

Expanded View Figures

COVID-19 patient #8 Protein score: 33

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1 MSSSSWLLLS LVAVTAAQST IEEQAKTFLD KFNHEAEDLF YQSSSLASWNY
51 NTNITEENVQ NNNNAGDKWS AFLKEQSTLA QMYPLEIQN LTVKLLQLAL
101 QQNGSSVLSE DKSKRLNTIL NTMSTIYSTG KVCNPNPQE CLLLEPGLNE
151 IMANSLDYNE RLWAWESWRS EVGQRLRPLY EEEVVLKNEM ARANHYEDYG
201 DYWRGDYEVN GVDGYDYSRG QLIEDVEHTF EEIKPLYEHL HAYVRAKLMN
251 AYPYSISPIG CLPAHLGLDM WGRFWTNLYS LTVFPQKPN IDVTDMVDQ
301 AWDAQRIFKE AEKFFVSVGL PMTQGFWEN SMLTDPGNVQ KAVCHPTAMD
351 LGKGFRLM CTKVTMDDFL TAHHEMGHIQ YDMAYAAQPF LLRNGANEGF
401 HEAVGEIMSL SAATPKHLKS IGLLSPDPQE DNETEINFL KQALITVGTL
451 PFTYMLEKWR WMVFKGEIIP DQMKKWMEM KREIVGVVEP VPHDETYCDP
501 ASLFHVSNDY SFIRYYTRTL YQFPQEQALC QAAKHEGPLH KCDISNSTEA
551 GQKLFNMLRL GKSEPTLAL ENNVGAKNMN VRPLLNLYFEP LFTWLKQDNK
601 NSFVWGSTDW SPYADQSIKV RISLSKALGD KAYEWNNDNM YLFRSSVAYA
651 MRQYFLKVKV QMILFGEEDV RVANLKPRIS FNFFVTAPKN VSDIIPRTEV
701 EKAIRMSRSR INDAFRLNND SLEFLGIQPT LGFPNQPPVS IWLIVFGVVM
751 GVIVGVIVIL IFTGIRDRKK KNKARSGENP YASIDISKGE NNPGFQNTDD
801 VQTSF
    
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COVID-19 patient #9 Protein score: 57

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1 MSSSSWLLLS LVAVTAAQST IEEQAKTFLD KFNHEAEDLF YQSSSLASWNY
51 NTNITEENVQ NNNNAGDKWS AFLKEQSTLA QMYPLEIQN LTVKLQLAL
101 QQNGSSVLSE DKSKRLNTIL NTMSTIYSTG KVCNPNPQE CLLLEPGLNE
151 IMANSLDYNE RLWAWESWRS EVGQRLRPLY EEEVVLKNEM ARANHYEDYG
201 DYWRGDYEVN GVDGYDYSRG QLIEDVEHTF EEIKPLYEHL HAYVRAKLMN
251 AYPYSISPIG CLPAHLGLDM WGRFWTNLYS LTVFPQKPN IDVTDMVDQ
301 AWDAQRIFKE AEKFFVSVGL PMTQGFWEN SMLTDPGNVQ KAVCHPTAMD
351 LGKGFRLM CTKVTMDDFL TAHHEMGHIQ YDMAYAAQPF LLRNGANEGF
401 HEAVGEIMSL SAATPKHLKS IGLLSPDPQE DNETEINFL KQALITVGTL
451 PFTYMLEKWR WMVFKGEIIP DQMKKWMEM KREIVGVVEP VPHDETYCDP
501 ASLFHVSNDY SFIRYYTRTL YQFPQEQALC QAAKHEGPLH KCDISNSTEA
551 GQKLFNMLRL GKSEPTLAL ENNVGAKNMN VRPLLNLYFEP LFTWLKQDNK
601 NSFVWGSTDW SPYADQSIKV RISLSKALGD KAYEWNNDNM YLFRSSVAYA
651 MRQYFLKVKV QMILFGEEDV RVANLKPRIS FNFFVTAPKN VSDIIPRTEV
701 EKAIRMSRSR INDAFRLNND SLEFLGIQPT LGFPNQPPVS IWLIVFGVVM
751 GVIVGVIVIL IFTGIRDRKK KNKARSGENP YASIDISKGE NNPGFQNTDD
801 VQTSF
    
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COVID-19 patient #10 Protein score: 53

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1 MSSSSWLLLS LVAVTAAQST IEEQAKTFLD KFNHEAEDLF YQSSSLASWNY
51 NTNITEENVQ NNNNAGDKWS AFLKEQSTLA QMYPLEIQN LTVKLLQLAL
101 QQNGSSVLSE DKSKRLNTIL NTMSTIYSTG KVCNPNPQE CLLLEPGLNE
151 IMANSLDYNE RLWAWESWRS EVGQRLRPLY EEEVVLKNEM ARANHYEDYG
201 DYWRGDYEVN GVDGYDYSRG QLIEDVEHTF EEIKPLYEHL HAYVRAKLMN
251 AYPYSISPIG CLPAHLGLDM WGRFWTNLYS LTVFPQKPN IDVTDMVDQ
301 AWDAQRIFKE AEKFFVSVGL PMTQGFWEN SMLTDPGNVQ KAVCHPTAMD
351 LGKGFRLM CTKVTMDDFL TAHHEMGHIQ YDMAYAAQPF LLRNGANEGF
401 HEAVGEIMSL SAATPKHLKS IGLLSPDPQE DNETEINFL KQALITVGTL
451 PFTYMLEKWR WMVFKGEIIP DQMKKWMEM KREIVGVVEP VPHDETYCDP
501 ASLFHVSNDY SFIRYYTRTL YQFPQEQALC QAAKHEGPLH KCDISNSTEA
551 GQKLFNMLRL GKSEPTLAL ENNVGAKNMN VRPLLNLYFEP LFTWLKQDNK
601 NSFVWGSTDW SPYADQSIKV RISLSKALGD KAYEWNNDNM YLFRSSVAYA
651 MRQYFLKVKV QMILFGEEDV RVANLKPRIS FNFFVTAPKN VSDIIPRTEV
701 EKAIRMSRSR INDAFRLNND SLEFLGIQPT LGFPNQPPVS IWLIVFGVVM
751 GVIVGVIVIL IFTGIRDRKK KNKARSGENP YASIDISKGE NNPGFQNTDD
801 VQTSF
    
