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Urine Measurements on the SomaScan® v4.1 Assay

Urine is a non-invasive sample type with strong potential for biomarker discovery. We have developed sample processing and data standardization strategies to now utilize urine in the SomaScan Assay. Performance characteristics for urine in the SomaScan Assay are described.

Introduction

Urine is an important biological fluid easily collected by non-invasive methods and already used in clinical diagnostics to identify a range of kidney related diseases, such as acute kidney injury, membranous nephropathy and diabetic nephropathy[1].

Studies using liquid chromatography-mass spectrometry (LC-MS) have now identified at least 6085 proteins in healthy urine[2]. With the increasing ability to identify proteins through a less invasive method, the urine proteome could be an important alternative to plasma and serum proteomes in clinical diagnostics.

Some notable uses include identifying and monitoring many different health conditions including heart disease, cancers, and inflammatory diseases. Additionally, the urine proteome could be used as an alternative or in combination with the blood proteomes in all stages of drug development from discovery to clinical trials to determine efficacy of drug treatments.

Today SomaLogic's proprietary technology, the SomaScan® Assay, delivers robust proteomic profiles in plasma and serum samples. We are now able to deliver that same quality of data using urine as a validated sample matrix. Details regarding the assay's power in determining proteomic profiles is detailed in our SomaScan Assay Technical White Paper (SL00000572).

Urine as a Sample Matrix

Compared to plasma and serum, urine can present significant challenges as a sample type, due to the variability in composition of urine between individuals and even from the same individual at different time points.

To maintain homeostasis of the blood, the kidney constantly varies the composition of urine, resulting in large concentration differences of salts, metabolites and proteins between samples. In order for urine to be a suitable sample type for the SomaScan Assay, we developed a method to normalize salts, metabolites, and total protein content in individual samples.

This is achieved by an automated buffer exchange of the samples into the SomaScan Assay buffer, followed by dilution to a standardized total protein concentration. The concentration range of proteins in urine is smaller than in plasma and serum; therefore, processed urine samples can be tested at a single total protein concentration with all SOMAmer® reagents together.

SomaScan Assay Data Standardization

When testing urine samples on the SomaScan Assay v4.1, around 61% of SOMAmer reagent measurements are at or near the limit of detection (LoD) in a large proportion of samples tested. In addition, about 0.4% of SOMAmer reagents often measure near or at saturation.

This distribution requires the use of a group-based normalization scheme during SomaScan Assay data standardization.

Three separate groups were defined during the validation procedure; data normalization is performed separately in each of them. The S1 group is comprised of reagents that are often measured at or below the LoD for most samples in the population reference. The reagents in the S3 group are those that are often close to saturation in most samples.

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The S2 group includes analytes that are typically above the LoD and below the saturation; these were defined as analytes not in the S1 or S3 groups.

The S2 group contains ~38.5 % of the SOMAmer reagents in the SomaScan Assay. The characterization metrics for the SomaScan urine assay were computed for the S2 group for reporting in Table 1.

Metric	Condition	Results
Precision (S2 group)	Median Total CV (SomaScan assay) 90th percentile CV (SomaScan assay)	5.6% 12.3%
Signal to Noise (S2 group)	Median Signal to Noise (S2 group)	1.7
Population F-Statistics (S2 group)	Percentage of reagents with population variance over assay variance, with 95% confidence	93%
Sample Volume	Urine (per sample)	550 µL

TABLE 1 Summary of SomaScan Assay v4.1 metrics to human targets in urine.

SomaScan Assay Characterization with Urine

The SomaScan Assay v4.1 has been validated using buffer-exchanged, protein-adjusted urine samples. The assay performance met all required acceptance criteria. The total median Coefficients of Variation (CV) of QC samples based on intra-run and inter-run data were less than 6.0% for the assay.

SomaScan Assay Characterization with Urine

The SomaScan Assay is a powerful, highly multiplexed tool well established for blood-based proteomics. We have developed methods to process urine samples for testing on the same Assay we use for plasma and serum samples. Table 1 summarizes the urine-specific metrics of the SomaScan Assay v4.1 (see the SomaScan technical note for additional metrics). SomaLogic's SomaScan Assay technology provides significant advantages in sample volume, cost, time, multiplexing capability, dynamic range, and flexibility of readout over many alternate protein biomarker Assays.

References

1. Kalantari S, et al. (2015) Human Urine Proteomics: Analytical Techniques and Clinical Applications in Renal Diseases. International Journal of Proteomics Volume 2015, Article ID 782798 (DOI:10.1155/2015/782798)
2. Zhao M, et al. (2017) A comprehensive analysis and annotation of human normal urinary proteome. Nature Scientific Reports 7: 3024 (DOI:10.1038/s41598-017-03226-6)

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