

## **Supplementary Information**

### **Variations in *O*-glycosylation Patterns Influence Viral Pathogenicity, Infectivity, and Transmissibility in SARS-CoV-2 Variants**

Sherifdeen Onigbinde <sup>1‡</sup>, Cristian D. Gutierrez Reyes <sup>1‡</sup>, Mojibola Fowowe <sup>1</sup>, Oluwatosin Daramola <sup>1</sup>, Mojgan Atashi <sup>1</sup>, Andrew I. Bennett <sup>1</sup>, and Yehia Mechref <sup>1,\*</sup>

<sup>1</sup>Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX 79409-1061

‡ These authors contribute equally

#### **\*Corresponding Author**

Department of Chemistry and Biochemistry

Texas Tech University

Lubbock, TX 79409-1061

Email: [Yehia.Mechref@ttu.edu](mailto:Yehia.Mechref@ttu.edu)

Tel: 806-742-3059

Fax: 806-742-1289

**Table of Contents:**

**Supplementary Figures:**

**Supplementary Figure S1.** Amino acid sequences and purity of the acquired S1 glycoproteins of eleven strains of SARS-CoV-2 that were expressed in human embryonic kidney 293 (HEK293) cells.

**Supplementary Figure S2.** Sialylation relative abundance on the receptor binding domain (RBD) of the variants S1 glycoproteins.

**Supplementary Figure S3.** Sialylation relative abundance on the receptor binding motif (RBM) of the variants S1 glycoproteins.

**Supplementary Figure S4.** Heatmap showing the relative abundance of individual *O*-glycoforms identified in **alpha**.

**Supplementary Figure S5.** Heatmap showing the relative abundance of individual *O*-glycoforms identified in **beta**.

**Supplementary Figure S6.** Heatmap showing the relative abundance of individual *O*-glycoforms identified in **gamma**.

**Supplementary Figure S7.** Heatmap showing the relative abundance of individual *O*-glycoforms identified in **delta**.

**Supplementary Figure S8.** Heatmap showing the relative abundance of individual *O*-glycoforms identified in **epsilon**.

**Supplementary Figure S9.** Heatmap showing the relative abundance of individual *O*-glycoforms identified in **kappa**.

**Supplementary Figure S10.** Heatmap showing the relative abundance of individual *O*-glycoforms identified in **iota**.

**Supplementary Figure S11.** Heatmap showing the relative abundance of individual *O*-glycoforms identified in **eta**.

**Supplementary Figure S12.** Heatmap showing the relative abundance of individual *O*-glycoforms identified in **lambda**.

**Supplementary Figure S13.** Heatmap showing the relative abundance of individual *O*-glycoforms identified in **mu**.

**Supplementary Figure S14.** Heatmap showing the relative abundance of individual *O*-glycoforms identified in **omicron**.

**Supplementary Figure S15.** EThcD tandem mass spectra of a tryptic/IMPa digested glycopeptide confirming the occupancy of both T323 and S325 *O*-glycosylation sites. Data extracted from eta variant (H29) with **Scan no., 3354; m/z, 751.6761; z, 3**.

**Supplementary Figure S16.** EThcD tandem mass spectra of a tryptic/IMPa digested glycopeptide confirming the occupancy of a mutation point (R190S) in Gamma.

**Supplementary Tables:**

**Supplementary Table S1:** List of *O*-glycopeptides identified in the different variants by Byonic software.

**Supplementary Table S2:** List of *O*-glycopeptides identified in the different variants by MetaMorpheus software.

**Supplementary Table S3:** Venn plot results showing the list of *O*-glycopeptides common and unique to Iota, Eta, Lambda, Mu, and Omicron.

**Supplementary Table S4:** List of O-glycopeptides on G446S mutation in Omicron.

## Supplementary Figure S1

100

Alpha **MFVFLVLLPL** VSSQCVNLTT RTQLPPAYTN SFRGVYYPD KVFRSSVLHS TQDLFLPFFS NVTWFHAI-- SGTNGTKRFD NPVLPFNDGV YFASTEKSNI  
 Beta **MFVFLVLLPL** VSSQCVN~~FTT~~ RTQLPPAYTN SFRGVYYPD KVFRSSVLHS TQDLFLPFFS NVTWFHAIHV SGTNGTKRF~~A~~ NPVLPFNDGV YFASTEKSNI  
 Gamma **MFVFLVLLPL** VSSQCVN~~FTN~~ RTQLPPAYTN SFRGVYYPD KVFRSSVLHS TQDLFLPFFS NVTWFHAIHV SGTNGTKRFD NPVLPFNDGV YFASTEKSNI  
 Delta **MFVFLVLLPL** VSSQCVNL~~RT~~ RTQLPPAYTN SFRGVYYPD KVFRSSVLHS TQDLFLPFFS NVTWFHAIHV SGTNGTKRFD NPVLPFNDGV YFASTEKSNI  
 Epsilon **MFVFLVLLPL** VSSQCVNL~~TT~~ RTQLPPAYTN SFRGVYYPD KVFRSSVLHS TQDLFLPFFS NVTWFHAIHV SGTNGTKRFD NPVLPFNDGV YFASTEKSNI  
 Kappa **MFVFLVLLPL** VSSQCVNL~~TT~~ RTQLPPAYTN SFRGVYYPD KVFRSSVLHS TQDLFLPFFS NVTWFHAIHV SGTNGTKRFD NPVLPFNDGV YFASTEKSNI  
 Iota **MFVFLVLLPL** VSSQCVNL~~TT~~ RTQLPPAYTN SFRGVYYPD KVFRSSVLHS TQDLFLPFFS NVTWFHAIHV SGTNGTKRFD NPVLPFNDGV YFASTEKSNI  
 Eta **MFVFLVLLPL** VSSQCVNL~~TT~~ RTQLPPAYTN SFRGVYYPD KVFRSSVLHS TQDLFLPFFS NVTWFHAIHV SGTNGTKRFD NPVLPFNDGV YFASTEKSNI  
 Lambda **MFVFLVLLPL** VSSQCVNL~~TT~~ RTQLPPAYTN SFRGVYYPD KVFRSSVLHS TQDLFLPFFS NVTWFHAIHV SGTN~~V~~KRFD NPVLPFNDGV YFASTEKSNI  
 Mu **MFVFLVLLPL** VSSQCVNL~~TT~~ RTQLPPAYTN SFRGVYYPD KVFRSSVLHS TQDLFLPFFS NVTWFHAIHV SGTNGTKRFD NPVLPFNDGV YFASTEKSNI  
 Omicron **MFVFLVLLPL** VSSQCVNL~~TT~~ RTQLPPAYTN SFRGVYYPD KVFRSSVLHS TQDLFLPFFS NVTWFH~~V~~I- SGTNGTKRFD NPVLPFNDGV YFASTEKSNI

