



August 30th, 2024, Paris-Saclay France

To the Editor,

We are pleased to submit our manuscript entitled "*Dual Fractions Proteomic Analysis of Silica Nanoparticles Interactions with Protein Extracts*" for consideration in the special issue "Applications of Silica and Silica-Based Composites" of the Materials journal.

This study investigates the complex interactions between nanoparticles and protein extracts using a novel dual-fraction nano-LC MS/MS mass spectrometry approach. While previous research has focused primarily on characterizing the corona, our work goes beyond this by analyzing both bound and unbound proteins in *Saccharomyces cerevisiae* protein extracts exposed to silica nanoparticles (SiNPs).

Our findings demonstrate the power of this dual-fraction mass spectrometry analysis:

- *Unique protein signatures*: We identified distinct protein profiles for each fraction, highlighting the diverse mechanisms involved in nanoparticle interaction with cellular components.
- *Comprehensive response*: Combining both fractions revealed a larger proteomic response to SiNP exposure compared to single-fraction analysis, suggesting a broader impact on cellular function.
- *Novel "impacted" proteins subset*: We identified 196 proteins demonstrably affected by SiNPs, likely undergoing conformational changes or aggregation due to nanoparticle exposure. This finding opens up new avenues for understanding the biological consequences of nanoparticle interaction at the proteomic level.

We believe this work contributes significantly to the field by providing a more comprehensive understanding of nanoparticle-protein interactions and identifying a novel class of "impacted" proteins.

The manuscript is well-structured, clearly written, and supported by robust data analysis. We are confident that it will be of interest to the readers of Materials.

We thank you for your time and consideration.

Sincerely,

Dr Pin and Dr Aude

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