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A review on viral metagenomics in extreme environments

Running title: Viral metagenomics in extreme environments

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Abstract

Viruses are the most abundant biological entities in the biosphere, and have the ability to infect Bacteria, Archaea and Eukaryotes. The virome is estimated to be at least ten times more abundant than the microbiome with 10^7 viruses per milliliter and 10^9 viral particles per gram in marine waters and sediments or soils, respectively. Viruses represent a largely unexplored genetic diversity, having an important role in the genomic plasticity of their hosts. Moreover, they also play a significant role in the dynamics of microbial populations. In recent years, metagenomic approaches have gained increasing popularity in the study of environmental viromes, offering the possibility of extending our knowledge related to both virus diversity and their functional characterization. Extreme environments represent an interesting source of both microbiota and their virome due to their particular physicochemical conditions, such as very high or very low temperatures and >1 atm hydrostatic pressures, among others. Despite the fact that some progress has been made in our understanding of the ecology of the microbiota in these habitats, few metagenomic studies have described the viromes present in extreme ecosystems. Thus, limited advances have been made in our understanding of the virus community structure in extremophilic ecosystems, as well as in their biotechnological potential. In this review, we critically analyse recent progress in metagenomic based approaches to explore the viromes in extreme environments and we discuss the potential for new discoveries, as well as methodological challenges and perspectives.

Table S1. Summary of studies metagenomics comparing to sequencing platforms, protocol extraction, and assembly and taxonomic tools

ID	Name of sample	ID sample	Number of reads or contigs	Type of sample	Country or Region	Type of sequencing	Method of extraction	Assembly	Taxonomic
SDEEP_ARCT_1a	EXPLODIVE	Arctic - Extra (2126)	27037	Sediment	Arctic Ocean	Pyrosequencing	CTAB/NaCl	CLC Genomics Workbench ver. 5.5	Megan
SDEEP_ATL_1a	EXPLODIVE	Atlantic - Extra (2125)	26826		Atlantic Ocean				
SDEEP_ATL_1b	EXPLODIVE	Atl_Vir (1157)	107090		Atlantic Ocean				
SDEEP_ARCT_1b	EXPLODIVE	Arct_Vir (1159)	63869		Arctic Ocean				
SDEEP_BKSEA_1a	EXPLODIVE	Black sea (1155)	784336		Black sea				
SDEEP_MED_1a	EXPLODIVE	Mediterrano (1161)	65340		Mediterraneo				
SDEEP_ATL_1c	EXPLODIVE	NE Atlancic (1156)	165517		Atlantic Ocean				
SDEEP_ARCT_1c	EXPLODIVE	Arctic Ocean (1158)	79646		Arctic Ocean				
SDEEP_JAP_2a	(Hado)pelagic sediments	Izu-Ogasawara Trench (164)	46458		Izu-Ogasawara Trench Japan				
SDEEP_JAP_2b	(Hado)pelagic sediments	Mariana Trench (165)	49584	Mariana Trench Japan					
SDEEP_JAP_2c	(Hado)pelagic sediments	off Shimokita Peninsula (166)	76498	Shimokita Peninsula Japon					
WDEEP_ITA_3a	Marine viromes	KM3 Ioinan Sea (3814)	9048	Deep sea-Seawater	Italy	Pyrosequencing	formamide/CTAB extraction	WI	Blast
WDEEP_CAN_4a	POV LineP transect	LJ12O (1394)	122565	Deep sea-Seawater	Canada	Pyrosequencing	WI	WI	WI
WDEEP_CAN_4b	POV LineP transect	LJ12D (1395)	49914						
WDEEP_CAN_4c	POV LineP transect	LA26O (1398)	70596						

