

Supporting Information for:

The Remarkable Selectivity of Nirmatrelvir

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		Compound IC50 (M)		Control IC50 (M)	Control ID
		NCGC00185682	Nirmatrelvir (PF-07321332)		
1	Calpain 1			3.09E-08	E64
2	Caspase 1	7.66E-09		1.73E-08	IETD-CHO
3	Caspase 2			1.09E-07	IETD-CHO
4	Caspase 3			1.03E-09	DEVD-CHO
5	Caspase 4			7.84E-07	IETD-CHO
6	Caspase 5	3.59E-07		6.44E-09	IETD-CHO
7	Caspase 6			2.32E-08	DEVD-CHO
8	Caspase 7			1.75E-09	DEVD-CHO
9	Caspase 8	9.67E-06		1.74E-09	IETD-CHO
10	Caspase 9	1.01E-06		2.17E-08	IETD-CHO
11	Caspase 10			1.25E-08	IETD-CHO
12	Caspase 11			8.60E-08	IETD-CHO
13	Caspase 14			5.66E-08	WEHD-CHO
14	Cathepsin B			3.15E-09	E64
15	Cathepsin C			7.35E-07	E64
16	Cathepsin H			2.50E-08	E64
17	Cathepsin K	6.73E-06	2.31E-07	4.74E-10	E64
18	Cathepsin L		**>1.00E-05	2.21E-09	E64
19	Cathepsin S		3.87E-06	1.74E-09	E64
20	Cathepsin V		2.90E-06	5.41E-09	E64
21	Papain		**>1.00E-05	1.50E-10	E64
22	SARS-CoV2-Mpro		3.62E-09	1.14E-08	GC376
23	SARS-CoV2-Plpro			8.99E-07	Plpro Inh.

Notes:

- 1) Nirmatrelvir (PF-07321332) and NCGC00185682 were tested in 10-dose IC50 singlet with a 3-fold serial dilution starting at 10 μ M.
- 2) Control compounds were tested in a 10-dose IC50 with a 3-fold serial dilution starting at 10 μ M.
- 3) Protease activities were monitored as a time-course measurement of the increase in fluorescence signal from fluorescently-labeled peptide substrate.
- 4) Empty cells indicate no inhibition or compound activity that could not be fit to an IC50 curve.
- 5) ** IC50 value higher than 10 μ M is estimated based on the best curve fitting available.