

Supplementary Material

Re-mining serum proteomics data reveals extensive post-translational modifications upon Zika and dengue infection

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Supplementary Figures

Figure S1: Modifications identified in spectral libraries

Modifications identified in spectral libraries generated from DDA samples. Libraries were generated with the following variable protein modifications: acetylation, carboxylation, formylation, glycosylation (monohexose (Hex), dihexose (Hex(2)), hexosamine (HexN), acetylhexosamine (HexNAc)), methylation (monomethylation, dimethylation), oxidation, phosphorylation, and sulfation. Carbamidomethylation (C) was set as a fixed modification. In total, 2,776 modifications were identified across the libraries.

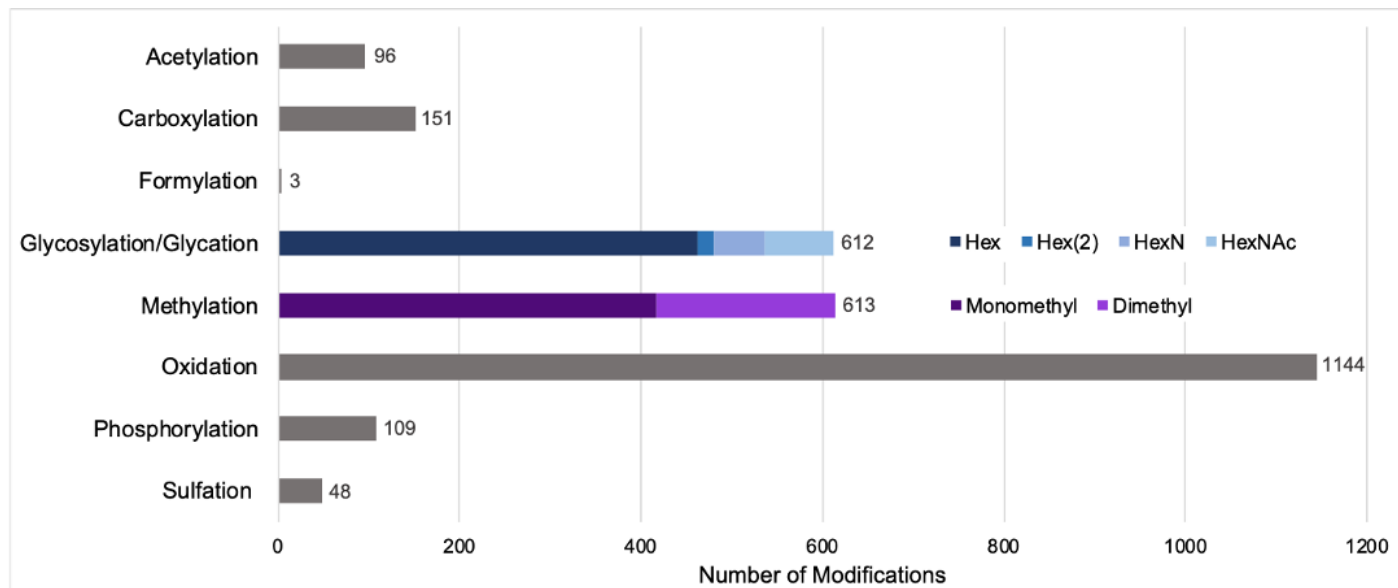


Figure S2: Glycosylation/glycation (GLY) modifications of peptides with significant differential abundance between Zika and dengue patient samples.

A) In the glycosylation/glycation category, 45 peptides with significant differential abundance between ZIKV and DENV patients containing 3 N-linked (N) and 20 O-linked (O) glycosylation modifications as well as 23 glycation (G) modifications were identified ($q\text{-value} \leq 0.05$). 14 of the 20 O-linked glycosylated peptides are more significantly abundant in ZIKV patients. **B)** 10 out of 11 modified immunoglobulin (IG) peptides are significantly more abundant in Zika patient samples. **C)** Modified serum albumin (ALB) peptides seem to be relatively evenly distributed between Zika and dengue patient samples (17 out of 27 more abundant in ZIKV). Thresholds for color coding: $q\text{-value} \leq 0.05$ (blue), absolute fold change (FC) ≥ 1.5 (green), beyond both thresholds (red), below both thresholds (grey).

