

**READDI EXP0139:**  
**Alphavirus Helicase Inhibitors**  
**CNP19 & 21**  
**Unwindase Covalent Hits**  
**RA0001821 SAR**

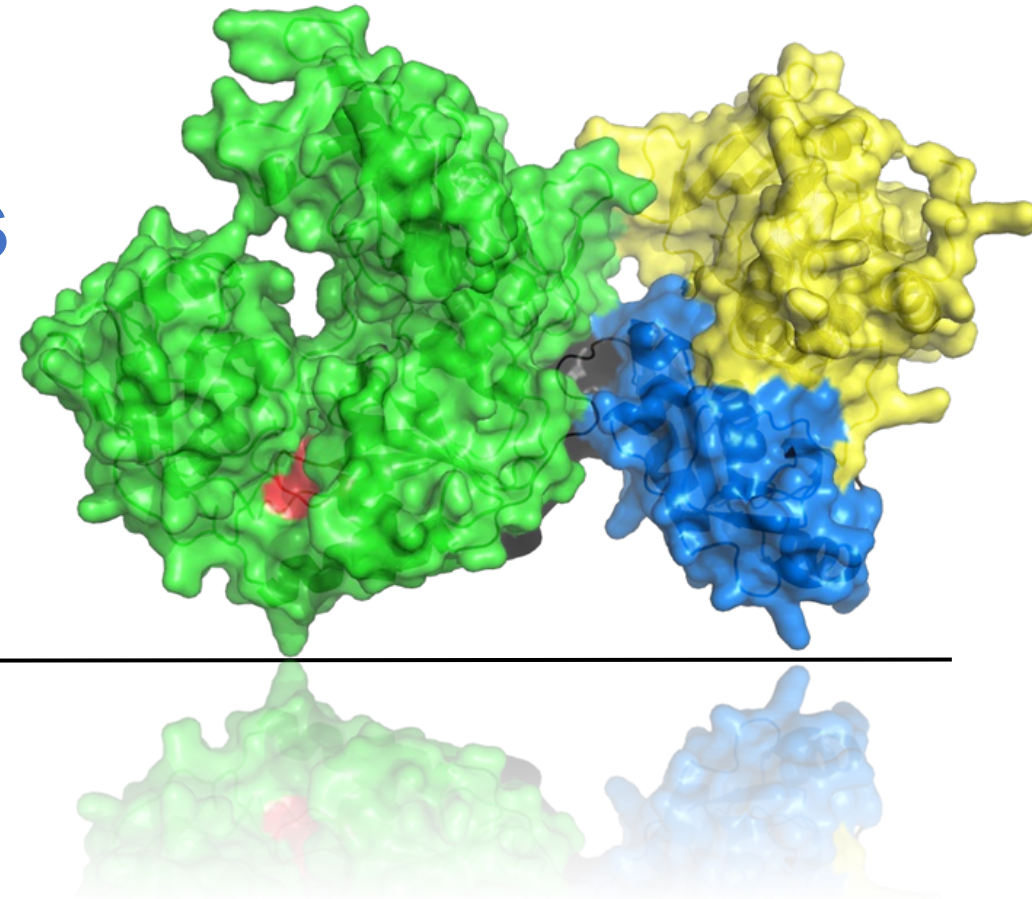
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**Jack Sears**

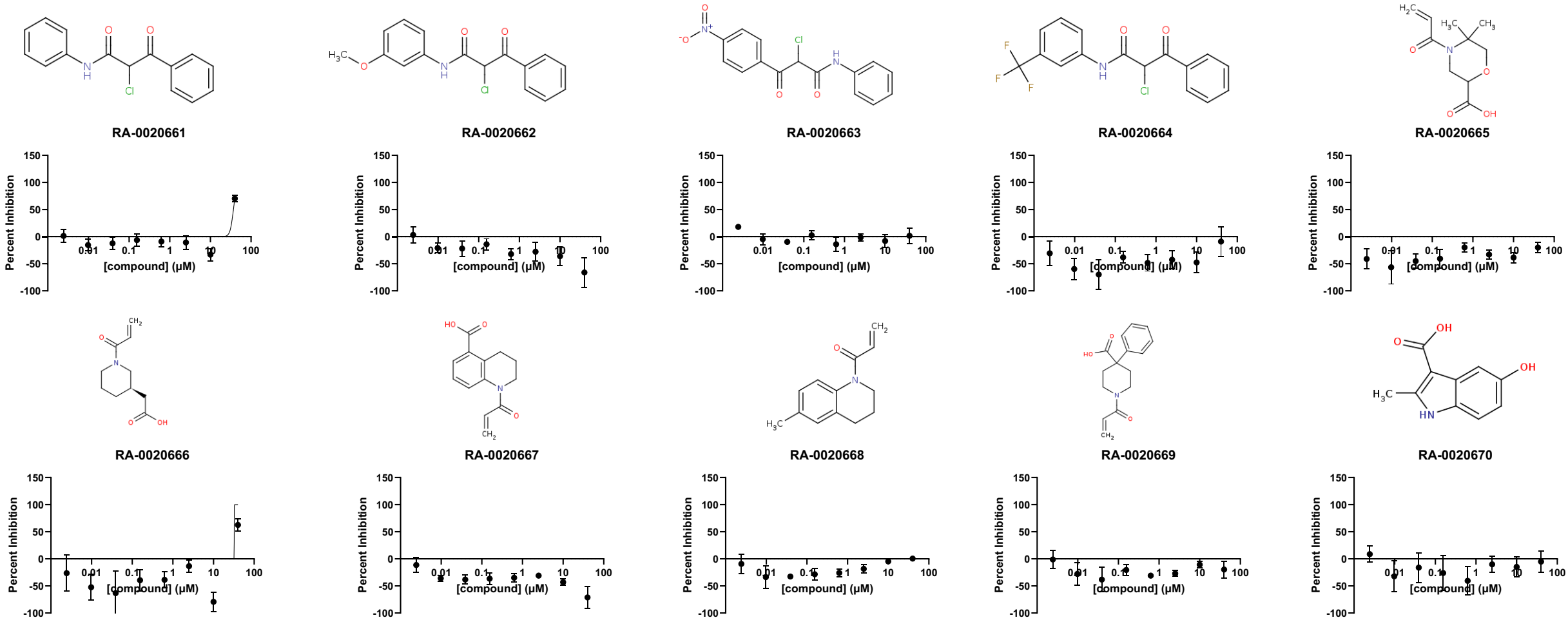
4<sup>TH</sup> Year Ph.D. Candidate

University of North Carolina – Chapel Hill

Department of Microbiology & Immunology – Heise & Moorman Laboratories

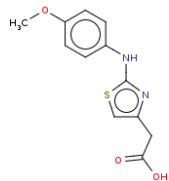


# EXP0139 CHKV 18125 nLuc Capsid Antiviral Assay

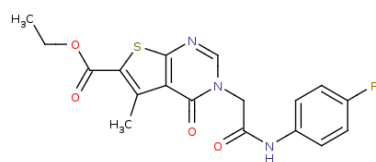
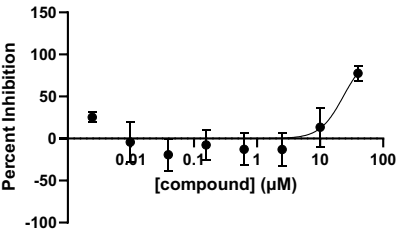