WDEEP_CAN_4d	POV LineP transect	LA26D (1400)	68516						
WDEEP_CAN_4e	POV LineP transect	LF26O (1403)	147537						
WDEEP_CAN_4f	POV LineP transect	LF26D (1404)	125896						
WDEEP_CAN_4g	POV LineP transect	LJ26O (1407)	101179						
WDEEP_CAN_4h	POV LineP transect	LJ26D (1408)	55332						
WDEEP_CAN_4i	POV LineP transect	LJ4O (1414)	97126						
WDEEP_CAN_4j	POV LineP transect	LJ4D (1415)	98478						
WDEEP_EUA_4a	POV MBARI transect	M6O1K (1432)	225833		United States				
WDEEP_EUA_4b	POV MBARI transect	M7O4K (1433)	144588		United States				
OMZ_CAN_5a	Saanich Inlet	Saanich_200m_r200 (2915)	1728968	Oxygen minimum zones	Canada	Illumina	e Gentra Puregene Blood kit (Qiagen)	Geneious v7.1	Blastx
OMZ_CAN_5b	Saanich Inlet	Saanich_fosmids (3286)	47		Pyrosequencing				
OMZ_CHL_6a	2008OMZst3viral200m (898)	Pyrosequencing	96706		Chile	Chile	CTAB/formamide	without assembly	Blastx
OMZ_CHL_6b	2008OMZst5viral200m (993)	Pyrosequencing	163531		Chile	Chile			
ARID_ATA_7a	Antarctic soil metaviromes	Antarctic hypolith reads (2726)	1057535	Hyperarid	Miers Valley; Antarctica	Illumina	WI	WI	WI
ARID_ATA_7b	Antarctic soil metaviromes	Antarctic open soil reads (2727)	870687		Miers Valley; Antarctica				
ARID_ATA_7c	Antarctic soil metaviromes	Antarctic hypolith contigs (2472)	32574		Miers Valley; Antarctica				
ARID_ATA_7d	Antarctic soil metaviromes	Antarctic open soil contigs (2473)	8442		Miers Valley; Antarctica				
ARID_NAM_8a	Namib Desert transect metaviromes	NAM_130 (5775)	3097		Namibia	Sanger	WI	WI	WI
ARID_NAM_8b	Namib Desert transect metaviromes	NAM_100 (5774)	2897			Sanger			
ARID_NAM_8c	Namib Desert transect metaviromes	NAM_70 (5773)	545			Sanger			
ARID_NAM_8d	Namib Desert transect metaviromes	NAM_40 ()							

ARID_NAM_8e	Namib hypolith 2012	Namib_hypolith_2012_contigs (2186)	4564			Illumina			
ARID_NAM_8f	Namib hypolith 2012	Namib_hypolith_2012_reads (2708)	841458			Illumina			
SALINE_NAM_9a	Archevir	P5_Ngallou (1700)	3018	Hypersaline	Namibia	Illumina	QIAamp DNA mini kit (Qiagen)	IDBA_UD	tBLASTx
SALINE_NAM_9b	Archevir	P2_Saloon(1701)	7302			Illumina			
SALINE_NAM_9c	Archevir	P6_Lake_Retba(1702)	884			Illumina			
SALINE_NAM_9d	Archevir	P7_Ngallou(1703)	1312			Illumina			
SALINE_NAM_9e	Archevir	P8_Ngallou(1704)	3212			Illumina			
SALINE_NAM_9f	Archevir	P9_Ngallou(1705)	529			Illumina			
SALINE_EUA_10a	Saltern ponds	Saltern medium - 112805 (23)	39439		United_States	Pyrosequencing	Ultra Clean Soil DNA Kit	WI	tBLASTx
SALINE_EUA_10b	Saltern ponds	Saltern medium - 111605 (24)	58319						
SALINE_EUA_10c	Saltern ponds	Saltern high - 111605 (25)	151180						
SALINE_EUA_10d	Saltern ponds	Saltern low - 0704 (26)	268049						
SALINE_EUA_10f	Saltern ponds	Saltern low - 111005 (27)	109836						
SALINE_EUA_10g	Saltern ponds	Saltern medium - 111005 (28)	39348						
SALINE_EUA_10h	Saltern ponds	Saltern medium - 112205 (29)	55142						
SALINE_EUA_10i	Saltern ponds	Saltern high - 120705 (30)	46628						
SALINE_EUA_10j	Saltern ponds	Saltern high - 112805 (31)	4536						
SALINE_EUA_10k	Saltern ponds	Saltern low - 112805 (32)	62363						
SALINE_EUA_11a	Freshwater	Tilapia Chanel 1105 (33)	264844	United_States	Pyrosequencing	CTAB/ formamide Ultra Clean Soil DNA kit	WI	tBLASTx	
SALINE_EUA_11b	Freshwater	Tilapia Channel 0406 (35)	60135						
SALINE_EUA_11c	Freshwater	Tilapia Channel 0806 (36)	56549						
SALINE_EUA_12a	Others	Tampa Bay induced(46)	279129	United_States	Pyrosequencing	WI	WI	WI	