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COVID-19 patient #11 Protein score: 41

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1 MSSSSWLLLS LVAVTAAQST IEEQAKTFLD KFNHEAEDLF YQSSSLASWNY
51 NTNITEENVQ NNNNAGDKWS AFLKEQSTLA QMYPLEIQN LTVKLLQLAL
101 QQNGSSVLSE DKSKRLNTIL NTMSTIYSTG KVCNPNPQE CLLLEPGLNE
151 IMANSLDYNE RLWAWESWRS EVGQRLRPLY EEEVVLKNEM ARANHYEDYG
201 DYWRGDYEVN GVDGYDYSRG QLIEDVEHTF EEIKPLYEHL HAYVRAKLMN
251 AYPYSISPIG CLPAHLGLDM WGRFWTNLYS LTVFPQKPN IDVTDMVDQ
301 AWDAQRIFKE AEKFFVSVGL PMTQGFWEN SMLTDPGNVQ KAVCHPTAMD
351 LGKGFRLM CTKVTMDDFL TAHHEMGHIQ YDMAYAAQPF LLRNGANEGF
401 HEAVGEIMSL SAATPKHLKS IGLLSPDPQE DNETEINFL KQALITVGTL
451 PFTYMLEKWR WMVFKGEIIP DQMKKWMEM KREIVGVVEP VPHDETYCDP
501 ASLFHVSNDY SFIRYYTRTL YQFPQEQALC QAAKHEGPLH KCDISNSTEA
551 GQKLFNMLRL GKSEPTLAL ENNVGAKNMN VRPLLNLYFEP LFTWLKQDNK
601 NSFVWGSTDW SPYADQSIKV RISLSKALGD KAYEWNNDNM YLFRSSVAYA
651 MRQYFLKVKV QMILFGEEDV RVANLKPRIS FNFFVTAPKN VSDIIPRTEV
701 EKAIRMSRSR INDAFRLNND SLEFLGIQPT LGFPNQPPVS IWLIVFGVVM
751 GVIVGVIVIL IFTGIRDRKK KNKARSGENP YASIDISKGE NNPGFQNTDD
801 VQTSF
    
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COVID-19 patient #12 Protein score: 29

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1 MSSSSWLLLS LVAVTAAQST IEEQAKTFLD KFNHEAEDLF YQSSSLASWNY
51 NTNITEENVQ NNNNAGDKWS AFLKEQSTLA QMYPLEIQN LTVKLLQLAL
101 QQNGSSVLSE DKSKRLNTIL NTMSTIYSTG KVCNPNPQE CLLLEPGLNE
151 IMANSLDYNE RLWAWESWRS EVGQRLRPLY EEEVVLKNEM ARANHYEDYG
201 DYWRGDYEVN GVDGYDYSRG QLIEDVEHTF EEIKPLYEHL HAYVRAKLMN
251 AYPYSISPIG CLPAHLGLDM WGRFWTNLYS LTVFPQKPN IDVTDMVDQ
301 AWDAQRIFKE AEKFFVSVGL PMTQGFWEN SMLTDPGNVQ KAVCHPTAMD
351 LGKGFRLM CTKVTMDDFL TAHHEMGHIQ YDMAYAAQPF LLRNGANEGF
401 HEAVGEIMSL SAATPKHLKS IGLLSPDPQE DNETEINFL KQALITVGTL
451 PFTYMLEKWR WMVFKGEIIP DQMKKWMEM KREIVGVVEP VPHDETYCDP
501 ASLFHVSNDY SFIRYYTRTL YQFPQEQALC QAAKHEGPLH KCDISNSTEA
551 GQKLFNMLRL GKSEPTLAL ENNVGAKNMN VRPLLNLYFEP LFTWLKQDNK
601 NSFVWGSTDW SPYADQSIKV RISLSKALGD KAYEWNNDNM YLFRSSVAYA
651 MRQYFLKVKV QMILFGEEDV RVANLKPRIS FNFFVTAPKN VSDIIPRTEV
701 EKAIRMSRSR INDAFRLNND SLEFLGIQPT LGFPNQPPVS IWLIVFGVVM
751 GVIVGVIVIL IFTGIRDRKK KNKARSGENP YASIDISKGE NNPGFQNTDD
801 VQTSF
    
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COVID-19 patient #13 Protein score: 37

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1 MSSSSWLLLS LVAVTAAQST IEEQAKTFLD KFNHEAEDLF YQSSSLASWNY
51 NTNITEENVQ NNNNAGDKWS AFLKEQSTLA QMYPLEIQN LTVKLLQLAL
101 QQNGSSVLSE DKSKRLNTIL NTMSTIYSTG KVCNPNPQE CLLLEPGLNE
151 IMANSLDYNE RLWAWESWRS EVGQRLRPLY EEEVVLKNEM ARANHYEDYG
201 DYWRGDYEVN GVDGYDYSRG QLIEDVEHTF EEIKPLYEHL HAYVRAKLMN
251 AYPYSISPIG CLPAHLGLDM WGRFWTNLYS LTVFPQKPN IDVTDMVDQ
301 AWDAQRIFKE AEKFFVSVGL PMTQGFWEN SMLTDPGNVQ KAVCHPTAMD
351 LGKGFRLM CTKVTMDDFL TAHHEMGHIQ YDMAYAAQPF LLRNGANEGF
401 HEAVGEIMSL SAATPKHLKS IGLLSPDPQE DNETEINFL KQALITVGTL
451 PFTYMLEKWR WMVFKGEIIP DQMKKWMEM KREIVGVVEP VPHDETYCDP
501 ASLFHVSNDY SFIRYYTRTL YQFPQEQALC QAAKHEGPLH KCDISNSTEA
551 GQKLFNMLRL GKSEPTLAL ENNVGAKNMN VRPLLNLYFEP LFTWLKQDNK
601 NSFVWGSTDW SPYADQSIKV RISLSKALGD KAYEWNNDNM YLFRSSVAYA
651 MRQYFLKVKV QMILFGEEDV RVANLKPRIS FNFFVTAPKN VSDIIPRTEV
701 EKAIRMSRSR INDAFRLNND SLEFLGIQPT LGFPNQPPVS IWLIVFGVVM
751 GVIVGVIVIL IFTGIRDRKK KNKARSGENP YASIDISKGE NNPGFQNTDD
801 VQTSF
    