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EC50	36.9	Unstable	Unstable	Unstable	Unstable	Unstable	Unstable	70.28	Unstable	Unstable
Hill Slope	10.63	Unstable	Unstable	Unstable	Unstable	Unstable	Unstable	9.658	Unstable	Unstable

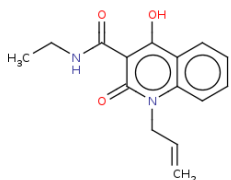
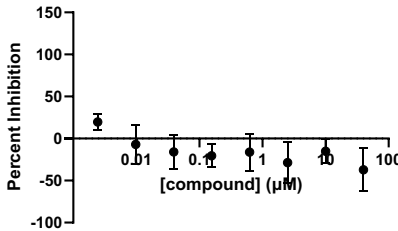
# EXP0139 CHKV 18125 nLuc Capsid Antiviral Assay



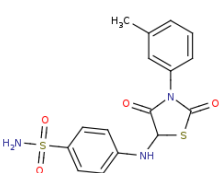
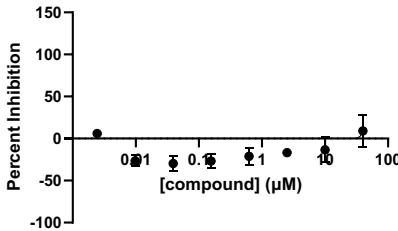
RA-0020671



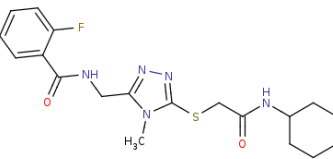
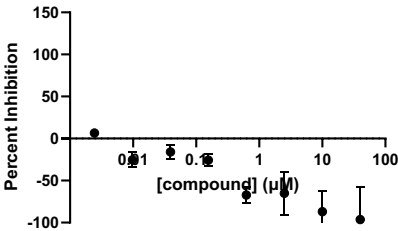
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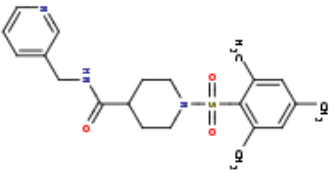
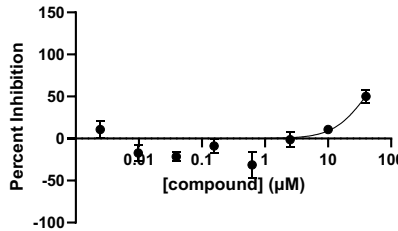
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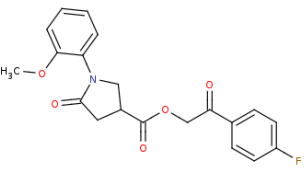
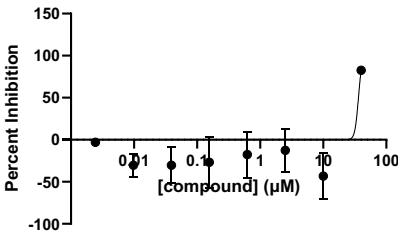
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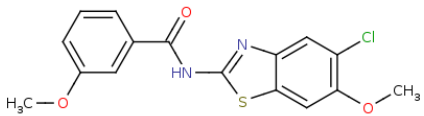
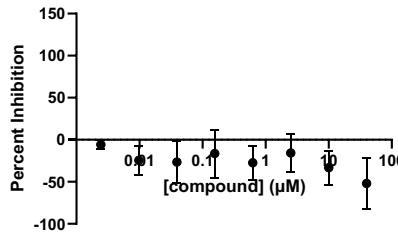
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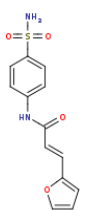
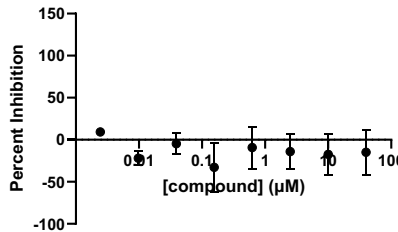
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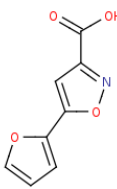
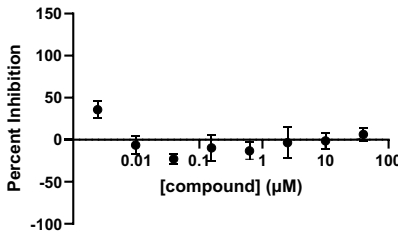
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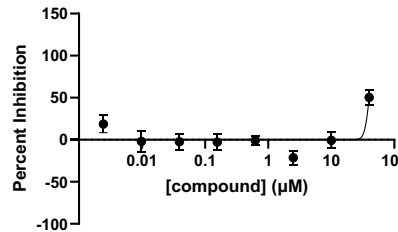
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RA-0001409

