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Supplemental information

Imatinib and methazolamide ameliorate COVID-19-induced metabolic complications via elevating ACE2 enzymatic activity and inhibiting viral entry

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Supplemental Information

Supplemental Information Inventory

Supplementary Figure Legends

Figure S1. ACE2 is a Key Molecule Potentially Linking COVID-19 to Associated Metabolic Defects, Related to Figure 1.

(**A-B**) HUVECs were infected by SARS-CoV-2 (MOI = 0.005) for 24 h and subjected to transcriptome study. Kyoto Encyclopedia of Genes and Genomes (**KEGG**) pathway enrichment (**A**) and Gene Ontology (**GO**) pathway enrichment (**B**) of differentially expressed genes after infection were shown. (**C**) HUVECs were treated with vehicle (-) or combination of 50 ng/ml of TNF-α, IL-4, IL-6 and IFN-γ for 48 h and were subjected to real-time PCR of *ACE2* (n = 3). Error bars represent SEM; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

Figure S2. ACE2 Plays an Important Role in Maintaining Metabolic Homeostasis, Related to Figure 2.

(**A-D**) HUVECs were transfected with ACE2 plasmid for overexpression for 72 h and subjected to real-time PCR (n = 4). (**E-N**) Eight-week-old male ob/ob mice were treated with intravenous injection of AAV9-CAG-humanACE2-EGFP (**ob/ob-ACE2**) or corresponding control virus (**ob/ob-Con**) and their wild type littermates with control virus (**WT-Con**), and all mice were sacrificed at 12 weeks after 6 h fasting. Livers were subjected to immunoblotting of ACE2 (**E**, blot shown on the left, quantification on the right; n = 4). The ratio of plasma Ang II to Ang-(1-7) (**F**) was shown (n = 5). Body weight gain at 4 weeks after virus injection was calculated as body weight on sacrificed day against body weight on virus injection day (**G**), epididymal fat index (**H**), food intake (**I**) and water intake (**J**) were shown (n = 6). Plasma triglyceride (**TG**) (**K**) and total cholesterol (**TC**) (**L**) were shown (n = 5). (**M**) H&E staining in livers was shown. (**N**) Quantifications of TC in liver were shown (n = 6). Error bars represent SEM, $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.001$. **Ang II**, angiotensin II; **Ang-(1-7)**, angiotensin (1-7).

Figure S3. Imatinib, Harpagoside and Methazolamide Are Identified as ACE2 Activators, Related to Figure 3.

(**A**) Conformational shuffling of ACE2 structure between closed (PDB code: 1R4L) and open state (PDB code: 1R42). (**B**) Knockdown efficiency of ACE2 siRNA in HUVECs was shown after real-time PCR analysis (n = 4). (**C**) Cell viability with the highest concentration of 15 compounds

in HUVECs was determined by lactate dehydrogenase (LDH) assay (n = 6). (**D-I**) HUVECs were treated with diminazene aceturate (**DIZE**, 100 μM), imatinib (**Ima**), harpagoside (**Har**) or methazolamide (**Met**) for 16 h and subjected to real-time PCR (n = 6). (**J-M**) HUVECs were treated with combination of 50 ng/ml TNF-α, IFN-γ, IL-4 and IL-6 for 32 h following imatinib, harpagoside or methazolamide for 16 h and subjected to real-time PCR (n = 6). The significance of Inflammatory factors versus Control was shown as #, Ima/Har/Met + Inflammatory factors versus Inflammatory factors as *. (**N-S**) HUVECs were treated with 10 nM control siRNA (**siCon**) or ACE2 siRNA (**siACE2**) for 8 h following imatinib, harpagoside or methazolamide for 16 h and subjected to real-time PCR (n = 4). (**T-W**) HUVECs were treated with imatinib, harpagoside or methazolamide for 16 h, and subjected to real-time PCR of *ACE2* (**T**) (n = 6), and immunoblotting (**U-W**, blot shown on the left, quantification on the right; n = 4). **L**, low concentration; **M**, medium concentration; **H**, high concentration; imatinib: 1 μM, 5 μM, 25 μM, respectively; harpagoside: 4 μM, 20 μM, 100 μM, respectively; methazolamide: 4 μM, 20 μM, 100 μM, respectively. Error bars represent SEM, $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.001$; $^{\#}p < 0.05$, $^{\#\#}p < 0.01$ and $^{\#\#\#}p < 0.001$.

Figure S4. Imatinib, Harpagoside and Methazolamide Directly Bind to and Activate ACE2, Related to Figure 4.

(**A**) Alignment of human and mouse ACE2 protein. Conserved amino acid residues for two proteins were labeled with asterisk (*****), as unconserved amino acid residues were highlighted in red. (**B**) Murine AML12 cells were treated with 10 nM control siRNA (**Con**) and ACE2 siRNA (**siACE2**) for 24 h and subjected to real-time PCR (n = 6). (**C-E**) AML12 cells were treated with imatinib, harpagoside or methazolamide for 16 h and subjected to real-time PCR (n = 5). **L**, low concentration; **H**, high concentration; imatinib: 1 μM, 25 μM, respectively; harpagoside: 4 μM, 100 μM, respectively; methazolamide: 4 μM, 100 μM, respectively. Error bars represent SEM, $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.001$.

Figure S5. Imatinib and Methazolamide Ameliorate Metabolic Defects in Insulin-resistant Mice via ACE2, Related to Figure 5.