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Healthy control #5 Protein score: 15

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1 MSSSSWLLLS LVAVTAAQST IEEQAKTFLD KFNHEAEDLF YQSSSLASWNY
51 NTNITEENVQ NNNNAGDKWS AFLKEQSTLA QMYPLEIQN LTVKLLQLAL
101 QQNGSSVLSE DKSKRLNTIL NTMSTIYSTG KVCNPNPQE CLLLEPGLNE
151 IMANSLDYNE RLWAWESWRS EVGQRLRPLY EEEVVLKNEM ARANHYEDYG
201 DYWRGDYEVN GVDGYDYSRG QLIEDVEHTF EEIKPLYEHL HAYVRAKLMN
251 AYPYSISPIG CLPAHLGLDM WGRFWTNLYS LTVFPQKPN IDVTDMVDQ
301 AWDAQRIFKE AEKFFVSVGL PMTQGFWEN SMLTDPGNVQ KAVCHPTAMD
351 LGKGFRLM CTKVTMDDFL TAHHEMGHIQ YDMAYAAQPF LLRNGANEGF
401 HEAVGEIMSL SAATPKHLKS IGLLSPDPQE DNETEINFL KQALITVGTL
451 PFTYMLEKWR WMVFKGEIIP DQMKKWMEM KREIVGVVEP VPHDETYCDP
501 ASLFHVSNDY SFIRYYTRTL YQFPQEQALC QAAKHEGPLH KCDISNSTEA
551 GQKLFNMLRL GKSEPTLAL ENNVGAKNMN VRPLLNLYFEP LFTWLKQDNK
601 NSFVWGSTDW SPYADQSIKV RISLSKALGD KAYEWNNDNM YLFRSSVAYA
651 MRQYFLKVKV QMILFGEEDV RVANLKPRIS FNFFVTAPKN VSDIIPRTEV
701 EKAIRMSRSR INDAFRLNND SLEFLGIQPT LGFPNQPPVS IWLIVFGVVM
751 GVIVGVIVIL IFTGIRDRKK KNKARSGENP YASIDISKGE NNPGFQNTDD
801 VQTSF
    
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Healthy control #10 Protein score: 29

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1 MSSSSWLLLS LVAVTAAQST IEEQAKTFLD KFNHEAEDLF YQSSSLASWNY
51 NTNITEENVQ NNNNAGDKWS AFLKEQSTLA QMYPLEIQN LTVKLQLAL
101 QQNGSSVLSE DKSKRLNTIL NTMSTIYSTG KVCNPNPQE CLLLEPGLNE
151 IMANSLDYNE RLWAWESWRS EVGQRLRPLY EEEVVLKNEM ARANHYEDYG
201 DYWRGDYEVN GVDGYDYSRG QLIEDVEHTF EEIKPLYEHL HAYVRAKLMN
251 AYPYSISPIG CLPAHLGLDM WGRFWTNLYS LTVFPQKPN IDVTDMVDQ
301 AWDAQRIFKE AEKFFVSVGL PMTQGFWEN SMLTDPGNVQ KAVCHPTAMD
351 LGKGFRLM CTKVTMDDFL TAHHEMGHIQ YDMAYAAQPF LLRNGANEGF
401 HEAVGEIMSL SAATPKHLKS IGLLSPDPQE DNETEINFL KQALITVGTL
451 PFTYMLEKWR WMVFKGEIIP DQMKKWMEM KREIVGVVEP VPHDETYCDP
501 ASLFHVSNDY SFIRYYTRTL YQFPQEQALC QAAKHEGPLH KCDISNSTEA
551 GQKLFNMLRL GKSEPTLAL ENNVGAKNMN VRPLLNLYFEP LFTWLKQDNK
601 NSFVWGSTDW SPYADQSIKV RISLSKALGD KAYEWNNDNM YLFRSSVAYA
651 MRQYFLKVKV QMILFGEEDV RVANLKPRIS FNFFVTAPKN VSDIIPRTEV
701 EKAIRMSRSR INDAFRLNND SLEFLGIQPT LGFPNQPPVS IWLIVFGVVM
751 GVIVGVIVIL IFTGIRDRKK KNKARSGENP YASIDISKGE NNPGFQNTDD
801 VQTSF
    
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Healthy control #6 (No ACE2 detected)

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1 MSSSSWLLLS LVAVTAAQST IEEQAKTFLD KFNHEAEDLF YQSSSLASWNY
51 NTNITEENVQ NNNNAGDKWS AFLKEQSTLA QMYPLEIQN LTVKLLQLAL
101 QQNGSSVLSE DKSKRLNTIL NTMSTIYSTG KVCNPNPQE CLLLEPGLNE
151 IMANSLDYNE RLWAWESWRS EVGQRLRPLY EEEVVLKNEM ARANHYEDYG
201 DYWRGDYEVN GVDGYDYSRG QLIEDVEHTF EEIKPLYEHL HAYVRAKLMN
251 AYPYSISPIG CLPAHLGLDM WGRFWTNLYS LTVFPQKPN IDVTDMVDQ
301 AWDAQRIFKE AEKFFVSVGL PMTQGFWEN SMLTDPGNVQ KAVCHPTAMD
351 LGKGFRLM CTKVTMDDFL TAHHEMGHIQ YDMAYAAQPF LLRNGANEGF
401 HEAVGEIMSL SAATPKHLKS IGLLSPDPQE DNETEINFL KQALITVGTL
451 PFTYMLEKWR WMVFKGEIIP DQMKKWMEM KREIVGVVEP VPHDETYCDP
501 ASLFHVSNDY SFIRYYTRTL YQFPQEQALC QAAKHEGPLH KCDISNSTEA
551 GQKLFNMLRL GKSEPTLAL ENNVGAKNMN VRPLLNLYFEP LFTWLKQDNK
601 NSFVWGSTDW SPYADQSIKV RISLSKALGD KAYEWNNDNM YLFRSSVAYA
651 MRQYFLKVKV QMILFGEEDV RVANLKPRIS FNFFVTAPKN VSDIIPRTEV
701 EKAIRMSRSR INDAFRLNND SLEFLGIQPT LGFPNQPPVS IWLIVFGVVM
751 GVIVGVIVIL IFTGIRDRKK KNKARSGENP YASIDISKGE NNPGFQNTDD
801 VQTSF
    