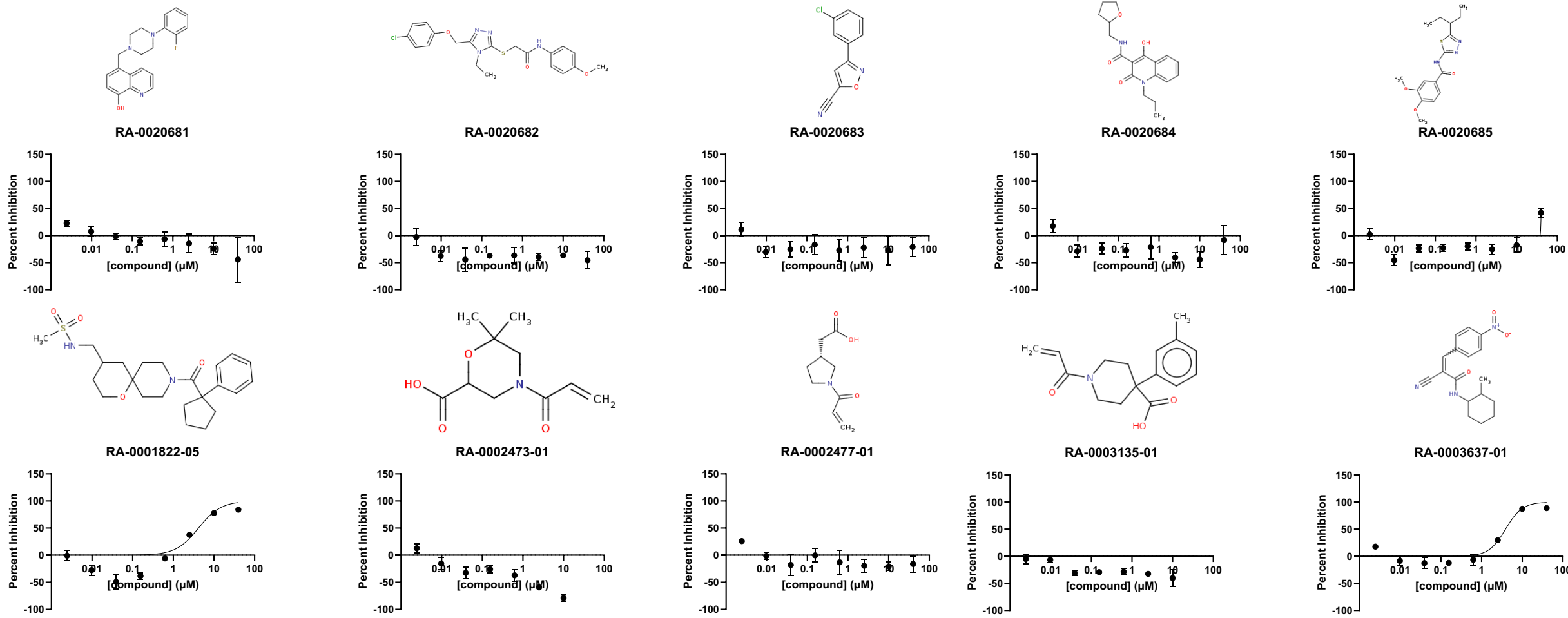


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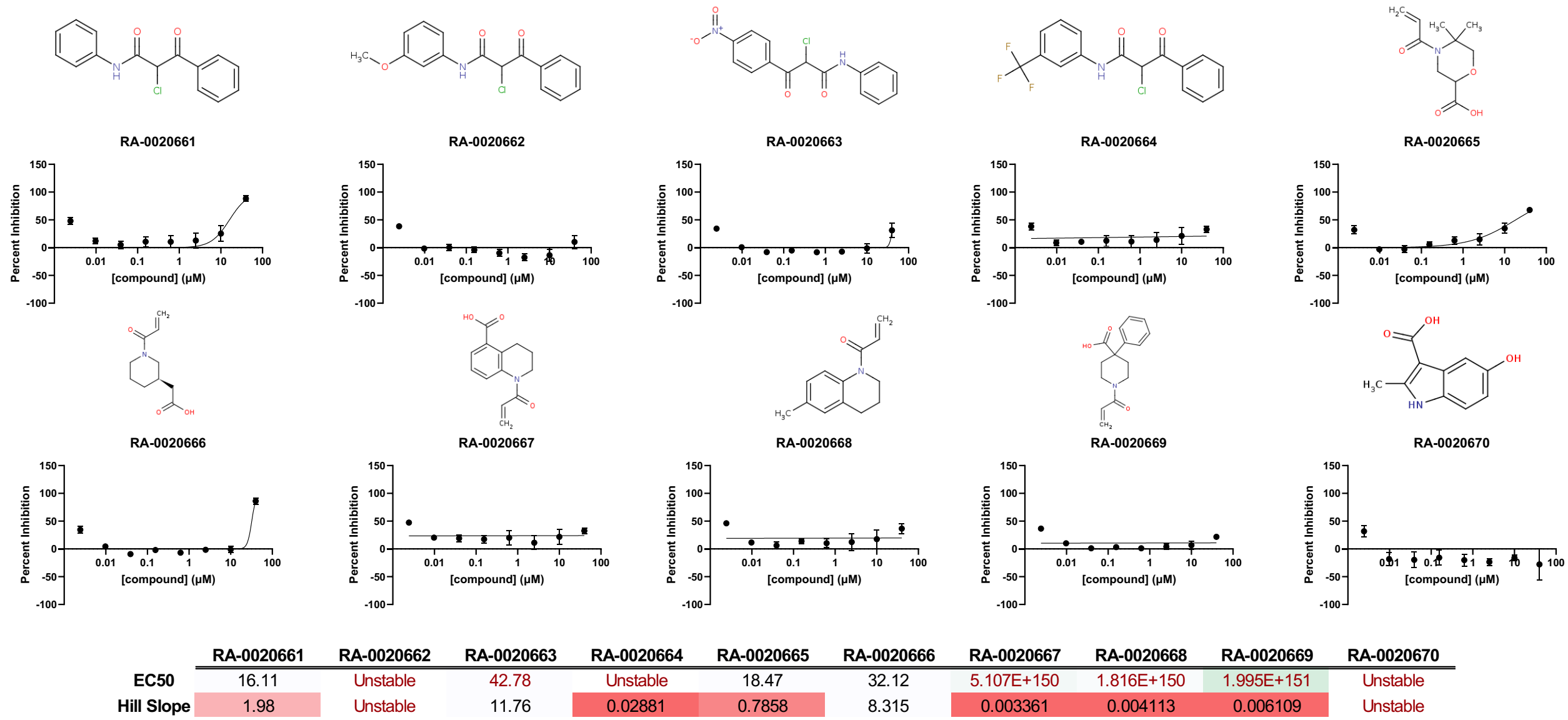
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EC50	23.32	Unstable	48.38	Unstable	39.52	36.18	Unstable	Unstable	52.12	39.95
Hill Slope	2.347	Unstable	12.09	Unstable	1.673	15.54	Unstable	Unstable	10.23	12.09

# EXP0139 CHKV 18125 nLuc Capsid Antiviral Assay

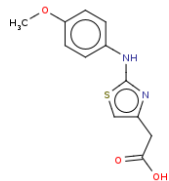


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EC50	Unstable	Unstable	Unstable	Unstable	40.18	4.174	Unstable	Unstable	Unstable	3.892
Hill Slope	Unstable	Unstable	Unstable	Unstable	Unstable	1.569	Unstable	Unstable	Unstable	2.113

