Mucosal tolerization to E-selectin for Prevention of Secondary Stroke

John Hallenbeck, M.D.
Chief of Intramural Stroke Branch
Senior Investigator, NIH/ NINDS

Recent Publications


Research Interests:

The Clinical Investigations Section of the Stroke Branch conducts translational research on stroke prevention and stroke treatment. In spontaneously hypertensive, stroke-prone rats, we are studying ways of preventing development of spontaneous brain infarcts. This work is focused on immunologic approaches that suppress the endothelial activation produced by inflammatory cytokines such as TNF and IL-1. Mucosal tolerization to E-selectin targets immunomodulation to vascular segments that are becoming activated and suppresses spontaneous strokes and hemorrhages. This work is being translated into clinical trials.

We also study endogenous neuroprotective mechanisms that induce tolerance to hypoxia and ischemia in brain cells. This work is focused on the intracellular signaling pathways and expressed genes that regulate tolerance to hypoxia and ischemia in hibernating animals (a model of natural tolerance), and in preclinical stroke models and primary cultures of brain microvessel endothelial cells, astrocytes, microglia, cortical neurons and transformed cell lines that have been preconditioned to induce tolerance (models of induced tolerance). Multifunctional regulatory mechanisms that are conserved in the several tolerance models are of particular interest. Findings in preclinical models that have robust potential to treat stroke are candidates for translation into proof of concept clinical trials.

Recent Publications:


Figure:

Comparisons are shown of the average number of brain infarcts per animal (A), the average area of brain infarcts per animal (B), the average number of brain intraparenchymal hemorrhages per animal (C), and the average area of brain intraparenchymal hemorrhages per animal (D) in each of 4 experimental groups. The experimental groups received either a single schedule of five every other day 5 μg doses of intranasally instilled ovalbumen or E-selectin, or they received booster repetition of these dosage schedules every three weeks to maintain any mucosal tolerance that had been induced.