200

Alpha **IRGWIFGTTL** GSKTQSLLIV NNATNVVIKV CEFQFCNDPF LGV-YHKNNK SWMESEFRVY SSANCTFEY VSQPLFMDLE GKQGNFKNL R EFVFKNIDGY  
 Beta **IRGWIFGTTL** GSKTQSLLIV NNATNVVIKV CEFQFCNDPF LGVYYHKNNK SWMESEFRVY SSANCTFEY VSQPLFMDLE GKQGNFKNL R EFVFKNIDGY  
 Gamma **IRGWIFGTTL** GSKTQSLLIV NNATNVVIKV CEFQCNYPF LGVYYHKNNK SWMESEFRVY SSANCTFEY VSQPLFMDLE GKQGNFKNL~~S~~ EFVFKNIDGY  
 Delta **IRGWIFGTTL** GSKTQSLLIV NNATNVVIKV CEFQFCNDPF LD~~V~~YYHKNNK SWMESG-VY SSANCTFEY VSQPLFMDLE GKQGNFKNL R EFVFKNIDGY  
 Epsilon **IRGWIFGTTL** GSKTQSLLIV NNATNVVIKV CEFQFCNDPF LD~~V~~YYHKNNK SWM~~K~~SEFRVY SSANCTFEY VSQPLFMDLE GKQGNFKNL R EFVFKNIDGY  
 Kappa **IRGWIFGTTL** GSKTQSLLIV NNATNVVIKV CEFQFCNDPF LD~~V~~YYHKNNK SWM~~K~~SEFRVY SSANCTFEY VSQPLFMDLE GKQGNFKNL R EFVFKNIDGY  
 Iota **IRGWIFGTTL** GSKTQSLLIV NNATNVVIKV CEFQFCNDPF LD~~V~~YYHKNNK SWMESEFRVY SSANCTFEY VSQPLFMDLE GKQGNFKNL R EFVFKNIDGY  
 Eta **IRGWIFGTTL** GSKTQSLLIV NNATNVVIKV CEFQFCNDPF LGV-YHKNNK SWMESEFRVY SSANCTFEY VSQPLFMDLE GKQGNFKNL R EFVFKNIDGY  
 Lambda **IRGWIFGTTL** GSKTQSLLIV NNATNVVIKV CEFQFCNDPF LGVYYHKNNK SWMESEFRVY SSANCTFEY VSQPLFMDLE GKQGNFKNL R EFVFKNIDGY  
 Mu **IRGWIFGTTL** GSKTQSLLIV NNATNVVIKV CEFQFCNDPF LGVSNHKNK SWMESEFRVY SSANCTFEY VSQPLFMDLE GKQGNFKNL R EFVFKNIDGY  
 Omicron **IRGWIFGTTL** GSKTQSLLIV NNATNVVIKV CEFQFCNDPF LD~~V~~YYHKNNK SWMESEFRVY SSANCTFEY VSQPLFMDLE GKQGNFKNL R EFVFKNIDGY

300

Alpha **FKIYSKHTPI** NLVRDLPQGF SALEPLVDLP IGINITRQFT LLALHRSYLT PGDSSSGWTA GAAAYYVGYL QPRTFLLKYN ENGTITDAVD CALDPLSETK  
 Beta **FKIYSKHTPI** NLVR~~G~~LPQGF SALEPLVDLP IGINITRQFT L-HISYLT PGDSSSGWTA GAAAYYVGYL QPRTFLLKYN ENGTITDAVD CALDPLSETK  
 Gamma **FKIYSKHTPI** NLVRDLPQGF SALEPLVDLP IGINITRQFT LLALHRSYLT PGDSSSGWTA GAAAYYVGYL QPRTFLLKYN ENGTITDAVD CALDPLSETK  
 Delta **FKIYSKHTPI** NLVRDLPQGF SALEPLVDLP IGINITRQFT LLALHRSYLT PGDSSSGWTA GAAAYYVGYL QPRTFLLKYN ENGTITDAVD CALDPLSETK  
 Epsilon **FKIYSKHTPI** NLVRDLPQGF SALEPLVDLP IGINITRQFT LLALHRSYLT PGDSSSGWTA GAAAYYVGYL QPRTFLLKYN ENGTITDAVD CALDPLSETK  
 Kappa **FKIYSKHTPI** NLVRDLPQGF SALEPLVDLP IGINITRQFT LLALHRSYLT PGDSSSGWTA GAAAYYVGYL QPRTFLLKYN ENGTITDAVD CALDPLSETK  
 Iota **FKIYSKHTPI** NLVRDLPQGF SALEPLVDLP IGINITRQFT LLALHRSYLT PGGSSSGWTA GAAAYYVGYL QPRTFLLKYN ENGTITDAVD CALDPLSETK  
 Eta **FKIYSKHTPI** NLVRDLPQGF SALEPLVDLP IGINITRQFT LLALHRSYLT PGDSSSGWTA GAAAYYVGYL QPRTFLLKYN ENGTITDAVD CALDPLSETK  
 Lambda **FKIYSKHTPI** NLVRDLPQGF SALEPLVDLP IGINITRQFT LLALHRSYLT PGDSSSGWTA GAAAYYVGYL QPRTFLLKYN ENGTITDAVD CALDPLSETK  
 Mu **FKIYSKHTPI** NLVRDLPQGF SALEPLVDLP IGINITRQFT LLALHRSYLT PGDSSSGWTA GAAAYYVGYL QPRTFLLKYN ENGTITDAVD CALDPLSETK

**EPE**

↓

Omicron **FKIYSKHTPI** **NIVRD**LPQGF SALEPLVDLP IGINITRQFT LLALHRSYLT PGDSSSGWTA GAAAYYVGYL QPRTFLLKYN ENGTITDAVD CALDPLSETK

