



Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:

Mueller, SN;Sloan, EK

Title:

Neuroimmune interactions at the crossroads of health and disease

Date:

2021-10-01

Citation:

Mueller, S. N. & Sloan, E. K. (2021). Neuroimmune interactions at the crossroads of health and disease. *Immunology and Cell Biology*, 99 (9), pp.922-923. <https://doi.org/10.1111/imcb.12502>.

Persistent Link:

<https://hdl.handle.net/11343/299046>

**SPECIAL FEATURE EDITORIAL**

Free-to-view

**Neuroimmune interactions at the crossroads of health and disease**Scott N Mueller<sup>1</sup> & Erica K Sloan<sup>2,3</sup>

<sup>1</sup>Department of Microbiology and Immunology, The University of Melbourne, The Peter Doherty Institute for Infection and Immunity, Melbourne, VIC 3000, Australia

<sup>2</sup>Drug Discovery Biology Theme, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, VIC 3052 Australia

<sup>3</sup>Division of Surgery, Peter MacCallum Cancer Center, VIC 3000, Australia

## Correspondence

Scott N Mueller and Erica K Sloan

E-mails: smue@unimelb.edu.au; erica.sloan@monash.edu

Running head: Neuroimmune interactions at the crossroads of health and disease

Keywords: Neuroimmunity, health, disease

Interactions between cells of the immune system and the nervous system play critical roles in tissue homeostasis and protect against disease. The brain signals to tissues via nerves that produce neurotransmitters that both directly and indirectly influence cells of the immune system. Although observations of wide-ranging communication between these two super systems of the body is well documented, mechanistically our understanding of neuroimmune regulation of cellular processes is still relatively poor. Deeper understanding of perturbations in neuroimmune interactions that contribute to inflammation, allergy and cancer are required for the identification of novel therapeutic targets.

**This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/IMCB.12502](https://doi.org/10.1111/IMCB.12502)**

This article is protected by copyright. All rights reserved

In this Special Feature, Wanrooy *et al.* examine neuroinflammatory processes in the brain in response to stroke.<sup>1</sup> Recruitment of neutrophils into the brain in ischemic stroke impacts astrocytes and glial cells and results in neuronal death. This review discusses heterogeneity in neutrophils and proposes that, although pro-inflammatory N1 neutrophils contribute to CNS pathology after stroke, immunosuppressive N2 neutrophils may contribute to neuronal remodeling and restore the integrity of the blood brain barrier after stroke. N2 neutrophils express arginase 1, CD206 and Ym-1 (chitinase 3-like protein), similar to M2 macrophages. The authors explore the potential therapeutic value in promoting N2 neutrophil responses as a way to promote neuronal viability and tissue repair in the CNS following stroke.

Neuroimmune pathways play important roles in guiding immune responses in mucosal tissues in response to allergy. Flayer *et al.* discuss neuroimmune interactions that guide type 2 immune responses to allergens and toxins.<sup>2</sup> They examine parallels between neuropeptides produced by sensory nerves with damage-associated molecular patterns (DAMPs) released from damaged or dying cells. The role of neuropeptides as key contributors to decision points that can direct the outcomes of type 2 immunity or tissue repair are discussed. A framework is proposed where immune outcomes are governed by interactions between DAMPs and neural signals, defined here as neuron-associated molecular patterns (NAMPs). This is an intriguing concept that has therapeutic implications through regulation of neural signals to dampen allergic responses.

The impacts of neuroimmune interactions on disease outcomes are increasingly being recognised in the context of cancer. Scheff and Saloman review the current findings from pre-clinical and clinical studies that investigated how neural signals can contribute to cancer outcomes.<sup>3</sup> Both autonomic (sympathetic and parasympathetic) and sensory nervous system activity has been shown to influence tumour development and responses to therapy. The authors discuss distinct findings in different cancers and tumour models, including the impact of stress and the sympathetic nervous system on tumour immunity, and the influence of pain in cancer progression. Implications for therapeutic targeting of the nervous system to improve responses in patients are discussed.

There exists a wealth of information pointing to bidirectional control of key immunological processes and regulation of immune responses to diverse diseases. Yet, many aspects of neuroimmune communication are yet to be revealed. Moreover, clinical benefits arising from targeting the nervous system to influence immunity will only begin to show full potential as our understanding of the mechanism involved in cross-talk between the peripheral nervous system and immune system become clearer. The reviews in this Special Feature provide a glimpse into some of the future directions in this burgeoning field.

#### **CONFLICTS OF INTEREST**

The authors declare no conflicts of interest.

#### **REFERENCES**

1. Wanrooy BJ, Wen SW, Wong CHY. Dynamic roles of neutrophils in post-stroke neuroinflammation. *Immunol Cell Biol* 2021; **99**, XXX-XXX.
2. Flayer CH, Perner C, Sokol CL. A decision tree model for neuroimmune guidance of allergic immunity. *Immunol Cell Biol* 2021; **99**, XXX-XXX.
3. Scheff NN, Saloman JL. Neuroimmunology of cancer and associated symptomology. *Immunol Cell Biol* 2021; **99**, XXX-XXX.

**NB. Wiley Production staff (not the authors) need to add page numbers to these ICB articles at Issue proof stage**