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Editor-in-Chief

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Dear Editor,

We are pleased to submit for consideration our original research article entitled "Serological Proteome Analysis (SERPA) Reveals Breast Cancer-Associated Autoantibodies Targeting Placental Antigens" for publication in the *Journal of Translational Medicine*.

In this study, we applied serological proteome analysis (SERPA) of human first-trimester placental proteins to identify breast cancer-associated autoantibody targets. We screened serum reactivity in 86 early-stage breast cancer patients and 86 non-cancer controls, identified 33 differentially reactive placental proteins by LC-MS/MS, and validated 12 candidates using ELISA and immunohistochemistry. Six proteins (PDIA3, STIP1, CCT2, PARK7, PRDX6, and LDHB) showed significantly elevated reactivity in breast cancer, and PARK7/PRDX6 showed distinct subcellular localization patterns in malignant versus normal breast tissues. Combinatorial analyses further yielded multi-marker panels (specificity 64–73%; sensitivity 77–97%) supporting the potential of placenta-reactive autoantibody signatures for non-invasive early breast cancer detection. Proteomics data are available via PRIDE/ProteomeXchange (dataset PXD071458).

We believe that this manuscript will be of interest to readers of the *Journal of Translational Medicine*, as it provides a experimentally validated approach for the discovery of blood-based immunodiagnostic biomarkers in early-stage breast cancer. The study further illustrates the potential of placenta-derived antigens as a source of serological biomarkers and contributes to a better understanding of tumor-associated humoral immune responses.

This study was approved by the Ethics and Review Boards of the Avicenna Research Institute (ARI) (Approval No. 1397.007), and all participants provided written informed consent. The manuscript has not been published previously, is not under consideration elsewhere, and all authors have approved its submission. The authors declare no conflict of interest.

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Sincerely,

Allan Stensballe, PhD
on behalf of all co-authors