400

Alpha **CTLKSFTVEK** GIYQTNSFRV QPTESIVRFP NITNLCPGFGE VFNATRFASV YAWNRKRISN CVADYSVLYN SASFSTFKCY GVSPTKLNDL CFTNVYADSF  
 Beta **CTLKSFTVEK** GIYQTNSFRV QPTESIVRFP NITNLCPGFGE VFNATRFASV YAWNRKRISN CVADYSVLYN SASFSTFKCY GVSPTKLNDL CFTNVYADSF  
 Gamma **CTLKSFTVEK** GIYQTNSFRV QPTESIVRFP NITNLCPGFGE VFNATRFASV YAWNRKRISN CVADYSVLYN SASFSTFKCY GVSPTKLNDL CFTNVYADSF  
 Delta **CTLKSFTVEK** GIYQTNSFRV QPTESIVRFP NITNLCPGFGE VFNATRFASV YAWNRKRISN CVADYSVLYN SASFSTFKCY GVSPTKLNDL CFTNVYADSF  
 Epsilon **CTLKSFTVEK** GIYQTNSFRV QPTESIVRFP NITNLCPGFGE VFNATRFASV YAWNRKRISN CVADYSVLYN SASFSTFKCY GVSPTKLNDL CFTNVYADSF  
 Kappa **CTLKSFTVEK** GIYQTNSFRV QPTESIVRFP NITNLCPGFGE VFNATRFASV YAWNRKRISN CVADYSVLYN SASFSTFKCY GVSPTKLNDL CFTNVYADSF  
 Iota **CTLKSFTVEK** GIYQTNSFRV QPTESIVRFP NITNLCPGFGE VFNATRFASV YAWNRKRISN CVADYSVLYN SASFSTFKCY GVSPTKLNDL CFTNVYADSF  
 Eta **CTLKSFTVEK** GIYQTNSFRV QPTESIVRFP NITNLCPGFGE VFNATRFASV YAWNRKRISN CVADYSVLYN SASFSTFKCY GVSPTKLNDL CFTNVYADSF  
 Lambda **CTLKSFTVEK** GIYQTNSFRV QPTESIVRFP NITNLCPGFGE VFNATRFASV YAWNRKRISN CVADYSVLYN SASFSTFKCY GVSPTKLNDL CFTNVYADSF  
 Mu **CTLKSFTVEK** GIYQTNSFRV QPTESIVRFP NITNLC~~P~~DE VFNATRFASV YAWNRKRISN CVADYSVLYN SAP~~F~~STFKCY GVSPTKLNDL CFTNVYADSF  
 Omicron **CTLKSFTVEK** GIYQTNSFRV QPTESIVRFP NITNLC~~P~~DE VFNATRFASV YAWNRKRISN CVADYSVLYN **LA**P~~F~~TFCKY GVSPTKLNDL CFTNVYADSF

500

Alpha **VIRGDEVROI** APGQTGKIA~~D~~ YNYKL~~P~~DDFT GCVIAWSNN LDSKVGGN~~Y~~ LYRLFRKS~~N~~ LKP~~F~~ERDIST E~~I~~YQAG~~S~~TPC NGVEG~~N~~CYF PLQSYGFQ~~P~~  
 Beta **VIRGDEVROI** APGQTG~~N~~IA~~D~~ YNYKL~~P~~DDFT GCVIAWSNN LDSKVGGN~~Y~~ LYRLFRKS~~N~~ LKP~~F~~ERDIST E~~I~~YQAG~~S~~TPC NGV~~K~~GFNCYF PLQSYGFQ~~P~~  
 Gamma **VIRGDEVROI** APGQTG~~T~~IA~~D~~ YNYKL~~P~~DDFT GCVIAWSNN LDSKVGGN~~Y~~ LYRLFRKS~~N~~ LKP~~F~~ERDIST E~~I~~YQAG~~S~~TPC NGV~~K~~GFNCYF PLQSYGFQ~~P~~  
 Delta **VIRGDEVROI** APGQTGKIA~~D~~ YNYKL~~P~~DDFT GCVIAWSNN LDSKVGGN~~Y~~ LYRLFRKS~~N~~ LKP~~F~~ERDIST E~~I~~YQAG~~S~~TPC NGV~~K~~GFNCYF PLQSYGFQ~~P~~  
 Epsilon **VIRGDEVROI** APGQTGKIA~~D~~ YNYKL~~P~~DDFT GCVIAWSNN LDSKVGGN~~Y~~ LYRLFRKS~~N~~ LKP~~F~~ERDIST E~~I~~YQAG~~S~~TPC NGV~~K~~GFNCYF PLQSYGFQ~~P~~  
 Kappa **VIRGDEVROI** APGQTGKIA~~D~~ YNYKL~~P~~DDFT GCVIAWSNN LDSKVGGN~~Y~~ LYRLFRKS~~N~~ LKP~~F~~ERDIST E~~I~~YQAG~~S~~TPC NGV~~K~~GFNCYF PLQSYGFQ~~P~~  
 Iota **VIRGDEVROI** APGQTGKIA~~D~~ YNYKL~~P~~DDFT GCVIAWSNN LDSKVGGN~~Y~~ LYRLFRKS~~N~~ LKP~~F~~ERDIST E~~I~~YQAG~~N~~TPC NGV~~K~~GFNCYF PLQSYGFQ~~P~~  
 Eta **VIRGDEVROI** APGQTGKIA~~D~~ YNYKL~~P~~DDFT GCVIAWSNN LDSKVGGN~~Y~~ LYRLFRKS~~N~~ LKP~~F~~ERDIST E~~I~~YQAG~~S~~TPC NGV~~K~~GFNCYF PLQSYGFQ~~P~~  
 Lambda **VIRGDEVROI** APGQTGKIA~~D~~ YNYKL~~P~~DDFT GCVIAWSNN LDSKVGGN~~Y~~ LYRLFRKS~~N~~ LKP~~F~~ERDIST E~~I~~YQAG~~S~~TPC NGV~~K~~GFNCYF PLQSYGFQ~~P~~  
 Mu **VIRGDEVROI** APGQTGKIA~~D~~ YNYKL~~P~~DDFT GCVIAWSNN LDSKVGGN~~Y~~ LYRLFRKS~~N~~ LKP~~F~~ERDIST E~~I~~YQAG~~S~~TPC NGV~~K~~GFNCYF PLQSYGFQ~~P~~  
 Omicron **VIRGDEVROI** APGQTG~~N~~IA~~D~~ YNYKL~~P~~DDFT GCVIAWS~~N~~ LDSKVGGN~~Y~~ LYRLFRKS~~N~~ LKP~~F~~ERDIST E~~I~~YQAG~~N~~TPC NGV~~A~~GFNCYF PLRSYSFRPT

