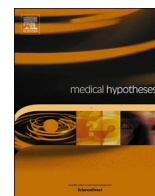




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## Correspondence

**Airways to heaven: Caution needed when exercising during COVID-19**

Dear Editor,

We read with particular interest the work of Heffernan et al. “*Exercise as medicine for COVID-19: On PPAR with emerging pharmacotherapy*” [1] which focuses on the protective role of exercise in SARS-Cov-2 infection, putatively by means of PPAR $\alpha$  upregulation. Although suggestive, the article presents a couple of questionable arguments.

The modulatory activity of PPAR $\alpha$  in the host-pathogen interaction is poorly characterized. For example, the study of Ehrlich et al. [2], reporting PPAR $\alpha$  upregulation upon fenofibrate application on isolated alveolar cells, also shows that the infection itself is capable of upregulating alveolar PPAR $\alpha$  gene (along with PPAR $\gamma$  and C/EBP), probably as a consequence of ER stress. Pharmacological stimulation of PPAR $\alpha$  was shown to suppress INF-I, a molecule whose deficiency gives rise to a more severe form of infection [3]. PPARs are also known to modulate oxidative stress, and specific ligands of each subtype may also display different results in regulating redox status. In addition, the efficacy of synthetic or dietary agonists in improving resistance to pathogen challenge is still controversial, making the role of PPAR $\alpha$  in infectious diseases a debatable issue.

Second, physical activity bears health benefits only within a specific range of time and intensity, occurrence that strictly applies to SARS-Cov-2 infection, in which a delicate balance between pro and anti-inflammatory responses influences clinical outcome, varyingly. Practicing habitual physical activity or training during the incubation/active period may have different health implications. Under certain circumstances, exercise may even worsen airways inflammation [4]. The augmented ventilation may enhance the spreading of infection to the lower airways, aggravating clinical conditions. Systemic response to SARS-Cov-2 represents an intricate pathophysiologic scenario, where the health outcomes rely on the interaction of multiple players. The mentioned variables coupled with the immunomodulatory effect of exercise [5] might blunt the presumptive health gain warranted by PPAR $\alpha$  upregulation, potentially reducing the effectiveness of physical activity.

**Declaration of Competing Interest**

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

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