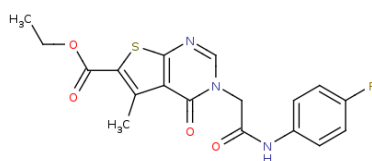
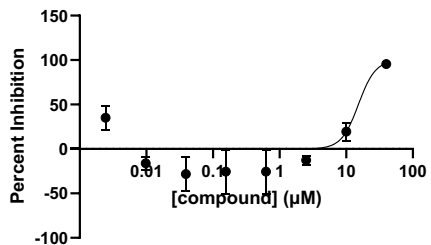
# EXP0139 VEEV TC83 nLuc Capsid Antiviral Assay



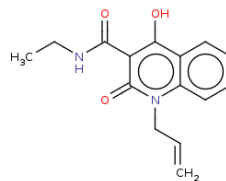
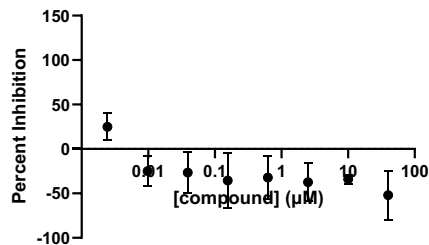
# EXP0139 VEEV TC83 nLuc Capsid Antiviral Assay



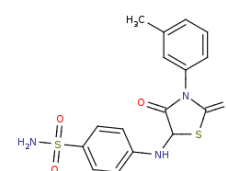
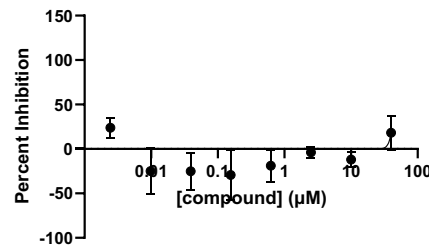
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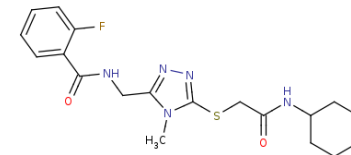
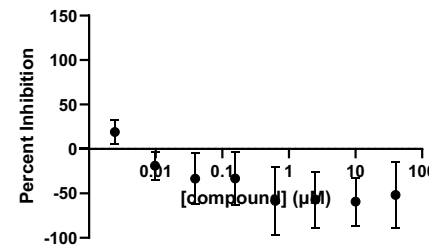
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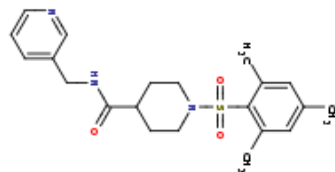
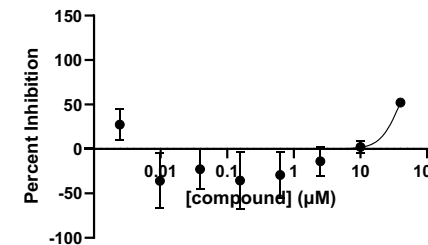
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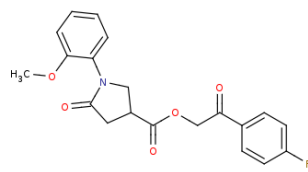
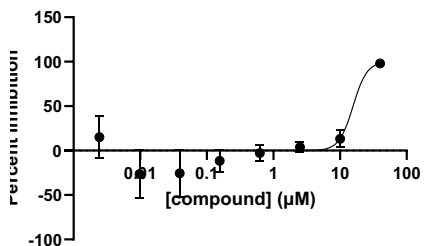
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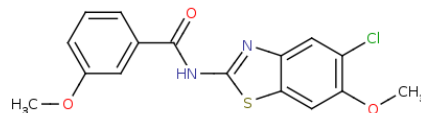
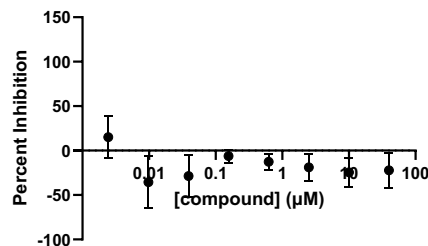
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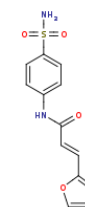
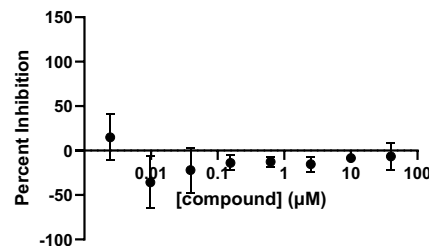
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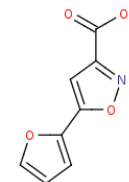
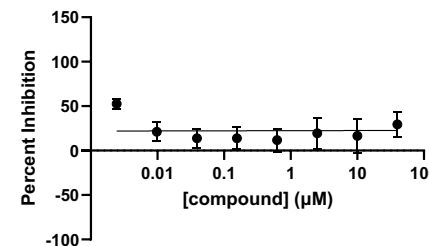
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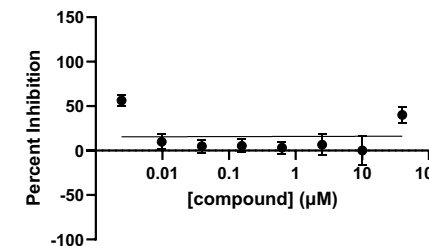
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RA-0001409

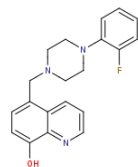


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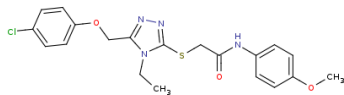
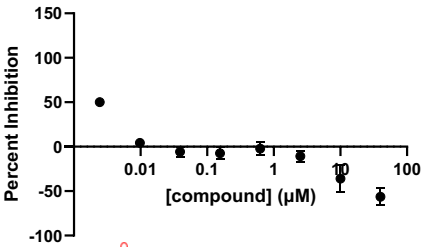


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EC50	15.24	Unstable	45.19	Unstable	38.83	15.69	Unstable	Unstable	1.609E+151	8.899E+133
Hill Slope	3.406	Unstable	12.3	Unstable	2.989	4.155	Unstable	Unstable	0.003571	0.005402

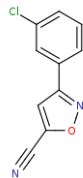
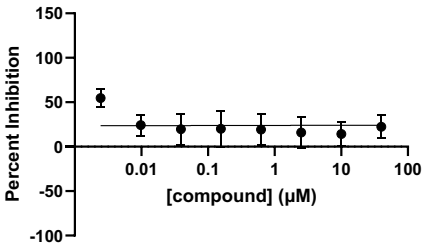
# EXP0139 VEEV TC83 nLuc Capsid Antiviral Assay