Alpha **YGVGVQPYRV** VVLSFELLHA PATVCPKKS TNLVKNKCVN FNFGNLGTG VLTESNKFL PFQQFGRD**I** DTTDAVRDPQ TLEILDITPC SFGGVS**VITP**  
 Beta **YGVGVQPYRV** VVLSFELLHA PATVCPKKS TNLVKNKCVN FNFGNLGTG VLTESNKFL PFQQFGRD**A** DTTDAVRDPQ **TLEILDITPC SFGGVS****VITP** Gamma  
**YGVGVQPYRV** VVLSFELLHA PATVCPKKS TNLVKNKCVN FNFGNLGTG VLTESNKFL PFQQFGRD**B** DTTDAVRDPQ TLEILDITPC SFGGVS**VITP** Delta  
 NGVGVQPYRV VVLSFELLHA PATVCPKKS TNLVKNKCVN FNFGNLGTG VLTESNKFL PFQQFGRD**C** DTTDAVRDPQ TLEILDITPC SFGGVS**VITP** Epsilon  
 NGVGVQPYRV VVLSFELLHA PATVCPKKS TNLVKNKCVN FNFGNLGTG VLTESNKFL PFQQFGRD**D** DTTDAVRDPQ TLEILDITPC SFGGVS**VITP** Kappa  
 NGVGVQPYRV VVLSFELLHA PATVCPKKS TNLVKNKCVN FNFGNLGTG VLTESNKFL PFQQFGRD**E** DTTDAVRDPQ TLEILDITPC SFGGVS**VITP** Iota  
 NGVGVQPYRV VVLSFELLHA PATVCPKKS TNLVKNKCVN FNFGNLGTG VLTESNKFL PFQQFGRD**F** DTTDAVRDPQ TLEILDITPC SFGGVS**VITP** Eta  
 NGVGVQPYRV VVLSFELLHA PATVCPKKS TNLVKNKCVN FNFGNLGTG VLTESNKFL PFQQFGRD**G** DTTDAVRDPQ TLEILDITPC SFGGVS**VITP** Lambda  
 NGVGVQPYRV VVLSFELLHA PATVCPKKS TNLVKNKCVN FNFGNLGTG VLTESNKFL PFQQFGRD**H** DTTDAVRDPQ TLEILDITPC SFGGVS**VITP**  
 Mu **YGVGVQPYRV** VVLSFELLHA PATVCPKKS TNLVKNKCVN FNFGNLGTG VLTESNKFL PFQQFGRD**I** DTTDAVRDPQ TLEILDITPC SFGGVS**VITP** Omicron  
**YGVGVQPYRV** VVLSFELLHA PATVCPKKS TNLVKNKCVN FNFGNL**K**GTG VLTESNKFL PFQQFGRD**J** DTTDAVRDPQ TLEILDITPC SFGGVS**VITP**

	601	685
Alpha	GTNTSNQAVV LYQGVNCTEV PVAIHADQLT PTWRYVSTGS NVFQTRAGCL IGAEHVNNSY ECDIPIGAGI CASYQTQTNs RRAR	
Beta	<b>GTNTSNQAVV LYQGVNCTEV PVAIHADQLT PTWRYVSTGS NVFQTRAGCL IGAEHVNNSY ECDIPIGAGI CASYQTQTNs RRAR</b>	
Gamma	GTNTSNQAVV LYQGVNCTEV PVAIHADQLT PTWRYVSTGS NVFQTRAGCL IGAEYVNNSY ECDIPIGAGI CASYQTQTNs RRAR	
Delta	GTNTSNQAVV LYQGVNCTEV PVAIHADQLT PTWRYVSTGS NVFQTRAGCL IGAEHVNNSY ECDIPIGAGI CASYQTQTNs RRAR	
Epsilon	GTNTSNQAVV LYQGVNCTEV PVAIHADQLT PTWRYVSTGS NVFQTRAGCL IGAEHVNNSY ECDIPIGAGI CASYQTQTNs RRAR	
Kappa	GTNTSNQAVV LYQGVNCTEV PVAIHADQLT PTWRYVSTGS NVFQTRAGCL IGAEHVNNSY ECDIPIGAGI CASYQTQTNs RRAR	
Iota	GTNTSNQAVV LYQGVNCTEV PVAIHADQLT PTWRYVSTGS NVFQTRAGCL IGAEHVNNSY ECDIPIGAGI CASYQTQTNs RRAR	
Eta	GTNTSNQAVV LYQGVNCTEV PVAIHADQLT PTWRYVSTGS NVFQTRAGCL IGAEHVNNSY ECDIPIGAGI CASYQTQTNs RRAR	
Lambda	GTNTSNQAVV LYQGVNCTEV PVAIHADQLT PTWRYVSTGS NVFQTRAGCL IGAEHVNNSY ECDIPIGAGI CASYQTQTNs RRAR	
Mu	GTNTSNQAVV LYQGVNCTEV PVAIHADQLT PTWRYVSTGS NVFQTRAGCL IGAEHVNNSY ECDIPIGAGI CASYQTQTNs RRAR	
Omicron	GTNTSNQAVV LYQGVNCTEV PVAIHADQLT PTWRYVSTGS NVFQTRAGCL IGAEYVNNSY ECDIPIGAGI CASYQTQTNs RRAR	

The percentage coverage for each protein determined by Proteome Discoverer is as follows: Alpha 87%; Beta 97%; Gamma 87%; Delta 89%; Epsilon 87%; Kappa 84%; Iota 86%; Eta 70%, Lambda 88%; Mu 85%; and omicron 91%.

