A SARS-CoV-2 impedimetric biosensor based on the immobilization of ACE-2 receptor-containing entire cell membranes as the biorecognition element

<u>Juliana Cancino-Bernardi</u>¹, Edson José Comparetti², Natália Noronha Ferreira², Renata Rank Miranda², Marco Montero², Isabella Sampaio do Nascimento², Paulo Inácio da Costa³, Valtencir Zucolotto⁴

¹University of São Paulo (*FFCLRP*) , ²University of São Paulo (*IFSC*) , ³São Paulo State University (*Department of Clinical Analysis*) , ⁴Universidade de São Paulo (*IFSC*)

e-mail: jucancino@usp.br

Biomimicking nanoparticles with cell membranes are one of the most innovative approaches to enhance performance, selectivity, and functionality for biomedical applications^{1,2}. The cell membrane coating provides several advantages such as enhanced biocompatibility, improved stability, and specific targeting capabilities due to inherit properties of the source cells. These advantages can be transferred to the biosensing scenario. For examples, to improve the specificity and selectivity of SARS-CoV-2 biosensors, the angiotensin-converting enzyme 2 (ACE-2) transmembrane receptor, that are overexpressed in respiratory model cells, was used as biorecognition element. In this new SARS-CoV-2 detection platform, cellular membranes from VeroCCL81 (mVero) and Calu-3 (mCalu) cells (which overexpress the ACE-2 transmembrane receptors) were extracted and immobilized as vesicles on an indium tin oxide electrode (ITO). Electrochemical impedance spectroscopy was used to optimize the performance of the developed devices for SARS-CoV-2 detection. The membrane biosensors showed limit of detection of 10.0 pg/mL and 7.25 pg/mL and limit of quantification of 30.4 pg/mL and 21.9 pg/mL were achieved with satisfactory accuracy for ITO-APTES-mVero and ITO-APTES-mCalu, respectively. Selectivity studies revealed that this platform was able to differentiate the target spike proteins from NS1 proteins from dengue and Zika viruses. The use of biorecognition between cell membranes that express the ACE-2 receptors and the virus spike protein may be a new and efficient way to diagnose SARS-CoV-2, especially in terms of the cost of production and isolation, when compared to other targets.

Acknowledgments: CNPq

References:

[1] J. Cancino-Bernardi, et al. Talanta, 2023, 253, 124008.

[2] N. F. Noronha, J. Cancino-Bernardi, et al. Chapter 13. In: Smart nanomaterials for bioencapsulation. Ed. Amsterdam: Elsevier, 2022, 223-232.