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LETTER TO EDITOR

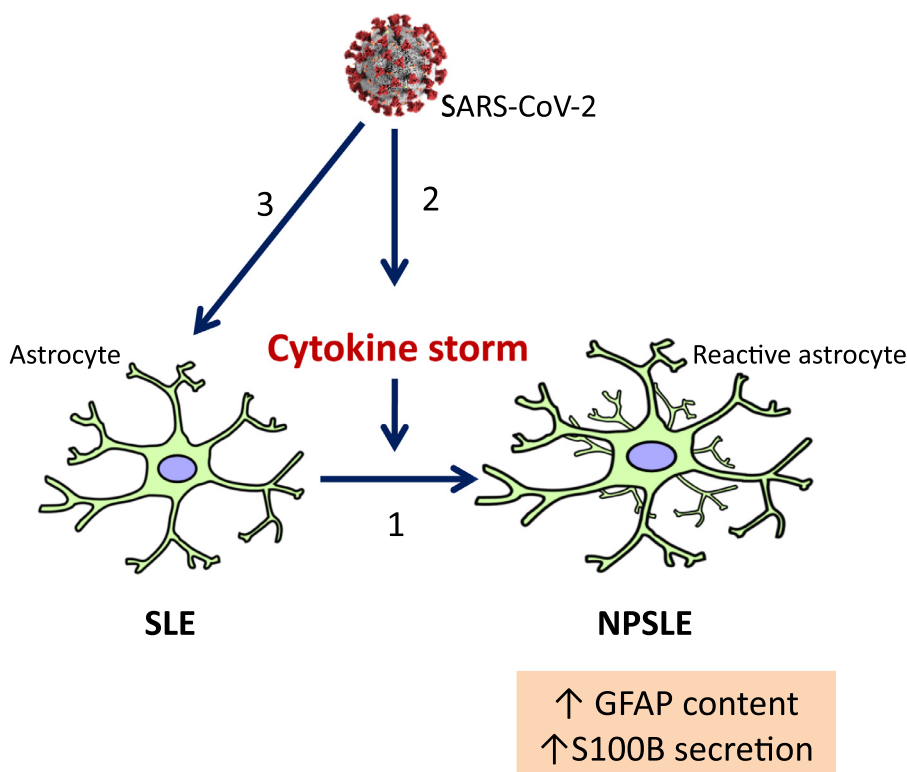
Utility of Serum S100B as A Marker in Systemic Lupus Erythematosus Patients During and After the SARS-CoV-2 Pandemic

Our attention was drawn by a publication in the *Archives of Medical Research* discussing how SARS-CoV-2 may be involved in the development and pathogenesis of autoimmune diseases, such as systemic lupus erythematosus (SLE) and multiple sclerosis (MS) (1). The authors mentioned the effects of COVID-19 on brain tissue, particularly in MS patients.

In fact, the severity of COVID-19 is not limited to the respiratory system; it affects many other systems, including the central nervous system (CNS). Neural changes are variable, including anosmia and ageusia, mood changes (especially depression), anxiety and even loss of conscious-

ness and cognitive deficits (2). At the beginning of the pandemic, the debate focused on whether direct effects on nerve cells occurred (neuroinfection), or whether these effects were secondary to systemic changes, such as hypercytokinemia, hypercoagulability or hypoxemia (3). The scenario is complex and both mechanisms are probably involved. Some markers of brain injury have been investigated in COVID-19, such as the astroglial proteins, GFAP (glial fibrillary acidic protein) and S100B (S100 calcium-binding protein B) (4,5).

We want to reinforce the hypothesis of autoimmune diseases being induced by SARS-CoV-2, as pointed out by



**Figure 1.** Potential mechanisms by which glial reactivity may be induced in NPSLE patients with COVID-19 (1). In the first condition, the inflammatory impact of the rheumatic disease on intact astrocytes in the CNS (in SLE) initially triggers the glial reactivity found in NPSLE, characterized by increased GFAP expression (with or without its release to the extracellular space) and increased secretion of S100B (2). In the second condition, the cytokine storm induced by SARS-CoV-2 (along with hypoxemia and thrombotic events) produces glial reactivity, which may or may not overlap with condition 1 (3). In the third condition, SARS-CoV-2 directly causes glial reactivity (neuroinfection), which may or may not overlap with condition 1.

Zhou S-Y et al., but also emphasize the difficulty of assessing the involvement of the CNS in cases of SLE. High scores of depression and anxiety were remotely identified in SLE patients and associated with isolation, difficulty in obtaining medication and access to health care services (6). The patients in that study were considered to be asymptomatic for COVID-19, but there was no laboratory test performed. This is important because of the overlap in symptoms that exists between active SLE and the manifestations of COVID-19, including fever, malaise and joint pain, making it difficult to differentiate between the two diagnoses. The vulnerability of SLE patients to depression and anxiety was also reported in another study (7), and is probably a common factor present in all patients with chronic diseases (8).

Neuropsychiatric manifestations in SLE (NPSLE) patients with COVID-19 are possibly due to the CNS involvement by SLE and aggravated by SARS-CoV-2 (Figure 1). However, we should not underestimate the capacity for viral aggression (direct or indirect) to occur independently of SLE, and the possibility that SARS-CoV-2 may trigger or even induce SLE and NPSLE.

Nevertheless, the involvement of the CNS in COVID-19 in SLE patients deserves a more detailed investigation. Indeed, CNS compromise in SLE patients with COVID-19 (confirmed with laboratory tests) is not trivial. In this case, serum S100B, which is increased in cases of brain injury caused by COVID-19, may be very useful in distinguishing NPSLE cases (9). Furthermore, considering that COVID-19 seems to leave long-term sequelae, including in the CNS, the measurement of serum S100B, among other markers, deserves investigation in SLE patients, both during the pandemic and to assess post-COVID damage (10).

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### Conflict of Interests

The authors declare that they have no conflicts of interest.

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ELENA NORIS-GARCÍA

*Instituto de Nefrología,*

*Departamento de Inmunología,*

*Havana, Cuba*

MARIA DE LOS

ANGELES ROBINSON-AGRAMONTE

*Universidad de Ciencias Médicas de La Habana*

*and Centro Internacional de Restauración Neurológica,*

*Departamento de Neuroinmunología,*

*Havana, Cuba*

CARLOS-ALBERTO GONÇALVES

*Universidade Federal do Rio Grande do Sul,*

*Programas de Pós-Graduação*

*em Bioquímica e Neurociências,*

*Porto Alegre, Brazil*

Address reprint requests to: Carlos-Alberto Gonçalves, Department of Biochemistry, Universidade Federal do Rio Grande do Sul Ramiro Barcelos, 2600-Anexo, Lab33, 90035-003, Porto Alegre, Brazil; Phone: (+55) (51) 330085567  
E-mail: [casg@ufrgs.br](mailto:casg@ufrgs.br)

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