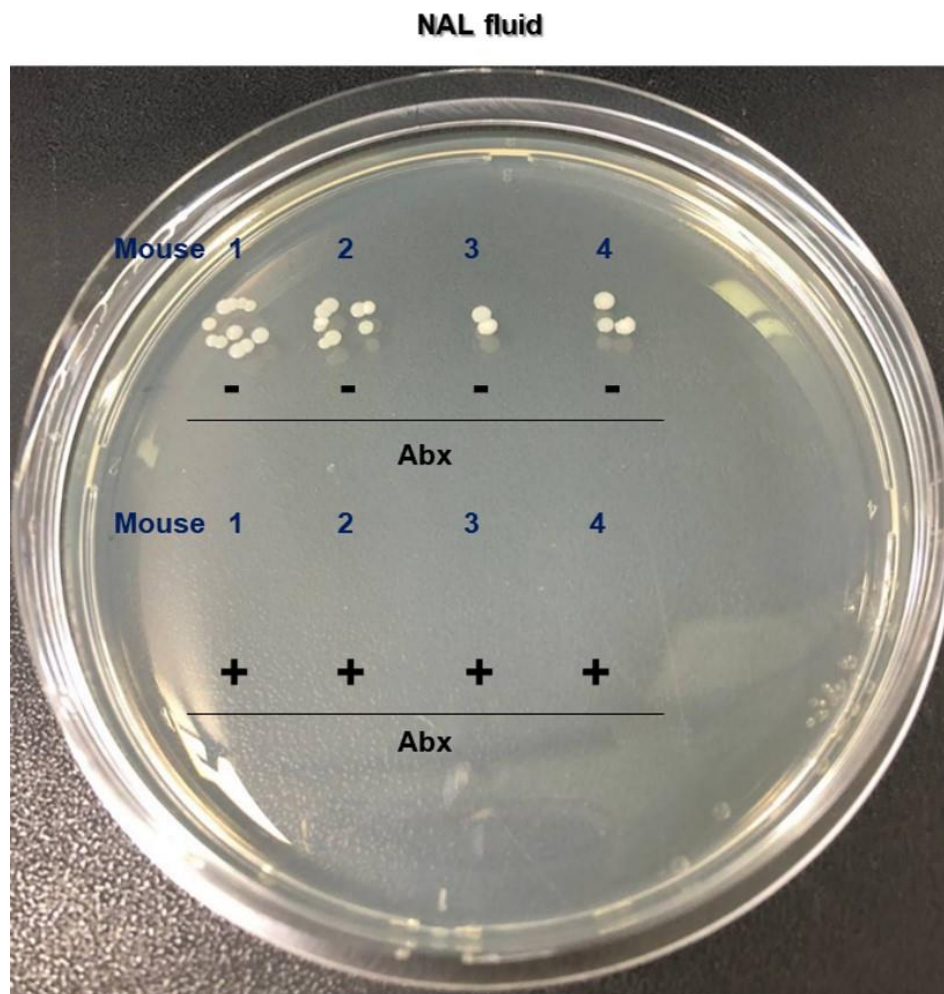
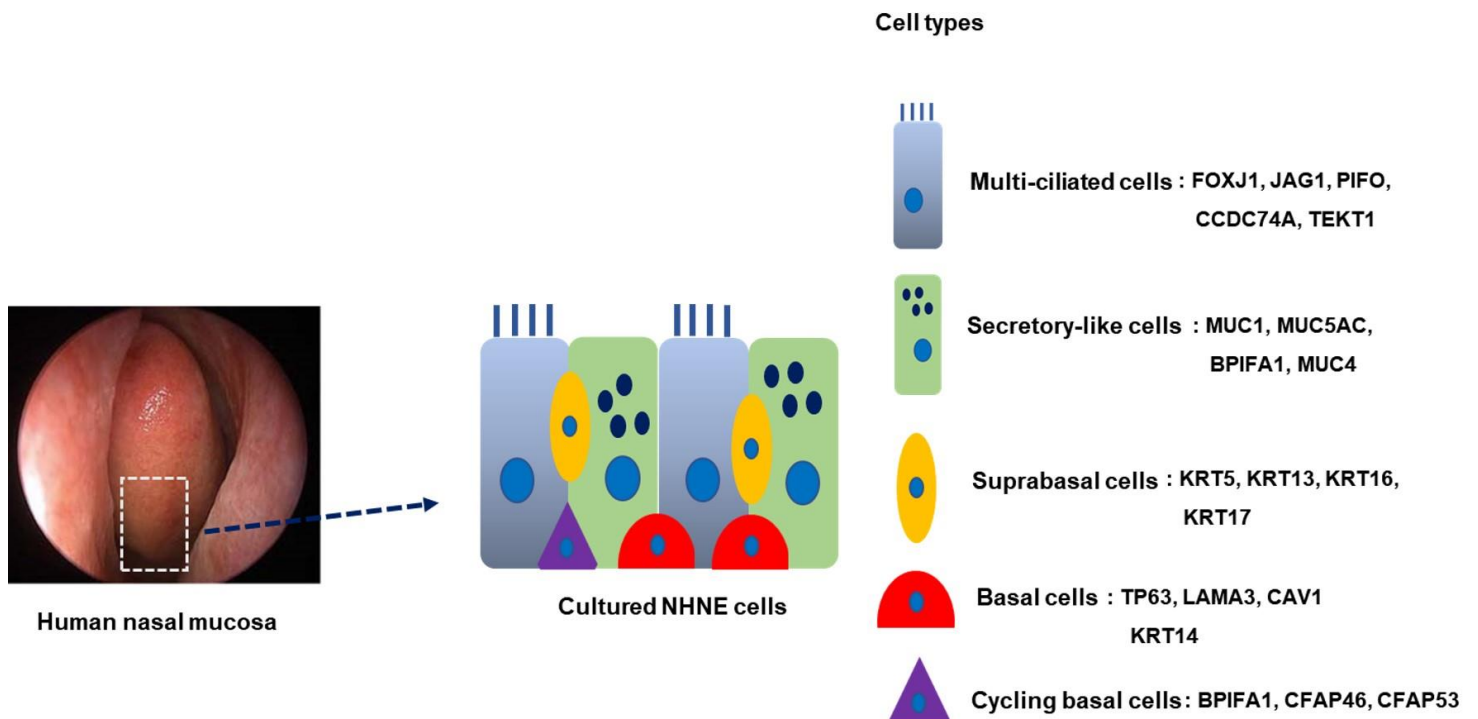