(**A-L**) Twenty-eight-week-old male mice with 23 weeks high-fat-diet treatment (**DIO**) and controlled lean mice (**Lean**) were treated with vehicle, 250 mg/kg of imatinib (**DIO + Ima**) or 100 mg/kg of methazolamide (**DIO + Met**) through gavage once each day for 4 weeks. At 32 weeks,

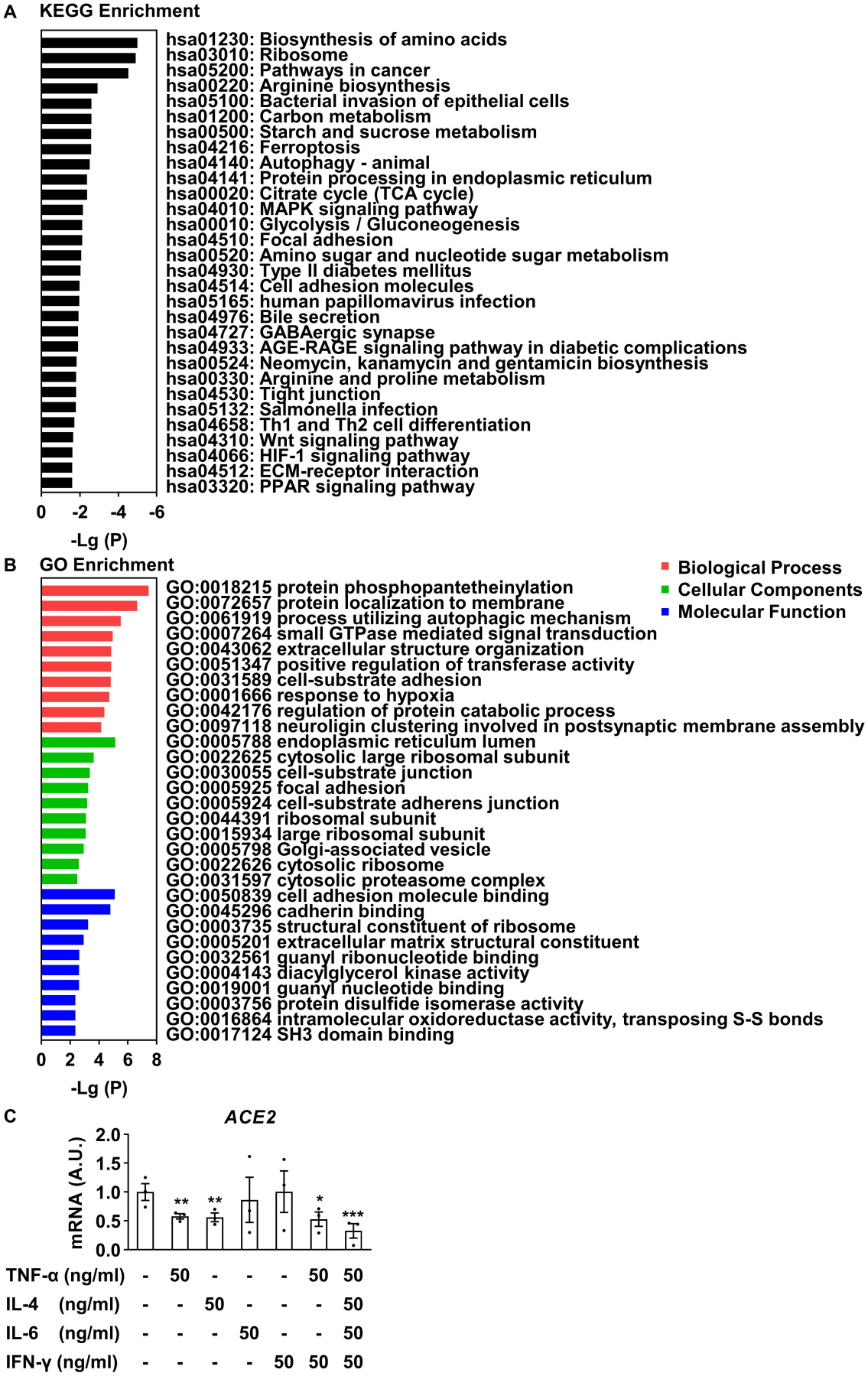
all mice were fasted for 6 h and sacrificed. Body weight (**A**), epididymal fat index (**B**), food intake (**C**) and water intake (**D**) were shown (n = 6). The significance of DIO versus Lean was shown as*, DIO+Met versus DIO as #. $^{*\#}p < 0.05$, $^{**\#\#}p < 0.01$ and $^{***\#\#\#}p < 0.001$. Plasma triglyceride (**TG**) (**E**), total cholesterol (**TC**) (**F**), alanine aminotransferase (**ALT**) (**G**) and aminotransferase (**AST**) (**H**) were shown. Livers were subjected to quantifications of TG (**I**) and TC (**J**) (n = 6) and immunoblotting of FoxO1 (**K**, blot shown on the left, quantification on the right; n = 6) and ACE2 (**L**, blot shown on the left, quantification on the right; n = 6). (**M-O**) For whole body knockdown of ACE2 (**ACE2 kd**), twenty-six-week-old male mice with 21 weeks high-fat-diet treatment (**DIO**) were treated with intravenous injection of AAV9-CAG-mACE2shRNA-EGFP or control virus. After two weeks recovery, all mice were given vehicle (**DIO** and **DIO + ACE2 kd**), 250 mg/kg of imatinib (**DIO + Ima** and **DIO + Ima + ACE2 kd**) or 100 mg/kg of methazolamide (**DIO + Met** and **DIO + Met + ACE2 kd**) through gavage once each day for 4 weeks. At 32 weeks, all mice were fasted for 6 h and sacrificed. Livers, kidneys and aortas were subjected to real-time PCR (**M**) (n = 3). Glucose tolerance testing (**GTT**) was performed at 30 weeks (**N**), and insulin tolerance testing (**ITT**) was performed at 31 weeks (**O**) (n = 6). The significance of Lean versus DIO was shown as *, DIO versus DIO + Ima as #, DIO versus DIO + Met as $, and DIO + Ima versus DIO + Ima + ACE2 kd as &. $^{*\#\$\&}p < 0.05$, $^{**\#\#\$\$\&\&}p < 0.01$ and $^{***\#\#\#\$\$\$\&\&\&}p < 0.001$. (**P**) Kidneys from kidney conditional knockdown of ACE2 (**ACE2 C-kd**) with transparenchymal renal pelvis injection of AAV9-CAG-mACE2shRNA-EGFP or control virus were subjected to real-time PCR for knockdown efficiency analysis (n = 6). (**Q**, **R**) Twenty-eight-week-old male mice with 23 weeks high-fat-diet treatment were treated with vehicle (**DIO**), 250 mg/kg of imatinib (**DIO + Ima**) or 100 mg/kg of methazolamide (**DIO + Met**) through gavage once each day for 4 weeks. At 32 weeks, all mice were fasted for 6 h and sacrificed. Kidneys (**Q**) and aortas (**R**) were subjected to real-time PCR (n = 4-6). Error bars represent SEM. $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.001$.

