

# Drug repurposing candidates against COVID-19

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The SARS-CoV-2 infection causes the respiratory illness COVID-19, the most recent member of the coronavirus family, declared a pandemic in early 2020. A working vaccine is optimistically estimated to be circulated in a year's time [1], thus global immunisation seems a million miles away. At the same time, big pharma's obsession with blockbuster drugs seems to have come to a halt, as researchers, executives and officials have realised that the much faster and less risky road for symptom alleviation and blocking viral reproduction is that of drug repurposing [2].

Currently the main three drug classes being considered are antivirals, antihypertensives and antiinflammatory agents, in order to stop the virus from reproducing and help with the accompanying heart and lung issues, respectively. Furthermore, a constantly increasing list comprising therapeutic targets is being compiled from the literature and primarily academic publications [3-6]. The list, among others, contains ACE2, AGTRs, PDEs, TLRs and CHRNs.

In order to aid this global crisis, we have deployed our computational platform comprising 90M models and 120M statistical enrichment calculations in order to suggest 27 *unfiltered* drug repurposing candidates, which may have been overlooked and warrant further exploration. These candidates are presented below with information on indication and known targets reproduced from DrugBank (<https://www.drugbank.ca/>). Note that the candidates are *not* presented in order of relevance. Immediately following the list of drugs, we provide *Table 1*, containing the matched GO Terms for the relevant predicted bioactivities. We urge fellow researchers to consider these drugs, consult with leading experts and proceed to their experimental validation.

## Bivalirudin

For thrombocytopenia and the prevention of thrombosis

Known targets: F2

Additional relevant predicted interaction: AGTR2, ACE2

## Carfilzomib

For multiple myeloma

Known Targets: PSMB5, PSMB8, PSMB1, PSMB9, PSMB2, PSMB10

Additional relevant predicted interaction: ACE2

### Sacubitril

For risk reduction of cardiovascular event for those with chronic heart failure

Known targets: MME

Additional relevant predicted interaction: ACE2

### Tropisetron

For the prevention of vomiting from cytotoxic therapy

Known targets: HTR3A

Additional relevant predicted interaction: CHRNA7

### Exenatide

For improving glycemic control in adults with type 2 diabetes mellitus

Known targets: GLP1R

Additional relevant predicted interaction: AGTR2, ACE2, CHRNA7

### Enfuvirtide

For HIV-1/AIDS combination therapy

Known targets: gp41

Additional relevant predicted interaction: ACE2

### Leuprolide

For the treatment of prostate cancer, endometriosis and uterine fibroids

Known targets: GNRHR

Additional relevant predicted interaction: ACE2, AGTR2 and HDAC11

### Teduglutide

For treating short bowel syndrome

Known targets: GLP2R

Additional relevant predicted interaction: ACE2

### Vorinostat

For T-cell lymphoma

Known targets: HDAC1, HDAC2, HDAC3, HDAC6, HDAC8, acuC1

Additional relevant predicted interaction: HDAC4, HDAC5, HDAC7, HDAC11

### Degarelix

For advanced prostate cancer

Known targets: GNRHR

Additional relevant predicted interaction: AGTR2, ACE2, CHRNA7

### Icatibant

For HAE attacks

Known targets: BDKRB2, ANPEP

Additional relevant predicted interaction: AGTR2, ACE2

#### Candesartan

For hypertension, congestive heart failure, systolic dysfunction, myocardial infarction and coronary artery disease

Known targets: AGTR1

Additional relevant predicted interaction: AGTR2

#### Hydroxyurea

For leukemia and other cancers, tested for pulmonary diseases

Known targets: RRM1

Additional relevant predicted interaction: HDAC5, HDAC7

#### Nateglinide

For non-insulin dependent-diabetes mellitus

Known targets: ABCC8, PPARG

Additional relevant predicted interaction: ACE2

#### Telmisartan

For hypertension and diabetic nephropathy

Known targets: AGTR1, PPARG

Additional relevant predicted interaction: AGTR2

#### Acetylcysteine

For mucolysis and paracetamol overdose

Known targets: ACY1, CHUK, IKBKB, GSS, SLC7A11, GRIN1, GRIN2A/2B/2D, GRIN3A

Additional relevant predicted interaction: ACE2

#### Primaquine

For the treatment of malaria

Known targets: KRT7, NQO2

Additional relevant predicted interaction: PDE4A, PDE4C

#### Tirofiban

For acute coronary syndrome (combination with heparin)

