Treatment of central nervous system injuries through targeted reduction of neuroinflammation

Published date: Feb. 12, 2018

Technology description

Background

Traumatic injuries to the brain and spinal cord are a leading cause of death among young people. Patients who are fortunate to survive the initial injury often deal with lifelong neurological impairment. With incident rates on the rise, TBI and SCI are poised to become a major contributor to the global epidemiological and economic burden among traumatic injuries.

The extent of the tissue damage suffered by TBI and SCI patients is determined not only by the primary injury sustained through mechanical forces applied to the tissues but through a secondary injury that occurs following the initial trauma. This secondary injury is the result of a complicated sequence of events initiated by the release of neurotoxic and endogenous inflammatory mediators by resident cells of the central nervous system. In SCI, secondary tissue damage and lesion expansion involve inflammatory events such as ischemia, oxidative damage, inflammatory cell infiltration and necrotic and apoptotic cell death. In TBI, microglia and astrocytes can produce pro-inflammatory cytokines and chemokines, together with the infiltrated leukocytes through the damaged blood-brain barrier. Despite different pathologies, an immunomodulatory therapeutic targeted at reducing the negative aspects of neuroinflammation may produce comparable efficacy in minimizing the extent of the secondary injury following the initial insult in TBI and SCI patients, along with related indications such as systemic inflammatory response syndrome (SIRS).

There is a significant unmet need to develop therapeutics for SCI and TBI in both the civilian and military populations. Many programs have shown promising results in pre-clinical trials but all have failed in humans. Accordingly there is ongoing desire to develop new therapeutic approaches to treat TBI and SCI.

Description of the Invention

Robarts Research Institute researchers at Western University have developed a suite of neuroprotective monoclonal antibodies targeting CD11d which plays a role in immune and inflammatory responses. CD11d is an important component of the CD11d/CD18 integrin expressed on the majority of circulating human neutrophils and monocytes/macrophages, NK, B and γδ T cells but not on αβT cells. Early treatment in animal (rat and mouse) models of SCI, TBI and SIRS prevents neuroinflammatory damage by neutrophils and macrophages resulting in improved neurological recovery. It is believed that these antibodies target CD11d expressed on the first wave of pro-inflammatory cells entering the

wound site whereby neutrophil and macrophage accumulation is reduced, overall secondary injury-associated cell death is decreased and more neuronal tissue is spared further injury leading to better functional recovery.

Keywords
Central Nervous System, Neuroinflammation, Traumatic Brain Injury, Spinal Cord Injury, Systemic Inflammatory Response Syndrome, Regenerative Medicine

Application area

• Spinal cord injury, Traumatic brain injury
• Systemic inflammatory response syndrome
• Additional potential applications (not yet investigated by Western): acute kidney injury, transplantation, heart lung bypass, subarachnoid hemorrhage, cervical spondylotic myelopathy, eosinophilic asthma, osteoarthritis, cardiovascular disease other than atherosclerosis.

Advantages

• Therapeutic candidates identified to a novel target with potential for further lead optimization
• Short treatment course immediately following injury
• Treatment is non-depleting and short acting – patients should maintain functional immune system during recovery Potential Applications

Institution

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