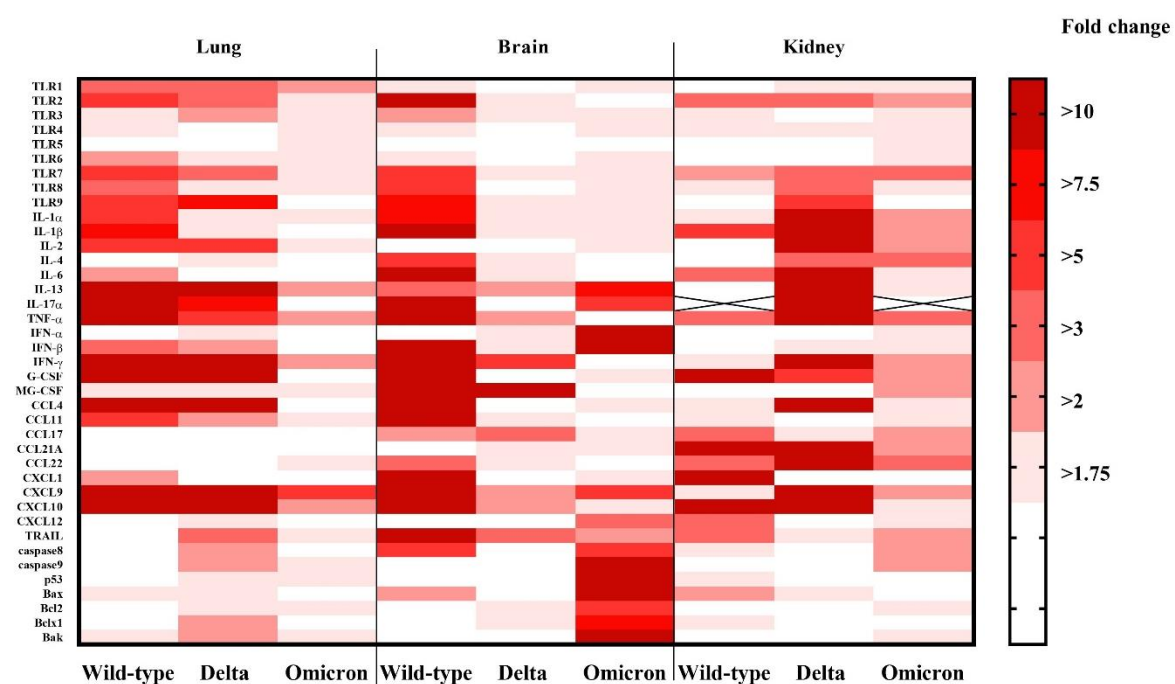
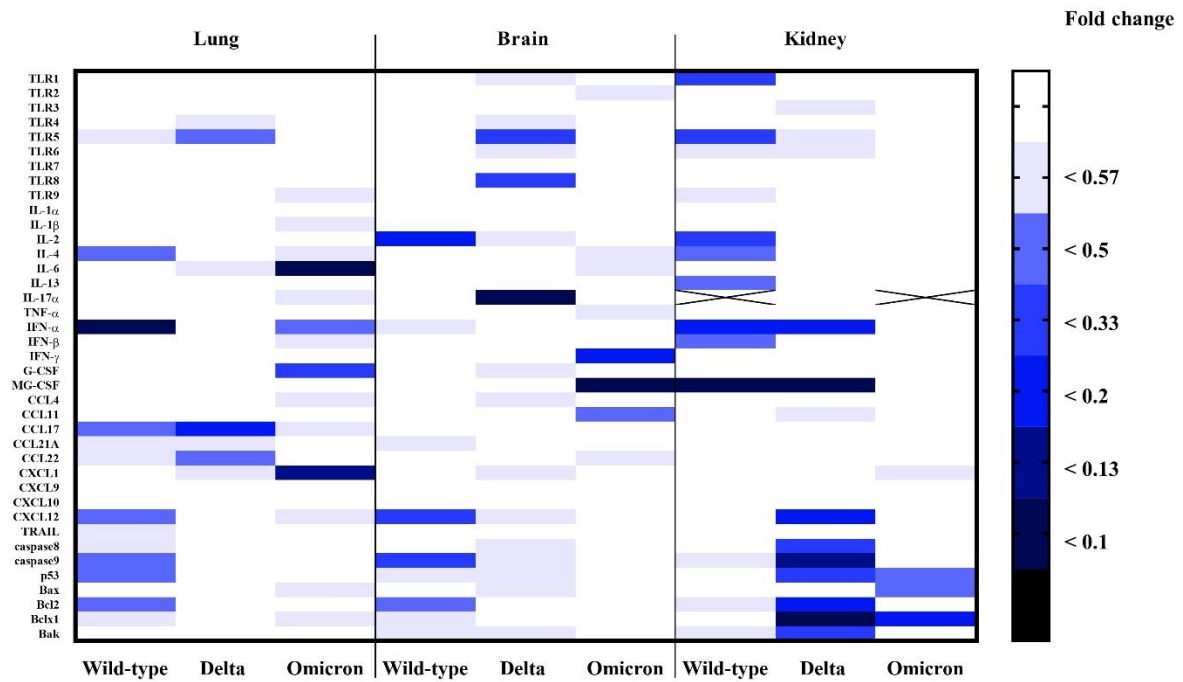
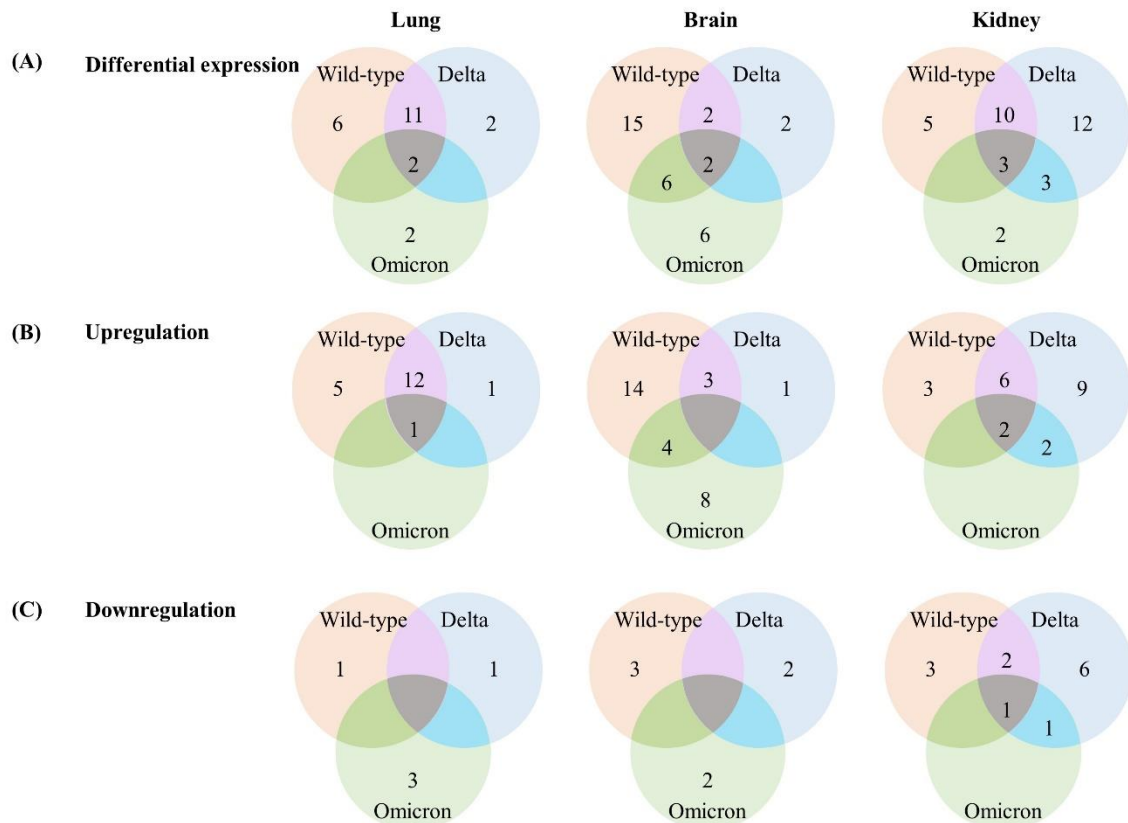




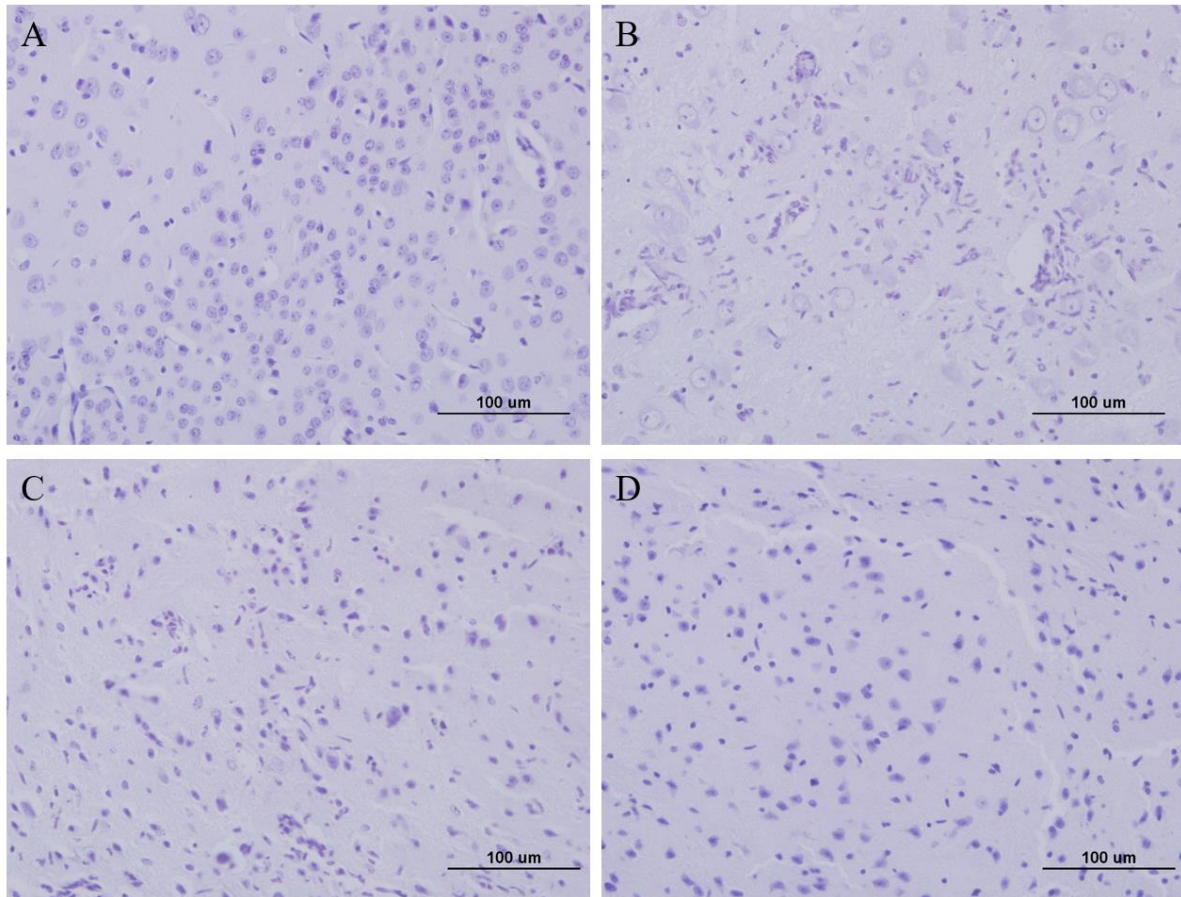
Supplementary Figure 1. Heat map of upregulated genes involved in the immune response of the lung, brain and kidney of hACE2 mice infected with Wild-type, Delta or Omicron. The basal expression level was considered as fold change 1-fold and upregulation was considered as >1-fold.



