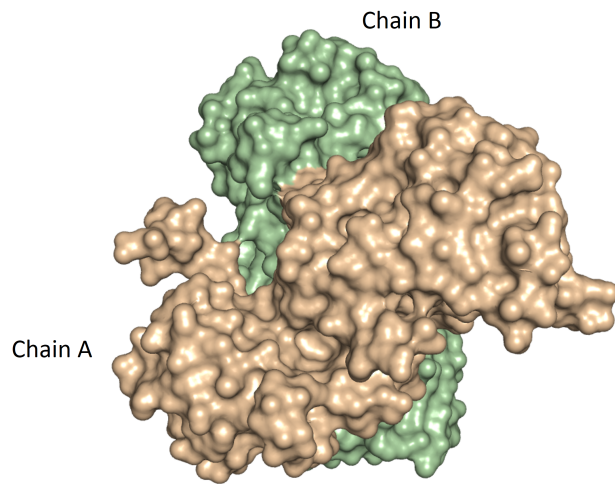
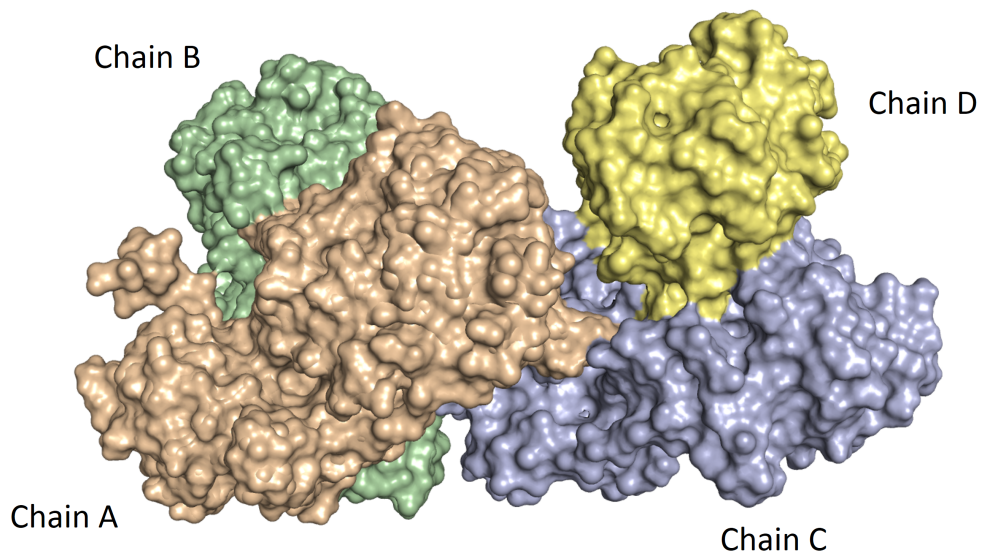


Supplemental information



Suppl. Fig. 1. Surface representation of the SeMet-CavV 3CL^{pro} dimer (PDB ID: 5LAC). Chains A and B are shown in wheat and green, respectively.



Suppl. Fig. 2. Surface representation of the structure of the CavV 3CL^{pro}/inhibitor complex (PDB ID: 5LAK), including chains A (wheat), B (green), C (blue), and D (yellow).

Suppl. Table 1. Nidovirus genomes used for phylogeny reconstruction.

