Glycosylation Changes as Non-Invasive Biomarkers for Lupus Nephritis Detection and Prognosis

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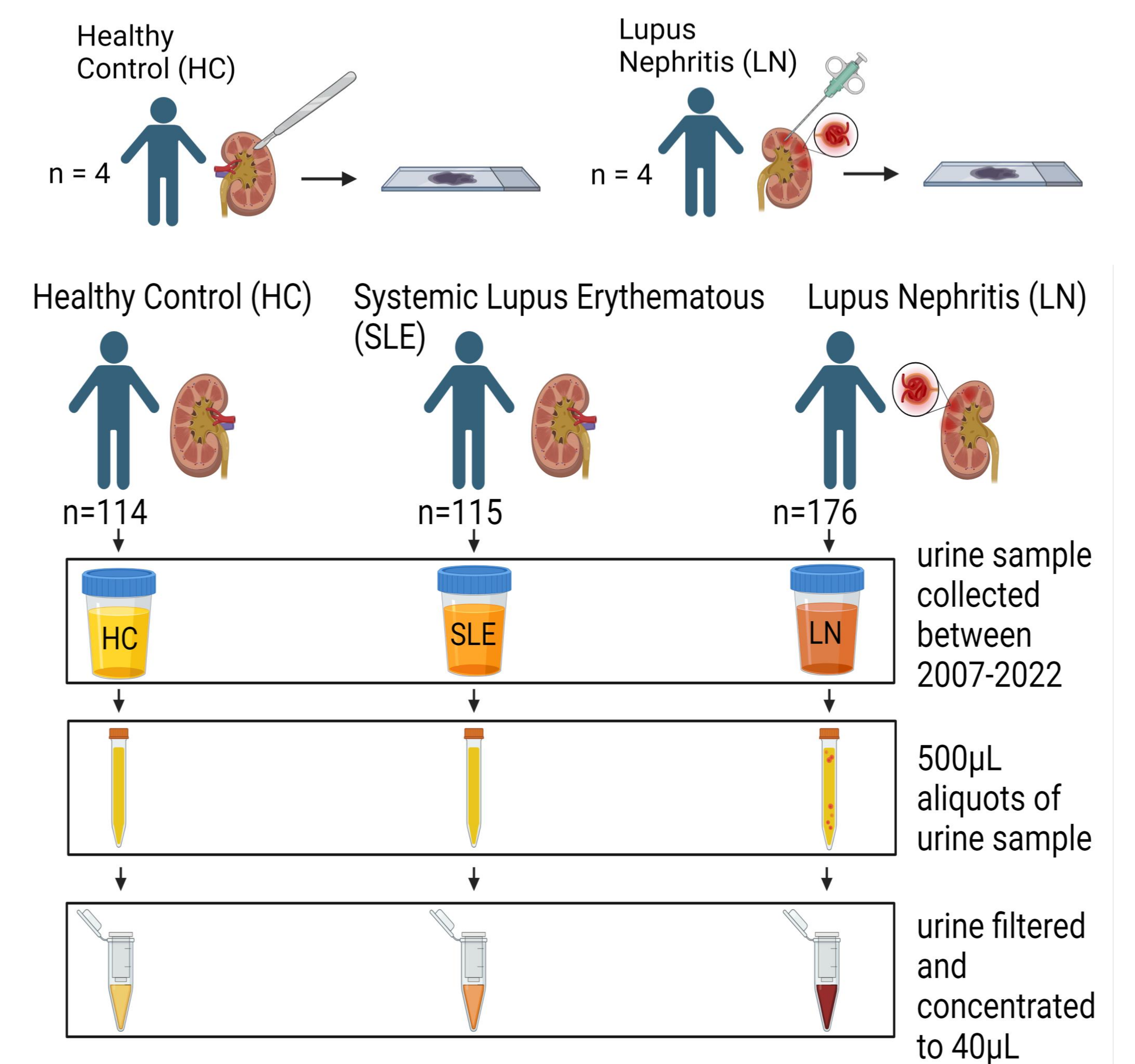
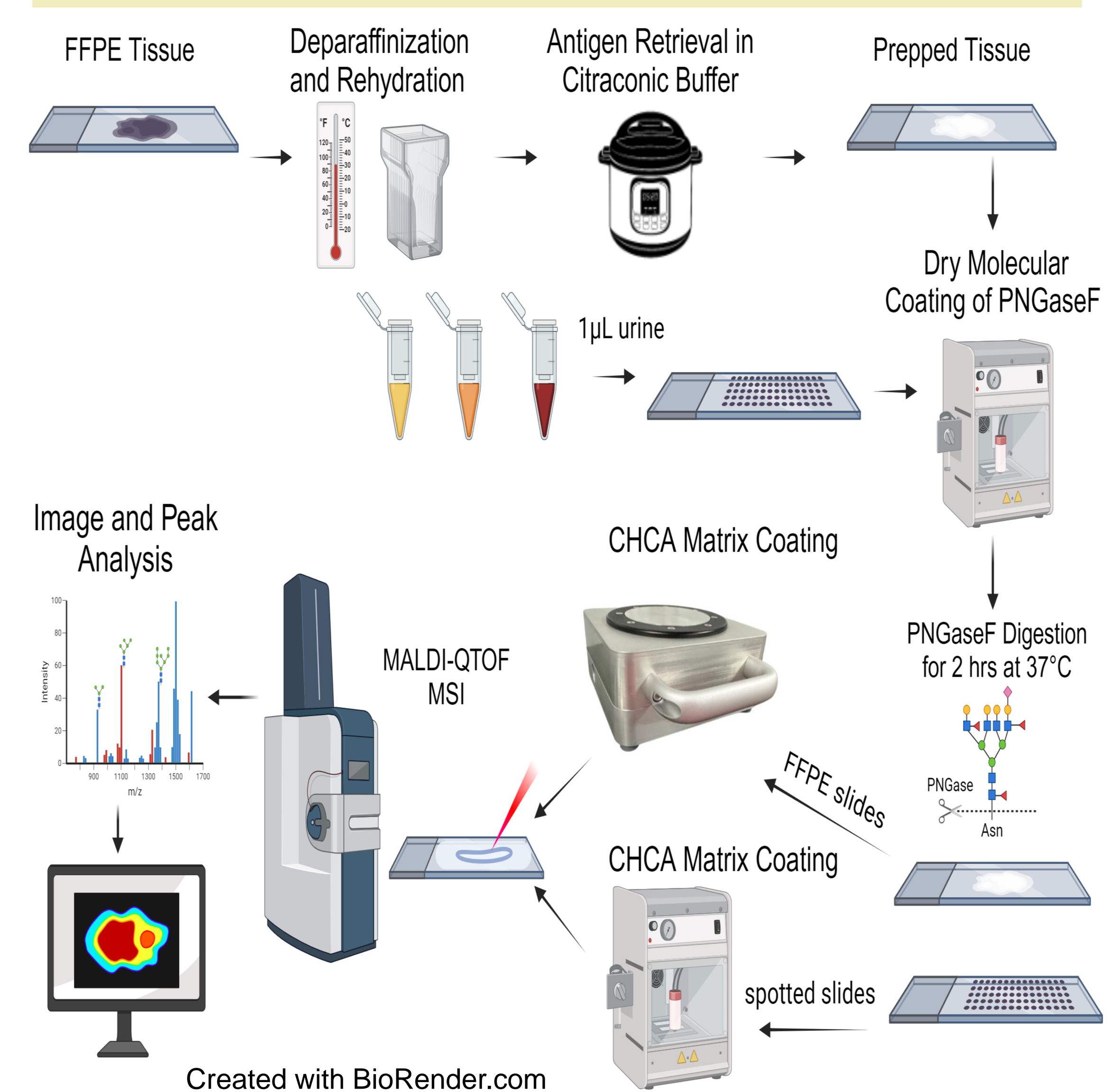
OVERVIEW

