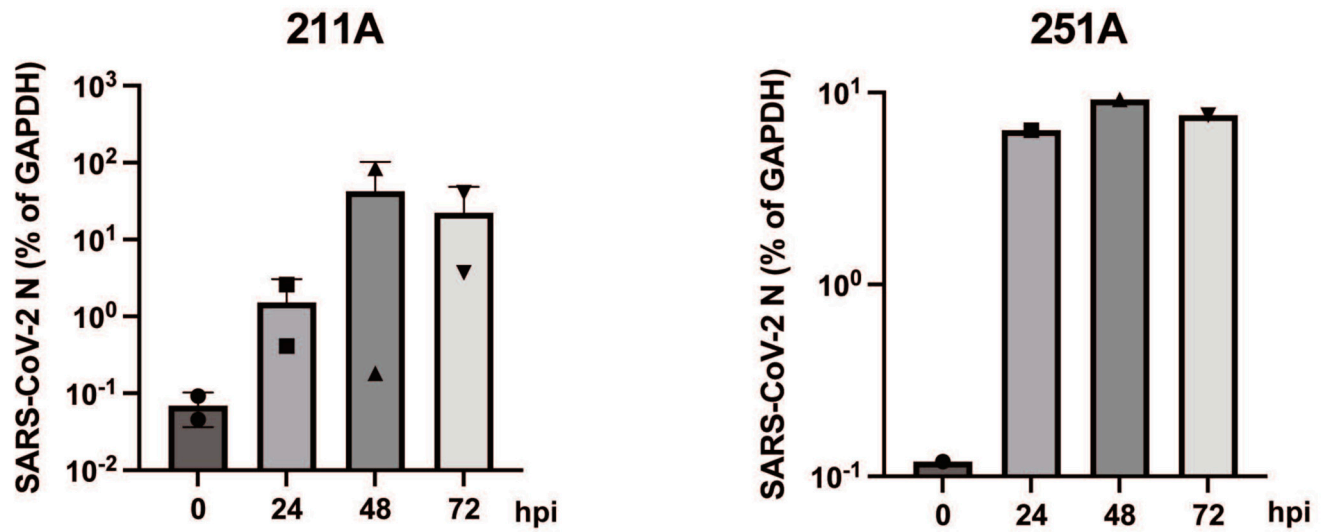
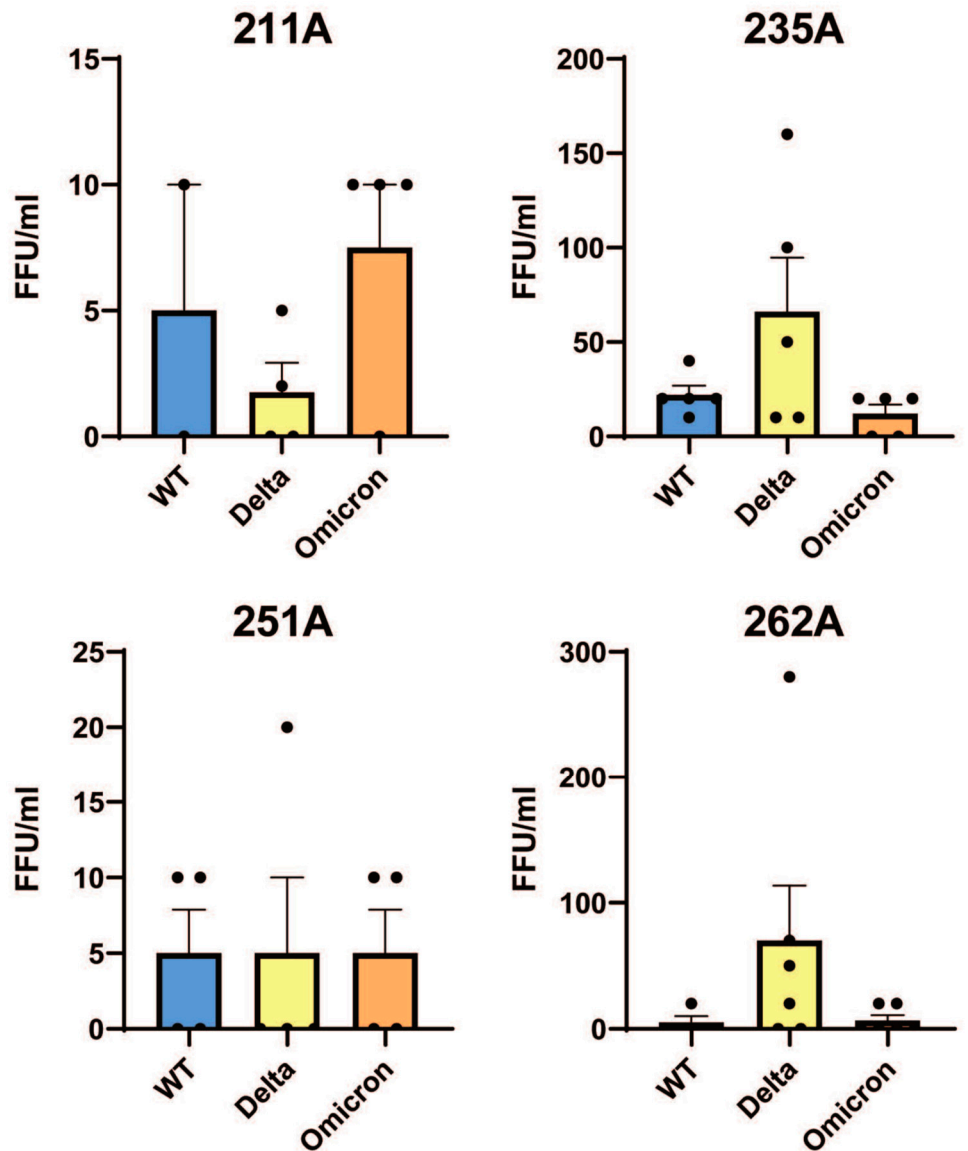