Figure S6. ACE2 Enzymatic Activators Improve Metabolic Defects and Inhibit Virus Entry upon SARS-CoV-2 Infection, Related to Figure 6.

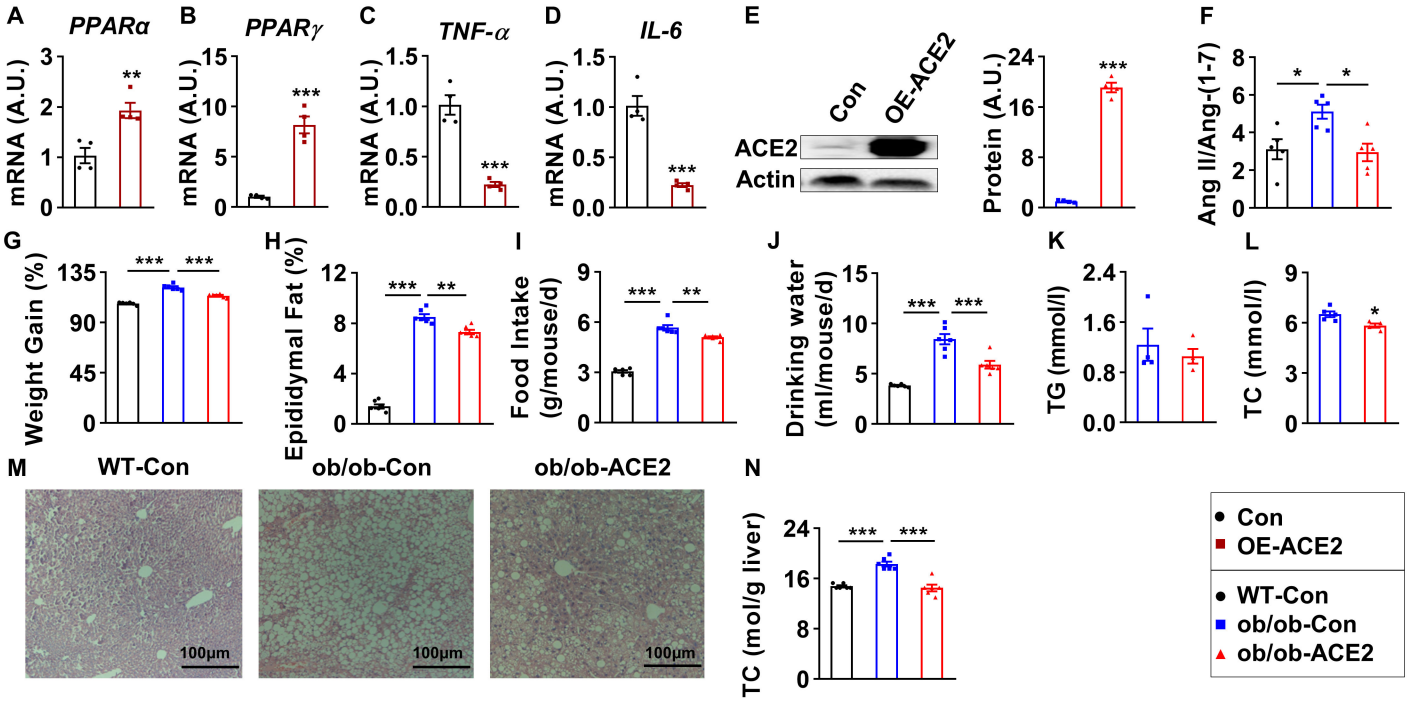
(**A**) Twelve-week-old human ACE2 transgenic mice were treated with vehicle (**Mock** and **CoV-2**), 250 mg/kg imatinib (**CoV-2 + Ima**) or 100 mg/kg methazolamide (**CoV-2 + Met**) through gavage once each day for 4 weeks after 6 weeks high-fat-diet treatment and were intranasally challenged with 4×10^4 FFU SARS-CoV-2. After 7 days post infection, all mice were fasted for 6 h and