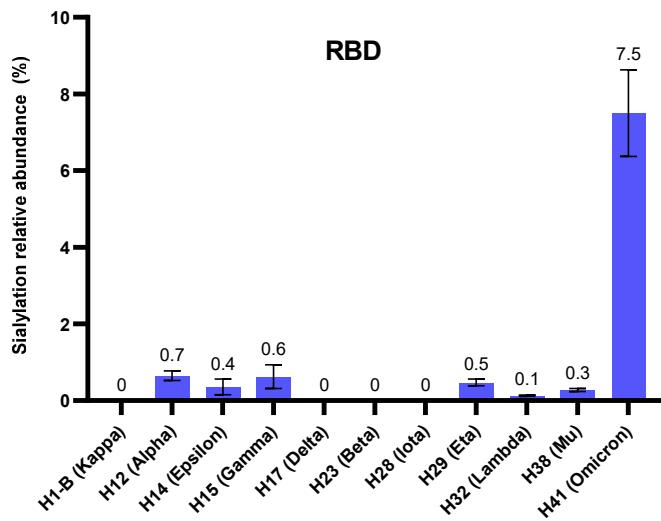
\*Sections highlighted in yellow show the protein percent coverage

\*Amino acid residues in red font are substituted

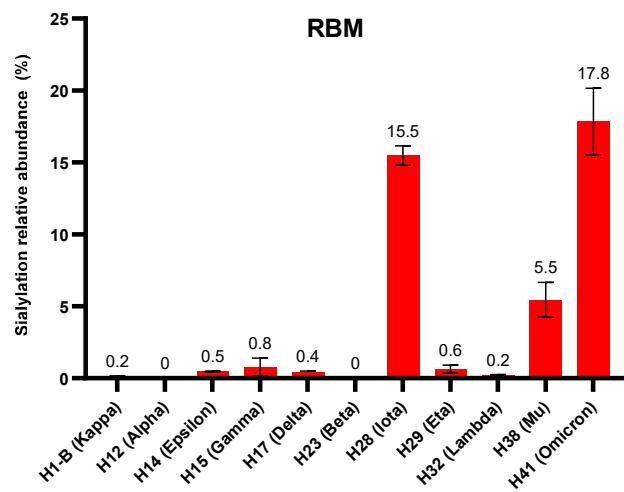
\* “\_” Represents deletions

\* “<img alt="downward arrow" data-bbox="218 881 238 896”/>” Indicates the point of insertion