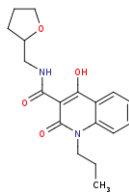
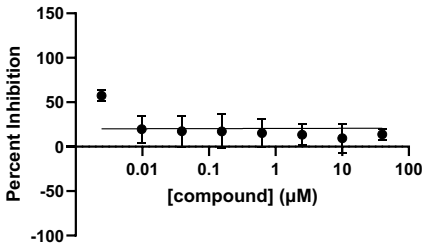
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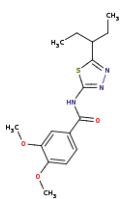
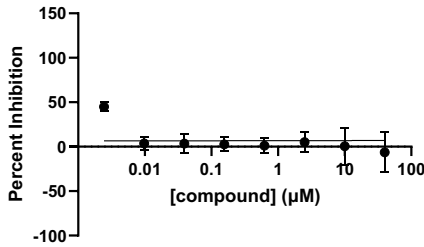
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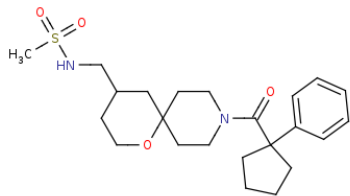
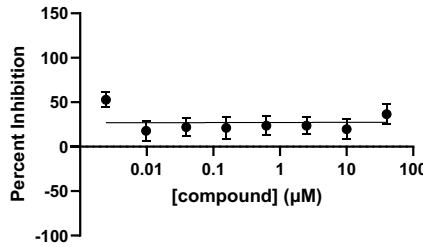
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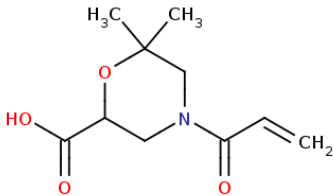
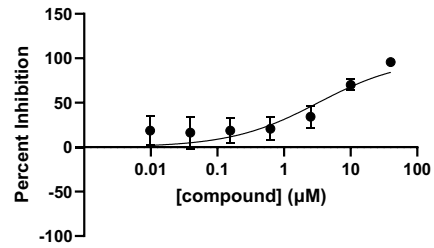
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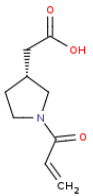
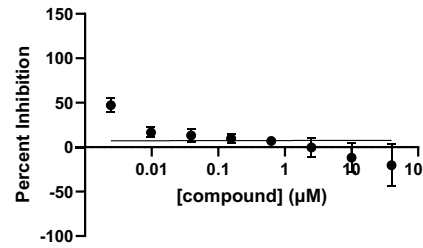
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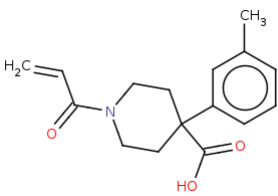
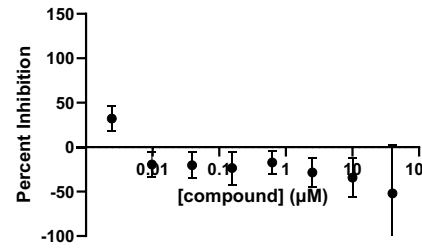
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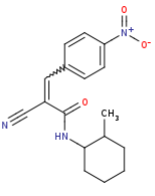
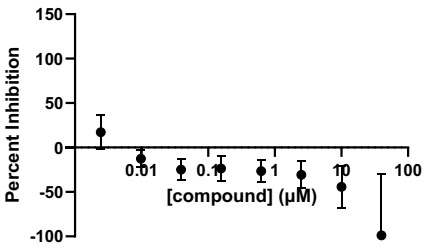
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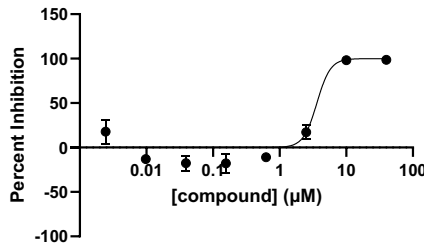
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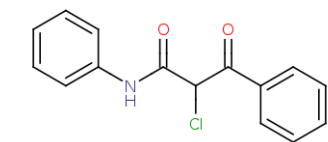


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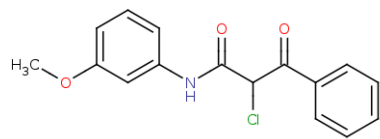
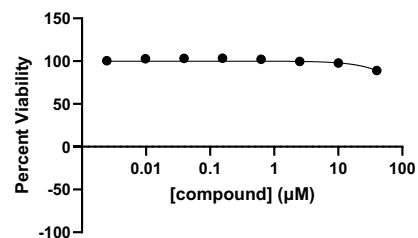


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EC50	Unstable	1.29E+151	1.709E+151	4.094E+151	5.538E+150	3.254	7.908E+151	Unstable	Unstable	3.622
Hill Slope	Unstable	0.003325	0.003894	0.00752	0.002832	0.6672	0.007188	Unstable	Unstable	4.276

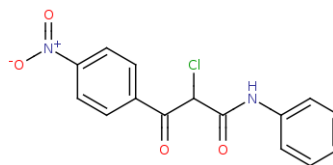
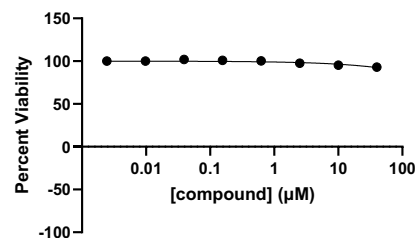
# EXP0139 Cell Titer Glo Viability Assay



