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Letter to the Editor

Letter to the Editor From Asadipooya: "Obesity and COVID-19: Mechanistic Insights From Adipose Tissue"

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To the Editor:

I read with interest the review article by Yu et al entitled "Obesity and COVID-19: Mechanistic Insights From Adipose Tissue." The authors stunningly explained the role of cell surface receptors, angiotensin-converting enzyme 2 (ACE2) and dipeptidyl peptidase 4 (DPP4) as the typical ways to infect host cells including adipocytes, which lead to a large reservoir for SARS-CoV-2 in obesity. They also discussed the potential detrimental roles of soluble ACE2 and overexpression of DPP4 in obesity, which can increase COVID-19 disease severity (1).

Soluble ACE2 exhibits a positive correlation with mortality rate due to cardiovascular and non-cardiovascular causes independent of age, sex, and ancestry (2). Moreover, changes in membrane flexibility besides viral weight and radius result in more engulfment into the host cells (3). Therefore, increases in disintegrin and metalloproteinase domain-containing protein 17 expression and ACE2 shedding in obesity (4) yield greater soluble ACE2 and loss of membrane ACE2, which diminish membrane flexibility. Consequently, SARS-CoV-2 can attach to soluble ACE2 and harvest the viral particles with higher weight and radius, leading to more engulfment (5).

DPP4 can interact with SARS-CoV-2, transduce metabolic signals, and modulate inflammation (1, 6, 7). DPP4 inhibitors potentially improve COVID-19 outcomes (1, 5). However, DPP4 inhibitor may increase ACE2 protein levels (8). Therefore, I argue that the use of DPP4 inhibitors in COVID-19 would be safer if combined with a medication that antagonizes the host protease and entry cofactors transmembrane protease serine protease-2 and metalloproteinase domain-containing protein 17 and reduces soluble ACE2 levels. As a result, the combination of DPP4 inhibitors and spironolactone not only reduces the SARS-CoV-2 entry into the host cells but will also provide anti-inflammatory, antithrombotic, antiproliferative, and antifibrotic effects (5).

Disclosures

The author has declared that no conflict of interest exists.

Data Availability

There is no data generation or analysis. Therefore, data sharing is not applicable to this article.

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