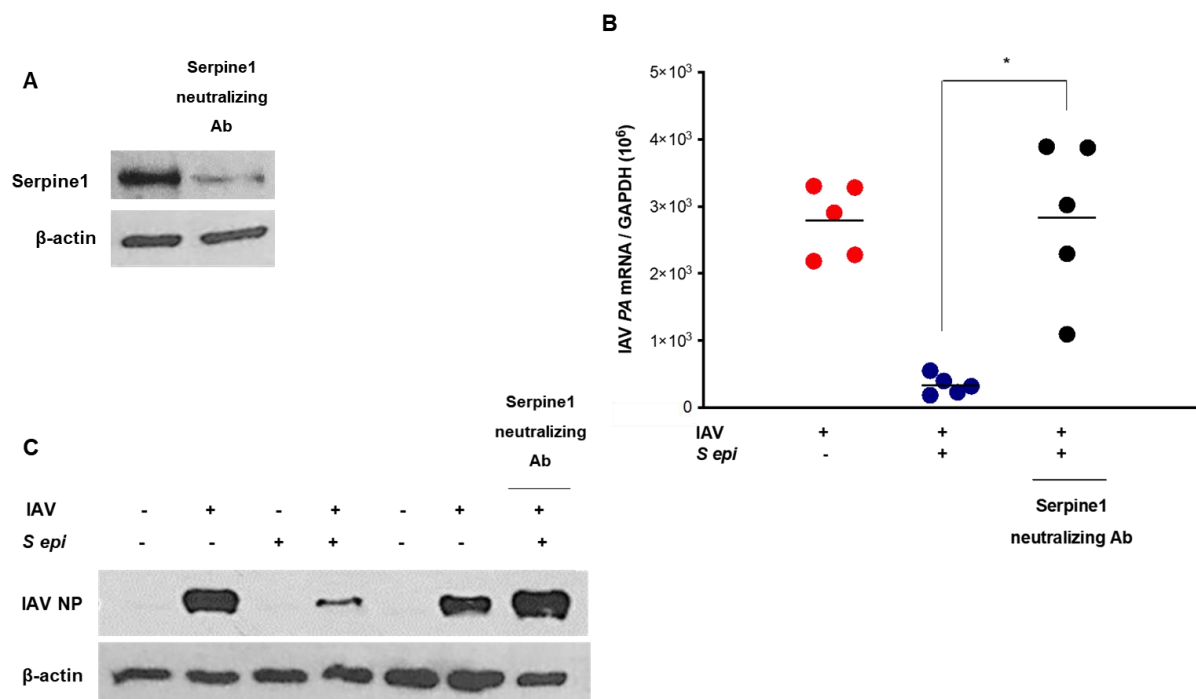
Supplementary figure 1. Colony assay using NAL fluid of C57BL/6 mouse depending on intranasal antibiotics treatment. For bacterial colony isolation, the NAL fluid of B6 mouse was placed on lysogeny broth (LB) plates for 1 day. No bacterial colony was observed in NAL fluid from B6 mouse with intranasal antibiotic treatment.



