

# Identifying SARS-CoV-2 Drugs Binding to the Spike Fatty Acid Binding Pocket Using In Silico Docking and Molecular Dynamics

## Supplementary Material

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
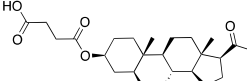
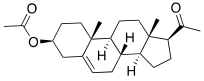
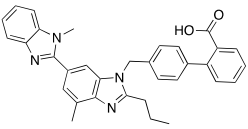
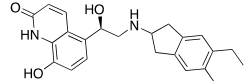
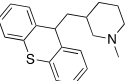
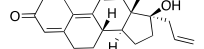
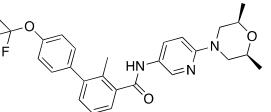
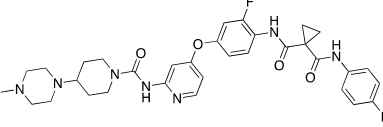
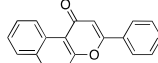
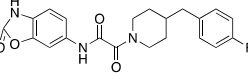
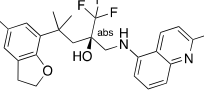
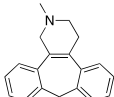
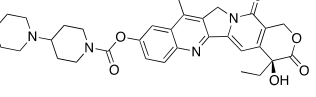
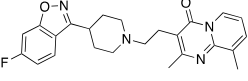
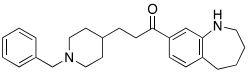
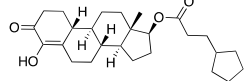
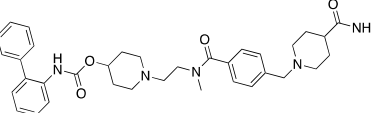
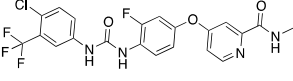
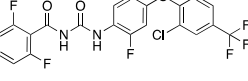
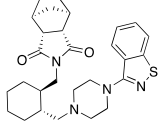
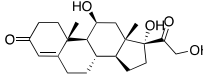
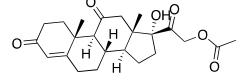
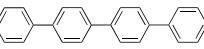
<sup>5</sup> School of Pharmacy, University of Nottingham, Nottingham NG7 2RD. UK