sacrificed. Lungs were subjected to immunohistochemistry stainings for viral nucleocapsid protein (**NP**). (**B-C**) Vero E6 cells were pre-treated with 25 μM imatinib, 100 μM harpagoside or 100 μM methazolamide for 6 h, followed by SARS-CoV-2 (MOI = 0.005) infection for 42 h, and focus formation assay for the titer of active virus in the supernatant was performed (**B**). (**C**) Infected Vero E6 cells were further subjected to real-time PCR (n = 6). (**D**) HEK293T cells expressing hACE2 were pre-treated with 25 μM imatinib, 100 μM harpagoside or 100 μM methazolamide for 6 h, followed by pseudovirions treatment for 66 h and were examined with lactate dehydrogenase (LDH) assay (n = 5). (**E**) The binding free energy of spike to ACE2 protein with or without imatinib or methazolamide was shown. (**F**, **G**) The structural conformations of spike and ACE2 protein before and after binding to imatinib (**F**, arrow) or methazolamide (**G**, arrow) were shown. Spike and ACE2 protein were labeled in gray before binding to the compounds, whereas spike protein in red, ACE2 in green (**F**) or blue (**G**) after binding. (**H**) meta-analysis of ACEi/ARB application and risk of severity and mortality in COVID-19 patients with hypertension were shown. CI, confidence interval. Error bars represent SEM. $^{**}p < 0.01$ and $^{***}p < 0.001$.

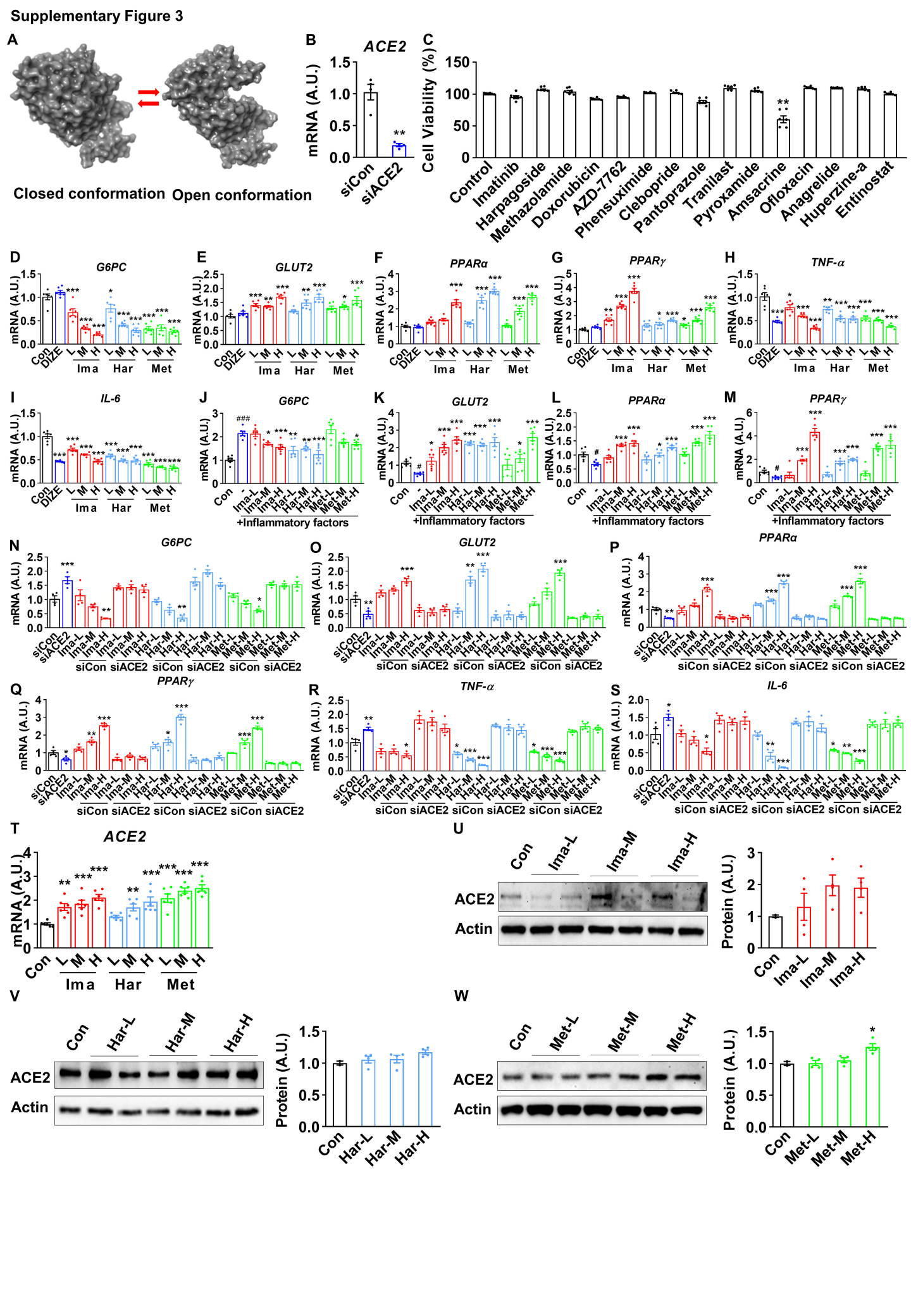
Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4

