

Blood Occludin Level as a Potential Biomarker for Early Blood Brain Barrier Damage

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Concern about intracerebral hemorrhage (ICH) is the primary reason for withholding tPA therapy from patients with ischemic stroke. Early blood brain barrier (BBB) damage is the major risk factor for fatal post-thrombolysis ICH, but rapidly assessing BBB damage before tPA administration is highly challenging. We recently reported that ischemia induced rapid degradation of tight junction protein occludin in cerebromicrovessels. The present study investigates whether the cleaved occludin is released into the blood stream and how blood occludin levels correlate to the extent of BBB damage using a rat model of ischemic stroke. Cerebral ischemia induced a time-dependent increase of blood occludin with a sharp increase at 4.5-hour post-ischemia onset, which concurrently occurred with the loss of occludin from ischemic cerebral microvessels and a massive BBB leakage at 4.5-hour post-ischemia. Two major occludin fragments were identified in the blood during cerebral ischemia. Furthermore, blood occludin levels remained significantly higher than its basal level within the first 24 hours after ischemia onset. Our findings demonstrate that blood occludin levels correlate well with the extent of BBB damage and thus may serve as a clinically relevant biomarker for evaluating the risk of ICH before tPA administration.

His research focuses on the mechanisms and neuroprotection of brain injury due to stroke. His research

program has been continuously funded by numerous NIH grants since 1997, resulting in over 200 peer-reviewed publications.