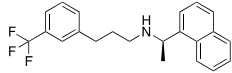
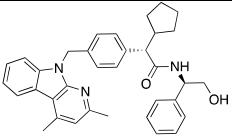
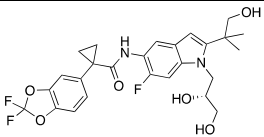
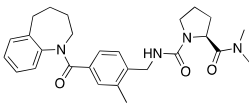
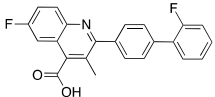
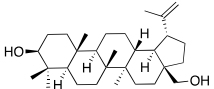
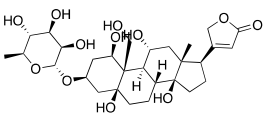
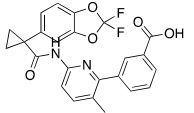
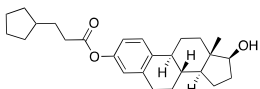
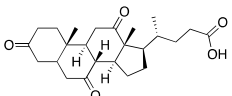
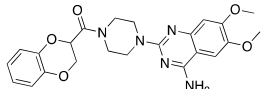
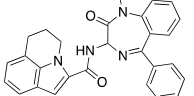
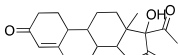
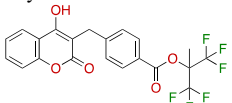
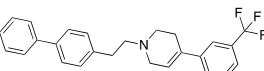
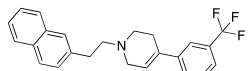
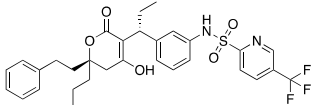
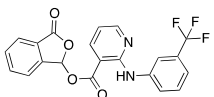
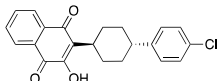
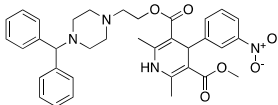
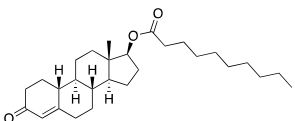
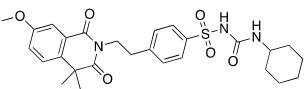
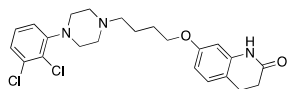
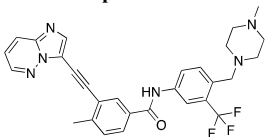
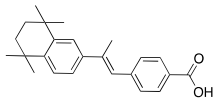
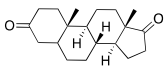
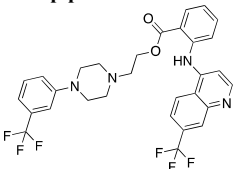
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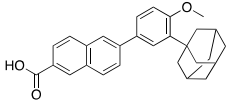
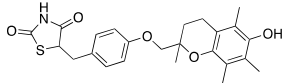
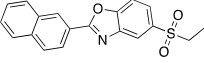
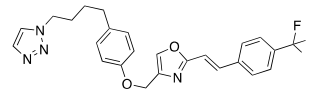
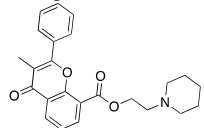
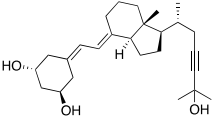
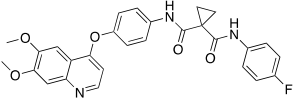
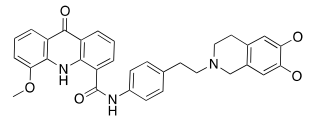
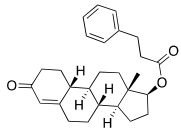
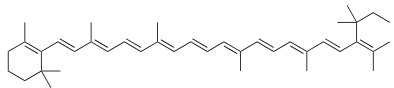
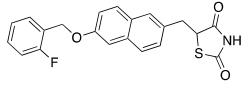
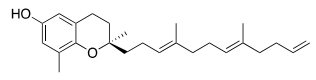
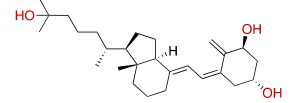
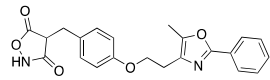
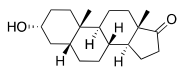
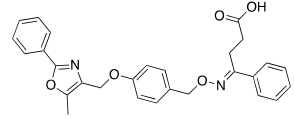
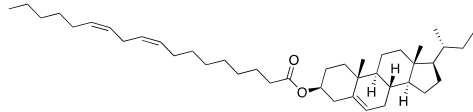
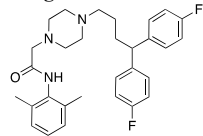
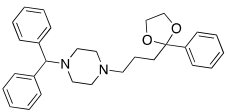
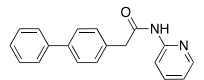
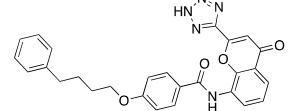
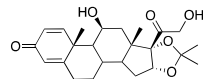
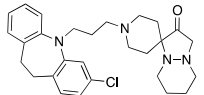
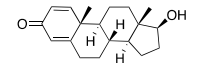
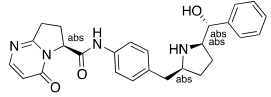
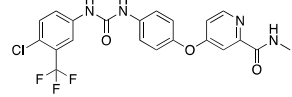
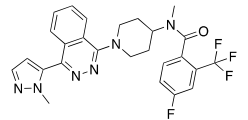
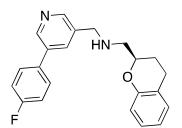
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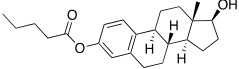
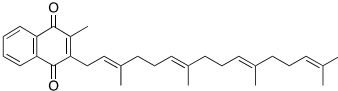
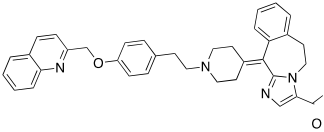
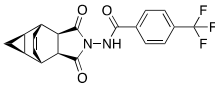
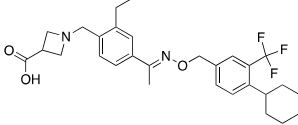
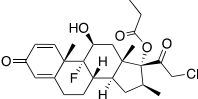
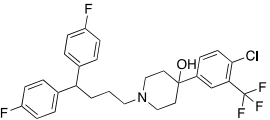
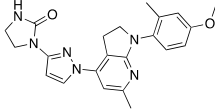
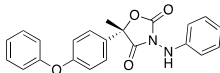
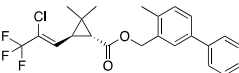
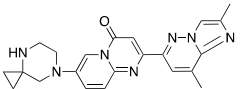
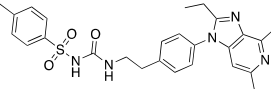
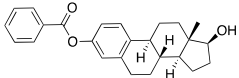
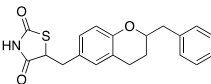
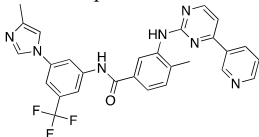
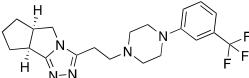
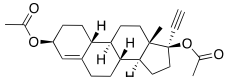
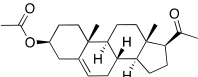
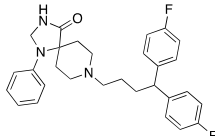
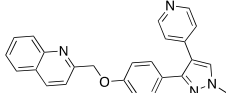
## Supplementary Information