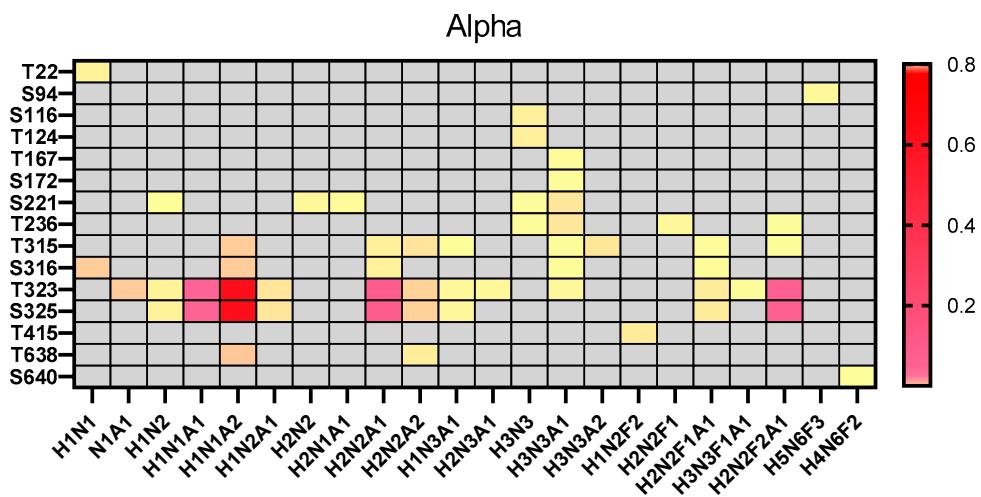
## Supplementary Figure S2



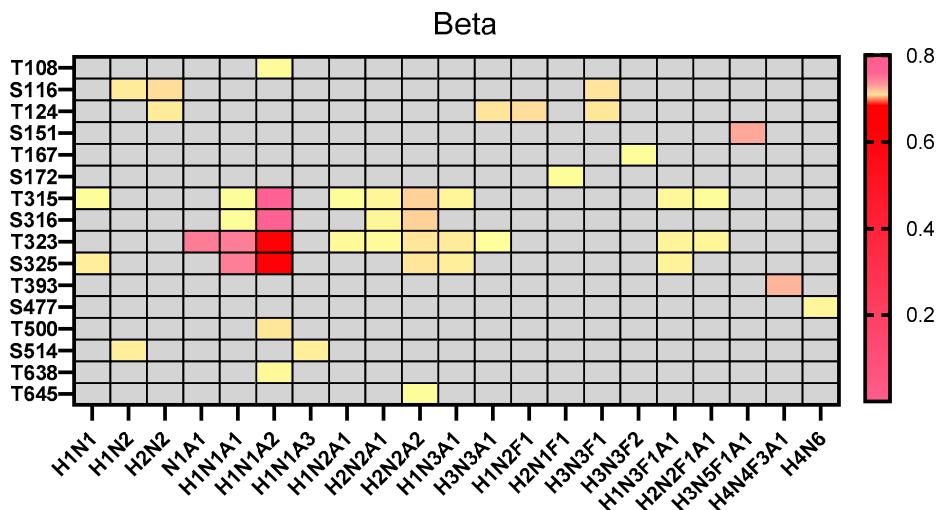
### Supplementary Figure S3



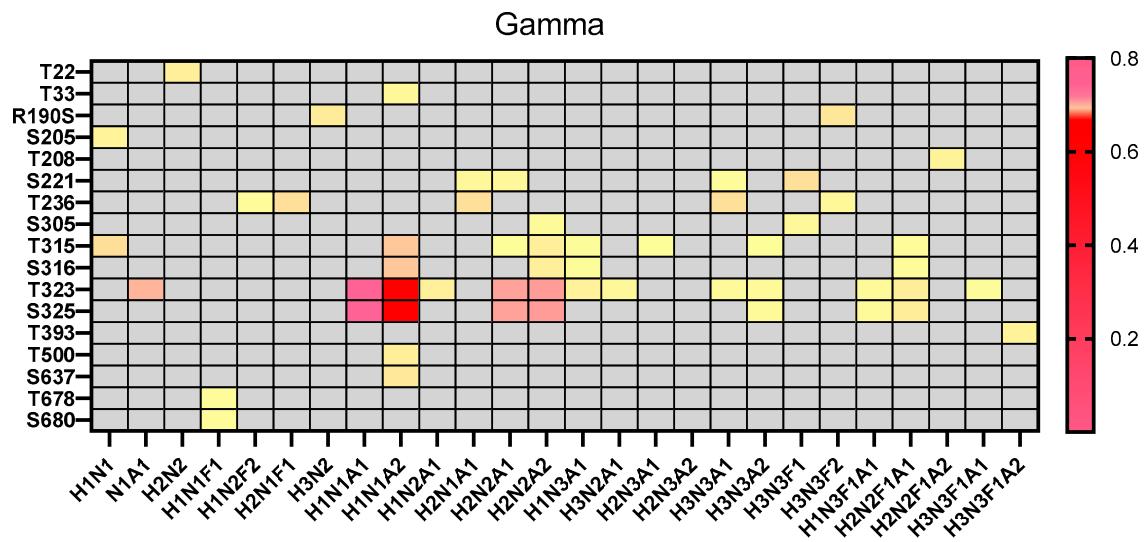
**Supplementary Figure S4**



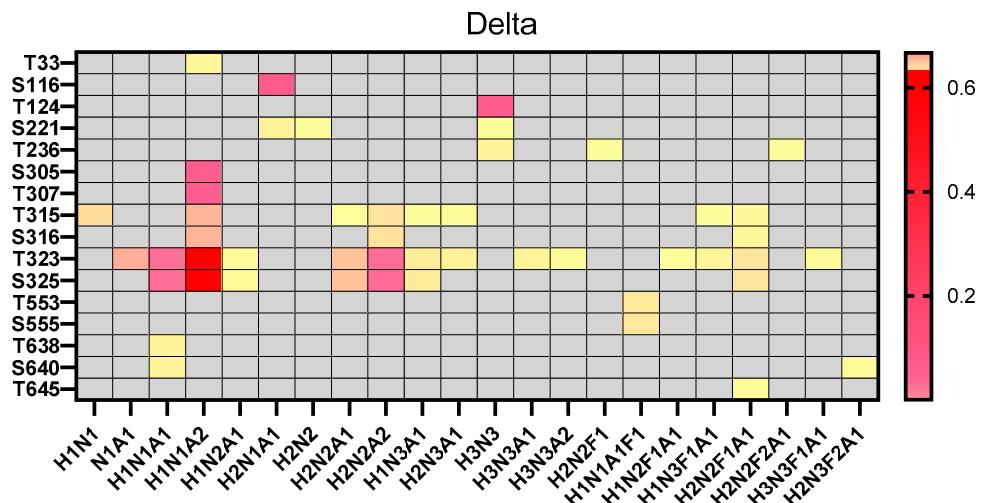
**Supplementary Figure S5**



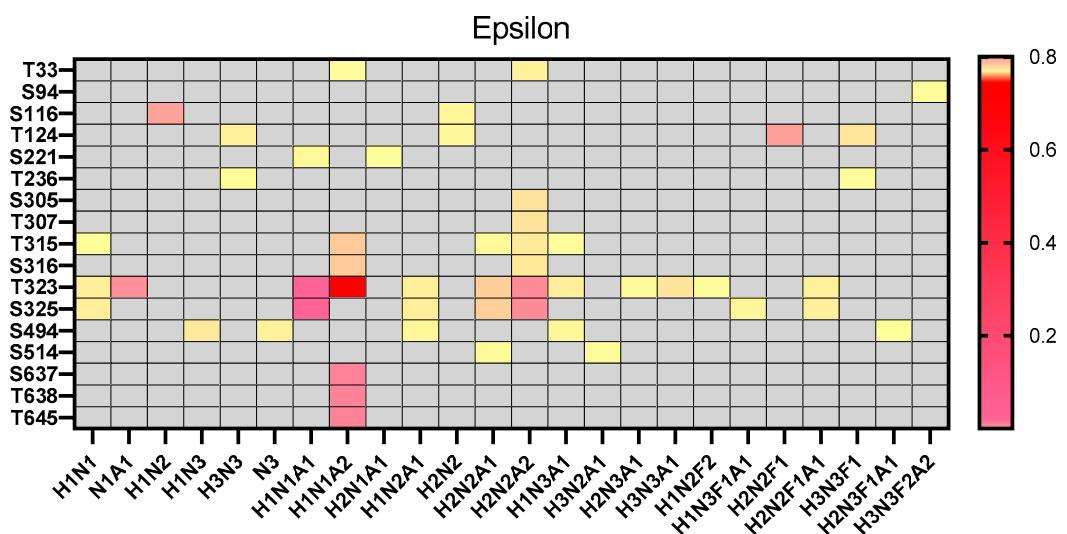