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Healthy control #7 (No ACE2 detected)

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1 MSSSSWLLLS LVAVTAAQST IEEQAKTFLD KFNHEAEDLF YQSSSLASWNY
51 NTNITEENVQ NNNNAGDKWS AFLKEQSTLA QMYPLEIQN LTVKLLQLAL
101 QQNGSSVLSE DKSKRLNTIL NTMSTIYSTG KVCNPNPQE CLLLEPGLNE
151 IMANSLDYNE RLWAWESWRS EVGQRLRPLY EEEVVLKNEM ARANHYEDYG
201 DYWRGDYEVN GVDGYDYSRG QLIEDVEHTF EEIKPLYEHL HAYVRAKLMN
251 AYPYSISPIG CLPAHLGLDM WGRFWTNLYS LTVFPQKPN IDVTDMVDQ
301 AWDAQRIFKE AEKFFVSVGL PMTQGFWEN SMLTDPGNVQ KAVCHPTAMD
351 LGKGFRLM CTKVTMDDFL TAHHEMGHIQ YDMAYAAQPF LLRNGANEGF
401 HEAVGEIMSL SAATPKHLKS IGLLSPDPQE DNETEINFL KQALITVGTL
451 PFTYMLEKWR WMVFKGEIIP DQMKKWMEM KREIVGVVEP VPHDETYCDP
501 ASLFHVSNDY SFIRYYTRTL YQFPQEQALC QAAKHEGPLH KCDISNSTEA
551 GQKLFNMLRL GKSEPTLAL ENNVGAKNMN VRPLLNLYFEP LFTWLKQDNK
601 NSFVWGSTDW SPYADQSIKV RISLSKALGD KAYEWNNDNM YLFRSSVAYA
651 MRQYFLKVKV QMILFGEEDV RVANLKPRIS FNFFVTAPKN VSDIIPRTEV
701 EKAIRMSRSR INDAFRLNND SLEFLGIQPT LGFPNQPPVS IWLIVFGVVM
751 GVIVGVIVIL IFTGIRDRKK KNKARSGENP YASIDISKGE NNPGFQNTDD
801 VQTSF
    
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Healthy control #8 (No ACE2 detected)

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1 MSSSSWLLLS LVAVTAAQST IEEQAKTFLD KFNHEAEDLF YQSSSLASWNY
51 NTNITEENVQ NNNNAGDKWS AFLKEQSTLA QMYPLEIQN LTVKLLQLAL
101 QQNGSSVLSE DKSKRLNTIL NTMSTIYSTG KVCNPNPQE CLLLEPGLNE
151 IMANSLDYNE RLWAWESWRS EVGQRLRPLY EEEVVLKNEM ARANHYEDYG
201 DYWRGDYEVN GVDGYDYSRG QLIEDVEHTF EEIKPLYEHL HAYVRAKLMN
251 AYPYSISPIG CLPAHLGLDM WGRFWTNLYS LTVFPQKPN IDVTDMVDQ
301 AWDAQRIFKE AEKFFVSVGL PMTQGFWEN SMLTDPGNVQ KAVCHPTAMD
351 LGKGFRLM CTKVTMDDFL TAHHEMGHIQ YDMAYAAQPF LLRNGANEGF
401 HEAVGEIMSL SAATPKHLKS IGLLSPDPQE DNETEINFL KQALITVGTL
451 PFTYMLEKWR WMVFKGEIIP DQMKKWMEM KREIVGVVEP VPHDETYCDP
501 ASLFHVSNDY SFIRYYTRTL YQFPQEQALC QAAKHEGPLH KCDISNSTEA
551 GQKLFNMLRL GKSEPTLAL ENNVGAKNMN VRPLLNLYFEP LFTWLKQDNK
601 NSFVWGSTDW SPYADQSIKV RISLSKALGD KAYEWNNDNM YLFRSSVAYA
651 MRQYFLKVKV QMILFGEEDV RVANLKPRIS FNFFVTAPKN VSDIIPRTEV
701 EKAIRMSRSR INDAFRLNND SLEFLGIQPT LGFPNQPPVS IWLIVFGVVM
751 GVIVGVIVIL IFTGIRDRKK KNKARSGENP YASIDISKGE NNPGFQNTDD
801 VQTSF
    
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Healthy control #9 (No ACE2 detected)