A

Protein alignment

Protein	Identity
ACE2_HUMAN	100.0%
ACE2_MOUSE	82.1%

```
ACE2_HUMAN   1 MSSSSWLLLSLVAVTAAQSTIEEQAKTFLDKFNHEAEDLFYQSSLASWNYNTNITEENVQ
ACE2_MOUSE   1 MSSSSWLLLSLVAVTTAQSLTEENAKTFLNNFNQEAEDLSYQSSLASWNYNTNITEENAQ
               ********************  ***   **  *****   **  *****  ********** *

ACE2_HUMAN  61 NMNNAGDKWSAFLKEQSTLAQMYPLQEIQNLTVKLQLQALQQNGSSVLSEDKSKRLNTIL
ACE2_MOUSE  61 KMSEAAAKWSAFYEEQSKTAQSFSLQEIQTPIIKRQLQALQQSGSSALSADKNKQLNTIL
               *  *  *****  ***  **  *****  *  *******  ***  **  **  * *****

ACE2_HUMAN 121 NTMSTIYSTGKVCNPDNPQECLLLEPGLNEIMANSLDYNERLWAWESWRSEVGKQLRPLY
ACE2_MOUSE 121 NTMSTIYSTGKVCNPKNPQECLLLEPGLDEIMATSTDYNSRLWAWEGWRAEVGKQLRPLY
               ************  ***********  ****  *  ***  ******  **  *********

ACE2_HUMAN 181 EEYVVLKNEMARANHYEDYGDYWRGDYEVNGVDGYDYSRGQLIEDVEHTFEEIKPLYEHL
ACE2_MOUSE 181 EEYVVLKNEMARANNYNDYGDYWRGDYEAEGADGYNYNRNQLIEDVERTFAEIKPLYEHL
               ********** * **********  *  ***  *  ********  **  *********

ACE2_HUMAN 241 HAYVRAKLMNAYPSYISPIGCLPAHLLGDMWGRFWTNLYSLTVPFGQKPNIDVTDAMVDQ
ACE2_MOUSE 241 HAYVRRKLMDTYPSYISPTGCLPAHLLGDMWGRFWTNLYPLTVPFAQKPNIDVTDAMMNQ
               *****  ***  ********* ********************  *****  **********  *

ACE2_HUMAN 301 AWDAQRIFKEAEKFFVSVGLPNMTQGFWENSMLTDPGNVQKAVCHPTAWDLGKGDFRILM
ACE2_MOUSE 301 GWDAERIFQEAEKFFVSVGLPHMTQGFWANSMLTEPADGRKVVCHPTAWDLGHGDFRIKM
               *** ***  ************  ******  *****  *  *  **********  *****  *

ACE2_HUMAN 361 CTKVTMDDFLTAHHEMGHIQYDMAYAAQPFLLRNGANEGFHEAVGEIMSLSAATPKHLKS
ACE2_MOUSE 361 CTKVTMDNFLTAHHEMGHIQYDMAYARQPFLLRNGANEGFHEAVGEIMSLSAATPKHLKS
               ********  ********************  ********************  *********

ACE2_HUMAN 421 IGLLSPDFQEDNETEINFLLKQALTIVGTLPFTYMLEKWRWMVFKGEIPKDQWMKKWWEM
ACE2_MOUSE 421 IGLLPSDFQEDSETEINFLLKQALTIVGTLPFTYMLEKWRWMVFRGEIPKEQWMKKWWEM
               ****  *****  ********************  *****  *****  **********

ACE2_HUMAN 481 KREIVGVVEPVPHDETYCDPASLFHVSNDYSFIRYYTRTLYQFQFQEALCQAAKHEGPLH