**Supplementary Figure S6**



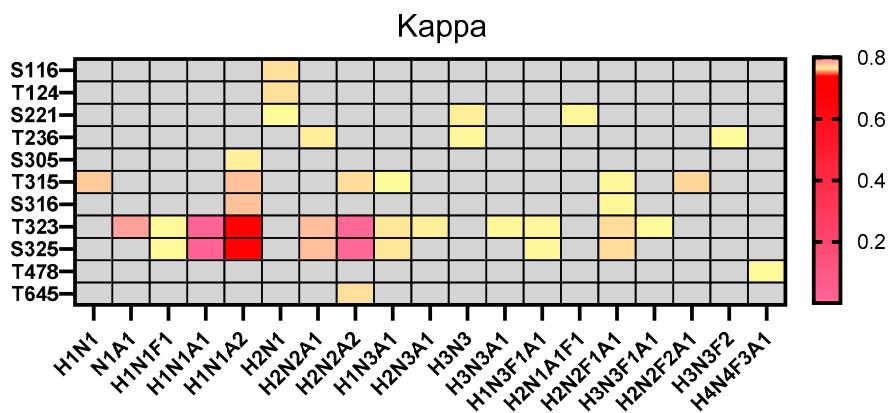
**Supplementary Figure S7**



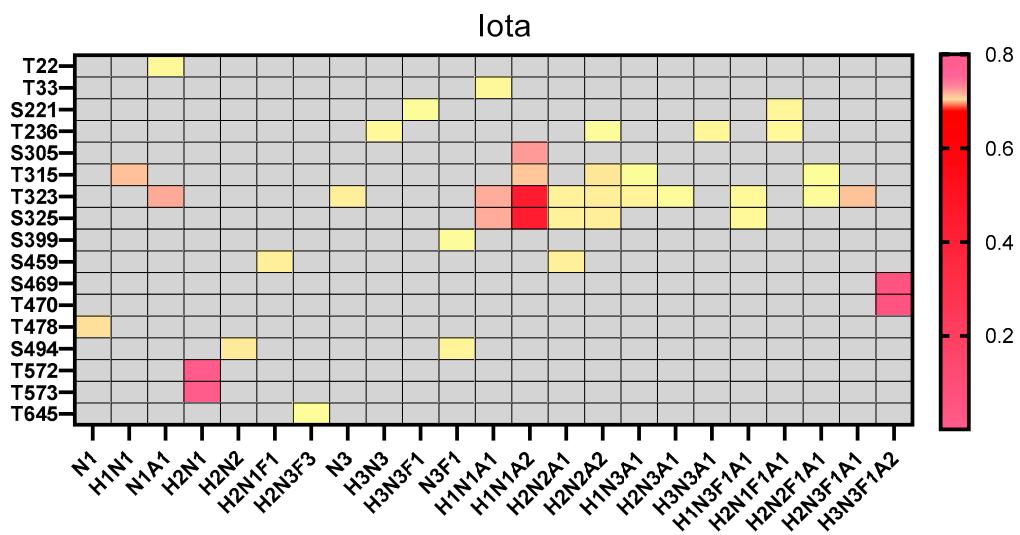
**Supplementary Figure S8**



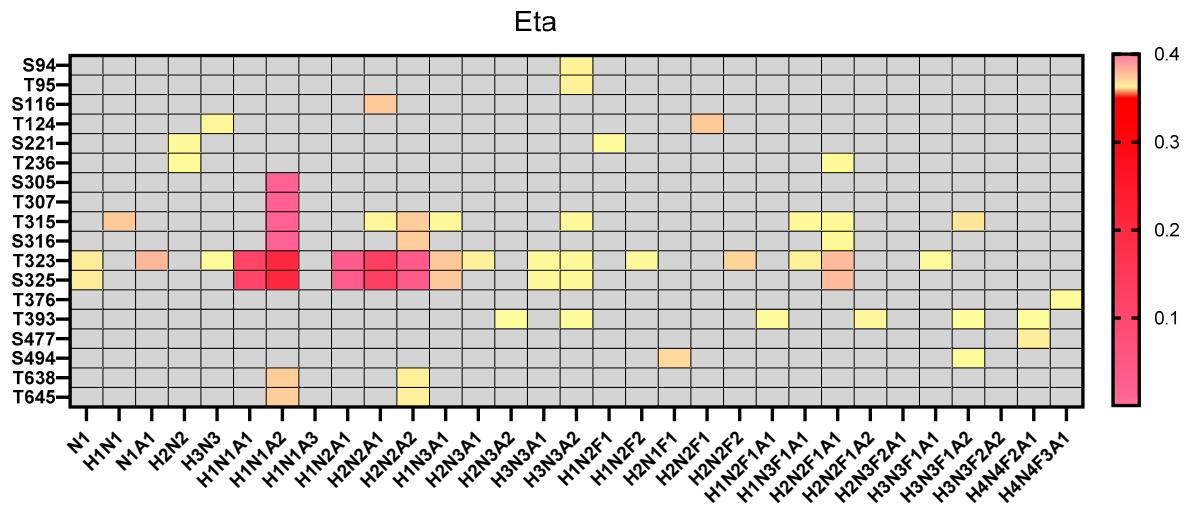
**Supplementary Figure S9**



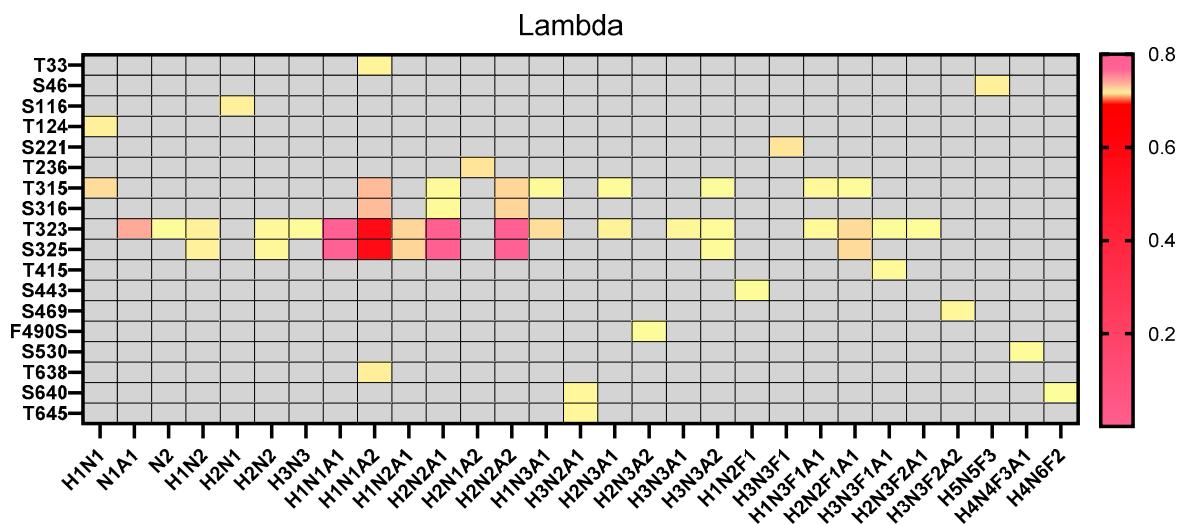
