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Targeting the splenic immune response as a novel therapeutic approach to stroke and traumatic brain injury

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There are an increasing number of reports citing that the immune response initiated from the spleen is responsible for the cellular degeneration associated with acute neural injury, including stroke and traumatic brain injury (TBI). Our laboratory has shown that splenectomy is protective in animal models of stroke and TBI. Our laboratory has found that the spleen elicits an inflammatory response that is mediated through interferon gamma. The administration of interferon gamma reversed the protective effect of splenectomy and blocking it's signaling with neutralizing antibodies reduced neurodegeneration after stroke. Further, interferon gamma does not directly induced cell death in cultured neurons or oligodendrocytes. Interferon gamma indirectly kills neural cells by activating microglia to release free radicals and other cellular toxins. Splenectomy immediately post-TBI reduced lesion volume and decreased CCL20 expression in the brain of rats subjected to TBI. We identified CCL20 as an inflammatory signal expressed 48 h post TBI in the damaged areas of the brain. CCL20 is a chemoattractant that induces the migration of T cells and dendritic cells to injury sites and peripheral lymphoid organs like the spleen via binding to the CCR6 receptor. This likely explains why the spleen and thymus upregulate CCL20 following TBI. Moreover, CCL20 is directly toxic to cultured neurons and oligodendrocytes. Only one other study demonstrated a role of this chemokine in the induction of cellular death. These studies demonstrate that identifying the inflammatory mediators originating from the spleen to target them for pharmaceutical intervention is a viable strategy to treat neural injury.

Biography

Keith Pennypacker completed his Ph.D. in pharmacology in 1987 from Penn State University followed by postdoctoral studies at the National Institute of Environmental Health Sciences. He is a Professor of the Molecular Pharmacology and Physiology Department in the Morsani College of Medicine at the University of South Florida. He has published 97 papers in reputed journals and is serving as an editorial board member for Translational Stroke Research and Pharmacology. He has filed several patents related to therapeutics to treat stroke and traumatic brain injury.

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