SALINE_EUA_12b	Others	Salton One (47)	55467						
SALINE_EUA_12c	Others	Salton Sea (46)	29814						
SALINE_EUA_12d	Others	Saltern Ponds fomids (1343)	42						
COLD_GRL_13a	Supraglacial	Cryoconite_viruses_curated (4314)	546	Cold Freshwater	Greenland icesheet plus Svalbard cryoconite	Illumina	QIAamp MinElute Virus Spin Kit	CLC Genomics Workbench	Qiime
COLD_ATA_14a	Lake limnopolar	Antartic Lake Spring	4132	Cold Freshwater	Antartic	Sanger	phenol-chloroform and ethanol precipitated.	WI	BLASTX
COLD_ATA_14b	Lake limnopolar	Antartic Lake Summer	387475	Cold Freshwater	Antartic	Sanger	phenol-chloroform and ethanol precipitated.	WI	BLASTX
HOT_EUA_15a	Yellowstone Hot Springs	Hot Spring Octopus (52)	22272	Hyperthermophile	United_States	Sanger	phenol-chloroform and ethanol precipitated.	ManSeq	BLASTx
HOT_EUA_15b	Yellowstone Hot Springs	Hot Spring Bear Paw (53)	8352	Hyperthermophile	United_States	Sanger			
HOT_TBV_16a	Brazos-Trinity Basin (IODP site 1320)	Brazos-Trinity 8mbsf (3813)	270730	Hyperthermophile	Mexico	Pyrosequencing	WI	WI	WI

*WI without information

Table S2. Structures of viral proteins derived from structural proteomic approaches or from the analysis of functionally unannotated open reading frames.

Family or order	Name	Extreme character	PDB ID	Molecule and function	Reference
<i>Mimiviridae</i>	<i>Megavirus chiliensis</i>	moderate salt	4XUL (XRAY)	Mg662 (GTP binding protein)	to be published
<i>Mimiviridae</i>	<i>Acanthamoeba polyphaga mimivirus</i>	moderate salt	4Z24, 5, 6 (XRAY)	R135 (outer layer protein, probably aryl alcohol oxidase)	Klose et al., 2015
<i>Nimaviridae</i>	White spot syndrome virus	moderate salt	2GJ2 (XRAY) 2GJI (NMR)	VP9 (hypothetical DNA binding protein)	Liu et al., 2006
<i>Ligamenvirales</i>	<i>Sulfolobus islandicus</i> rod-shaped virus 1	high temperature and low pH	2X5T, G, H, (XRAY) 2X3G (XRAY) 2X48 (XRAY) 2X4I (XRAY)	ORF131 ORF119 ORF55 ORF114a (Scottish Structural Proteomics Facility)	Oke et al., 2010
<i>Ligamenvirales</i>	<i>Acidianus filamentous</i> virus 1	high temperature and low pH	3II2, 3, 3ILD, E (XRAY)	ORF157 (nuclease)	Goulet et al., 2010
<i>Ligamenvirales</i>	<i>Acidianus filamentous</i> virus 1	high temperature and low pH	3DF6, 3DJW (XRAY)	Afv1-99 (unknown)	Goulet et al., 2009a
<i>Ligamenvirales</i>	<i>Acidianus filamentous</i> virus 1	high temperature and low pH	2WB6 (XRAY)	Afv1-102 (unknown)	Keller et al., 2009
<i>Ligamenvirales</i>	<i>Sulfolobus islandicus</i> filamentous virus	high temperature and low pH	2H36 (XRAY)	ORF14 (putative structural protein)	Goulet et al., 2009b
<i>Ligamenvirales</i>	<i>Acidianus filamentous</i> virus 3	high temperature and low pH	2J6B, C (XRAY)	Afv3-109 (DNA binding protein)	Keller et al., 2007
<i>Globuloviridae</i>	<i>Pyrobaculum spherical</i> virus	high temperature	2X3M (XRAY) 2X5R (XRAY) 2X4J (XRAY) 2X5C (XRAY) 2VXZ (XRAY)	ORF239 ORF126 ORF137 ORF131 gp04 (Scottish Structural Proteomics Facility)	Oke et al., 2010
<i>Fuselloviridae</i>	<i>Sulfolobus spindle-shape</i> virus 1	high temperature and low pH	2VQC (XRAY)	F112 (hypothetical DNA binding protein)	Menon et al., 2008
<i>Fuselloviridae</i>	<i>Sulfolobus spindle-</i>	high temperature	1SKV (XRAY)	D-63 (hypothetical	Kraft et al., 2004

	shape virus 1	and low pH		adaptor protein)	
<i>Bicaudaviridae</i>	Acidianus two-tailed virus	high temperature and low pH	4ART (XRAY) 4ATS (XRAY)	ORF273 (novel fold)	Felisberto-Rodrigues et al., 2012
<i>Bicaudaviridae</i>	Acidianus two-tailed virus	high temperature and low pH	3FAJ (XRAY)	P131 (unknown)	to be published
<i>satellite virus</i>	<i>Sulfolobus islandicus</i> pSSVx	high temperature and low pH	3O27 (XRAY)	C68 (DNA binding protein)	Contursi et al., 2011