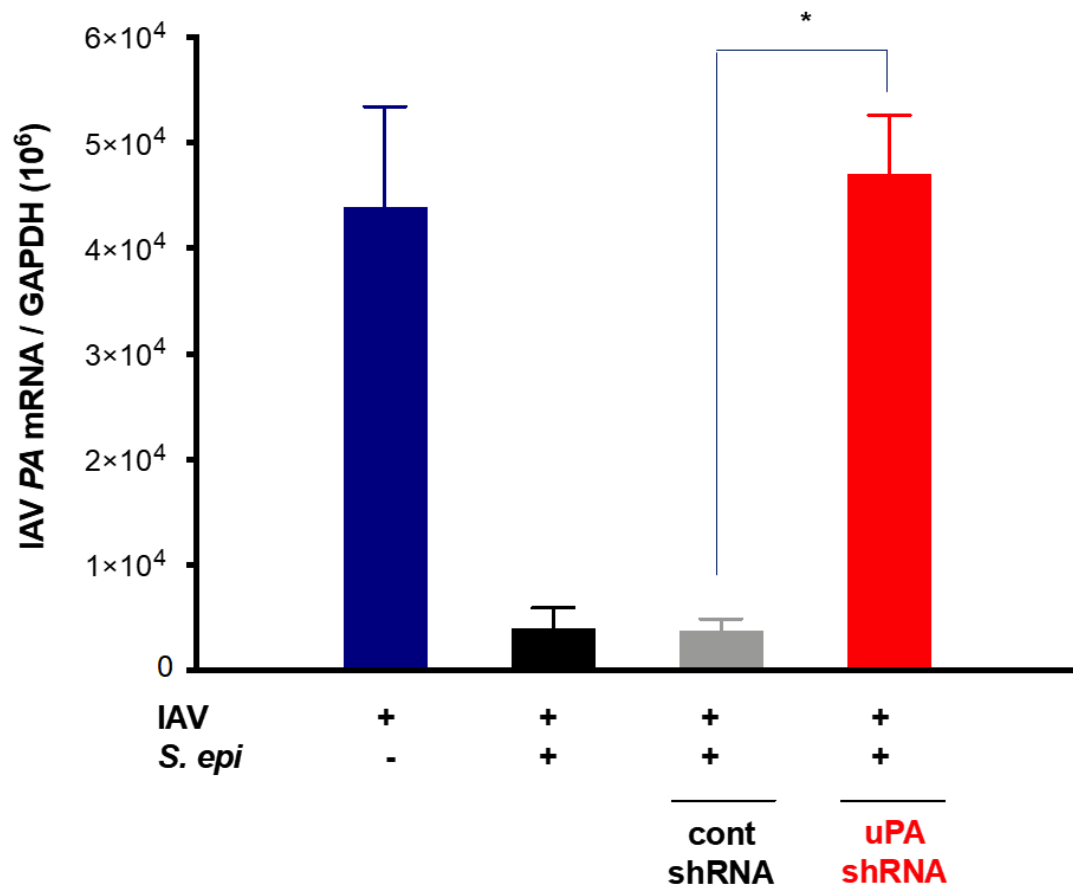
Supplementary figure 2. Schematic illustration depicts the sampling location of surgical nasal mucosa specimen (middle turbinate) for primary nasal epithelial culture and overview of the major cell types in the nasal epithelial cells for single cell RNA sequencing.