**Table S1.** MMPBSA binding energies (kcal/mol) of top 100 docking candidates. Physical properties computed by Cactvs 3.4.8.18

Drug (logP N <sub>donor</sub> N <sub>acceptor</sub> N <sub>rot-bonds</sub> )	ΔG	Drug	ΔG	Drug	ΔG	Drug	ΔG
 <b>Caprospinol</b> 8.2 0 4 6	-38.89	 <b>5-α-pregnane-3-β-ol hemisuccinate</b> 4.9 1 5 6	-29.60	 <b>Pregnenolone acetate</b> 4.8 0 3 3	-27.75	 <b>Telmisartan</b> 6.9 1 4 7	-
 <b>Indacaterol</b> 3.3 4 4 6	-35.99	 <b>Metixene</b> 4.9 0 2 2	-29.50	 <b>Altrenogest</b> 2.8 1 2 2	-27.58	 <b>Sonidegib</b> 5.8 1 8 5	23.88
 <b>Golvatinib</b> 4.1 3 9 8	-35.37	 <b>β-Naphthoflavone</b> 4.4 0 2 1	-29.32	 <b>Radiprodil</b> 3.0 2 5 3	-27.40	 <b>Mapracorat</b> 6.2 2 8 6	-
 <b>Setiptiline</b> 3.3 0 1 0	-35.04	 <b>Irinotecan</b> 3.0 1 8 5	-29.24	 <b>Ocaperidone</b> 3.3 0 6 4	-27.36	 <b>Zanafezil</b> 4.9 1 3 6	23.29
 <b>Oxabolone cypionate</b> 5.7 1 4 5	-34.78	 <b>Revefenacin</b> 4.1 2 6 11	-29.16	 <b>Regorafenib</b> 4.2 3 8 5	-27.31	 <b>Flufenoxuron</b> 6.3 2 9 4	-
 <b>Lurasidone</b> 5.4 0 6 5	-33.04	 <b>Hydroxycortisone (Cetacort)</b> 1.6 3 5 2	-29.16	 <b>Cortisone acetate</b> 2.1 1 6 4	-27.16	 <b>p-quaterphenyl</b> 7.3 0 0 3	22.62

Drug (logP N <sub>donor</sub> N <sub>acceptor</sub> N <sub>rot-bonds</sub> )	ΔG	Drug	ΔG	Drug	ΔG	Drug	ΔG
 <b>Cinacalcet</b> 6.1 1 4 6	-33.02	 <b>Implipitape</b> 7.3 2 3 8	-29.11	 <b>Tezacafort</b> 2.9 4 9 8	-26.85	 <b>Fedovapagon</b> 3.2 1 3 4	22.44
 <b>Brequinar</b> 5.6 1 5 3	-32.94	 <b>Betulin</b> 8.3 2 2 2	-28.83	 <b>Ouabain</b> -1.7 8 12 4	-26.83	 <b>Lumacaftor</b> 4.4 2 8 5	22.33
 <b>Estradiol cypionate</b> 7.1 1 3 5	-32.94	 <b>Dehydrocholic acid</b> 2.6 1 5 4	-28.82	 <b>Doxazosin</b> 2.5 1 9 4	-26.59	 <b>Tarazepide</b> 4.6 1 3 3	21.94
 <b>Segesterone</b> 2.3 1 3 1	-32.80	 <b>Tecarfarin</b> 5.5 1 11 5	-28.80	 <b>Paliroden</b> 6.6 0 4 5	-26.56	 <b>Xaliproden</b> 6.2 0 4 4	21.92
 <b>Tipranavir</b> 7.0 2 10 11	-32.39	 <b>Talniflumate</b> 5.3 1 9 5	-28.56	 <b>Mepron (atovaquone)</b> 5.2 1 3 2	-26.35	 <b>Manidipine</b> 5.6 1 9 11	21.63
 <b>Nandrolone decanoate</b> 7.3 0 3 10	-32.33	 <b>Gliquidone</b> 4.6 2 6 7	-28.54	 <b>Aripiprazole</b> 4.6 1 4 7	-25.96	 <b>Ponatinib</b> 4.1 1 8 6	21.19
 <b>Arotinoid acid</b> 7.5 1 2 3	-32.05	 <b>Androstanedione</b> 3.6 0 2 0	-28.54	 <b>Bifeprunox</b> 4.2 1 4 4	21.16		

