

## Letters

### TO THE EDITOR

## Is Platelet-Activating Factor the Missing Link Between COVID-19 and Atherosclerosis?



We read with interest the recent review by Chidambaram et al.<sup>1</sup> However, we need to point out the lack of reference to the role of platelet-activating factor (PAF) as the missing link between COVID-19 and atherosclerosis. PAF is the most potent lipid inflammatory factor,<sup>2</sup> which has gained attention for its dual role in COVID-19 and atherosclerosis.<sup>3</sup>

PAF is known to play a pivotal role in the pathogenesis of atherosclerosis by promoting endothelial dysfunction, inflammation, and platelet aggregation.<sup>4</sup> Interestingly, SARS-CoV-2 induces a hyper-inflammatory state, often termed a "cytokine storm," which can exacerbate pre-existing atherosclerotic conditions or initiate new vascular inflammatory events that can lead to or exacerbate cardiovascular symptomatology.

PAF is implicated in inflammation which can trigger a local vascular reaction within arterial plaques, resulting in thrombosis, plaque disruption, and acute ischemic events.<sup>2</sup> Endothelial cell dysfunction, an early event, and the subsequent platelet activation and adhesion to the activated endothelium are central to both atherosclerosis and COVID-19. Moreover, SARS-CoV-2 spike protein can stimulate the release of PAF from monocytes, triggering cytokine release and perivascular inflammation.<sup>5</sup>

Understanding the role of PAF in COVID-19 could open new therapeutic avenues. Targeting PAF signaling pathways may not only mitigate the severe inflammatory responses associated with the virus but

also reduce the cardiovascular complications that contribute significantly to the morbidity and mortality of COVID-19 patients. Recognizing the role of PAF in this context can enhance our approach to treatment and potentially improve outcomes for patients affected by both COVID-19 and atherosclerosis.

Constantinos A. Demopoulos, PhD<sup>a</sup>

\*Smaragdi Antonopoulou, PhD<sup>b</sup>

Theoharis C. Theoharides, MS, MPhil, PhD, MD<sup>c</sup>

\*Department of Nutrition and Dietetics  
School of Health Science and Education  
Harokopio University

Athens, Greece

E-mail: [antonop@hua.gr](mailto:antonop@hua.gr)

From the <sup>a</sup>National and Kapodistrian University of Athens, Athens, Greece; <sup>b</sup>School of Health Science and Education, Harokopio University, Athens, Greece; and the <sup>c</sup>Institute for Neuro-Immune Medicine, Nova Southeastern University, Clearwater, Florida, USA.

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

### REFERENCES

1. Chidambaram V, Kumar A, Sadaf IM. COVID-19 in the initiation and progression of atherosclerosis pathophysiology during and beyond the acute phase. *JACC: Adv.* 2024;3:1-21.
2. Lordan R, Tsoupras A, Zabetakis I, et al. Forty Years since the structural elucidation of Platelet-Activating Factor (PAF): historical, current, and future research perspectives. *Molecules.* 2019;24(23):4414.
3. Demopoulos C, Antonopoulou S, Theoharides TC. COVID-19, microthromboses, inflammation, and platelet activating factor. *Biofactors.* 2020;46(6):927-933.
4. Antonopoulou S, Demopoulos CA. Protective effect of olive oil microconstituents in atherosclerosis: emphasis on PAF implicated atherosclerosis theory. *Biomolecules.* 2023;13(4):700.
5. Antonopoulou S, Petsini F, Detopoulou M, et al. Is there an interplay between the SARS-CoV-2 spike protein and platelet-Activating factor? *Biofactors.* 2022;48(6):1271-1283.