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“Pharmacogenomic Influence of ApoE and Mimetic Peptide on Neurologic Outcomes as a Paradigm for Targeted Therapeutic Development in a Murine Model of Intracerebral Hemorrhage”

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Summary: As a frequent admitting diagnosis to neurosurgical intensive care units, intracerebral hemorrhage (ICH) is vastly understudied but known to generate marked neuroinflammatory response with poor clinical outcome. The aim is to develop rational, targeted pharmacogenomic therapies by using a murine model of ICH in transgenic systems. By setting up a series of experiments utilizing mice expressing human apolipoproteinE isoforms (apoE3 and apoE4), the isoform-specific effects on neuroinflammation after ICH can be identified. Thus, testing the specific hypothesis that endogenous expression of apoE modifies neurological deficits by modulating glial activation in an isoform-specific manner will allow for the development of rationally-derived mimetic peptides to manipulate these effects. By examining cytokine generation with complementary histochemical techniques, determination of the extent to which apoE and mimetic peptides confer neuroprotection through neuroinflammatory modulation will be made, demonstrating apoE as a compelling target for pharmacogenomic therapy to improve recovery for critically ill patients with ICH.