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1 MSSSSWLLLS LVAVTAAQST IEEQAKTFLD KFNHEAEDLF YQSSSLASWNY
51 NTNITEENVQ NNNNAGDKWS AFLKEQSTLA QMYPLEIQN LTVKLLQLAL
101 QQNGSSVLSE DKSKRLNTIL NTMSTIYSTG KVCNPNPQE CLLLEPGLNE
151 IMANSLDYNE RLWAWESWRS EVGQRLRPLY EEEVVLKNEM ARANHYEDYG
201 DYWRGDYEVN GVDGYDYSRG QLIEDVEHTF EEIKPLYEHL HAYVRAKLMN
251 AYPYSISPIG CLPAHLGLDM WGRFWTNLYS LTVFPQKPN IDVTDMVDQ
301 AWDAQRIFKE AEKFFVSVGL PMTQGFWEN SMLTDPGNVQ KAVCHPTAMD
351 LGKGFRLM CTKVTMDDFL TAHHEMGHIQ YDMAYAAQPF LLRNGANEGF
401 HEAVGEIMSL SAATPKHLKS IGLLSPDPQE DNETEINFL KQALITVGTL
451 PFTYMLEKWR WMVFKGEIIP DQMKKWMEM KREIVGVVEP VPHDETYCDP
501 ASLFHVSNDY SFIRYYTRTL YQFPQEQALC QAAKHEGPLH KCDISNSTEA
551 GQKLFNMLRL GKSEPTLAL ENNVGAKNMN VRPLLNLYFEP LFTWLKQDNK
601 NSFVWGSTDW SPYADQSIKV RISLSKALGD KAYEWNNDNM YLFRSSVAYA
651 MRQYFLKVKV QMILFGEEDV RVANLKPRIS FNFFVTAPKN VSDIIPRTEV
701 EKAIRMSRSR INDAFRLNND SLEFLGIQPT LGFPNQPPVS IWLIVFGVVM
751 GVIVGVIVIL IFTGIRDRKK KNKARSGENP YASIDISKGE NNPGFQNTDD
801 VQTSF
    
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Figure EV1. ACE2 proteins are detected in the serum exosomes of all six COVID-19 patients.
 The identified peptide sequences (red color) of endogenous ACE2 by mass spectrometry analyses using exosomes isolated from the sera of six COVID-19 patients and six healthy controls (Cohort #3). All six COVID-19 patients but only two of six healthy controls showed exosomal ACE2 proteins in the serum exomes. Exosomes were sequentially isolated using ExoQuick kits and then ExoQuick ULTRA columns. Exosomes were further purified by immunoprecipitation using a combination of anti-CD9, anti-CD63, and anti-CD81 magnetic beads. The protein score is the sum of the highest ions score of MS/MS search for each distinct peptide.

A UBR4 protein sequence

1 MATSGGEEAA AAAPAPGTPA TGADTTPGWE VAVRPLLSAS YSAFEMKELP
 51 QLVASVIESE SEILHHEKQY EPFYSFVVAL SHYITTVCS LIPRNLQKSV
 101 AAACKVLIIEF SLLRLENPE ACASVQKHLLI LLIKGLCTCG SRLDRTEIIT
 151 FTAMMKSARK PQTVKTLSDV EDQKELASPV SPELRQKEVQ MNFLNQLTSV
 201 FNPRTVASQP ISTQTLVEGE NDEQSSDQQA SAIKTKNVFI AQNVASLQEL
 251 GGSEKLLRVC LNLPLYFLRY NRFQDAVLAN SFFIMPATVA DATAVRNGFH
 301 SLVIDVTMAL DTLSLPVEFP LNPRLQDVT VLSLSCLYAG VSVATCMAIL
 351 HVGSAQQVVRT GSTSSKEDDY ESDAATIVQK CLEIYDMIGQ AISSSRRAGG
 401 EHYQNFQLL AWCLLNSLFL ILNLSPTALA DKGKEDPLA ALRVDRILSR
 451 TKEGVSPPKL GPGKGHQGFG VLSVILANHA IKLLTSLFQD LQVEALHKGW
 501 ETDGPPAALS IMAQSTSIQR IQRLIDSVP L MNLLTLLST SYRKACVLQR
 551 QRKGMSSDA SASDSTNYE EDDFSSTEED SSQDDSEPI LGWAFQETIS
 601 PSKEKAAPP PPPPPLESS PRVKSQKQA PGEKGNILAS RKDPELFLGL
 651 ASNILNFITS SMLNSRNNFI RNYLSVLSLE HHMATLASII KEVDKDLKLG
 701 SSDEEFAAAL YHFNHSLVTS DLQSPNLQNT LLQQLGVAFP SEGWPPLYIH
 751 PQSLSVLSRL LLIHQHKASA QGDPDVPECL KVWDRFLSTM KQNALQGVVP
 801 SETEDLNVEH LQMLLLIFHN FTETGRRAIL SLFVQIQEL SVNMDAQMRF
 851 VPLILARLLL IFDYLLHQYS KAPVYLFEQV QHNLLSPPFG WASGSDSNS
 901 RRATTPLYHG FKEVEENWSK HFSSDAVPHF RFYCVLSPEA SEDDLNRLDS
 951 VACDVLFSKL VKYDELIAAL TALLAAGSQL DTVRRKENKN VTALEACALQ
 1001 YYFLILWRIL GILPPSKTYI NQLSMNSPEM SECILHTRL WSSRLRISY
 1051 VNWIKDHLIK QGMKAHEASS LLELASTTIC SSVKYDVEIV EEFYFARQISS
 1101 FCSIDCTTIL QLHEIPSLQS IYTLDAIAISK VQVSLDEHFS KMAAETDPHK
 1151 SSEITKNLLP ATLQLIDTYA SFTTARXLLQN FNEEGTEKP SKEALQGFAA
 1201 VLAIGSSRCK ANTLGPTLVQ NLPSSVQTV C ESWNININTNE FPNIGSWRNA
 1251 FANDTIPSES YISAVQAAHL GTLCSQSLPL AASLKHTLLS LVRLTGDLIV
 1301 WSDENMPPQV IRTLLPLLE SSTESVAEIS SNSLERILGP AESDEFLAVR
 1351 YEKLITGCYN ILANHNDPNS LQYLEKLEEC SQARKAMEEF
 1401 FSDSGELVQI MMATANENLS AKFCNRVLKF PTKLFQLTEK SPNPSLLHLC
 1451 GSLAQLACVE PVRLQAWLFR MTTSPPKDSD QLDVIQENRQ LLQLLTYIV
 1501 RENSQVGEV CAVLLGTLTP MATEMLANG GTGFPPELMVV MATLASAGQG
 1551 AGHLQLHNA VDWLSRCKKY LSQKNVVEKL NANVMHGKHV MILECTCHIM
 1601 SYLADVTNAL SQSNGQGPSH LSVDGEEAII EVDSDWVEEL AVEEDSQAE
 1651 DSDEDSLCKN LCTFTITQKE FMNQHWHYCH TCKMVDGVGV CTVCARVCHK
 1701 DHEISYAKYG SFFCDGCAKE DGSLCALVLR TPSSGMSSTM KESAFQSEPR
 1751 ISELSVRHAS TSSPADKAV TISDGVVADE EKPKKSSLCR TVEGCRELEQ
 1801 NQANFSFAPL VLDMLNFLMD AIQTNFQQAS AVGSSSRAQQ ALSELHTVEK
 1851 AVEMTDQLMV PTLGSGEGAF ENVMRMYSGD QGQTIRQLIS AHVLRKVAAC
 1901 VLSSPHGRRL HLAVSHEK GK ITVQLSALL KQADSSKRKL TLRTHASAPV
 1951 PFTVLSLTGN PCKEDYLAVC GLKDCHVLT F SSSGSVSDHL VHPQLATGN
 2001 FIIKAVWLPG SQTELAIVTA DFKIYDLCV DALSPTFYFL LPSSKIROVT
 2051 FLFNEEGKNI IVIMSSAGYI YTLQMEEASS AQQGPFYVFN VLEINHEDLK
 2101 DSNQVAGGG VSVYVSHVQL MLFFSYCQKG SFAATISRRT LEVLQLFPIN
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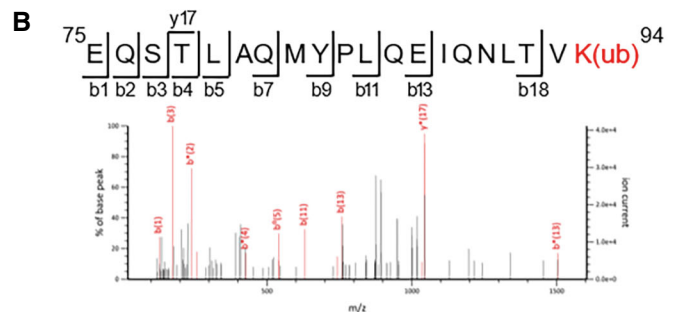