ACE2_MOUSE 481 KREIVGVVEPLPHDETYCDPASLFHVSNDYSFIRYYTRTIYQFQFQEALCQAAKYNGSLH
               ********** ********************  ********************  *  **

ACE2_HUMAN 541 KCDISNSTEAGQKLFNMLRLGKSEPWTLALENVVGAKNMNVRPLLNYFEPLFTWLKDQNK
ACE2_MOUSE 541 KCDISNSTEAGQKLLKMLSLGNSEPWTKALENVVGARNMDVKPLLNYFQPLFDWLKEQNR
               **********  **  **  *****  ********  **  *  ******  ***  ***  **

ACE2_HUMAN 601 NSFVGWSTDWSPYADQSIKVRISLKSALGDRAYEWNDNEMYLFRSSVAYAMRQYFLKVKN
ACE2_MOUSE 601 NSFVGWNTEWSPYADQSIKVRISLKSALGANAYEWTNNEMFLFRSSVAYAMRKYFSIIKN
               ******  *  ********************  ****  ***  **********  **  **

ACE2_HUMAN 661 QMILFGEEDVRVANLKPRISFNFFVTAPKNVSDIIPRTEVEKAIRMSRSRINDAFRLNDN
ACE2_MOUSE 661 QTVPFLEEDVRVSDLKPRVSFYFFVTSPQNVSDVIPRSEVEDAIRMSRGRINDVFGLNDN
               *  *  ******  ****  **  ****  *  ****  ***  ***  ******  ****  *  ****

ACE2_HUMAN 721 SLEFLGIQPTLGPPNQPPVSIWLIVFGVVMGVIVVGIVILIFTGIRDRKKKNKARSGENP
ACE2_MOUSE 721 SLEFLGIHPTLEPPYQPPVTIWLIIFGVVMALVVVGIIILIVTGIKGRKKKNETKREENP
               ********  ***  **  ****  ****  *****    ****  ***  ***   *****      ***

ACE2_HUMAN 781 YASIDISKGENNPGFQNTDDVQTSF
ACE2_MOUSE 781 YDSMDIGKGESNAGFQNSDDAQTSF
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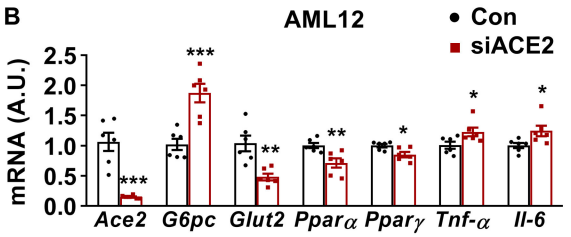
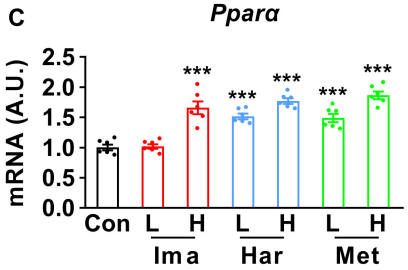
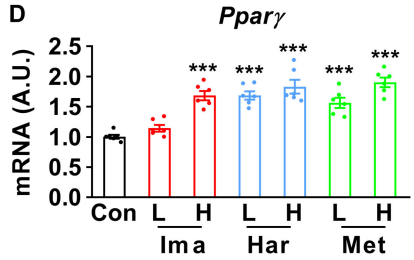
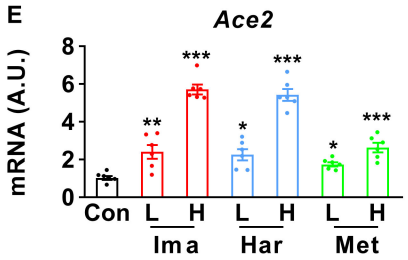
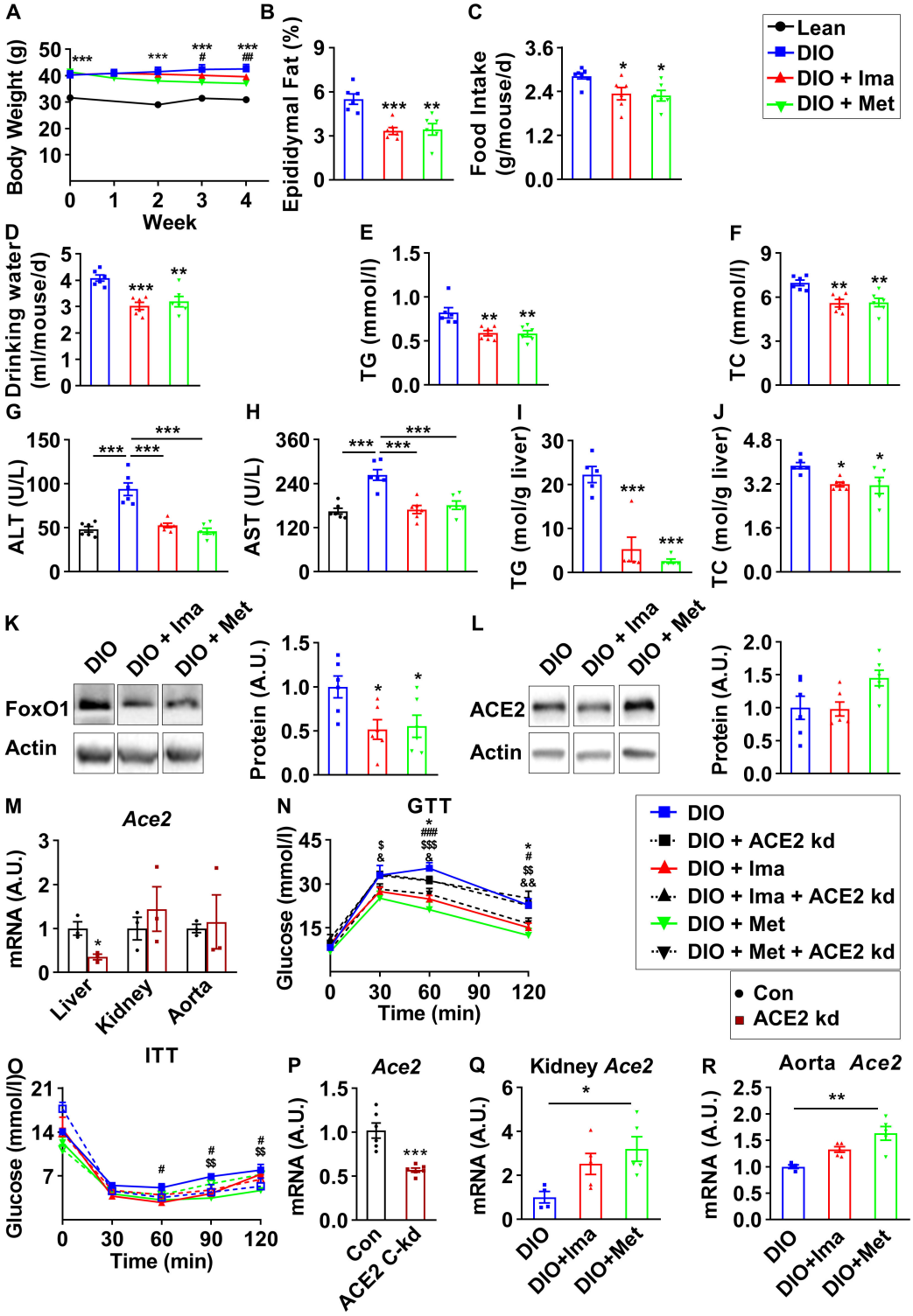




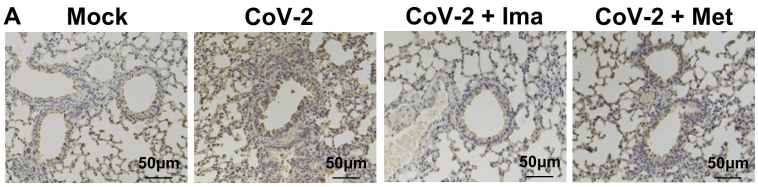


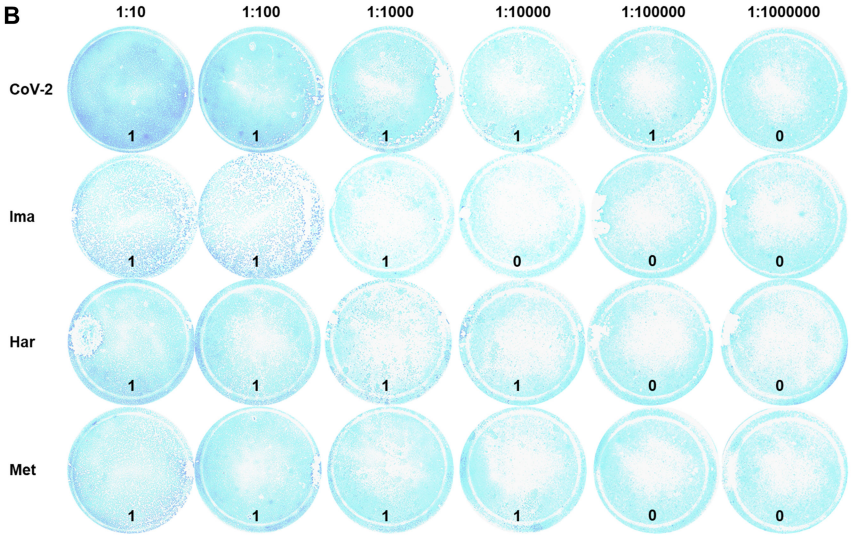


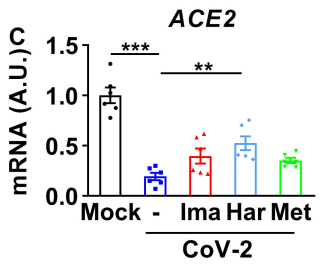
Supplementary Figure 5

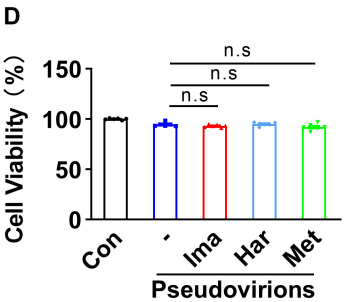


Supplementary Figure 6





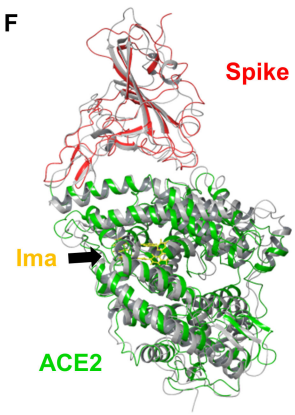


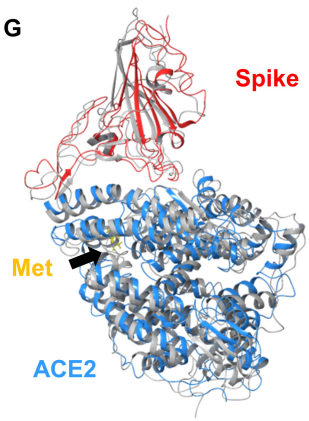


E

Molecular dynamics simulation

System	Interaction Types	Binding free energy (kcal/mol)
Spike protein-ACE2 system	Spike protein to ACE2	-264.784±28.139
Spike protein-ACE2-Drug system	Spike protein to ACE2 (Imatinib)	-249.744±30.329
	Spike protein to ACE2 (Methazolamide)	-258.103±29.533





H