Drug (logP $N_{\text{donor}}$ $N_{\text{acceptor}}$ $N_{\text{rot-bonds}}$ )	$\Delta G$	Drug	$\Delta G$	Drug	$\Delta G$	Drug	$\Delta G$
 <b>Adapalene</b> 7.7 1 3 4	-32.03	 <b>Troglitazone</b> 5.1 2 6 5	-28.53	 <b>Antrafenine</b> 7.5 1 12 8	-25.86	 <b>Mubritinib</b> 5.4 0 8 10	20.81
 <b>Flavoxate</b> 4.3 0 5 6	-31.70	 <b>Inecalcitol</b> 4.4 3 3 4	-28.26	 <b>Cabozantinib</b> 5.4 2 7 8	-25.81	 <b>Elacridar</b> 5.6 2 7 8	20.28
 <b>Nandrolone phenpropionate</b> 5.1 0 3 5	-31.52	 <b><math>\beta</math>-carotene</b> 13.5 0 0 10	-28.26	 <b>Netoglitazone</b> 4.9 1 5 5	-25.53	 <b>Tocotrienol</b> 8.2 1 2 9	20.11
 <b>Calcitriol</b> 5.1 3 3 6	-31.06	 <b>Reglitazar</b> 4.0 1 6 7	-28.25	 <b>Etiocolanolone</b> 3.7 1 2 0	-25.44	 <b>Imiglitazar</b> 5.1 1 7 11	20.09
 <b>Cholesteryl linoleate</b> 15.9 0 2 21	-30.98	 <b>Lidoflazine</b> 6.0 1 5 9	-28.11	 <b>Dotarizine</b> 4.9 0 4 8	-25.16	 <b>Difenpiramide</b> 3.8 1 2 4	19.56
 <b>Pranlukast</b> 4.2 2 7 9	-30.79	 <b>Desonide</b> 2.7 2 6 2	-28.08	 <b>Mosapramine</b> 5.4 1 4 4	-24.87	 <b>1-Testosterone</b> 4.0 1 2 0	19.31
 <b>Vibegron</b> 1.8 3 5 6	-30.72	 <b>Sorafenib</b> 4.1 3 7 5	-28.04	 <b>Mosapramine</b> 5.4 1 4 4	-24.73	 <b>1-Testosterone</b> 4.0 1 2 0	18.99

Drug (logP $N_{\text{donor}}$ $N_{\text{acceptor}}$ $N_{\text{rot-bonds}}$ )	$\Delta G$	Drug	$\Delta G$	Drug	$\Delta G$	Drug	$\Delta G$
	-30.60		-27.98		-24.72		-
<b>Estradiol valerate</b> 6.0 1 3 5	-30.60	<b>Menatetrenone</b> 8.9 0 2 11	-27.98	<b>Laniquidar</b> 5.8 0 6 8	-24.72	<b>Tecovirimat</b> 2.6 1 6 1	17.77
	-30.58		-27.95		-24.67		-
<b>Siponimod</b> 4.8 1 8 9	-30.58	<b>Clobetasol propionate</b> 3.8 1 6 5	-27.95	<b>Penfluridol</b> 7.3 1 7 7	-24.67	<b>Emicerfont</b> 2.9 1 5 4	17.57
	-30.11		-27.78		-24.05		-
<b>(S)-famoxadone</b> 5.0 1 5 5	-30.11	<b>Bifenthrin</b> 6.0 0 5 6	-27.78	<b>Risdiplam</b> 0.5 1 6 2	-24.05	<b>Grapiprant</b> 4.6 2 5 7	17.33
	-29.87		-27.75		-24.03		-
<b>Estradiol benzoate</b> 4.5 1 3 3	-29.87	<b>Englitazone</b> 4.4 1 4 4	-27.75	<b>Nilotinib</b> 4.9 2 9 6	-24.03	<b>Lorpiprazole</b> 3.3 0 7 4	15.96
	-29.75		-27.75		-23.95		-
<b>Ethynodiol diacetate</b> 3.9 0 4 5	-29.75	<b>Pregnenolone acetate</b> 4.8 0 3 3	-27.75	<b>Fluspirilene</b> 5.6 1 5 7	-23.95	<b>Mardepodect</b> 4.2 0 4 5	15.31

**Table S2.** Correlations between physical properties of ligands and binding energies

	logP	N <sub>donor</sub>	N <sub>acceptor</sub>	N <sub>rotate</sub>	$\Delta G$
logP	1.00				
N <sub>donor</sub>	-0.38	1.00			
N <sub>acceptor</sub>	-0.29	0.41	1.00		
N <sub>rotate</sub>	0.57	0.02	0.23	1.00	
$\Delta G$	-0.14	-0.08	0.12	-0.04	1.00