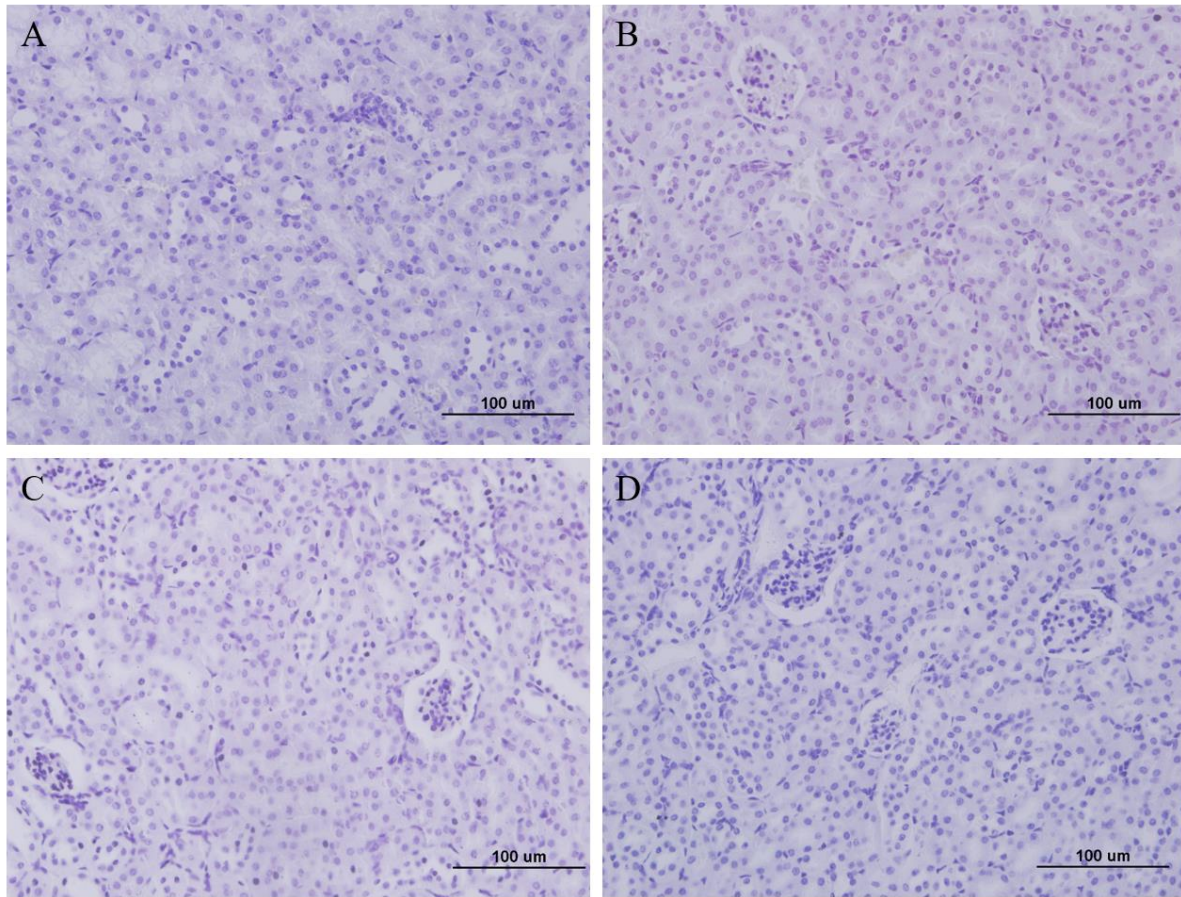
Supplementary Figure 2. Heat map of downregulated genes involved in the immune response of the lung, brain and kidney of hACE2 mice infected with Wild-type, Delta or Omicron. The basal expression level was considered as fold change 1-fold and downregulation was considered as <1-fold.



Supplementary Figure 3. Venn-diagram demonstrating the overlapping and unique differentially expressed genes in hACE2 mice infected with SARS-CoV-2 variants. (A) The number of common genes which differentially expressed in lung, brain and kidney upon the SARS-CoV-2 infections. The number of Common and unique genes (B) upregulated, (C) downregulated by each variant sample. Upregulation = > 3-folds and downregulation = < 3-folds



Supplementary Figure 4. Brain histopathology of K18-hACE2 transgenic mice infected with variants of SARS-CoV-2. A) Brain tissue of PBS mock infected mice. B) Brain tissue of wild-type virus infected mice. C) Brain tissue of Delta variant infected mice. D) Brain tissue of Omicron infected mice.



Supplementary Figure 5. Kidney histopathology of K18-hACE2 transgenic mice infected with variants of SARS-CoV-2. A) Kidney tissue of PBS mock infected mice. B) Kidney tissue of wild-type virus infected mice. C) Kidney tissue of Delta variant infected mice. D) Kidney tissue of Omicron infected mice.