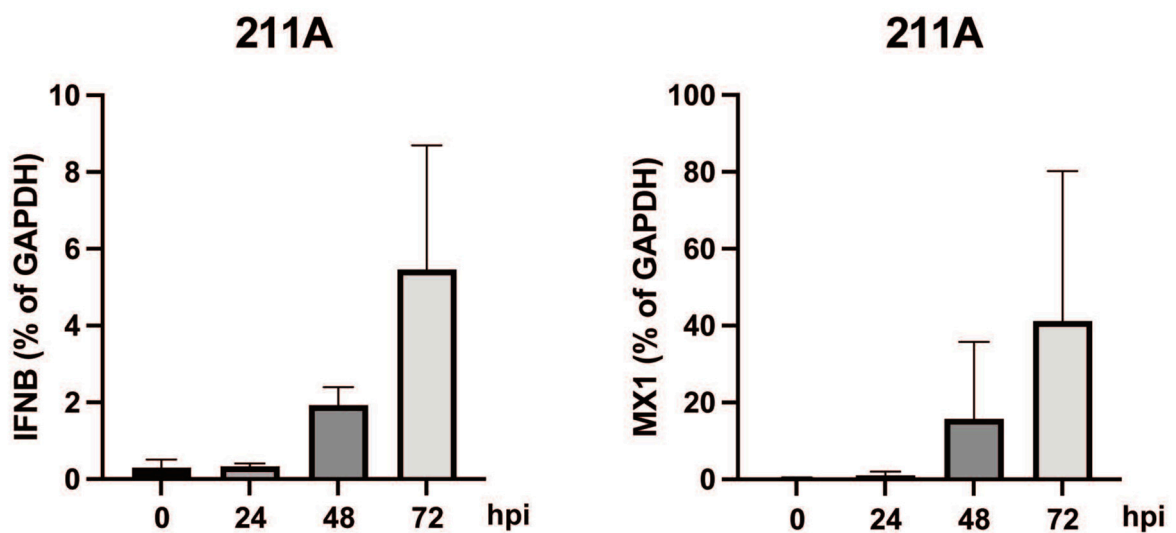
Supplementary Materials



Supplemental Figure S1. Kinetics of SARS-CoV-2 replication in human colonoids. Colonoid lines in 2D transwell monolayers derived from two donors were infected with indicated SARS-CoV-2 variants at an MOI of 0.01. RNA was harvested at 24, 48, or 72 hours post infection and SARS-CoV-2 N level was quantified by RT-qPCR and normalized to GAPDH.



Supplemental Figure S2. Production of virus progeny from multiple SARS-CoV-2 variants. Quantification of infectious viral particles in the supernatants collected from the apical compartments of corresponding transwells at 24 hours post infection by a focus forming unit assay.



Supplemental Figure S3. Temporal dynamics of type I IFN expression. IFNB and MX1 mRNA levels were quantified by RT-qPCR and normalized to GAPDH in colonoids infected with WA1 and harvested at 24, 48, and 72 hours post infection. (Mean with SEM).

Table S1. Virus sequencing results: Spike Mutations in SARS-CoV-2 variants sequenced by NovaSeq.

Omicron B.1.1.529	Delta B.1.617.2	WT WA1
T95I, G142D, V143del, Y144del, Y145del, N211I, L212del, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F, D1146	T19R, G142D, E156G, F157del, R158del, L452R, T478K, D614G, P681R, F855S, D950N, C1235F	No spike mutations

Table S2. qPCR Primers and Probes.

Primer name	Sequences
SARS-CoV-2 N	Forward: ATGCTGCAATCGTGCTACAA Reverse: GACTGCCGCCTCTGCTC Probe: FAM/TCAAGGAACAACATTGCCAA/TAMRA
Human GAPDH	Forward: GGAGCGAGATCCCTCCAAAAT Reverse: GGCTGTTGTCATACTTCTCATGG
IFNL3	Forward: TAAGAGGGCCAAAGATGCCTT Reverse: CTGGTCCAAGACATCCCCC
IFNB	Forward: ATGACCAACAAGTGTCTCCTCC Reverse: GGAATCCAAGCAAGTTGTAGCTC
MX1	Forward: GTGGCTGAGAACAACCTGTG Reverse: GGCATCTGGTCACGATCCC

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Table S3. Background of the colonoids donors.

Patient ID	Patient Diagnosis (N = non-IBD/healthy, CD = Crohn's, UC = ulcerative colitis, FAP = Familial)	Center Biopsy Collected At	Intestinal region	Age @ Access	Sex 1=Male 2=Female	Race 1=White 2=Black 3=Asian 4=Hispanic 5=Multiple/Other 6=Native American	
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	aden. Poly.						
H211	N	WashU	Rectum	55	2	2	
H235	N	WashU	Rectum	51	2	2	
H251	N	WashU	Rectum	63	1	1	
H262	N	WashU	Rectum	56	2	1	