Peripheral Immune Response to CNS Injury

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Despite considerable research effort in the area of acute neural injury, no therapeutic breakthroughs have been discovered in recent years. Alternative approaches for pharmacological intervention are needed to target the processes associated with these neuropathologies. The peripheral immune system plays a role in the delayed neurodegeneration occurring in stroke and traumatic brain injury as well as in chronic neural diseases. Broadly inhibiting the immune response to neural injury has not been successful. A further understanding of the immune–brain interaction during injury could provide more specific targets for treatment. This issue is devoted to examination of the immune response to neural injury and provides insight into potential molecular targets for drug treatment.

Dr. Becker reviews her laboratory's work examining the cellular immune responses directed toward brain antigens in both animal models of stroke and patients after ischemic stroke. These responses have been identified as TH1(+) linked to exacerbated stroke outcome and antigen-specific TREG which results in a more positive outcome. The development of a TH1(+) response is correlated with an inflammatory background, such as a systemic inflammatory stimulus in experimental stroke or a systemic infection in stroke patients. The conclusion is that systemic inflammation alters the microenvironment in the brain and lymph nodes leading to the development of an autoimmune response to brain antigens after cerebral ischemic injury.

Dr. Garbuzova examines the involvement of innate and adaptive immune systems in amyotrophic lateral sclerosis (ALS). Modulation of the immune system has been reported to provide beneficial outcome in ALS animal models, but these results have not translated to human patients.

Regulatory B lymphocytes in experimental stroke are a potential protective cell type as cited by Drs. Offner and Hurn.

Lack of B cells leads to increased infarct volume while restoration of B cells reverses this effect. Regulatory B cells that produce IL-10 are protective. Agents that enhance their presence would be applicable as a novel therapy for stroke.

The manuscript of Hetz et al. describes that when cellular therapies are used to treat traumatic brain injury (TBI), there is a reduction in cellular degeneration due to decreased inflammation. These cell therapies interact with reactive macrophages in the spleen. This interaction at the spleen culminates in the systemic immune response switching to an anti-inflammatory mode.

The report from Dr. Yenari's laboratory furthers the role of inflammation in contributing to the exacerbation of stroke. This review examines the use of bone marrow chimeras to understand the relative contributions of the brain resident and the peripheral inflammatory response to stroke-induced neurodegeneration.

Minocycline as a treatment for stroke is reported to decrease inflammation in patients following acute ischemic stroke (Switzer et al.). Since IL-6 correlates with poorer stroke outcome, the expression of this cytokine was utilized as biomarker for inflammation. This study shows that it is likely that even low doses of minocycline have a potent anti-inflammatory effect with no difference in baseline stroke severity.

Targeting cannabinoid receptors (CBR) is a novel approach in treating experimental stroke. The study by Zhang et al. aimed to identify the type of cannabinoid receptor that participated in the protective effect following experimental stroke. The cellular protection was provided through the CBR2 as well as the 5HT1A receptors.

Leonardo et al. shows that the expression of the chemokine, CCL20, in oligodendrocytes and neurons after TBI appears to be a marker for cellular degeneration. The presence of CCL20 causes death of cultured oligodendrocytes under normoxic and oxygen glucose deprivation (OGD) but only to cultured neurons exposed to OGD. Since CCL20 is produced in the spleen prior to the expression in the injured brain following TBI, this chemokine could be a potential therapeutic target for a treatment for TBI.

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