Table S1: Primer Sequences of Toll-like receptor, cytokine, chemokine and apoptosis-related genes

Gene	Forward primer sequence (5'-3')	Reverse primer sequence (5'-3')
<i>Beta-actin</i>	TGG AAT CCT GTG GCA TCC ATG AAA C	TAA AAC GCA GCT CAG TAA CAG TCC G
<i>TLR1</i>	GTG TGC AGC TGA TTG CTC AT	CAA ACC GAT CGT AGT GCT GA
<i>TLR2</i>	TGC TTT CCT GCT GGA GAT TT	TGT AAC GCA ACA GCT TCA GG
<i>TLR3</i>	CGC CCT CTT CGT AAC TTG AC	AGA CAG CCC CTT CAG GAA AT
<i>TLR4</i>	AGT GGC CCT ACC AAG TCT CA	GTG CTG AAA ATC CAG GTG CT
<i>TLR5</i>	CTG GGG ACC CAG TAT GCT AA	ACA GCC GAA GTT CCA AGA GA
<i>TLR6</i>	CAA AGG AGG CGC TAT ACT CG	GGT GGA ACA GCC TTG AAA AA
<i>TLR7</i>	CCT GTT CTA CTG GGG TCC AA	GCC TCA AGG CTC AGA AGA TG
<i>TLR8</i>	CTT CCA AAC TTG GCA ACC AT	GAA GAC GAT TTC GCC AAG AG
<i>TLR9</i>	TTC TCT TCA TGG ACG GGA AC	CCC AGC TTG ACA ATG AGG TT
<i>IL-1alpha</i>	CCC GTC CTT AAA GCT GTC TG	AAT TGG AAT CCA GGG GAA AC
<i>IL-1beta</i>	GCC CAT CCT CTG TGA CTC AT	AGG CCA CAG GTA TTT TGT CG
<i>IL-2</i>	CCC ACT TCA AGC TCC ACT TC	ATC CTG GGG AGT TTC AGG TT
<i>IL-4</i>	TCA ACC CCC AGC TAG TTG TC	TGT TCT TCG TTG CTG TGA GG
<i>IL-6</i>	AGT TGC CTT CTT GGG ACT GA	TCC ACG ATT TCC CAG AGA AC
<i>IL-13</i>	CAG CTC CCT GGT TCT CTC AC	CCA CAC TCC ATA CCA TGC TG
<i>IL-17alpha</i>	TCC AGA AGG CCC TCA GAC TA	AGC ATC TTC TCG ACC CTG AA
<i>IFN beta</i>	CCC TAT GGA GAT GAC GGA GA	CTG TCT GCT GGT GGA GTT CA
<i>IFN alpha</i>	CTG CTG GCT GTG AGG AAA TA	GGC TCT CCA GAC TTC TGC TC
<i>IFN gamma</i>	GGC TGT TTC TGG CTG TTA CTG	TCT GGC TCT GCA GGA TTT TC
<i>TNF alpha</i>	CCA CCA CGC TCT TCT GT CTA	TGG GCT ACA GGC TTG TCA CT
<i>G-CSF</i>	CTC AAC TTT CTG CCC AGA GG	TAG GTG GCA CAC AAC TGC TC

<i>GM-CSF</i>	GGC CTT GGA AGC ATG TAG AG	CCG TAG ACC CTG CTC GAA TA
<i>MIO-1beta(CCL4)</i>	CCC ACT TCC TGC TGT TTC TC	GAG GAG GCC TCT CCT GAA GT
<i>Eotaxin(CCL11)</i>	TCC ACA GCG CTT CTA TTC CT	CTA TGG CTT TCA GGG TGC AT
<i>TARC(CCL17)</i>	AGT GGA GTG TTC CAG GGA TG	CTG GTC ACA GGC CGT TTT AT
<i>6CKine(CCL21A)</i>	ATG TGC AAA CCC TGA GGA AG	TCC TCT TGA GGG CTG TGT CT
<i>CCL22</i>	GTC CTA GGG AGG AGG ACC TG	GAA GGG GGA TAA GCT GGA AG
<i>CXCL1</i>	GCT GGG ATT CAC CTC AAG AA	AGG TGC CAT GAG AGC AGT CT
<i>CXCL9</i>	AAA ATT TCA TCA CGC CCT TG	TCT CCA GCT TGG TGA GGT CT
<i>CXCL10</i>	GGA TGG CTG TCC TAG CTC TG	ATA ACC CCT TGG GAA GAT GG
<i>CXCL12</i>	AGT AGT GGC TCC CCA GGT TT	GAG ACA GTC TTG CGG ACA CA
<i>TRAIL</i>	CCC TGC TTG CAG GTT AAG AG	GGC CTA AGG TCT TTC CAT CC
<i>caspase8</i>	CCT AGA CTG CAA CCG AGA GG	GCA GGC TCA AGT CAT CTT CC
<i>caspase9</i>	TGC CCT TGC CTC TGA GTA GT	AAC AAA GAA ACG CCC ACA AC
<i>p53</i>	AGA GAC CGC CGT ACA GAA GA	CTG TAG CAT GGG CAT CCT TT
<i>Bax</i>	TGC AGA GGA TGA TTG CTG AC	GAT CAG CTC GGG CAC TTT AG
<i>BCL-2</i>	AGG AGC AGG TGC CGA CAA GA	GCA TTT TCC CAC CAC TGT CT
<i>Bcl-XL</i>	CAA AAG CGG GTA CCT TAC CA	CGA ATG GTG TGT GTG TCC TC
<i>Bak</i>	CCA ACA TTG CAT GGT GCT AC	AGG AGT GTT GGG AAC ACA GG