Figure EV2. UBR4 is identified as an ACE2-interacting protein by mass spectrometry.

A The identified peptide sequences (red color) of endogenous UBR4 by mass spectrometry analyses using ACE2 immunocomplexes. ACE2-overexpressing HEK293T cells were treated with the proteasome inhibitor MG132 (25 μ M) for 2 h.

B Besides Lys26, Lys112, and Lys114 residues, Lys94 residue was also identified as an ACE2 ubiquitination site. Mass spectrometry analysis of the ACE2 peptide containing the ubiquitination residue Lys94 from ACE2-transfected HEK293T cells treated with MG132.

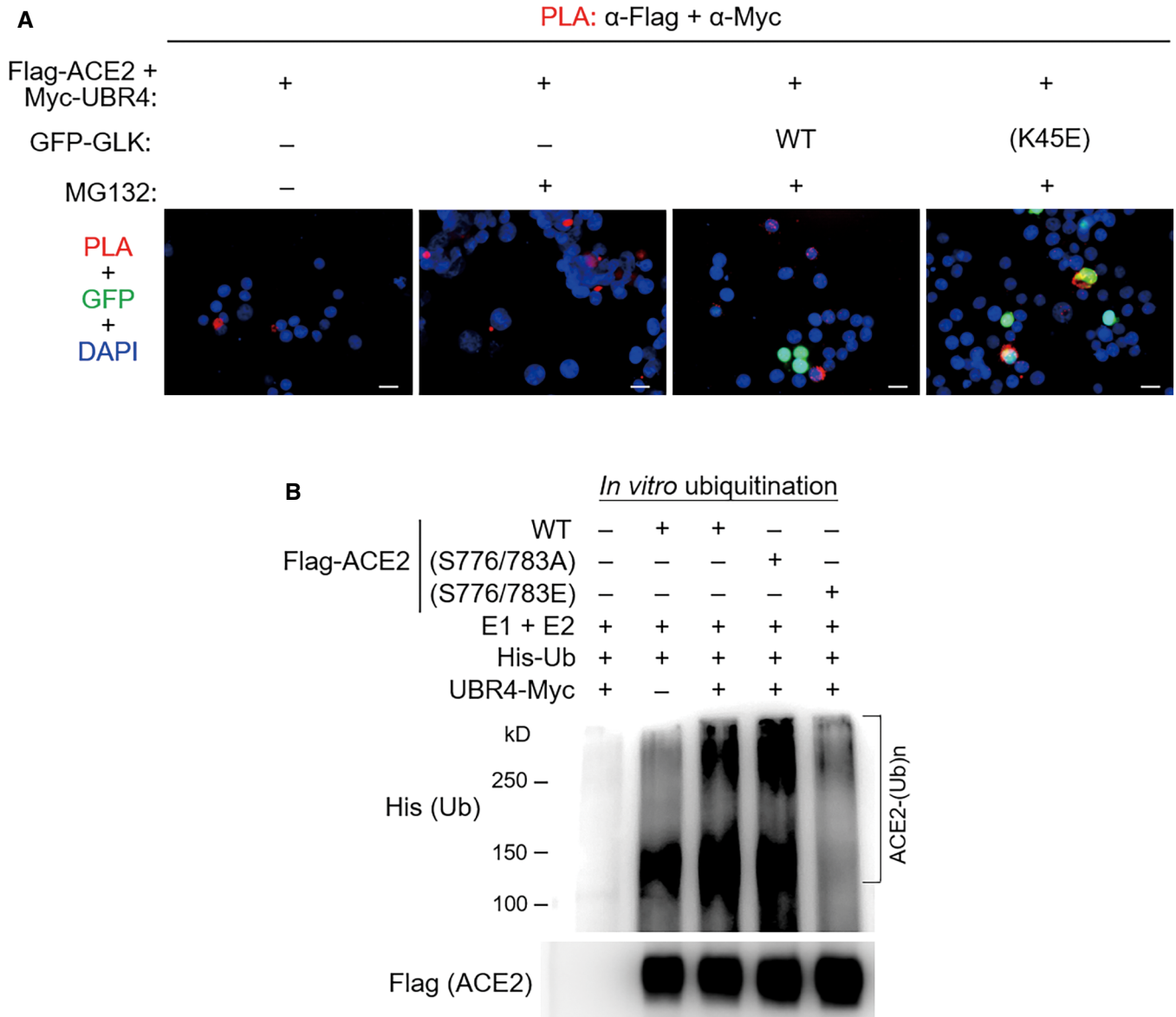


Figure EV3. GLK-induced ACE2 phosphorylation blocks the ACE2-UBR4 interaction and subsequent ACE2 ubiquitination.

A *In situ* PLA assays of the interaction between Flag-tagged ACE2 and Myc-tagged UBR4 proteins in HEK293T cells. Cells were co-transfected with