Clinical Chemistry

Correlations Within and Between Highly Multiplexed Proteomic Assays of Human Plasma

Article:
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Correlations Within and Between Highly Multiplexed Proteomic Assays of Human Plasma.
Clin Chem 2025; 71(6): 677–87. https://doi.org/10.1093/clinchem/hvaf030

Guest: Dr. Mary Rooney from the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health and the Welch Center for Prevention, Epidemiology, and Clinical Research.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the Association for Diagnostics & Laboratory Medicine. I'm Bob Barrett. Researchers in many fields, including biomarker discovery, drug development, and clinical diagnostics, rely on the simultaneous measurement of thousands of proteins.

This proteomic approach enables scientists to discover new protein networks or identify patterns of change that can't be seen when performing single-protein measurements. Several commercial proteomic platforms have been developed, with the most prominent undergoing several rounds of expansion to include an ever-increasing array of protein targets. Since results generated by these platforms drive important downstream decisions, they must be accurate and reliable, but to this point, little is known about how the multiplex platforms compare to one another. Are they essentially interchangeable? If not, is one approach preferred? Are the takeaway points from proteomic studies reproducible, or are they dependent on the proteomic platform chosen?

A new research article, appearing in the June 2025 issue of *Clinical Chemistry*, addresses these questions, comparing two of the leading proteomic platforms head-to-head using a panel of plasma specimens from participants throughout the United States. In this podcast, we are joined by the article's author. Dr. Mary Rooney is an Assistant Research Professor in the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health. She is also Core Faculty at the Welch Center for Prevention, Epidemiology, and Clinical Research.

So Dr. Rooney, before we discuss the study's findings, let's get a little basic. Can you briefly introduce us to the concept of proteomics and the SomaScan and Olink platforms that you are comparing?

Mary Rooney: Of course. So, proteomics is all about measuring the proteins in our bodies. It's this powerful tool for discovery and hypothesis-generating research. As you mentioned, the two

main proteomics platforms that researchers are using includes the SomaScan platform and also the Olink platform.

So the SomaScan platform uses an actimer-based technology, whereas the Olink platform is antibody-based. We've seen in the last decade that the number of assays on these proteomic platforms has grown sizably. So now the SomaScan platform is capable of quantifying over 10,000 assays on the SomaScan 11K, while Olink's latest platform, the Olink Explore HT, is capable of quantifying over 5,000 assays.

Just briefly, we know from prior research that these earlier versions of the platforms can have some variable agreement. We just haven't seen a head-to-head comparison of the agreement of these latest platforms, the SomaScan 11K and Olink Explore HT.

Bob Barrett: Well, that leads me right into this next question. On the SomaScan 11K and the Olink Explore HT, only about 10% of the overlapping proteins had high cross-platform agreement. How should researchers interpret or reconcile findings across these latest platforms when the agreement across platforms is this variable?

Mary Rooney: That's a great question. As you mentioned, the cross-platform agreement can be quite variable, especially for the prior versions of the SomaScan and Olink platforms, which had fewer measurable assays. It's important for researchers to be aware that even if these platforms are nominally measuring the same protein, they might actually be detecting different modifications of the same protein.

With that in mind, the lack of replication across platforms doesn't necessarily mean that one platform is wrong per se, but confirming these key findings using complementary methods can help strengthen confidence in the results across these platforms.

Bob Barrett: In this paper, you explored various methods for handling data below the limit of detection. How did the handling of values below the limit of detection affect your interpretation of the data, particularly for Olink?

Mary Rooney: That's an important point. We found that for these different approaches for handling the values below the limit of detection, that it can have a substantial impact on our measures of precision. In our study, the Olink Explore-HT data had numerous proteins with high variability, especially for those proteins that were below the platform's limit of detection.

But for example, when we replaced those low or undetectable values with half the limit of detection, precision improved substantially. Researchers working with these proteomics data will really want to think about how they handle low abundance proteins in their analyses. These imputation methods, they can reduce noise and help improve reliability, but these approaches should be applied thoughtfully with an understanding of the underlying data distribution.

But on the other hand, the SomaScan 11k platform had nearly all of the assays with the vast majority of protein values above the limit of detection.

Bob Barrett: Finally, Dr. Rooney, in your opinion, what's the most important message for researchers using these proteomic platforms going forward?

Mary Rooney: My key takeaway is that proteins are very complex. Validation will just continue to be an ongoing and important effort for researchers. We'll need additional data that'll be very helpful for the field of proteomics going forward.

But in the meantime, it's really important for researchers to be aware of the strengths and limitations of these platforms and also some of the technical nuances of the assays that they're planning to use. Also, our analysis only focused on one aspect of the comparison in terms of precision. In our study, we found that SomaScan 11k did maintain precision at a large scale. However, we know that there are other considerations that we weren't able to consider given our sample size, such as which platform may have more assays that are associated with genetic variants in the protein encoding region. It'd be really interesting to see how the SomaScan 11k and Olink Explore HC compare in this regard going forward.

Bob Barrett: That was Dr. Mary Rooney from Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. She wrote a research article in the June 2025 issue of *Clinical Chemistry* comparing multiplexed proteomic assays, and she's been our guest in this podcast on that topic. I'm Bob Barrett. Thanks for listening.