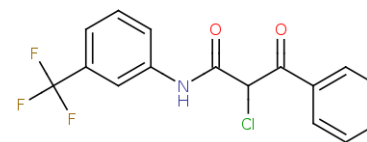
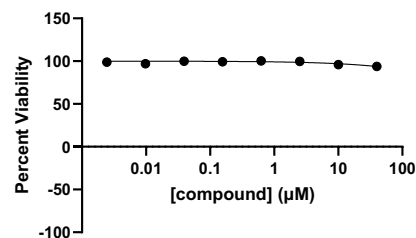
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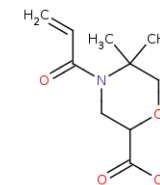
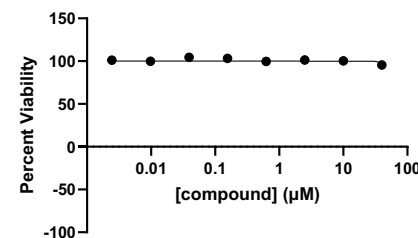
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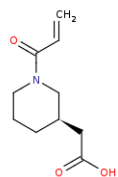
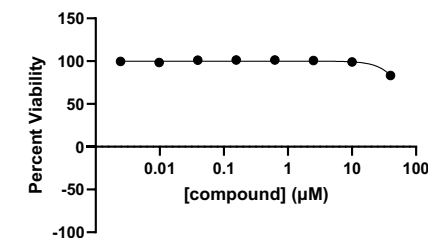
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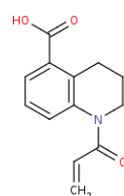
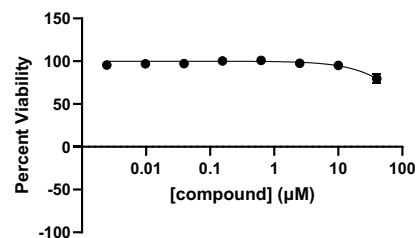
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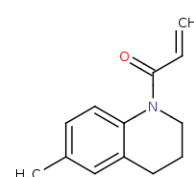
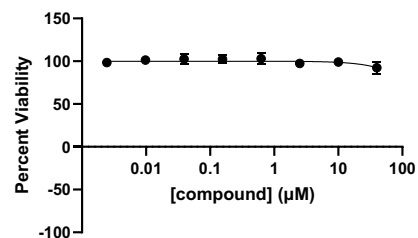
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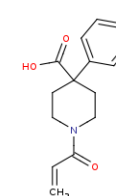
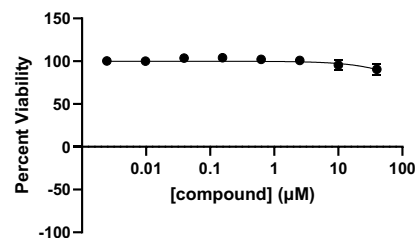
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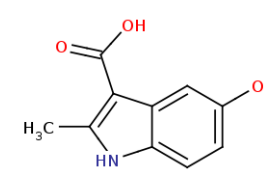
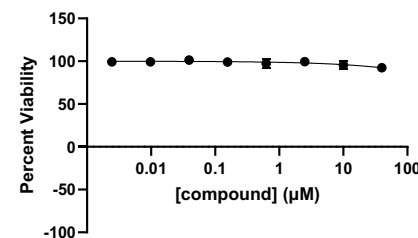
RA-0020667



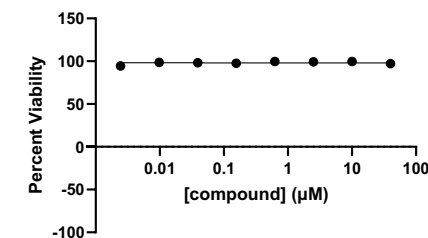
RA-0020668



RA-0020669



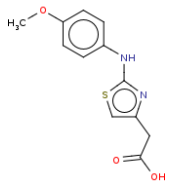
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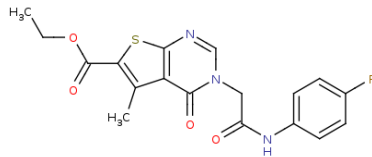
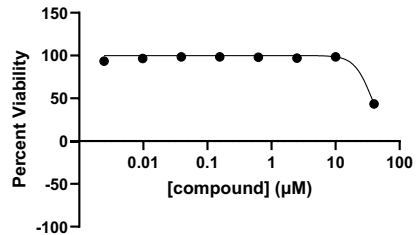
	RA-0020661	RA-0020662	RA-0020663	RA-0020664	RA-0020665	RA-0020666	RA-0020667	RA-0020668	RA-0020669	RA-0020670
CC50	197.7	3318	5147	52.52	80.47	140.6	284.1	377.2	5773	Unstable
Hill Slope	-1.304	-0.568	-0.5572	-11.23	-2.3	-1.089	-1.283	-0.987	-0.5001	-0.01064



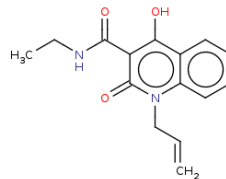
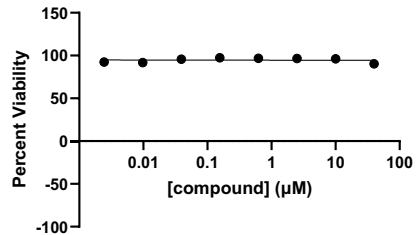
# EXP0139 Cell Titer Glo Viability Assay



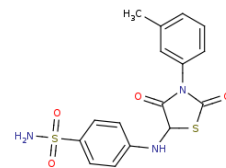
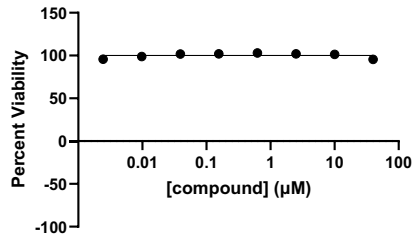
RA-0020671



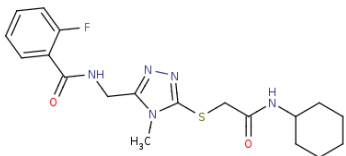
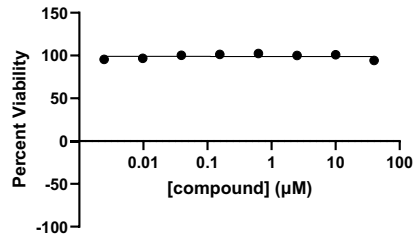
RA-0020672



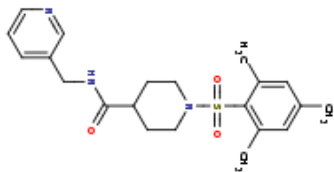
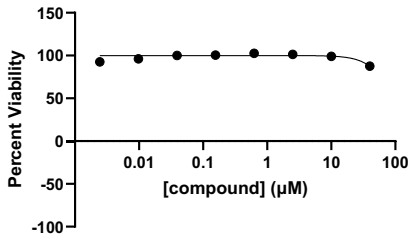
RA-0020673



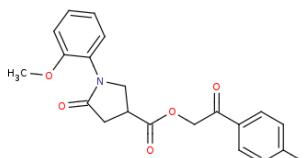
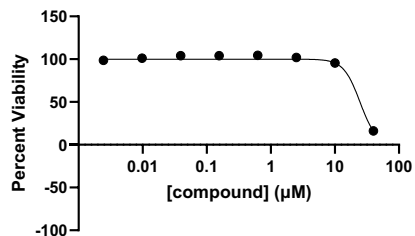
RA-0020674



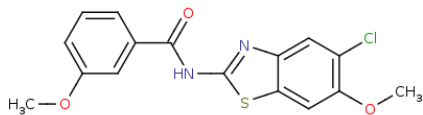
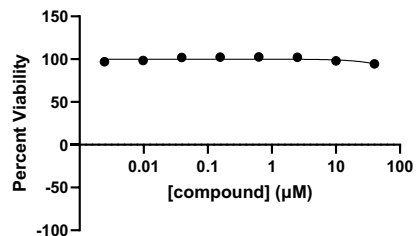
RA-0020675