Meta-analysis	ACEi/ARB group		Non-ACEi/ARB group		Heterogeneity		Odds Ratio 95% CI
	Total events	Total patients	Total events	Total patients	I^2	*P*	
Severity	452	1501	673	2022	48%	0.69	0.95 [0.74, 1.22]
Mortality	2969	15483	2935	14089	70%	0.0003	0.74 [0.63, 0.87]

Table S4. Oligos used in this study, Related to STAR Methods.

Oligo name		Sequence (5'–3')	Purpose
Mouse *G6pc*	Forward	AGGTCGTGGCTGGAGTCTTGTC	qPCR
	Reverse	GTAGCAGGTAGAATCCAAGCGC	qPCR
Mouse *Glut2*	Forward	GTTGGAAGAGGAAGTCAGGGCA	qPCR
	Reverse	ATCACGGAGACCTTCTGCTCAG	qPCR
Mouse *Pgc1α*	Forward	TGCCTGCATGAGTGTGTGCT	qPCR
	Reverse	GGCTGGTCCTCACCAACCAG	qPCR
Mouse *Pparα*	Forward	GAGTGCAGCCTCAGCCAAG	qPCR
	Reverse	TCCAGAGCTCTCCTCACCGA	qPCR
Mouse *Pparγ*	Forward	ACGCGGAAGAAGAGACCTGG	qPCR
	Reverse	TGCGAGTGGTCTTCCATCACG	qPCR
Mouse *Tnfα*	Forward	GGTGCCTATGTCTCAGCCTCTT	qPCR
	Reverse	GCCATAGAACTGATGAGAGGGAG	qPCR
Mouse *Il-1β*	Forward	TGGACCTTCCAGGATGAGGACA	qPCR
	Reverse	GTTCATCTCGGAGCCTGTAGTG	qPCR
Mouse *Il-6*	Forward	TACCACTTCACAAGTCGGAGGC	qPCR
	Reverse	CTGCAAGTGCATCATCGTTGTTC	qPCR
Mouse *Pck1*	Forward	GGCGATGACATTGCCTGGATGA	qPCR
	Reverse	TGTCTTCACTGAGGTGCCAGGA	qPCR
Mouse *Gyg1*	Forward	CCAGAGTTTCTGAACCTGTGGTG	qPCR
	Reverse	CCAAAGGACAGGTCTGACAAGG	qPCR
Mouse *Sglt1*	Forward	ATGCTACACACCGAGGGCTG	qPCR
	Reverse	TTCTTGGCCGAGAGGCATCG	qPCR
Mouse *Dgat2*	Forward	CTGTGCTCTACTTCACCTGGCT	qPCR
	Reverse	CTGGATGGGAAAGTAGTCTCGG	qPCR
Mouse *Fasn*	Forward	CACAGTGCTCAAAGGACATGCC	qPCR
	Reverse	CACCAGGTGTAGTGCCTTCCTC	qPCR
Mouse *Col3a1*	Forward	GACCAAAAGGTGATGCTGGACAG	qPCR
	Reverse	CAAGACCTCGTGCTCCAGTTAG	qPCR
Mouse *Gpt1*	Forward	CCACTCAGTCTCTAAGGGCTAC	qPCR
	Reverse	ACACAACCGCACGCTCATCAGT	qPCR
Mouse *Srebp1*	Forward	CGACTACATCCGCTTCTTGCAG	qPCR
	Reverse	CCTCCATAGACACATCTGTGCC	qPCR
Mouse *Vim*	Forward	CGGAAAGTGGAATCCTTGCAGG	qPCR
	Reverse	AGCAGTGAGGTCAGGCTTGGAA	qPCR
Mouse *Cd36*	Forward	GGACATTGAGATTCTTTTCCTCTG	qPCR
	Reverse	GCAAAGGCATTGGCTGGAAGAAC	qPCR
Mouse *Mcp1*	Forward	GCTACAAGAGGATCACCAGCAG	qPCR
	Reverse	GTCTGGACCCATTCCTTCTTGG	qPCR
Mouse *Msr1*	Forward	CGCACGTTCAATGACAGCATCC	qPCR
	Reverse	GCAAACACAAGGAGGTAGAGAGC	qPCR