XRAY: obtained by X-ray crystallography; NMR: obtained by Nuclear Magnetic Resonance

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Table S3. Structural proteins from extremophile viruses.

<i>Family or order</i>	Name	Extreme character	PDB ID	Molecule	Reference
<i>Siphoviridae</i>	marine siphovirus TW1	moderate salt	5WK1 (EM)	major capsid protein	Wang et al., 2018
<i>Podoviridae</i>	Procholococcus cyanophage P-SSP7	moderate salt	2XD8 (EM)	capsid	Liu et al., 2010
<i>Inoviridae</i>	Thermus phage PH75	high temperature	1HGV, Z, 1HH0 (FD)	capsid	Pederson et al., 2001
<i>Sphaerolipoviridae</i>	Thermus virus P23-77	high temperature	3ZMN, O, 3ZN4, 5, 6 (XRAY)	VP16 and VP17 capsid proteins	Rissanen et al., 2013
<i>Turriviridae</i>	Sulfolobus turreted icosahedral virus 1	high temperature and low pH	6BO3 (XRAY)	turret protein	to be published
<i>Turriviridae</i>	Sulfolobus turreted icosahedral virus 1	high temperature and low pH	3J31 (EM) 4IL7 (XRAY)	virus structural protein	Veesler et al., 2013
<i>Turriviridae</i>	Sulfolobus turreted icosahedral virus 1	high temperature and low pH	4IND (XRAY)	turret	to be published
<i>Turriviridae</i>	Sulfolobus turreted icosahedral virus 1	high temperature and low pH	3RKL (XRAY)	structural protein	to be published
<i>Turriviridae</i>	Sulfolobus turreted icosahedral virus 1	high temperature and low pH	2BBD (XRAY)	major capsid protein	Khayat et al., 2005
<i>Nimaviridae</i>	White spot syndrome virus	moderate salt	5HLJ (XRAY)	envelope protein VP24	Sun et al., 2016
<i>Nimaviridae</i>	White spot syndrome virus	moderate salt	2ED6, M (XRAY)	major envelope proteins VP26 and VP28	Tang et al., 2007
<i>Ligamenvirales</i>	Sulfolobus filamentous virus 1	high temperature and low pH	6D5F (EM)	virus	Liu et al., 2018
<i>Ligamenvirales</i>	Acidianus filamentous virus 1	high temperature and low pH	5W7G (EM)	viral envelope with lipid monolayer	Kasson et al., 2017
<i>Ligamenvirales</i>	Sulfolobus islandicus rod-shaped virus 2	high temperature and low pH	3J9X (EM)	virion	DiMaio et al., 2015
<i>Ligamenvirales</i>	Acidianus filamentous virus 1	high temperature and low pH	3FBL, Z (XRAY)	coat protein	Goulet et al., 2009
<i>Liigamenvirales</i>	Sulfolobus islandicus rod-shaped virus 1	high temperature and low pH	3F2E (XRAY)	coat protein	Szymczynna et al., 2009
<i>Corticoviridae</i>	Pseudoalteromonas	moderate salt	2W0C (XRAY)	virus	Abrescia et al., 2008

	phage PM2		2VVD (XRAY) 2VVE (XRAY) 2VVF (XRAY)	spike protein P1 spike protein P1 capsid protein P2	
<i>Bicaudaviridae</i>	Acidianus tailed spindle virus	high temperature and low pH	5EQW (XRAY)	major capsid protein	Hochstein et al., 2018
<i>Lavidaviridae</i>	Cafeteriavirus-dependent mavirus (virophage)	moderate salt	6G41, 2, 3, 4, 5 (XRAY)	major capsid protein, full length and truncated, penton protein	Born et al., 2018
<i>Lavidaviridae</i>	Sputnik virophage 3	moderate salt	3J26 (EM)	virus	Zhang et al., 2012
<i>Satellite virus</i>	Sputnik virophage	moderate salt	3KK5 (EM)	virus	Sun et al., 2009

XRAY: obtained by X-ray crystallography; NMR: obtained by Nuclear Magnetic Resonance; EM: obtained by cryo-electron microscopy; FD: obtained by fiber diffraction

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Table S4. DNA binding proteins and proteins that bind histones from extremophilic viruses.