Flag-ACE2 and Myc-UBR4 plus either GFP-GLK (green) or GFP-GLK (K45E) kinase-dead mutant (green) plasmids. Nuclei were stained with DAPI. Red dots represent direct interaction signals. Yellow color represents the co-existence of PLA signal (red) and GLK (K45E) mutant protein (green). Original magnification, ×200. Scale bars, 20 μm.

B *In vitro* ubiquitination assays using Myc-tagged UBR4 and Flag-tagged ACE2 proteins with E1 ubiquitin-activating enzyme, E2 ubiquitin-conjugating enzyme, and His-tagged ubiquitin. ACE2 ubiquitination and ACE2 were detected by immunoblotting with anti-His and anti-Flag antibodies, respectively. Data shown are representative results of three independent experiments.

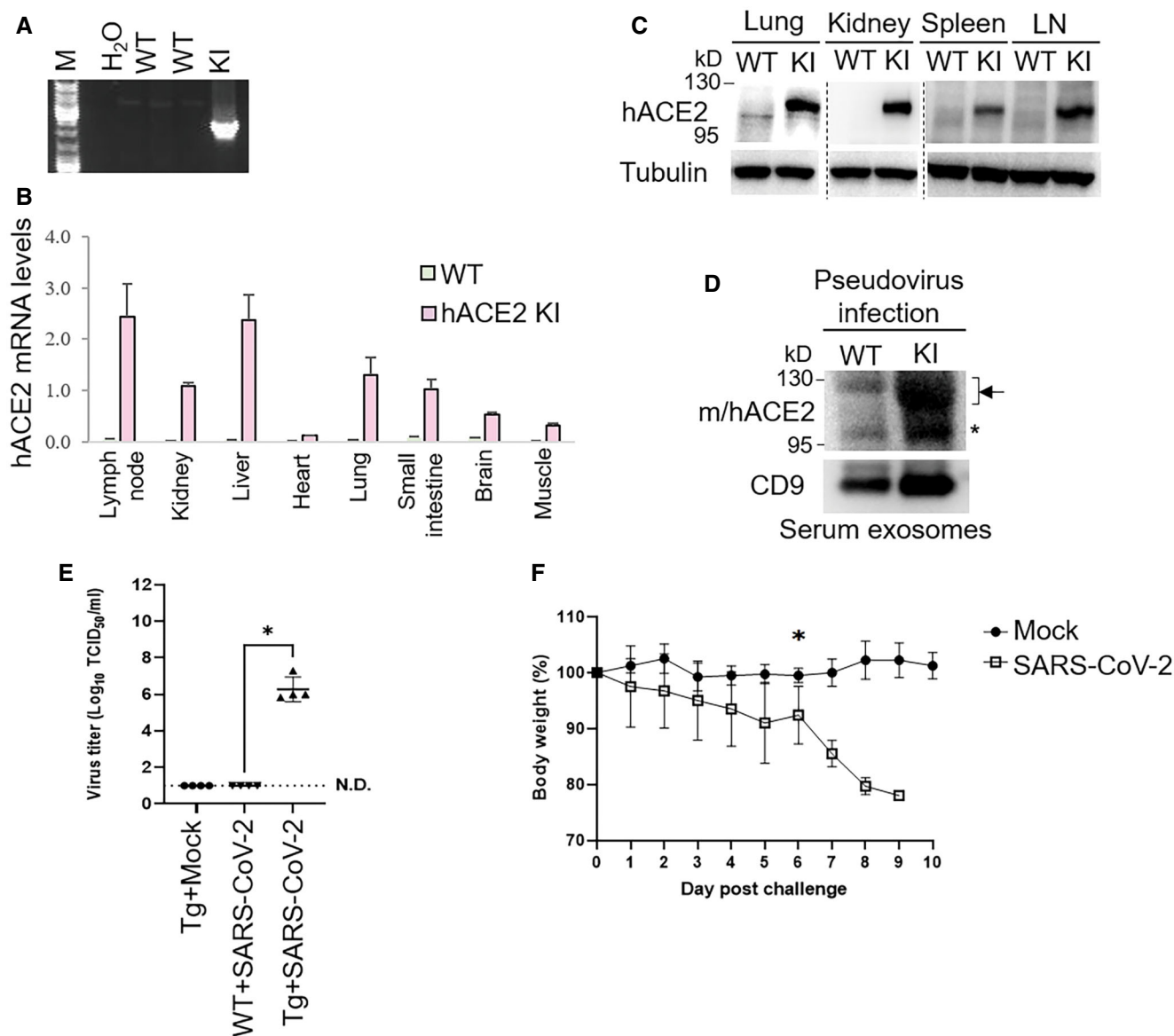


Figure EV4. Infection of hACE2 knockin mice and EF1 α -hACE2 transgenic mice with SARS-CoV-2 pseudovirus or live SARS-CoV-2.