- Lupus Nephritis (LN) affects nearly 50% of patients with Systemic Lupus Erythematosus (SLE) and is linked to poor outcomes[1-2]. Current urine markers, such as the protein-to-creatinine ratio, lack specificity for detecting glomerular damage, often requiring repeated kidney biopsies to monitor disease progression[2].
- Using MALDI-MSI, unique N-glycan signatures were identified in renal biopsies and urine samples from LN patients and controls (healthy or SLE), suggesting that LN-specific glycosylation changes could serve as non-invasive biomarkers for early glomerular injury.



METHOD



BIOPSY RESULTS

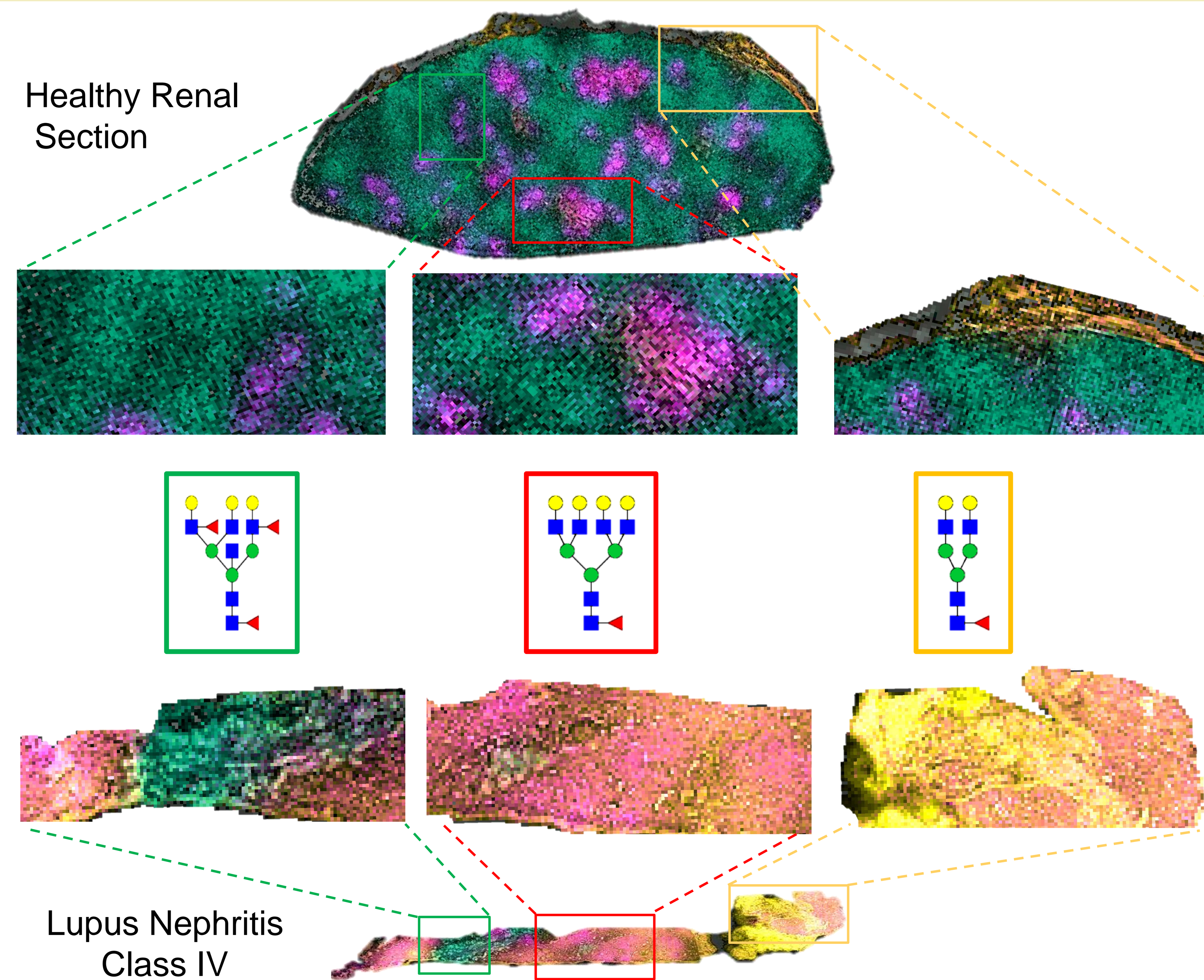


Figure 1. MALDI-MSI of Healthy kidney and Lupus Nephritis (LN) Biopsy. Three N-glycans are displayed: 2669 m/z (green/teal), localized in the proximal convoluted tubule; 2539 m/z (pink/fuchsia), localized in the glomeruli; and1809 m/z (yellow), associated with fibrosis