Family or order	Name	Extreme character	PDB ID	molecule	Reference
<i>Iridoviridae</i>	Singapore grouper iridovirus	moderate salt	3RJ2 (XRAY)	H3 binding protein	Tran et al., 2011
<i>Turriviridae</i>	Sulfolobus turreted icosahedral virus 1	high temperature and low pH	2J85 (XRAY)	DNA binding protein	Larson et al., 2007
<i>Turriviridae</i>	Sulfolobus turreted icosahedral virus 1	high temperature and low pH	2CO5 (XRAY)	DNA binding protein	Larson et al., 2007a
<i>Nimaviridae</i>	White spot syndrome virus	moderate salt	2ZUG (XRAY)	histone-binding DNA-like protein	Wang et al., 2008
<i>Ligamenvirales</i>	Acidianus filamentous virus 1	high temperature and low pH	2LVH (NMR)	DNA binding protein (Zn finger)	Guilliere et al., 2013
<i>Ligamenvirales</i>	Acidianus filamentous virus 6	high temperature and low pH	4HV0 (XRAY)	transcription regulator	Peixeiro et al., 2013
<i>Ligamenvirales</i>	Sulfolobus islandicus rod-shaped virus 1	high temperature and low pH	2KEL (NMR)	transcriptional regulator SvtR	Guilliere et al., 2009
<i>Fuselloviridae</i>	Sulfolobus spindle-shape virus 1	high temperature and low pH	4LID (XRAY)	DNA binding protein	to be published
<i>Fuselloviridae</i>	Sulfolobus islandicus plasmid-virus pSSVx	high temperature and low pH	2MLG (NMR)	transcription factor Stf76	Contursi et al., 2014
<i>Fuselloviridae</i>	Sulfolobus virus Ragged Hills	high temperature and low pH	4AAI (NMR)	DNA binding protein E73	Schlenker et al., 2012
<i>Fuselloviridae</i>	Sulfolobus spindle-shape virus 1	high temperature and low pH	2WBT (XRAY)	zinc finger protein	to be published
<i>Fuselloviridae</i>	Sulfolobus spindle-shape virus 1	high temperature and low pH	1TBX (XRAY)	DNA binding protein F-93	Kraft et al., 2004

XRAY: obtained by X-ray crystallography; NMR: obtained by Nuclear Magnetic Resonance

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Table S5. Enzymes from extremophilic viruses.

Family or order	Name	Environment	PDB ID	Molecule	Reference
<i>Caudovirales</i>	Thermus phage G20c	high temperature	6IBG (XRAY)	portal protein	Bayfield et al., 2019
<i>Myoviridae</i>	Prochlorococcus phage P-HM1	moderate salt	5HI8 (XRAY)	phycobiliprotein lyase	Gasper et al., 2017
<i>Myoviridae</i>	cyanophage S-TIM5	moderate salt	4P9C, D, E (XRAY)	deoxycytidylate deaminase	Marx and Alian 2014
<i>Myoviridae</i>	Synechococcus phage S-SSM7	moderate salt	3UWA, B (XRAY)	peptide deformylase	Frank et al., 2013
<i>Phycodnaviridae</i>	Ostreococcus tauri virus 2	moderate salt, high copper	4B8N (XRAY)	cytochrome b5	Reid et al., 2013
<i>Mimiviridae</i>	Acanthamoeba polyphaga mimivirus	moderate salt	5YEU, T (XRAY)	Cas4-like protein	Dou et al., 2018
<i>Mimiviridae</i>	Acanthamoeba polyphaga mimivirus	moderate salt	6AX6, 7 (XRAY)	lysyl hydroxylase	Guo et al., 2018
<i>Mimiviridae</i>	Acanthamoeba polyphaga mimivirus	moderate salt	5XC3, 5 (XRAY)	Rab GTPase	Ku et al., 2017
<i>Mimiviridae</i>	Acanthamoeba polyphaga mimivirus	moderate salt	5X55 (XRAY)	uracil-DNA glycosylase	Kwon et al., 2017
<i>Mimiviridae</i>	Megavirus chiliensis	moderate salt	4P37, 4WSE (XRAY)	polyadenylate synthase	Priet et al., 2015
<i>Mimiviridae</i>	Megavirus chiliensis	moderate salt	4U4I (XRAY)	superoxide dismutase	Lartigue et al., 2014
<i>Mimiviridae</i>	Megavirus chiliensis	moderate salt	4TQG (XRAY)	UDP-GlcNac 4,6-dehydratase 5-epimerase	Piacente et al., 2014
<i>Mimiviridae</i>	Acanthamoeba polyphaga mimivirus	moderate salt	4NRW (XRAY)	DNA glycosylase Nei1-G86D	Prakash et al., 2014
<i>Mimiviridae</i>	Acanthamoeba	moderate salt	4MB7 (XRAY)	DNA glycosylase	Prakash et al., 2013