Mouse *Lox1*	Forward	GTCATCCTCTGCCTGGTGTTGT	qPCR
	Reverse	TGCCTTCTGCTGGGCTAACATC	qPCR
Mouse *Mmp2*	Forward	CAAGGATGGACTCCTGGCACAT	qPCR
	Reverse	TACTCGCCATCAGCGTTCCCAT	qPCR
Mouse *Srb1*	Forward	ACACCCGAATCCTCGCTGGAAT	qPCR
	Reverse	CCGTTGGCAAACAGAGTATCGG	qPCR
Mouse *Ace2*	Forward	CACTCTGGGAATGAGGACACGG	qPCR
	Reverse	TTTCCCCGTGCGCCAAGAT	qPCR
Mouse *Gapdh*	Forward	CATCACTGCCACCCAGAAGACTG	qPCR
	Reverse	ATGCCAGTGAGCTTCCCGTTCAG	qPCR
Human *G6PC*	Forward	AGGTCGTGGCTGGAGTCTTGTC	qPCR
	Reverse	GTAGCAGGTAGAATCCAAGCGC	qPCR
Human *GLUT2*	Forward	TGCCACACTCACACAAGACCTG	qPCR
	Reverse	TGGAAGGAACCCAGCACAGC	qPCR
Human *PGC1α*	Forward	ATTGGAGCCCCATGGATGAAGG	qPCR
	Reverse	ATTCGCCAGCGGCTGTTACT	qPCR
Human *PPARα*	Forward	AGCTGTCACCACAGTAGCTTG	qPCR
	Reverse	ATGACCGAGCCATCTGAGCC	qPCR
Human *PPARγ*	Forward	AGCCTGCATTTCTGCATTCTGC	qPCR
	Reverse	CCACGGAGCTGATCCCAAAGT	qPCR
Human *TNFα*	Forward	GAGGCGCTCCCCAAGAAGAC	qPCR
	Reverse	CAGGCTTGTCACTCGGGGTT	qPCR
Human *IL-1β*	Forward	TCGAGGCACAAGGCACAACA	qPCR
	Reverse	TCACTGGCGAGCTCAGGTACT	qPCR
Human *IL-6*	Forward	GCAAGGGTCTGGTTTCAGCCT	qPCR
	Reverse	TCGCTCCCTCTCCCTGTAAGT	qPCR
Human *IL-10*	Forward	TGCAAAACCAAACCACAAGACAG	qPCR

	Reverse	TTCACTCTGCTGAAGGCATCTCG	qPCR
Human *ICAM-1*	Forward	TGCCCTGATGGGCAGTCAAC	qPCR
	Reverse	TCTCTCCTCACCAGCACCGT	qPCR
Human *VCAM-1*	Forward	TGGTCGTGATCCTTGGAGCC	qPCR
	Reverse	GATGTGGTCCCCTCATTCGT	qPCR
Human *MMP9*	Forward	TGTGCCTTTGAGTCCGGTGG	qPCR
	Reverse	AAGACCGAGTCCAGCTTGCG	qPCR
Human *ACE2*	Forward	TGAGGACACTGAGCTCGCTT	qPCR
	Reverse	TTGAACTTGGGTTGGGCGCT	qPCR
Human *GAPDH*	Forward	GCCATGTTGCAACCGGGAAG	qPCR
	Reverse	TAGCCTCGCTCCACCTGACT	qPCR
SARS-CoV-2 *Spike*	Forward	TCCTGGTGATTCTTCTTCAGGT	qPCR
	Reverse	TCTGAGAGAGGGTCAAGTGC	qPCR
pcDNA3.1-Flag-GFP -ACE2(human)	Forward	CTTGGTACCGAGCTCGGATCC GCCACCATGTCAAGCTCTTCCTGGCT	Cloning
	Reverse	GAAGGGCCCTCTAGACTCGA GAAAGGAGGTCTGAACATCATCAGTG	Cloning
siACE2(human)		GAAGACCTGTTCTATCAAA	siRNA
siACE2(mouse)		GAGATAAACTTCCTAACTGAAA	siRNA
shACE2(mouse)		CCGATCATCAAGCGTCAAC TACTCGAGTAGTTGACGCTT GATGATCGGTTTTT	shRNA