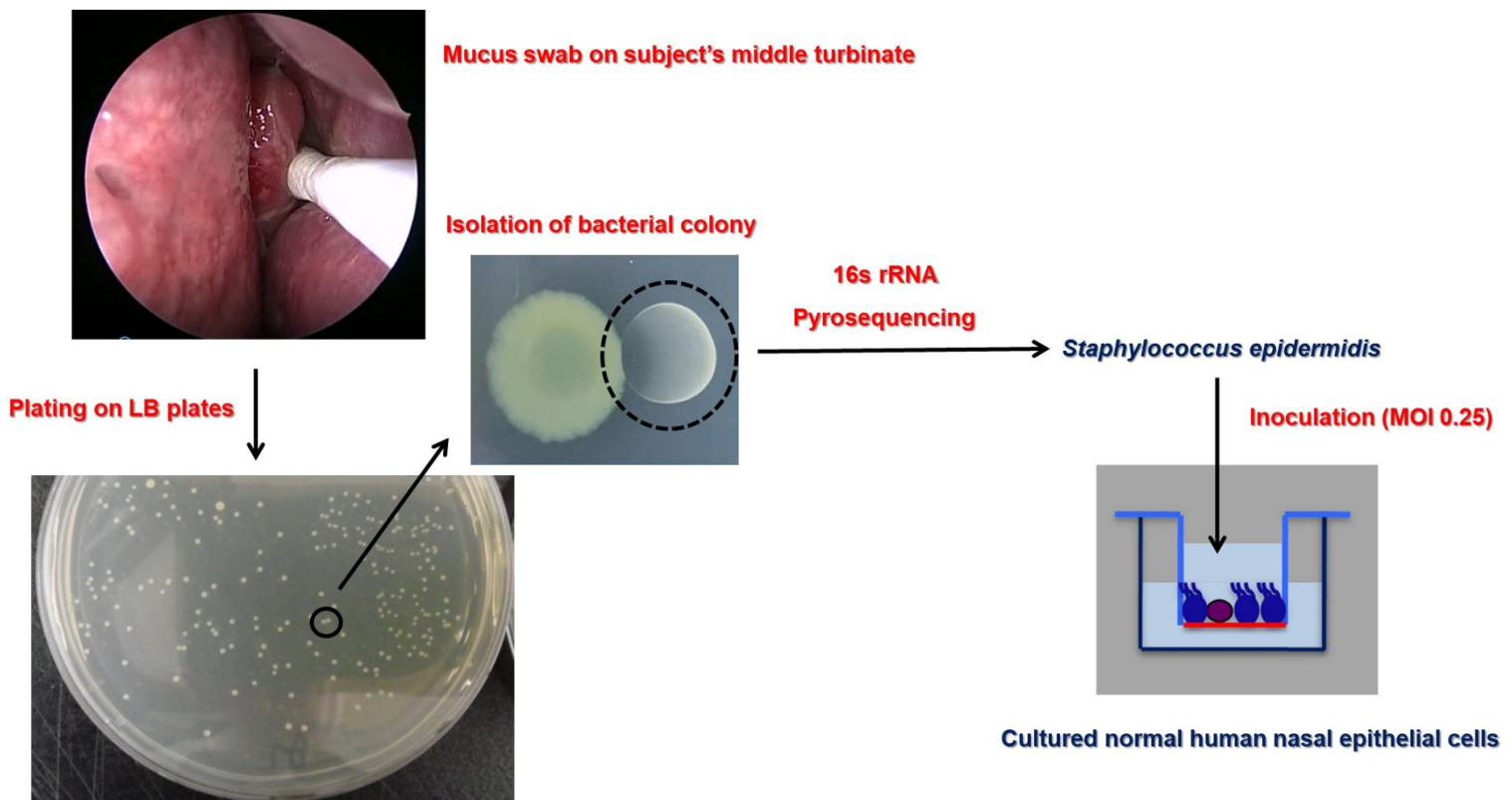
Supplementary figure 3. Serpine1 blocking peptide (2.5ug/ 5ul) was inoculated into the nasal cavity of B6 mice at 1 days prior to antibiotics treatment and then, *S. epidermidis* was inoculated with inoculated to the mice two days before IAV (2,130 pfu/30 μ l, PBS) infection. (A) Serpine1 protein level was measured using western blot analysis. (B) IAV PA mRNA and (C) NP levels were assessed in the nasal mucosa of *S. epidermidis*-inoculated B6 mice following IAV infection depending on the neutralization of Serpine1.