	polyphaga mimivirus			Nei2	
<i>Mimiviridae</i>	Acanthamoeba polyphaga mimivirus	moderate salt	4AMQ (XRAY)	nucleotidyl transferase	to be published
<i>Mimiviridae</i>	Megavirus chiliensis	moderate salt	4AMS (XRAY)	nucleotidyl transferase	to be published
<i>Mimiviridae</i>	Acanthamoeba polyphaga mimivirus	moderate salt	3TD7 (XRAY)	sulfhydryl oxidase	Hakim et al., 2012
<i>Mimiviridae</i>	Acanthamoeba polyphaga mimivirus	moderate salt	3VK7, 8 (XRAY)	DNA glycosylase Nei1	Imamura et al., 2012
<i>Mimiviridae</i>	Acanthamoeba polyphaga mimivirus	moderate salt	3DKD, 3GPA, 3GP9, 3G2X, 3FCW, 3FCV, 3FC9, 3FBF, 3FBE, 3FBC, 3FBB, 3EVW, 3EVO, 3EVM, 3ETM, 3ENA, 3EMT, 3EM1, 3ELH, 3EJM, 3EIC, 3EE3, 3DDI, 3B6B, 2B8Q, 2B8P (XRAY)	nucleoside diphosphate kinase, wild type and mutants	Jeudy et al., 2009
<i>Mimiviridae</i>	Acanthamoeba polyphaga mimivirus	moderate salt	3A42, 5, 6 (XRAY)	DNA glycosylase Nei1	Imamura et al., 2009
<i>Mimiviridae</i>	Acanthamoeba polyphaga mimivirus	moderate salt	3GWN (XRAY)	sulfhydryl oxidase	Hakim and Fass, 2009
<i>Iridoviridae</i>	grouper iridovirus	moderate salt	5VMN, O (XRAY)	Bcl-2 protein apoptosis inhibitor	Banjara et al., 2018
<i>Iridoviridae</i>	grouper iridovirus	moderate salt	3KHS (XRAY)	purine nucleoside	Kang et al., 2010

				phosphorylase	
<i>Turriviridae</i>	Sulfolobus turreted icosahedral virus 1	high temperature and low pH	4R2H, I (XRAY)	DNA packing ATPase B204	Dellas et al., 2015
<i>Turriviridae</i>	Sulfolobus turreted icosahedral virus 2	high temperature and low pH	4KFR, S, T, U (XRAY)	DNA packing ATPase B204	Happonen et al., 2013
<i>Turriviridae</i>	Sulfolobus turreted icosahedral virus 1	high temperature and low pH	2C0N (XRAY)	glycosyltransferase	Larson et al., 2006
nimaviridae	White spot syndrome virus	moderate salt	5Y5O, P, Q (XRAY)	dUTPase	Zang et al., 2018
ligamenvirales	Sulfolobus islandicus rudivirus 3	high temperature and low pH	6EXP (XRAY)	anti-CRISPR protein	He et al., 2018
ligamenvirales	Acidianus filamentous virus 1	high temperature and low pH	3II2, 3, 3ILD, E (XRAY)	nuclease ORF157	Goulet et al., 2010
fuselloviridae	Sulfolobus spindle-shape virus 1	high temperature and low pH	3VCF, 4DKS (XRAY)	integrase	Zhan et al., 2012
fuselloviridae	Sulfolobus spindle-shape virus 1	high temperature and low pH	3UXU (XRAY)	integrase	Eilers et al., 2012
fuselloviridae	Sulfolobus virus Ragged Hills	high temperature and low pH	2W8M (XRAY)	PD-(D/E)XK nuclease	Menon et al., 2010

XRAY: obtained by X-ray crystallography

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