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Letter to the Editor

COVID-19 fatal outcomes: Role of the endothelial glycocalyx in both cell adhesion and migration

Gerardo Tricarico [a,b], *Valter Travagli* [c,*]

[a] *COVID-19 Unit, Presidio Ospedaliero Sant'Andrea, Vercelli, Italy*
[b] *UCM United Campus of Malta, Msida, Malta*
[c] *Università degli Studi di Siena, Dipartimento di Biotecnologie, Chimica e Farmacia — Dipartimento di Eccellenza Nazionale 2018-2022, Siena, Italy*

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Dear Editor-in-Chief,

We read with great interest the review regarding the correlation between the systemic inflammatory microvascular endotheliopathy and the endothelial glycocalyx damage in COVID-19 [1]. We have found what is reported there thoroughly adequate. In this regard, we would like to suggest food for thought that could lead to further study, also with a view to the appropriateness of therapeutic treatments in relation to the developmental stages of the disease [2]. First, in our opinion, the involvement of the cell membrane of the endothelial cell is an active part in determining the prognostic evolution [3]. In detail, the retracting action of the actin fibrils integral with the glycocalyx plays a fundamental role in the non-physiological recruitment of some corpuscular elements at the level of the circulatory bloodstream. Among these, we can include platelets, the cause of thrombotic phenomena and CD8+ lymphocytes of the immune system. Among other things, the induction of arrhythmias and myocarditis can also be correlated with the abnormal migration of CD8+ lymphatic cells and their consequent cytotoxic action. These effects are directly correlated with the shear stress variations deriving from the morphological variations of the glycocalyx in the various anatomical districts, inducing potential cellular changes, also via epigenetics. This aspect opens the way to the evaluation of a hypothesized upstream genetic polymorphism [4], capable of at least partially explaining the severity of the pathological evolution in a small cohort of patients, correlated with the mechanism by which the cell expresses and produces the glycocalyx.

Secondly, understanding these aspects would make it possible to identify personalized therapeutic treatments. Probably, the reported administration of sialic acid may not give the desired results. Instead, it may be more effective to find therapies that can restore homeostatic conditions and induce the endothelial cell to produce glycocalyx with characteristics more appropriate to the function envisaged for that anatomical district. Although, as known, an excessive development of ROS damages the glycocalyx, a regulated increase could instead act as an action inducing its restoration, according to a principle of balance between distress and eustress. To confirm this hypothesis, there is evidence in which patients affected by neurodegenerative disorders treated with paradoxical oxidative therapies manage to overcome the critical phase of the disease [5].

Ultimately, the partial or complete reduction of the glycocalyx layer alone is not enough to explain the phenomenon of parenchymal damage. The increase in CD8+ activity with the automatism generated by the close adhesion at the endothelial cell-lymphocyte/platelet level and at the same time lymphopenia with a decrease in circulating CD8+ lymphocytes resulting from their increased adhesion to the vascular wall

* *Corresponding author*. Università degli Studi di Siena, Dipartimento di Biotecnologie, Chimica e Farmacia — Dipartimento di Eccellenza Nazionale 2018-2022, Viale Aldo Moro, 2, 53100, Siena, Italy.
E-mail address: valter.travagli@unisi.it (V. Travagli).
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gives rise to a further transendothelial migration that on the one hand generates disseminated intravascular coagulation, on the other generates parenchymal damage.

Conflicts of interest

G. Tricarico and V. Travagli 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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