CONGRESUL CONSACRAT ANIVERSĂRII A 75-A DE LA FONDAREA USMF „NICOLAE TESTEMIȚANU”
20 23 octombrie 2020

# IMMUNOMODULATION AFTER ISCHEMIC STROKE. MECHANISMS AND THERAPEUTIC IMPLICATIONS

Danu Glavan, Alexandru Gasnaș, Stanislav Groppa

Department of Neurology no. 2, "Nicolae Testemițanu" State University of Medicine and Pharmacy, Chișinău, Republic of Moldova

## Introduction

Inflammation of brain tissue after ischemic stroke leads to local and systemic effects. Immunity suppression by the nervous system results in the protection of nerve tissue from subsequent inflammatory damage. At the same time, it increases the susceptibility of the whole body to infections.

## Keywords

Ischemic stroke, immunity, immunomodulation, inflammation

## Purpose

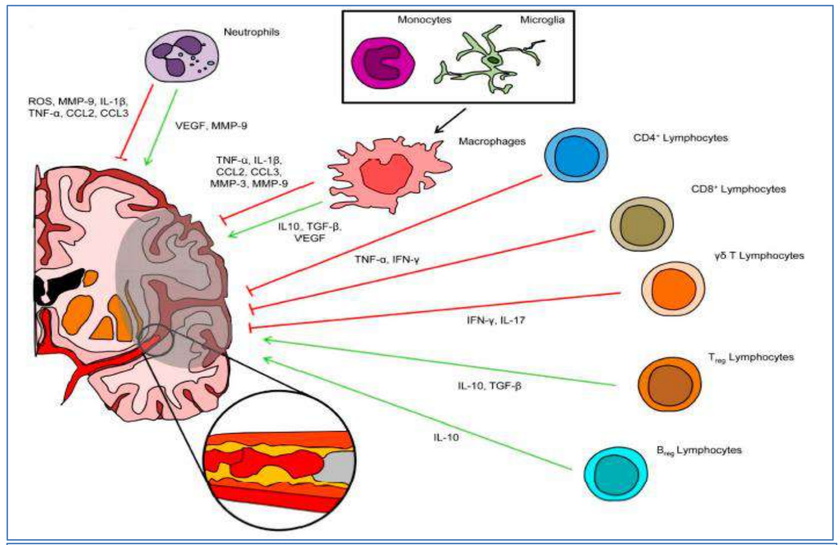
Description of local and systemic immune changes that occur after an ischemic stroke, outlining the mechanisms of immunosuppression induced by cerebral ischemia and the potential therapeutic implications of these phenomena.

## Material and methods

Articles in English were searched on the PubMed Central and Google Scholar, using the keywords “ischemic stroke”, “inflammation”, “infection”, “immunomodulation”, “immunity” and “autoimmunity”. Representative papers were selected that provided data on pathogenetic pathways and inflammatory markers in ischemic stroke and their possible therapeutic approaches.

## Results

Inflammatory mechanisms are currently considered as an important target for stroke therapy. There is evidence that immune signals and mediators can have both detrimental and beneficial effects in particular stages of the disease process. As an ischemic stroke occurs, an inflammatory cascade is triggered with cellular elements: neutrophils, microglia, monocytes/macrophages, T and B lymphocytes and humoral ones: cytokines, free radicals, damage-associated molecular pattern, autoantibodies, etc. These may be diagnostic and prognostic factors in ischemic stroke, as well as potential therapeutic targets for the control of ischemic injury and possible complications.




**Inflammatory cells in post-ischemic brain injury and reparation**
Bonaventura A, Liberale L, Vecchié A, et al. Update on Inflammatory Biomarkers and Treatments in Ischemic Stroke. *Int J Mol Sci*. 2016;17(12):1967. Published 2016 Nov 25. doi:10.3390/ijms17121967

Currently, the target of immunomodulation translated into clinical trials is focused on the early phase of toxic neuroinflammation. However, the neuroinflammatory reaction after acute brain injury continues for months. One of the studied therapies, Fingolimod, a sphingosine-1-phosphate receptor modulator, which inhibits T lymphocytes, is shown to be promising by reducing the volume of infarction, the risk of hemorrhagic transformation and disability in Asians.

There is increasing evidence that dysregulation of the immune response after the stroke might be an important predisposing factor for infection.

## Conclusions

Evidence suggests that post-ischemic oxidative stress and inflammation contribute to brain injury and to the expansion of the ischemic lesion. On the other hand, an adequate adaptive immune response after acute brain ischemia also plays an important role in response to ischemic injury, preventing secondary infarct growth by counteracting the production of proinflammatory cytokines and by modulating the activation of lymphocytes and microglia.

Immunomodulatory therapy seems promising in certain subgroups of patients with ischemic stroke. By now there are modest data on the benefit of this therapy, collected from small populations, further studies which will help us select these subgroups being needed.

## References

1. Veltkamp R, Gill D. Clinical Trials of Immunomodulation in Ischemic Stroke. *Neurotherapeutics*. 2016;13(4):791-800. doi:10.1007/s13311-016-0458-y
2. Zhang S, Zhou Y, Zhang R, et al. Rationale and design of combination of an immune modulator Fingolimod with Alteplase bridging with Mechanical Thrombectomy in Acute Ischemic Stroke (FAMTAIS) trial. *International Journal of Stroke*. 2017;12(8):906-909. doi:10.1177/1747493017710340
3. Pagram H, Bivard A, Lincz LF, Levi C. Immunity and stroke, the hurdles of stroke research translation. *International Journal of Stroke*. 2017;12(2):123-131. doi:10.1177/1747493016676622