Supplementary figure 4. *Staphylococcus epidermidis*-induced uPA production was involved in IAV replication in NHNE cells. IAV PA mRNA levels were monitored by real-time PCR following *S. epidermidis* inoculation at 1 dpi with transfection with cont shRNA and uPA shRNA.

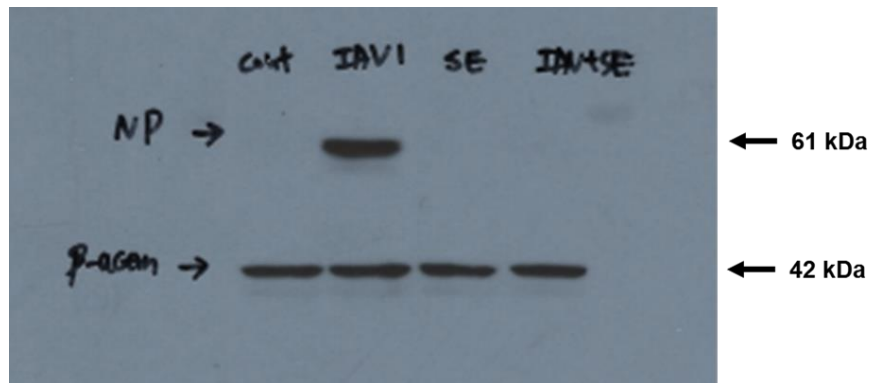


Supplementary figure 5. Schematic illustration of step-by-step experiments from *S. epidermidis* isolation to inoculation of NHNE cells. For bacterial colony isolation, nasal mucus of healthy subjects was obtained using a cotton swab and was used to inoculate Lysogeny Broth (LB) plates. After 2 days of incubation, bacterial colonies were obtained from the LB plates, *S. epidermidis* colonies were identified using GS-FLX 454 pyrosequencing by 16S rRNA gene amplification, and *S. epidermidis* was used to inoculate NHNE cells (MOI 0.25).

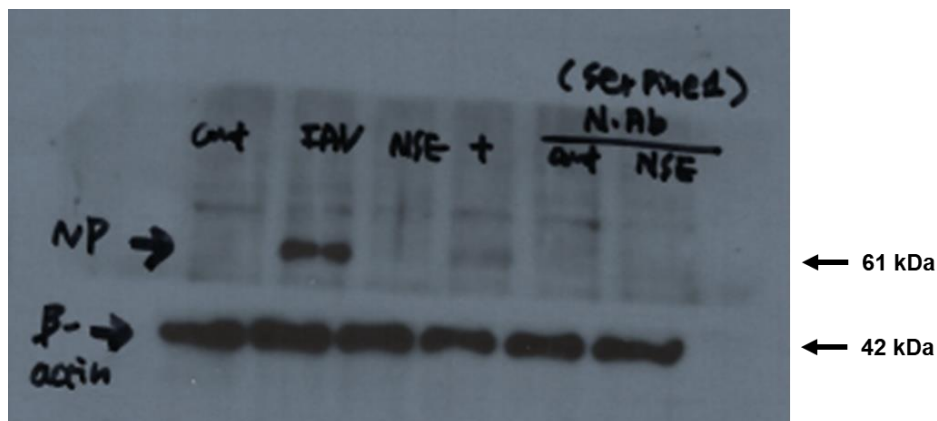


Supplementary figure 6 The full uncropped scans of the western blots included into the main documents