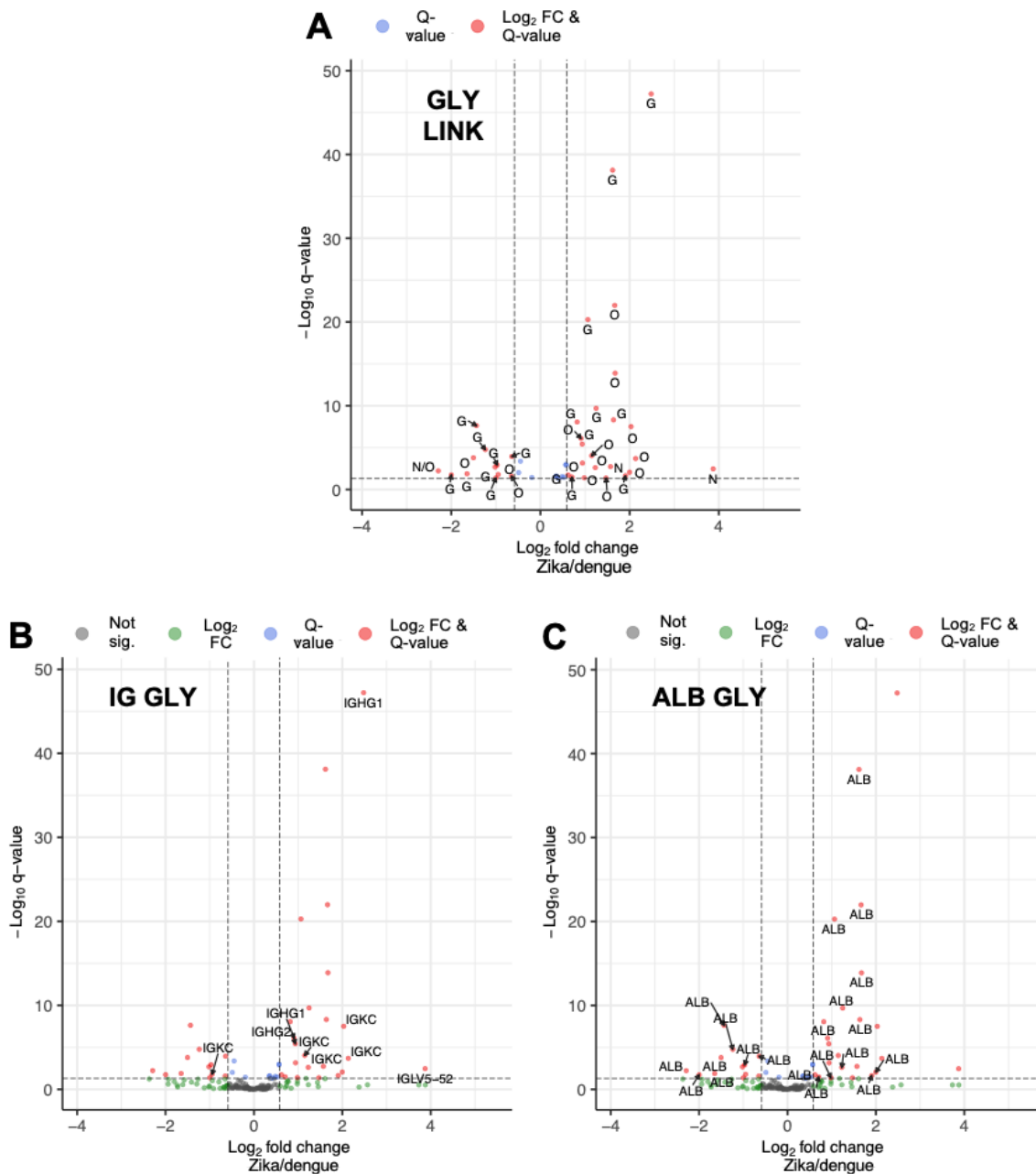
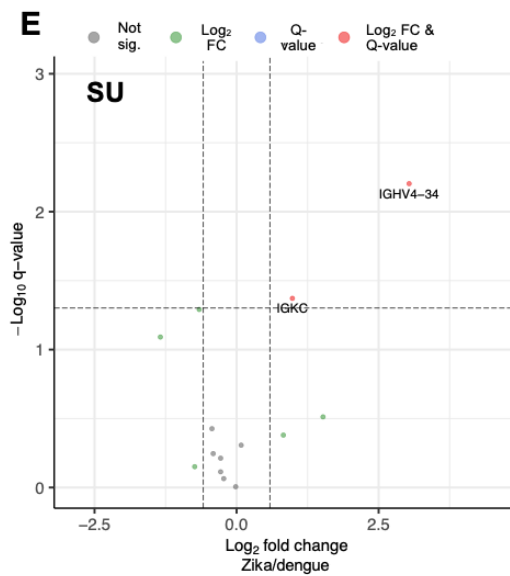
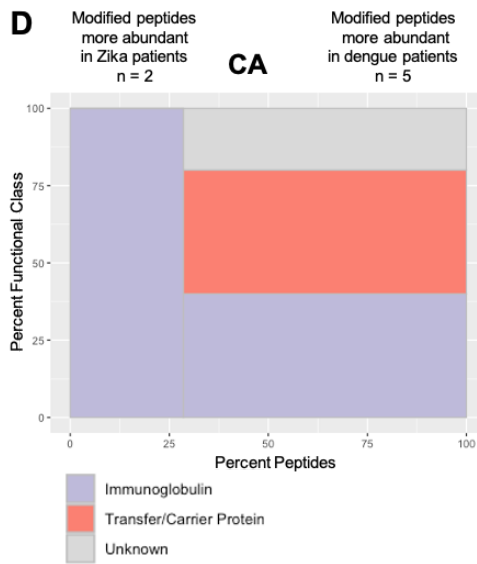
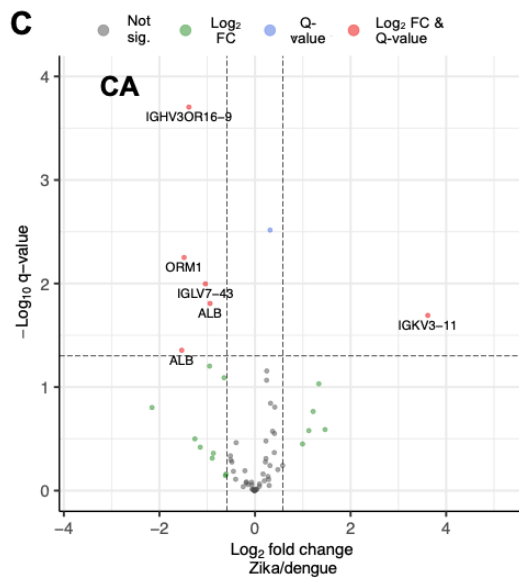
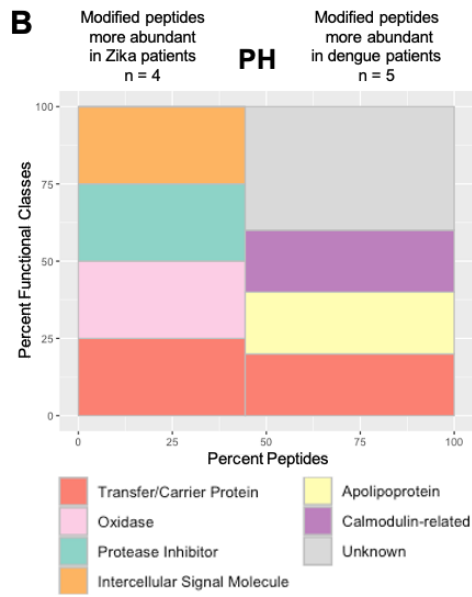
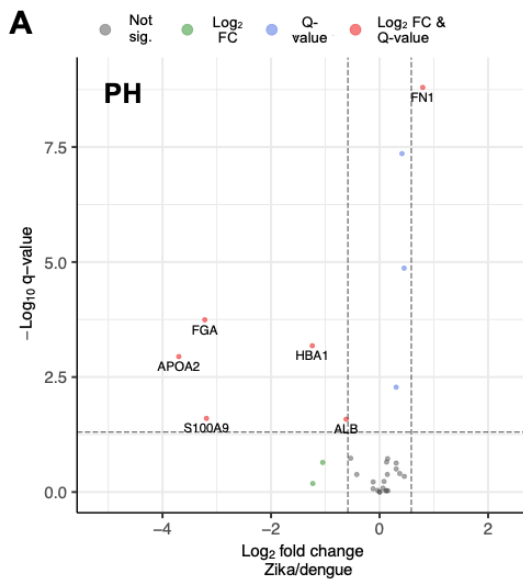