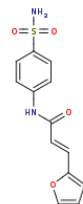
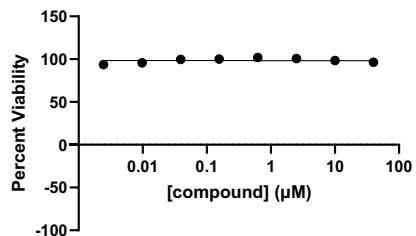
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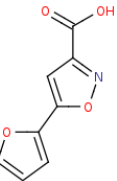
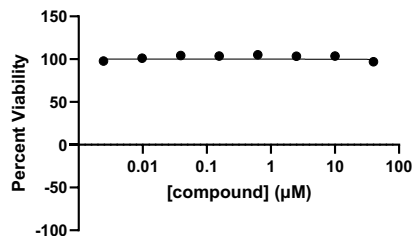
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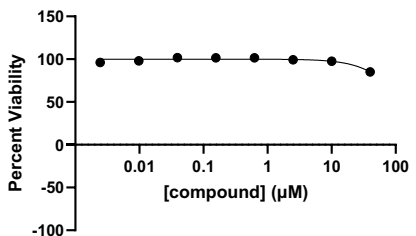
RA-0020678



RA-0001409

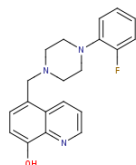


RA-0020680

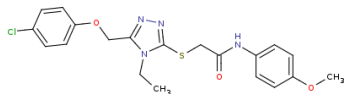
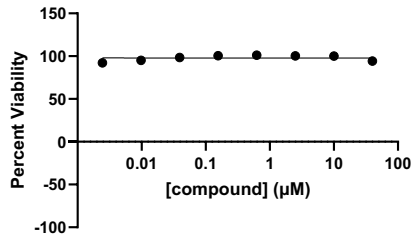


	RA-0020671	RA-0020672	RA-0020673	RA-0003261	RA-0020675	RA-0020676	RA-0020677	RA-0020678	RA-0020679	RA-0020680
EC50	36.81	Unstable	Unstable	Unstable	98.03	24.62	337.5	Unstable	52.16	138.2
Hill Slope	-3.185	-0.007741	-0.9129	-0.01229	-2.17	-3.392	-1.329	-0.01101	-13.05	-1.399

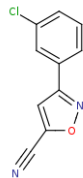
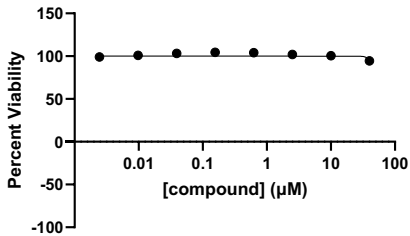
# EXP0139 Cell Titer Glo Viability Assay



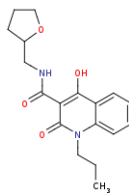
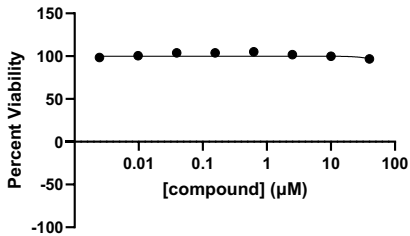
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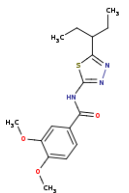
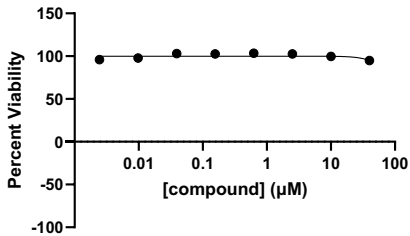
RA-0020682



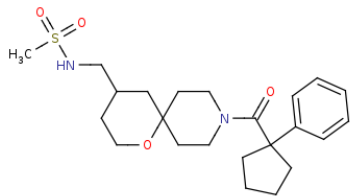
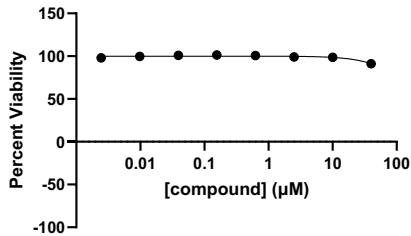
RA-0020683



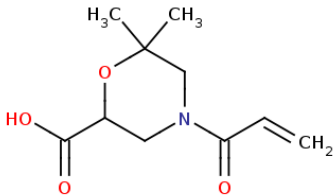
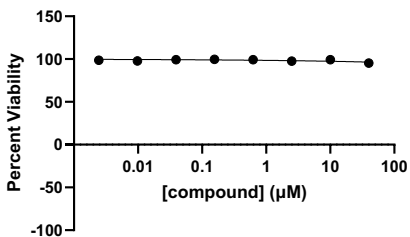
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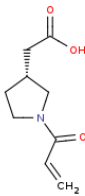
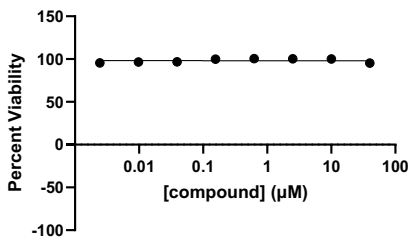
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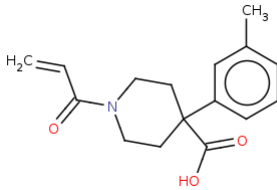
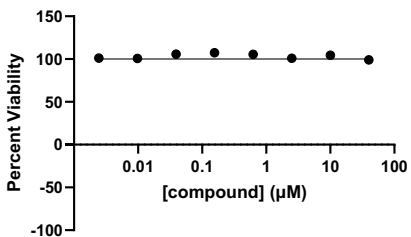
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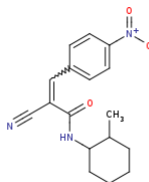
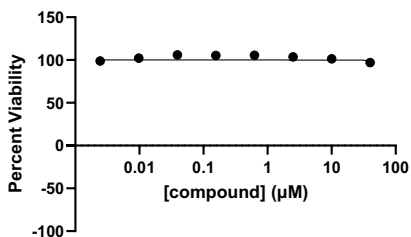
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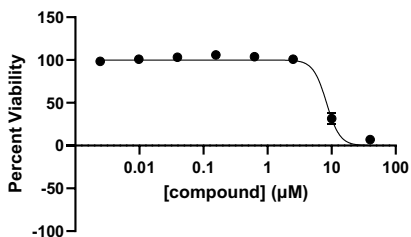
RA-0002477-01