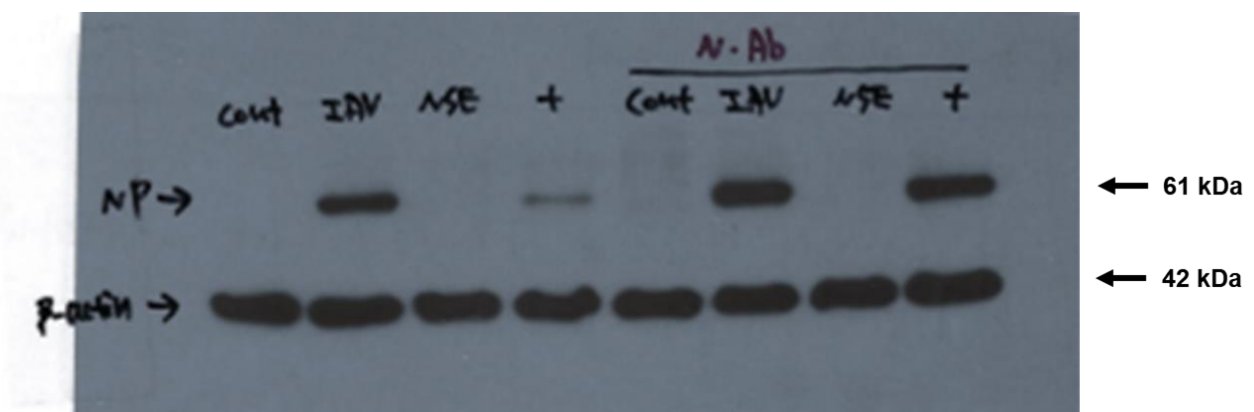
(A) Figure 2G



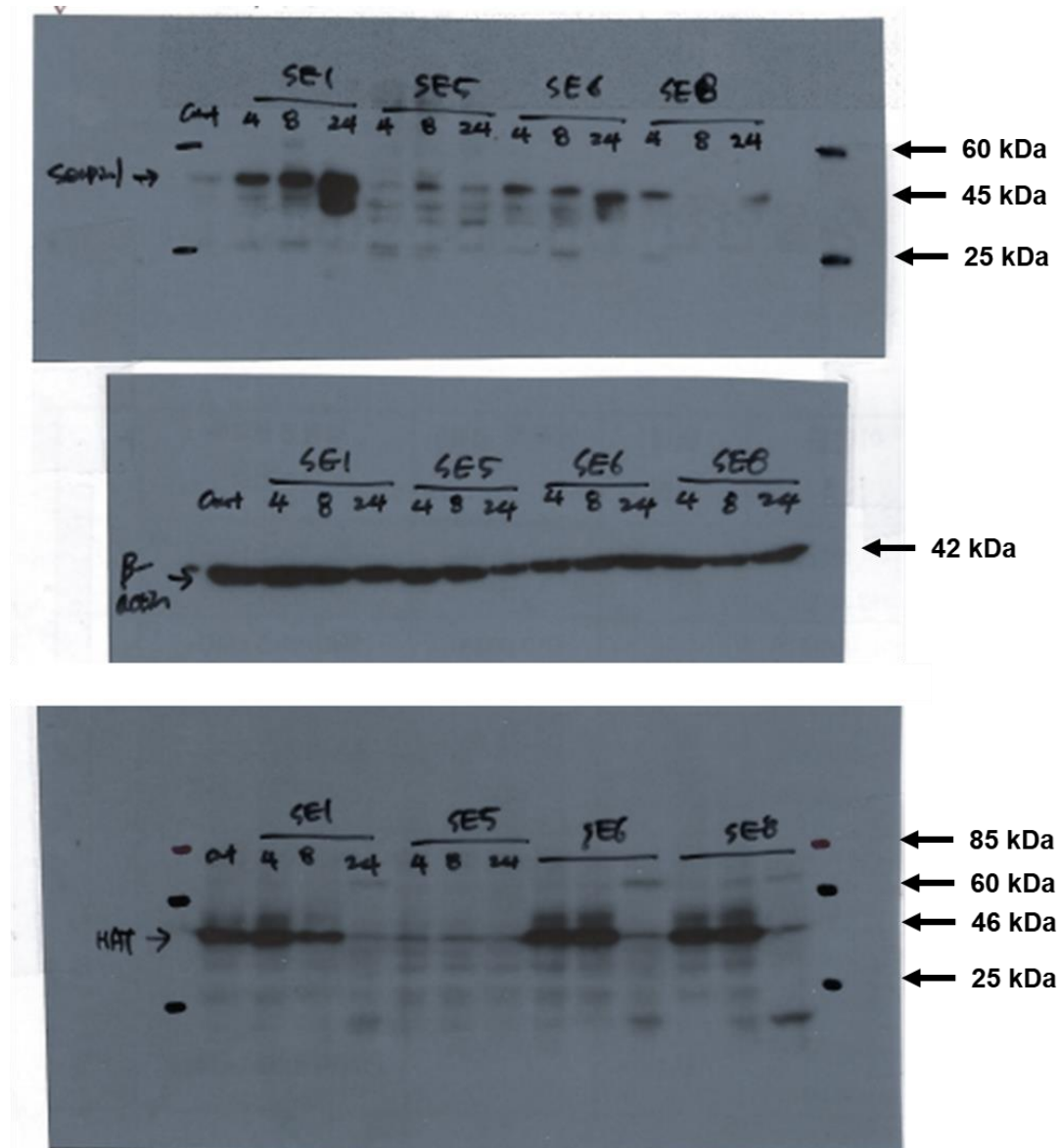
(B) Figure 2H



(C) Figure 3L



(D) Figure 4G



Supplementary table 1. The list of DEGs linked with biological processes enriched GO categories in *S. epidermidis*-inoculated NHNE cells (determined by DAVID analysis).

GO category	ID	Gene symbol	<i>S.epidermidis</i> /control (fold)
Defense response to virus	20989	IL23A	4.725
	19461	DDIT4	4.194
	771	ZC3H12A	3.217
	10611	MICA	3.12
	14656	POLR3D	3.12
	20074	BNIP3	3.041
	29546	BPIFA1	2.51
	33245	IFNGR2	2.439
	24881	ISG20	2.135
	12690	TRIM56	0.403
	27955	TRIM25	0.394
	6414	DTX3L	0.333
	13019	ZC3HAV1	0.314
	25456	PLA2G10	0.24
Modulation by symbiont of entry into host	32704	LGALS1	24.363
	7707	CXCL8	12.98
	12821	CAV1	5.171
	10694	HLA-DRB1	4.101
	18646	TMPRSS4	0.418
	27955	TRIM25	0.394
	27174	LGALS9	0.379
	10408	TRIM38	0.361
	19834	TRIM8	0.361

Serine peptidase inhibitor	5214	SERPINE2	40.804
	12691	SERPINE1	17.155
	5869	COL7A1	5.426
	9772	SPINK1	5.147
	9567	SPOCK1	5.062
	11097	CD109	3.635
	23566	SERPINA3	2.633
	29022	SERPINA7	2.482
	29016	SERPINB5	2.367
Serine peptidase	4659	FAP	11.843
	19503	PLAU	5.627
	18646	TMPRSS4	0.418
Virus entry to host	12821	CAV1	5.171
	20909	ITGA5	5.141
	30459	ICAM1	4.253
	22451	EFNB2	3.907
	24191	VPS18	3.219
	7043	CLDN1	3.008
	12326	EGFR	2.592
	22537	GAS6	2.193
	22184	KPNA3	0.492
	4654	DPP4	0.231