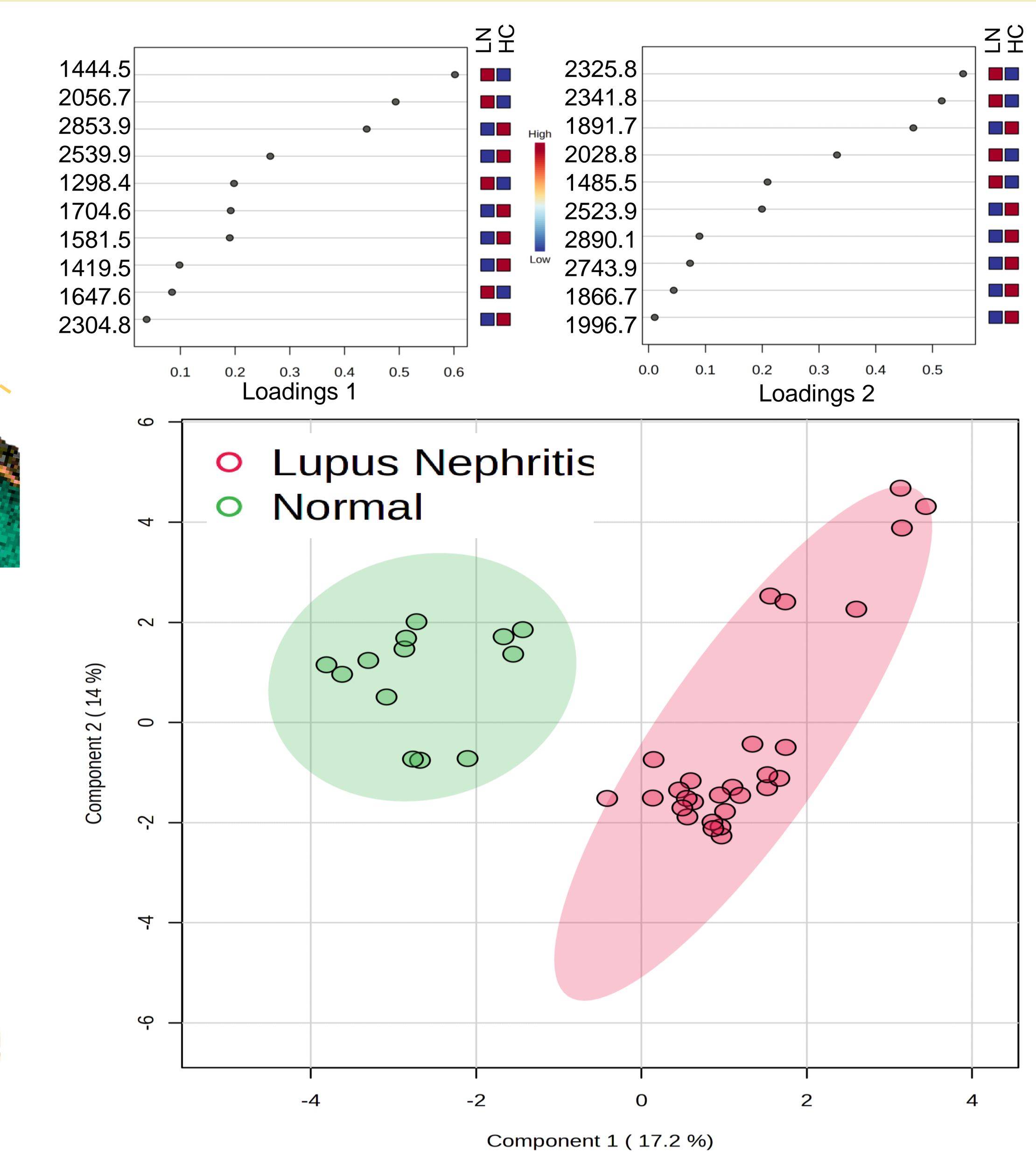


Figure 2. Sparse PLS-DA of N-Glycans Identified in Biopsies. The loading plots highlight the 20 N-glycans that contribute most to distinguishing between biopsy types. Loadings 1 (x-axis) and Loadings 2 (y-axis) represent the two components used in the analysis, with features retained after applying the sparsity penalty. The plot demonstrates clear separation between healthy controls (n=4) and LN samples (n=4).