Species	Acronym	Accession number
<i>Alphaarterivirus equid</i>	EAV	X53459.3
<i>Gammaarterivirus lacdeh</i>	LDV	U15146.1
<i>Betaarterivirus suid 1</i>	PRRSV-1	M96262.2
<i>Betaarterivirus suid 2</i>	PRRSV-2	U87392.3
<i>Betaarterivirus chinrav 1</i>	RatAV	KP280006.1
<i>Deltaarterivirus hemfev</i>	SHFV	AF180391.2
<i>Iotaarterivirus kibreg 1</i>	KRTGV	JX473849.1
<i>Zetaarterivirus ugarco 1</i>	KRCV-1	KC787630.1
<i>Etaarterivirus ugarco 1</i>	KRCV-2	KC787658.1
<i>Thetaarterivirus mikelba 1</i>	MYBV-1	KM110938.1
<i>Epsilonarterivirus hemcep</i>	SHEV	KM677927.1
<i>Iotaarterivirus debrazmo</i>	DeMAV	KP126831.1
<i>Deltaarterivirus pejah</i>	PBJV	KR139839.1
<i>Thetaarterivirus kafuba</i>	KKCBV	KT447550.1
<i>Epsilonarterivirus safriver</i>	FSVV	KR862307.1
<i>Lambdaarterivirus afriporav</i>	APRAV	KP026921.1
<i>Kappaarterivirus wobum</i>	WPDV	JN116253.3
<i>Alphacoronavirus 1</i>	TGEV	AJ271965.2
<i>Human coronavirus 229E</i>	HCoV_229E	AF304460.1
<i>Human coronavirus NL63</i>	HCoV_NL63	AY567487.2
<i>Miniopterus bat coronavirus 1</i>	Mi-BatCoV_1A	EU420138.1
<i>Miniopterus bat coronavirus HKU8</i>	Mi-BatCoV_HKU8	EU420139.1
<i>Porcine epidemic diarrhea virus</i>	PEDV	AF353511.1
<i>Rhinolophus bat coronavirus HKU2</i>	Rh-BatCoV_HKU2	EF203065.1
<i>Scotophilus bat coronavirus 512</i>	Sc-BatCoV_512	DQ648858.1
<i>Bat coronavirus HKU10</i>	BtCoV_HKU10	JQ989271.1
<i>Bat coronavirus CDPHE15</i>	BtCoV_CDPHE15	KF430219.1
<i>Mink coronavirus 1</i>	MCoV	HM245925.1
<i>Betacoronavirus 1</i>	HCoV_OC43	AY585228.1
<i>Human coronavirus HKU1</i>	HCoV_HKU1	AY597011.2
<i>Murine coronavirus</i>	MHV	AY700211.1
<i>Pipistrellus bat coronavirus HKU5</i>	Pi-BatCoV_HKU5	EF065509.1
<i>Rousettus bat coronavirus HKU9</i>	Ro-BatCoV_HKU9	EF065513.1
<i>Severe acute respiratory syndrome-related coronavirus</i>	SARS-CoV	AY274119.3
<i>Tylonycteris bat coronavirus HKU4</i>	Ty-BatCoV_HKU4	EF065505.1
<i>Middle East respiratory syndrome-related coronavirus</i>	MERS-CoV	JX869059.2
<i>Hedgehog coronavirus 1</i>	EriCoV	KC545383.1
<i>Avian coronavirus</i>	IBV	M95169.1
<i>Beluga whale coronavirus SW1</i>	BWCoV	EU111742.1
<i>Bulbul coronavirus HKU11</i>	BuCoV_HKU11	FJ376619.2
<i>Bulbul coronavirus HKU11</i>	ThCoV_HKU12	FJ376621.1
<i>Munia coronavirus HKU13</i>	MuCoV_HKU13	FJ376622.1

Species	Acronym	Accession number
<i>Coronavirus HKU15</i>	PoCoV_HKU15	JQ065043.2
<i>White-eye coronavirus HKU16</i>	WECoV_HKU16	JQ065044.1
<i>Night heron coronavirus HKU19</i>	NHCoV_HKU19	JQ065047.1
<i>Wigeon coronavirus HKU20</i>	WiCoV_HKU20	JQ065048.1
<i>Common moorhen coronavirus HKU21</i>	CMCoV_HKU21	JQ065049.1
<i>Bovine torovirus</i>	BRV	AY427798.1
<i>Porcine torovirus</i>	PToV	JQ860350.1
<i>White bream virus</i>	WBV	DQ898157.1
<i>Fathead minnow nidovirus 1</i>	FHMNV	GU002364.2
<i>Chinook salmon nidovirus 1</i>	CSV	KJ681496.1
<i>Ball python nidovirus 1</i>	BPNV	KJ541759.1
<i>Bovine nidovirus 1</i>	BoNV	KM589359.1
<i>Alphamesonivirus 1</i>	CavV	HM746600.1
<i>Alphamesonivirus 2</i>	KSaV	KC807171.1
<i>Alphamesonivirus 3</i>	DKNV	AB753015.2
<i>Alphamesonivirus 4</i>	CASV	KJ125489.1
<i>Alphamesonivirus 5</i>	HanaV	JQ957872.1
<i>Alphamesonivirus 8</i>	NseV	JQ957874.1
<i>Alphamesonivirus 9</i>	MenoV	JQ957873.1
<i>Gill-associated virus</i>	GAV	AF227196.1
<i>Infratovirus 1</i>	INTOV	KX883638.1
<i>Sectovirus 1</i>	SECTOV	KX883637.1
<i>Turrinivirus 1</i>	TurrNV	KX883629.1
<i>Charybnavirus 1</i>	CharNV	KX883628.1
<i>Decronivirus 1</i>	DecNV	KX883636.1
<i>Paguronivirus 1</i>	PagRV	KX883627.1

Suppl. Table 2. 3CL^{pro} PDB entries used to produce the structure-based MSA.

PDB ID	Chain	Acronym
5LAC	B	CavV
2Q6D	A	IBV
4YO9	A	Ty-BatCoV_HKU4
4RSP	A	MERS-CoV
1UJ1	A	SARS-CoV
1P9S	A	HCoV_229E
3TLO	A	HCoV_NL63
5HYO	A	PEDV
1LVO	A	TGEV