

## **Educational Note**

# Antigen-specific autoreactive T cell responses targeting the central nervous system

Running title: Autoreactive T cells and central nervous system

## Efthimios Dardiotis<sup>1\*</sup>, <sup>1</sup> Dimitrios P. Bogdanos<sup>2</sup>

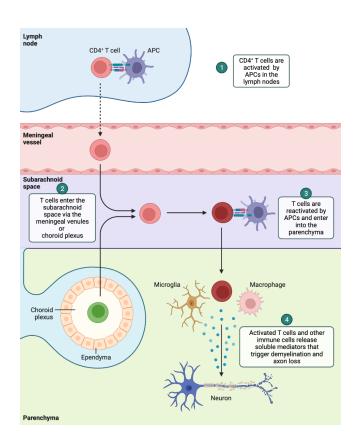
<sup>1</sup>Department of Neurology, Faculty of Medicine, School of Health Sciences, University of Thessaly, University General Hospital of Larissa, 41110 Larissa, Greece

<sup>2</sup>Department of Rheumatology and Clinical Immunology, Faculty of Medicine, School of Health Sciences, University of Thessaly, University General Hospital of Larissa, 41110 Larissa, Greece

\*Corresponding Author's e-mail: edar@med.uth.gr

### (submitted 25 May 2022; revised 5 June 2022; accepted 7 June 2022)

Keywords- Autoimmuniity; Adverse reactions; autoimmunity; autoimmune rheumatic diseases; cyclosporine; gum hypertrophy; treatment







*Fig. 1* Activation of antigen-specific autoreactive CD4+ T lymphocytes showing the possible paths of activated T cell entry Based on a consise review by (1).  $CD4^+$  T cells are most likely primed in the periphery by professional antigen presenting cells (APC) i.e. dendritic cells (DCs), which present autoantigenic epitopes such as myelin or other disease-related epitopes (2). In turn, APCs residing in the central nervous system (CNS) can seize these autoantigens *in situ* and migrate them to the lymph nodes. Antigen-specific autoreactive CD4<sup>+</sup> T cells cross the blood–cerebrospinal fluid (CSF) barrier and enter the subarachnoid space.

Those T cells are re-activated within the subarachnoid space by HLA class II-expressing macrophages and DCs expressing various autoepitopes enter the subarachnoid space in the choroid plexus. Reactivated T cells and their immune counterparts release soluble mediators and trigger a series of events damaging the myelin sheath, ultimately leading to demyelination (1-5) (prepared using a template by BioRender under a license to DPB).

### References

1. Goverman J. Autoimmune T cell responses in the central nervous system. Nat Rev Immunol. 2009;9(6):393-407.

2. Baron JL, Madri JA, Ruddle NH, Hashim G, Janeway CA, Jr. Surface expression of alpha 4 integrin by CD4 T cells is required for their entry into brain parenchyma. J Exp Med. 1993;177(1):57-68.

3. Florou DT, Mavropoulos A, Dardiotis E, Tsimourtou V, Siokas V, Aloizou AM, et al. Tetracyclines Diminish In Vitro IFN-gamma and IL-17-Producing Adaptive and Innate Immune Cells in Multiple Sclerosis. Front Immunol. 2021;12:739186.

4. Kivisakk P, Imitola J, Rasmussen S, Elyaman W, Zhu B, Ransohoff RM, et al. Localizing central nervous system immune surveillance: meningeal antigen-presenting cells activate T cells during experimental autoimmune encephalomyelitis. Ann Neurol. 2009;65(4):457-69.

5. Vasileiadis GK, Dardiotis E, Mavropoulos A, Tsouris Z, Tsimourtou V, Bogdanos DP, et al. Regulatory B and T lymphocytes in multiple sclerosis: friends or foes? Auto Immun Highlights. 2018;9(1):9.

AUTHORS CONTRIBUTION The authors prepared the manuscript and the artwork. The authors approves the final version of the manuscript.

CONFLICT OF INTEREST The Authors declare no conflict of interest