Figure S3: Phosphorylation (PH), carboxylation (CA), and sulfation (SU) modifications of peptides with significant differential abundance between Zika and dengue patient samples.

Note that the function categories displayed signify function annotation, not an enrichment of any of the functions compared to control. **A)** Volcano plot of modified peptides with phosphorylation sites. Out of 30 modified peptides, 9 differed significantly between Zika and dengue patients with a q-value ≤ 0.05 (blue and red combined). **B)** Mosaic plot of protein function classification for significant peptides with phosphorylated residues. Four peptides are significantly more abundant in ZIKV patients (left), 5 are significantly more abundant in DENV patients (right). **C)** Volcano plot of modified peptides with carboxylation sites. Out of 66 modified peptides, 7 differed significantly between ZIKV and DENV patients with a q-value ≤ 0.05 (blue and red combined). **D)** Mosaic plot of protein function classification for significant peptides with carboxylated residues. 2 peptides are significantly more abundant in ZIKV patients (left), 5 are significantly more abundant in dengue patients (right). **E)** Sulfated peptides with significant differential abundance between Zika and dengue patients. Out of 14 modified peptides, two peptides from immunoglobulin components differed significantly between Zika and dengue patients (red), both being more abundant in ZIKV. Thresholds for volcano plot color coding: q-value ≤ 0.05 (blue), absolute fold change (FC) ≥ 1.5 (green), beyond both thresholds (red), below both thresholds (grey). Protein function classification was retrieved from the PANTHER Classification System.



Supplemental Tables

Table S1: Identification - 1,806 modifications in 1,652 peptides from 251 proteins

Table S2: Significant difference between Zika and dengue - 272 modifications in 246 peptides from 97 proteins

Table S3: C-linked glycosylation with consensus sequence Trp-X-X-Trp.

The modifications in complement components have been described previously. The modification in the immunoglobulin component has not been annotated. Residue refers to the position of modified residue according to the UniProt sequence. Dengue/Zika present refers to the number of DENV and ZIKV patient serum samples in which the modified peptide was detected (out of 68 DENV and 54 ZIKV samples).