impairment, and therefore has both healthcare and social implications. While several neuroimaging studies have shown white matter abnormalities in septic patients, there has been limited correlation with neuropathologic studies.

Therefore, our project goal is to better understand the cognitive dysfunction caused by sepsis with a focus on white matter injury. The proposed project will include a preliminary retrospective analysis of approximately 20 autopsy brains of septic patients from our institution. All histologic sections will be screened for evidence of global ischemic injury, septic emboli, and other lesions. Five standardized brain sections from each case will initially be evaluated using immunohistochemistry for acute axonal injury using an Amyloid Precursor Protein (APP) stain. The evaluation of the APP immunostains will include both morphologic patterns of injury as well as semiquantitative assessments of both the extent and severity of injury. Based on the APP results, subsequent immunohistochemical studies will be performed to evaluate other pathobiologic features including gliosis, microglial activation, and endothelial activation.

We are also currently in the initial phases of a prospective, post-mortem Diffuse Tensor Imaging (DTI) study to evaluate the white matter integrity of septic patients. This study will be performed in close collaboration with our colleagues in radiology and will allow us to better correlate radiologic findings with histopathological abnormalities and enhance our understanding of the pathobiological processes underlying sepsis-associated white matter injury.

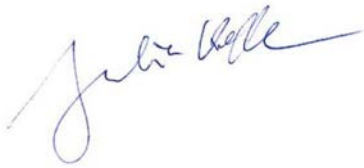
The grant funding will aid in the cost of performing the immunohistochemical stains for the initial retrospective study, with an estimated budget of \$5000. Additional financial support will be available through institutional funds from the Department of Pathology at the University of Pittsburgh.

Thank you for your consideration of this proposal, and please let us know if there is anything we can provide to help in the review process.

Sincerely,

A handwritten signature in blue ink, appearing to read "Anne M. Shepler".

Anne M. Shepler, MD
Neuropathology Fellow
shepleram@upmc.edu

A handwritten signature in blue ink, appearing to read "Julia Kofler".

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