URINE RESULTS

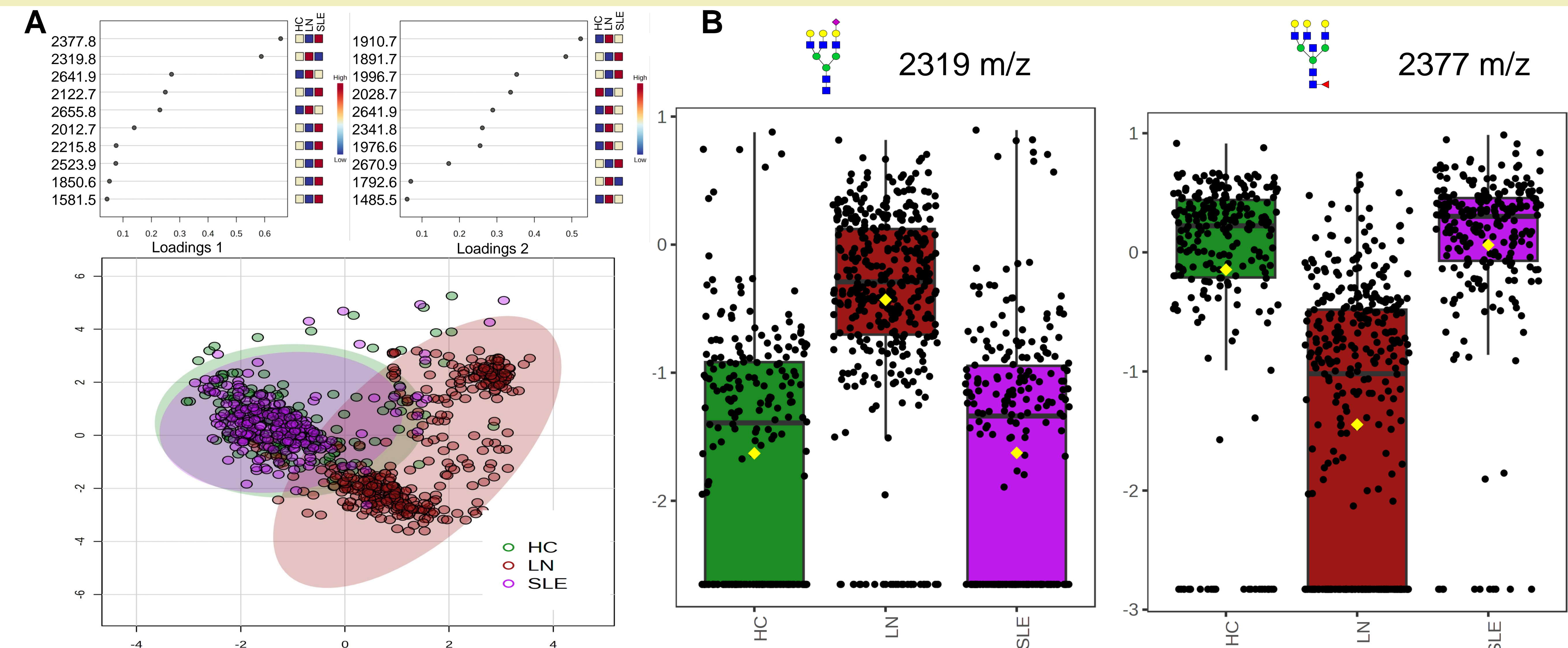


Figure 3. Sparse PLS-DA and Heatmap of N-Glycans Identified in Urine Samples
A) Sparse PLS-DA analysis of N-glycans in urine reveals clear separation between LN (N=176) and HC (N=114), SLE (N=114) samples.
B) Boxplots highlight two statistically significant N-glycans from a one-way ANOVA (p-value = 0.000005): 2319 m/z, a sialylated N-glycan upregulated in LN compared to controls, and 2377 m/z, a core-fucosylated N-glycan downregulated in LN compared to controls.

CONCLUSIONS AND FUTURE DIRECTIONS

Main Takeaways

- Healthy and lupus nephritis (LN) tissues have distinct N-glycan profiles; in healthy biopsies, N-glycans are highly localized to critical areas like the glomeruli, while LN tissues show more diffuse and weaker signals.
- Both healthy control (HC) and lupus nephritis (LN) biopsy tissues exhibited distinct glycomic signatures, with urine findings reflecting these differences. This suggests that urine could serve as a non-invasive alternative for glycomic analysis.

Future Directions

- Investigate how distinct N-glycan profiles in LN correlate with clinical outcomes, such as disease severity, kidney damage, and treatment response, to advance personalized medicine approaches for LN management.
- Explore the underlying mechanisms that contribute to the altered glycan patterns observed in LN and assess how these changes drive disease progression.

REFERENCES

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2. Bomback, Andrew S, and Gerald B Appel. "Lupus Nephritis: Diagnosis and Classification." UpToDate, 19 Oct. 2022.

ACKNOWLEDGMENTS

1. Department of Defense (DoD) Congressionally Directed Medical Research Programs (W81XWH-16-1-0640 and W81XWH-22-1-0330 awarded to T.N.). Opinions and interpretations are those of the authors and are not necessarily endorsed by the DoD.
2. 2023 LRA Administrative Supplement to Promote diversity in Lupus Research (award 1253588 to T.N. in support of A.A.)

Department of Pathology for providing patient biopsy samples and the Department of Rheumatology and the MUSC Core Center for Clinical Research biorepository for providing patient urine samples.

Figures were created using SCiLS lab, BioRender, and MetaboAnalyst

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