Supplementary table 2. Top 10 significant GO Biological Process and DEGs in *S. epidermidis*-inoculated NHNE cells (determined by ErichR analysis).

term	p-value	overlap_genes
positive regulation of cytokine production (GO:0001819)	1.27E-12	GBP5.CD274.IL33.CCBE1.CSF2.PRKDC.GATA3.HLAG. TRIM6.RGCC.NIRP10.IL23A.LEP.IRF1.PDE4B.CHI3L1. FFAR2.IL6ST.TLR5.TLR3
cellular response to cytokine stimulus (GO:0071345)	2.41E-12	GBP5.CEF2.PNPT1.CCL22.CCL20.IL1R2.DOCK8. RC3H1.GATA3.CBL.MMP9.IL1F10.TRIM6.SOCS1. IL23A.IRF1.IL2RB.ANKRD1.CHI3L1.VIM.SOX9.IL6ST.GBP1
cytokine-mediated signaling pathway (GO:0019221)	1.01E-11	CSF2.PELI2.IFIT5.GATA3.CBL.SAMHD1.IL1RL1.SOCS1. GBP1.IL33.CCL22.CCL20. IL1R2.HLA-GMMP9.IL17RB.IL1F10.IL23A.LEP.IRF1. IL2RB.VIM.IL6ST.MAP3K14.IL17C
regulation of interleukin-8 production (GO:0032677)	1.96E-07	NLRP10.C5AR2.LEP.OTUD7B.CHI3L1.FFAR2.TLR5.TLR3
regulation of inflammatory response (GO:0050727)	5.52E-07	IL33.NLRP10.IK23A.NAPEPLD.S100A12.FFAR2.GATA3.MMP9. VAMP2.TLR3.BRD4
neutrophil degranulation (GO:0043312)	9.09E-07	RAB3A.RAB5C.DDX3X.SERPINA1.CALML5.ATG1.KRT1.IQGAP2. MMP9.OSCAR.GLIPR1.DOK3.LRG1.S100A12.CHI3L1.VAMP2
positive regulation of intracellular signal transduction (GO:1902533)	1.01E-06	DDX3X.PELI2.IFIT5.GATA3.FGF1.CBL.TRIM6.IL23A.LEP. REL.S100A12.CHI3L1.SOX9. MAP3K14.IKBKE.TLR3.BRD4
neutrophil activation involved in immune response (GO:0002283)	1.01E-06	RAB3A.RAB5C.DDX3X.SERPINA1.CALML5.ARG1.KRT1. IQGAP2.MMP9.OSCAR. GLIPR1. DOK3.LRG1.S100A12. CHI3L1.VAMP2
neutrophil mediated immunity (GO:0002446)	1.10E-06	RAB3A.RAB5C.DDX3X.SERPINA1.CALML5.ARG1.KRT1. IQGAP2.MMP9.OSCAR.GLIPR1. DOK3.LRG1.S100A12.CHI3L1.VAMP2
regulation of T cell proliferation (GO:0042129)	1.88E-06	CD274.RIPK3.ARG1.IL23A.LEP.IL6ST.HLA-G

Supplementary table 3. The list of DEGs linked with GO category: Serine type endopeptidase inhibitor in *S. epidermidis*-inoculated secretory and suprabasal NHNE cells (determined by DAVID analysis).

GO: Serine type endopeptidase inhibitor	ID	Gene symbol	<i>S.epidermidis</i>/control (fold)
Secretory cells	2938	AGT	0.4
	5869	COL7A1	2.851
	9567	SPOCK1	2.042
	9772	SPINK1	4.227
	12691	SERPINE1	14.413
	29022	SERPINB7	2.163
	29722	WFDC5	3.796
	29724	PI3	2.052
	29740	WFDC6	0.44
Suprabasal cells	5214	SERPINE2	2.122
	5869	COL7A1	3.374
	11097	CD109	2.592
	12562	TFPI2	2.702
	12691	SERPINE1	12.387
	29016	SERPINB5	2.273
	29022	SERPINB7	3.107
	29722	WFDC5	4.721
	29737	WFDC2	0.377