Supporting Information

Computational and Experimental Approaches Identify Beta-blockers as Potential SARS-CoV-2 Spike Inhibitors

Ana C. Puhl[†*], Melina Mottin[‡, §], Carolina Q. Sacramento[&, #], Tatyana Almeida Tavella[%], Gabriel Gonçalves Dias[‡], Natalia Fintelman-Rodrigues[&, #], Jairo R. Temerozo[¥, µ], Suelen S. G. Dias[&], Paulo Ricardo Pimenta da Silva Ramos[‡], Eric M. Merten[±], Kenneth H. Pearce[±, £], Fabio Trindade Maranhão Costa[%], Lakshmanane Premkumar[¶], Thiago Moreno L. Souza[&, #], Carolina Horta Andrade[‡*] and Sean Ekins[†*]

[†] Collaborations Pharmaceuticals, Inc., 840 Main Campus Drive, Lab 3510, Raleigh, NC 27606, USA.

[‡] LabMol - Laboratory of Molecular Modeling and Drug Design, Faculdade de Farmácia, Universidade Federal de Goiás, Goiânia, GO, 74605-170, Brazil.

[§] Pathogen-Host Interface Laboratory, Department of Cell Biology, University of Brasilia, Brasilia, Brazil.

[&] Laboratory of Immunopharmacology, Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, RJ, Brazil

[#] Center of Technological Development in Health (CDTS)/National Institute of Science and Technology for Innovation on Neglected Population Diseases (INCT-IDPN), Rio de Janeiro, RJ, Brazil

[%] Laboratory of Tropical Diseases – Prof. Dr. Luiz Jacinto da Silva, Department of Genetics, Evolution, Microbiology and Immunology, University of Campinas-UNICAMP, Campinas, SP, Brazil.

[¥] Laboratory on Thymus Research, Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, RJ, Brazil.

[µ] National Institute for Science and Technology on Neuroimmunomodulation (INCT/NIM), Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, RJ, Brazil.

[±] Center for Integrative Chemical Biology and Drug Discovery, Chemical Biology and Medicinal Chemistry, Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, North Carolina 27599, USA.

[£] UNC Lineberger Comprehensive Cancer Center, Chapel Hill, North Carolina 27599, USA.

[¶] Department of Microbiology and Immunology, University of North Carolina School of Medicine, Chapel Hill, NC 27599, USA.

*To whom correspondence should be addressed: Ana C. Puhl, E-mail address: ana@collaborationspharma.com; Carolina Horta Andrade E-mail address: carolina@ufg.br, Sean Ekins, E-mail address: sean@collaborationspharma.com, Phone: +1 215-687-1320.

Table S1: Compounds tested using nanoDSF.

Compound	Tm	ΔTm
Pindolol	58.6°C	-0.2°C
Carvedilol	58.0°C	0.3°C
Carteolol	58.4°C	0.0

Table S2: Cytotoxicity of compounds in Vero and A549 cells

	CC_{50} (µM)	
Compound	**Vero**	**A549**
Atenolol	(133 – 400)	(133 - 400)
Carvedilol	29.2	17.8
Pindolol	(20 – 60)	-
Propranolol	86.1	73.3
Carteolol	(133 – 400)	(133 – 400)
(±)-Bisoprolol hemifumarate	(10 – 30)	-

* Numbers in parentheses represent the concentration range containing the compound CC_{50}

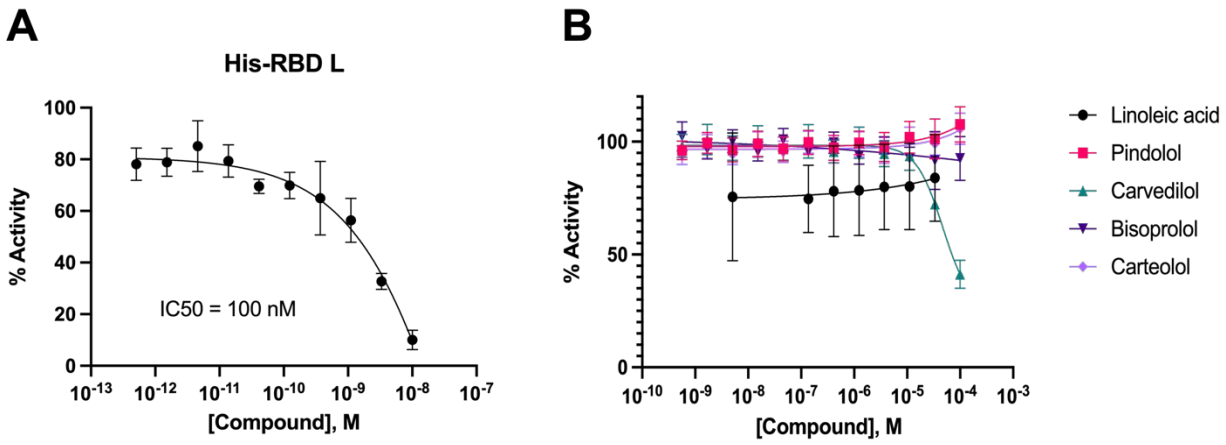

Figure S1: Lumit SARS-CoV 2 Spike RBD: hACE2 Immunoassay. **A)** Positive control, his-RBD showed an IC50 100 nM. **B)** Beta blockers and linoleic acid.