**Supplementary Figure S10**



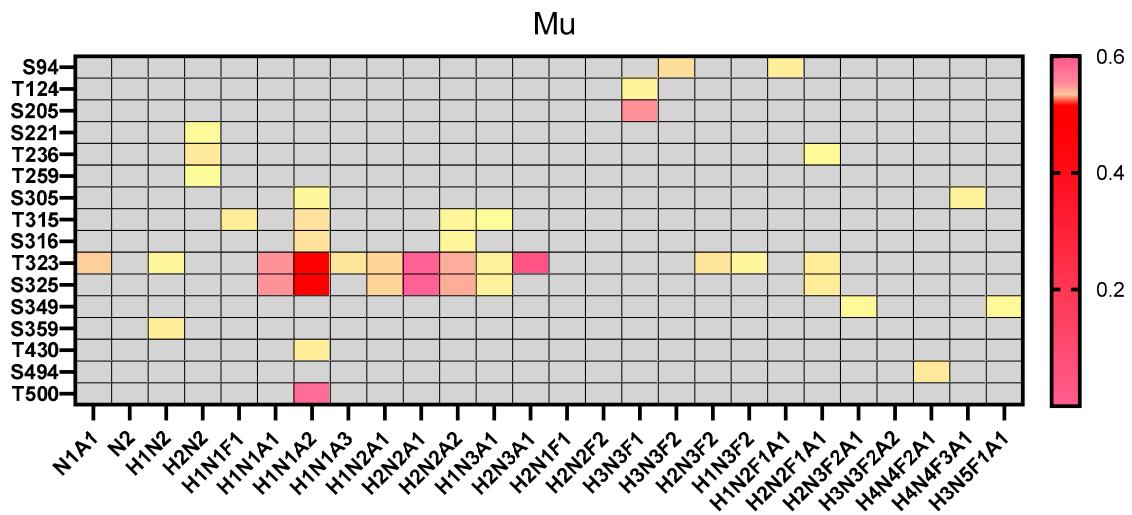
**Supplementary Figure S11**



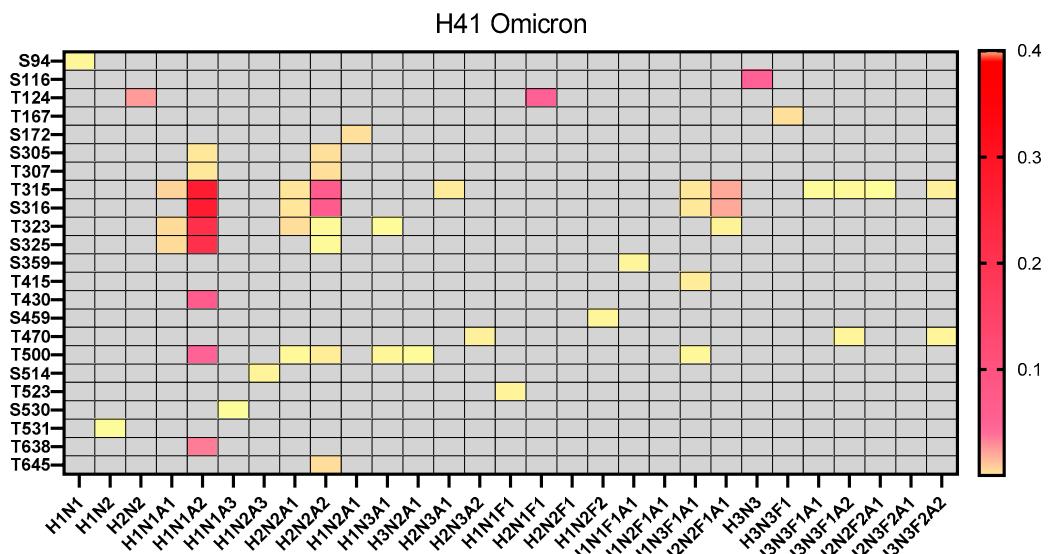
**Supplementary Figure S12**



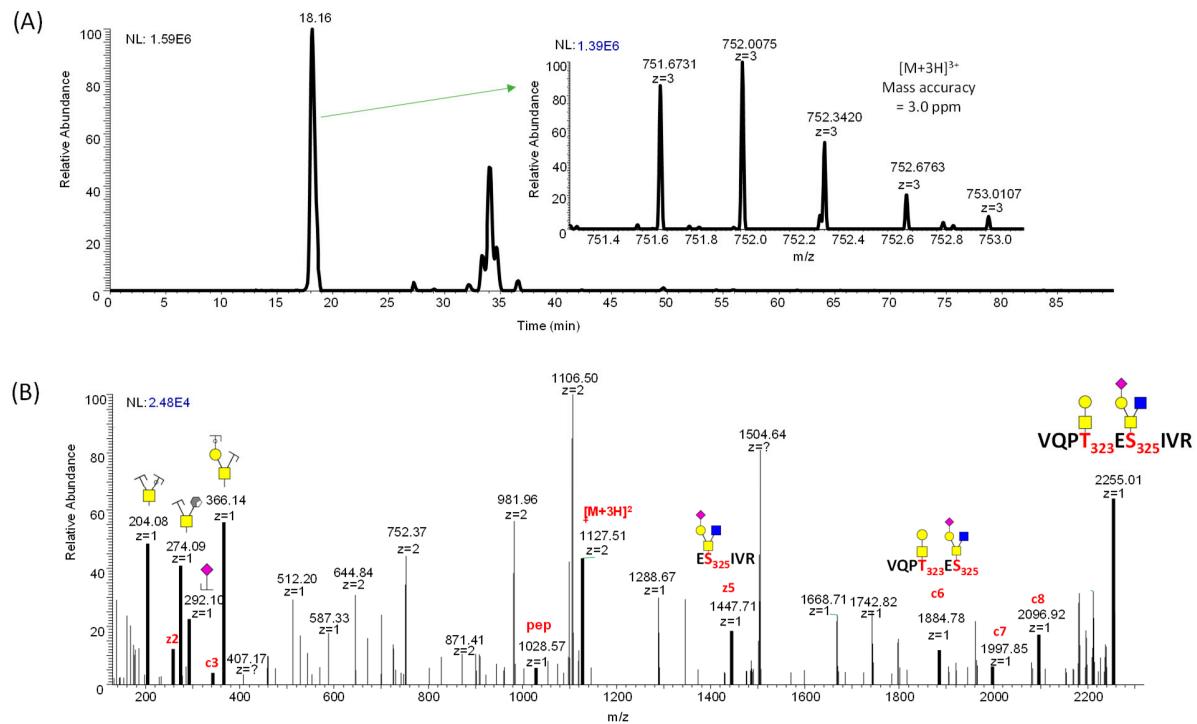
**Supplementary Figure S13**



**Supplementary Figure S14**



## Supplementary Figure S15



## Supplementary Figure S16