Known targets: ITGA2B, ITGB3

Additional relevant predicted interaction: ACE2

#### Amantadine

For symptoms of infection caused by various strains of influenza A virus

Known targets: GRIN3A, DRD2

Additional relevant predicted interaction: CHRNA7

Esomeprazole

For GERD and prevention of gastrointestinal bleeds with NSAID use

Known targets: ATP4A

Additional relevant predicted interaction: IRAK1

Fosinopril

For hypertension use as an adjunct in treating congestive heart failure

Known/Predicted targets: ACE, *No additional targets of interest*

Lovastatin

For hypercholesterolemia and primary prevention of coronary heart disease

Known/Predicted targets: HMGCR, ITGAL, HDAC2, *No additional targets of interest*

Milrinone

For the treatment of congestive heart failure

Known targets: PDE3A

Additional relevant predicted interaction: IRAK1

Nicardipine

For management of chronic stable angina and treatment of hypertension

Known targets: CACNA1C, CACNB2, CACNA1D, CACNA2D1, PDE1A, PDE1B, ADRA1A, ADRA1B, ADRA1D, CHRM1, CHRM2, CHRM3, CHRM4, CHRM5, CALM1

Additional relevant predicted interaction: AChE

Pantoprazole

For short-term treatment of erosive esophagitis

Known targets: ATP4A

Additional relevant predicted interaction: IRAK1

Pravastatin

For the treatment of hypercholesterolemia and to reduce the risk of cardiovascular disease

Known targets: HMGCR

Additional relevant predicted interaction: HDAC2

Varenicline

For use as an aid in smoking cessation

Known/Predicted targets: CHRNA4, CHRNA7, CHRNA3, CHRNA6, *No additional targets of interest*

**Table 1.** Associated GO Terms with the relevant predicted bioactivities for the 27 drug repurposing candidates outlined in the above document.

GO Level1	GO Level2	GO Levels3+	Go Term ID	
biological process	cellular component assembly	macromolecular complex assembly	GO:0065003	
	locomotion	cell motility	GO:0048870	
	metabolic process		biosynthetic process	GO:0009058
			catabolic process	GO:0009056
			cellular nitrogen compound metabolic process	GO:0034641
			DNA metabolic process	GO:0006259
			nucleobase-containing compound catabolic process	GO:0034655
			cellular protein modification process	GO:0006464
			drug metabolic process	GO:0017144
			lipid metabolic process	GO:0006629
			phosphorylation	GO:0016310
			proteolysis	GO:0006508
	protein processing	GO:0016485		
	small molecule metabolic process	GO:0044281		
regulation of catalytic activity	positive regulation of catalytic activity	GO:0043085		
response to toxic substance	response to antibiotic	GO:0046677		
transport		transmembrane transport	GO:0055085	
		vesicle-mediated transport	GO:0016192	
cellular component	membrane	plasma membrane	GO:0005886	
	organelle	Golgi apparatus	GO:0005794	
		cilium	GO:0005929	
		lipid particle	GO:0005811	
		nucleus	GO:0005634	
molecular function	catalytic activity	hydrolase activity	GO:0016787	
		acting on carbon-nitrogen (but not peptide) bonds	GO:0016810	
		acting on ester bonds	GO:0016788	
		cholinesterase activity	GO:0004104	
		acetylcholinesterase activity	GO:0003990	
		phosphoric diester hydrolase activity	GO:0008081	
		peptidase activity	GO:0008233	
		transferase activity	GO:0016740	
		transferring phosphorus-containing groups, kinase activity	GO:0016301	
		nucleic acid binding	DNA binding	GO:0003677
	RNA binding		GO:0003723	
	nucleotide binding	adenyl nucleotide binding	GO:0030554	
	peptide binding	beta-amyloid binding	GO:0001540	
	protein binding		enzyme binding	GO:0019899
			identical protein binding	GO:0042802
			protein homodimerization activity	GO:0042803
			protein heterodimerization activity	GO:0046982
			protein self-association	GO:0043621
			receptor binding	GO:0005102
			transcription factor binding	GO:0008134
receptor activity		G-protein coupled receptor activity	GO:0004930	
		virus receptor activity	GO:0001618	
transporter activity	transmembrane transporter activity	GO:0022857		

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