A PCR analyses of hACE2 knockin allele in the genomic DNA from mouse tails. The PCR product of the 2,379-bp band indicates the hACE2 knockin allele.

B Real-time PCR analyses of knockin human ACE2 (hACE2) mRNA levels in the lymph nodes, kidneys, liver, heart, lungs, small intestine, brain, and muscle from wild-type or hACE2 KI mice. The human ACE2 mRNA levels were normalized to mouse GAPDH mRNA levels. $n = 2$ (technical replicates) per group.

C Immunoblotting analyses of hACE2, tubulin, and human ACE2 proteins in the lungs, kidneys, spleen, and lymph nodes of wild-type and hACE2 KI mice.

D Immunoblotting of hACE2, GLK, and CD9 proteins in the exosomes isolated from the sera of the SARS-CoV-2 pseudovirus-infected mice. Exosomes were isolated sequentially using ExoQuick kits and then ExoQuick ULTRA columns. Arrowheads denote glycosylated hACE2 proteins; asterisk denotes unglycosylated hACE2 proteins.

E, F EF1 α -hACE2 Tg and wild-type mice were infected intranasally with 2×10^5 pfu of live SARS-CoV-2. $n = 4$ (biological replicates) per group. EF1 α -hACE2 Tg mice were treated intranasally with PBS (Mock) as controls. On day 3 postinfection, the mice were sacrificed, and the lung tissues were homogenized for the TCID₅₀ assay (E). The survival rate of EF1 α -hACE2 Tg mice challenged with live SARS-CoV2 was monitored (F). WT, wild-type mice; KI, hACE2 knockin mice; Tg, EF1 α -hACE2 transgenic mice. The number of infected mice was less than 3 from day 7 due to deaths; thus, the statistical analysis of panel F was only performed on data up to day 6 postinfection.

Data information: In (B), data are presented as means \pm SD. In (E), data are presented as means \pm SEM. * P -value < 0.05 (Kruskal–Wallis test). In (F), data are presented as means \pm SEM. * P -value < 0.05 (Mann–Whitney test).

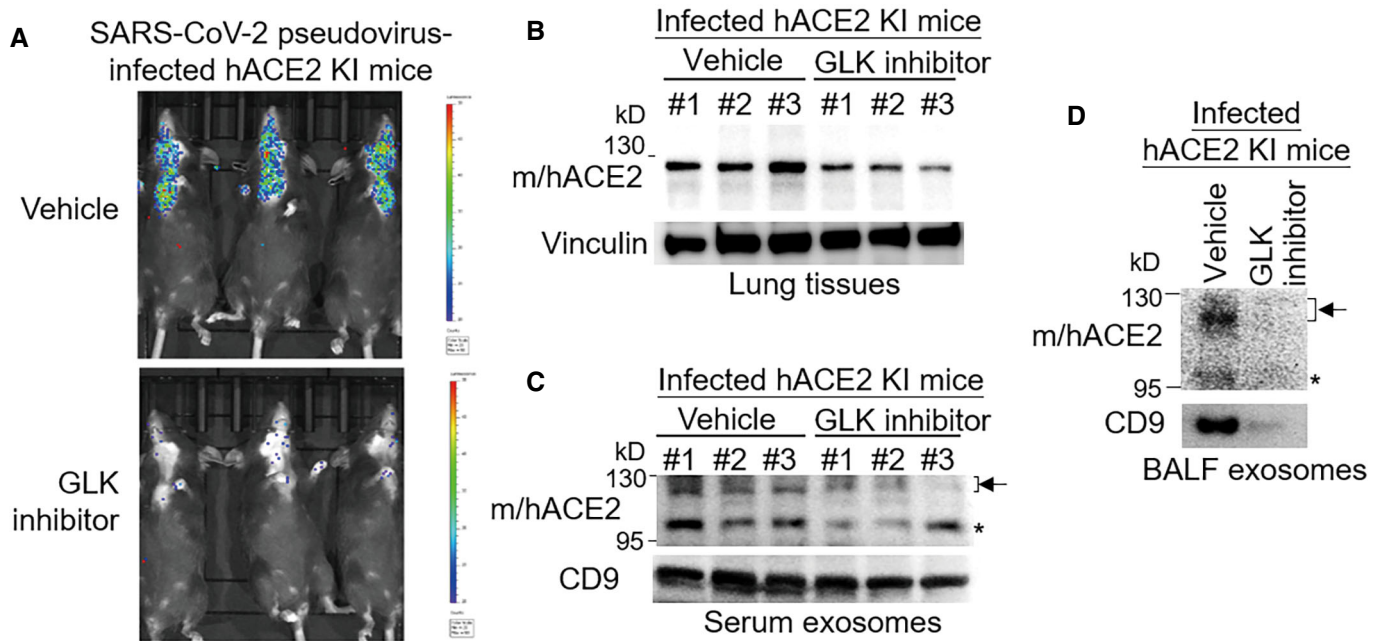


Figure EV5. GLK inhibitor attenuates ACE2 protein levels, ACE2-containing exosomes, and SARS-CoV-2 pseudovirus infection.

A–D Human ACE2 KI mice were intranasally infected with SARS-CoV-2 pseudovirus on Day 0 and Day 1. Mice were also treated with the GLK inhibitor verteporfin on Day 0 after infection. $n = 3$ (biological replicates) per group. Infection efficiencies of SARS-CoV-2 pseudovirus in mouse tissues were measured by IVIS and presented as luminescence counts on Day 2 (A). Immunoblotting of ACE2 and vinculin in the lung tissues of the infected hACE2 KI mice with/without the GLK inhibitor verteporfin (10 μ M in 100 μ l) treatment (B). Immunoblotting of ACE2 and CD9 in exosomes isolated from the sera (C) and BALF (D) of the infected mice with/without the GLK inhibitor verteporfin (10 μ M in 100 μ l) treatment. Arrowhead denotes glycosylated ACE2 proteins; asterisk denotes unglycosylated ACE2 proteins.

Data information: WT, wild-type mice; KI, hACE2 knockin mice.