RA-0003135-01



RA-0003637-01



	RA-0020681	RA-0020682	RA-0020683	RA-0020684	RA-0020685	RA-0001822-05	RA-0002473-01	RA-0002477-01	RA-0003135-01	RA-0003637-01
EC50	Unstable	51.16	142.9	125.9	223.8	Unstable	Unstable	Unstable	54.73	8.326
Hill Slope	-0.01028	-11.57	-2.679	-2.551	-1.354	-0.2366	-0.01066	Unstable	-11.15	-4.177

Summary – CNP19 & CNP21

READDI ID	Description	CHKV			VEEV			Viability		
		% Inhibition 10uM	EC50	Hill Slope	% Inhibition 10uM	EC50	Hill Slope	% Viability 10uM	CC50	Hill Slope
RA-0020661	nsp2 helicase Covalent set (CNP19)	70.215523	36.9	10.63	88.1531419	16.11	1.98	88.98175	197.7	-1.304
RA-0020662	nsp2 helicase Covalent set (CNP19)	-66.12386	Unstable	Unstable	10.385729	Unstable	Unstable	92.96812	3318	-0.568
RA-0020663	nsp2 helicase Covalent set (CNP19)	1.5313876	Unstable	Unstable	31.2307018	42.78	11.76	93.93069	5147	-0.5572
RA-0020664	nsp2 helicase Covalent set (CNP19)	-9.060457	Unstable	Unstable	33.1251138	Unstable	0.02881	95.51304	52.52	-11.23
RA-0020665	nsp2 helicase Covalent set (CNP19)	-20.03485	Unstable	Unstable	67.7508245	18.47	0.7858	83.30772	80.47	-2.3
RA-0020666	nsp2 helicase Covalent set (CNP19)	62.638633	Unstable	Unstable	86.1078274	32.12	8.315	79.66769	140.6	-1.089
RA-0020667	nsp2 helicase Covalent set (CNP19)	-71.19012	Unstable	Unstable	32.592216	5.1E+150	0.003361	92.48369	284.1	-1.283
RA-0020668	nsp2 helicase Covalent set (CNP19)	0.4309616	70.28	9.658	36.6229221	1.8E+150	0.004113	90.46852	377.2	-0.987
RA-0020669	nsp2 helicase Covalent set (CNP19)	-19.68599	Unstable	Unstable	21.7683131	2E+151	0.006109	92.34456	5773	-0.5001
RA-0020670	nsp2 helicase Asinex set (CNP21)	-5.191962	Unstable	Unstable	-27.814431	Unstable	Unstable	97.20253	Unstable	-0.01064
RA-0020671	nsp2 helicase Asinex set (CNP21)	77.57272	23.32	2.347	95.5748657	15.24	3.406	43.42525	36.81	-3.185
RA-0020672	nsp2 helicase Asinex set (CNP21)	-37.18745	Unstable	Unstable	-51.995473	Unstable	Unstable	90.29867	Unstable	-0.00774
RA-0020673	nsp2 helicase Asinex set (CNP21)	9.1122113	48.38	12.09	18.2297233	45.19	12.3	95.5855	Unstable	-0.9129
RA-0003261	nsp2 helicase Asinex set (CNP21)	-96.26813	Unstable	Unstable	-51.575341	Unstable	Unstable	94.30285	Unstable	-0.01229
RA-0020675	nsp2 helicase Asinex set (CNP21)	50.161337	39.52	1.673	52.2120991	38.83	2.989	87.50149	98.03	-2.17
RA-0020676	nsp2 helicase Asinex set (CNP21)	82.645668	36.18	15.54	98.0933071	15.69	4.155	16.1607	24.62	-3.392
RA-0020677	nsp2 helicase Asinex set (CNP21)	-52.06567	Unstable	Unstable	-22.178135	Unstable	Unstable	94.54369	337.5	-1.329
RA-0020678	nsp2 helicase Asinex set (CNP21)	-14.83009	Unstable	Unstable	-6.5575393	Unstable	Unstable	96.36352	Unstable	-0.01101
RA-0001409	nsp2 helicase Asinex set (CNP21)	6.2539011	52.12	10.23	29.4437259	1.6E+151	0.003571	96.96624	52.16	-13.05
RA-0020680	nsp2 helicase Asinex set (CNP21)	50.40782	39.95	12.09	40.024093	8.9E+133	0.005402	85.00816	138.2	-1.399
RA-0020681	nsp2 helicase Asinex set (CNP21)	-44.26446	Unstable	Unstable	-56.439688	Unstable	Unstable	94.32375	Unstable	-0.01028
RA-0020682	nsp2 helicase Asinex set (CNP21)	-45.62496	Unstable	Unstable	22.4089415	1.3E+151	0.003325	94.50413	51.16	-11.57
RA-0020683	nsp2 helicase Asinex set (CNP21)	-20.99128	Unstable	Unstable	13.7880827	1.7E+151	0.003894	96.8222	142.9	-2.679
RA-0020684	nsp2 helicase Asinex set (CNP21)	-8.314951	Unstable	Unstable	-6.4255207	4.1E+151	0.00752	94.90023	125.9	-2.551
RA-0020685	nsp2 helicase Asinex set (CNP21)	42.254178	40.18	Unstable	36.6481529	5.5E+150	0.002832	91.13404	223.8	-1.354

# Summary – Unwindase Covalent Hits

READDI ID	Description	CHKV			VEEV			Viability		
		% Inhibition 10uM	EC50	Hill Slope	% Inhibition 10uM	EC50	Hill Slope	% Viability 10uM	CC50	Hill Slope
RA-0002473-01	CHIKV NSP2 Helicase Unwindase Covalent Hits follow-up	-100.3821	Unstable	Unstable	-20.31147	7.9E+151	0.007188	95.30888	Unstable	-0.01066
RA-0002477-01	CHIKV NSP2 Helicase Unwindase Covalent Hits follow-up	-16.07851	Unstable	Unstable	-51.808864	Unstable	Unstable	99.15723	Unstable	Unstable
RA-0003135-01	CHIKV NSP2 Helicase Unwindase Covalent Hits follow-up	-129.7594	Unstable	Unstable	-98.772963	Unstable	Unstable	97.05244	54.73	-11.15
RA-0003637-01	CHIKV NSP2 Helicase Unwindase Covalent Hits follow-up	88.819976	3.892	2.113	98.7388839	3.622	4.276	7.063782	8.326	-4.177
RA-0003639-01	CHIKV NSP2 Helicase Unwindase Covalent Hits follow-up	85.694563	28.08	5.059	91.9441405	34.56	16.63	113.9651	8.45E+09	-26.11