Brief summary of evidence of lab-made 2019 nCoV

From 2017-2019, a series academic papers about a novel zoonotic coronavirus isolated from bats in Zhoushan, Zhejiang (in short, ZS bat-CoV) were published in English (1) and Chinese

(1. post-graduate thesis: Preliminary study about bat-virus in South-east coastland http://le.cnki.net/kmobile/Master/detail/SYJT_PHAM/1017235765.nh)

(2. Molecular identification and analyse of bat-coronavirus in Zhoushan area

<u>http://kns.cnki.net/kcms/detail/detail.aspx?filename=JSCY201901004&dbcode=CJFQ</u> <u>&dbname=CJFDTEMP&v=</u>).

The main investigators were from Chinese military institution (The Third Military Medical University and Military medical institute of Nanjing Command) (*Pic. 1-3*).



Pic. 2

Pic. 1

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物分类学 > 摘要

舟山地区蝙蝠轮状病毒分子鉴定和分析

《寄生虫与医学昆虫学报》2019年 第1期 | 何婷 朱长强 艾乐乐 胡丹 吕 瑞辰 谭伟龙 王长军 钱晖 江苏大学医学院 江苏镇江212000 东部战区 疾病预防控制中心 江苏南京210000 中国人民解放军疾病预防控制中心 北京100071

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摘 要:为监测东南沿海舟山地区蝙蝠携带轮状病毒的流行情况,探索 其流行机制,2015-2018年,在浙江省舟山地区采集蝙蝠,以蝙蝠肠组织为 模板,设计针对轮状病毒VP3序列的特异引物进行RT-PCR检测。结果显 示,2015年采集的65只蝙蝠,轮状病毒阳性率为6.15%(4/65),2016年采集的 48只蝙蝠,阳性率为2.08%(1/48),2017年采集的70只蝙蝠,阳性率为2.86%(2/70),而2018年采集的101只蝙蝠,未检测到轮状病毒序列。针对2017年 小菲菊头蝠Rhinolophus hipposideros体内发现的一株轮状病毒进行基因 组扩增,获取部分基因组序列并进行生物信息学分析,发现VP7基因序列 与蝙蝠源轮状病毒相似度最高,同源性为96%;VP3基因序列与人源轮状 病毒同源性为90%;VP6基因序列与猫同源性为95%。根据上述结果,我们 推测舟山蝙蝠来源轮状病毒是一株重组病毒株,具有潜在跨种传播给人 类的可能性。本研究系首次在东南沿海舟山地区蝙蝠体内检测到轮状病 毒,对该地区轮状病毒的监测和预警具有一定的公共卫生意义。

【分类】	【生物科学】 > 动物学 > 动物分类学(系统动物学) > 哺乳
	<u>纲 > 真兽亚纲 > 翼手目</u>
【关键词】	<u>蝙蝠轮状病毒进化分析</u>
【出处】	《寄生虫与医学昆虫学报》2019年 第1期 22-29页 共8页
【收录】	中文科技期刊数据库

Pic. 3

It means the novel ZS bat-CoV was owned by Chinese military labs only. In the papers above, they have clarified that ZS bat-CoV has potential cross-species

transmission, including human, also emphasized that it is significant for public health. The full genome sequence of certain strains of ZS bat-CoV were released in Genbank of NIH (accession numbers MG772844 through MG772934), provided by Nanjing

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Bat SAR genome	S-like coronavirus isolate bat-SL-CoVZC45, complete	Bat SARS-li genome	ke coronavirus isolate bat-SL-CoVZXC21, complete		
GenBank: MC	3772933 1	GenBank: MG7729	34.1		
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LOCUS DEFINITION ACCESSION VERSION KEYWORDS SOURCE ORGANISM	MG772933 MG772933.1 Bat SARS-like coronavirus	DEFINITION Bat ACCESSION MG7 VERSION MG7 KEYWORDS . SOURCE Bat ORGANISM Bat	72934 29732 bp RNA linear VRL 28-MAR-2018 SARS-like coronavirus isolate bat-SL-CoVZXC21, complete genome. 72934 1 ZARS-like coronavirus SARS-like coronavirus		
REFERENCE AUTHORS TITLE	stage; Nidovirales; Coronaviridae; Coronavirinae; Betacoronavirus. 1 (bases 1 to 29802) Hu,D. Genomic Characterization and Infectivity of A Novel SARS-like coronavirus in Chinese Bats	stag REFERENCE 1 AUTHORS Hu,I TITLE Geno	omic Characterization and Infectivity of A Novel SARS-like		
JOURNAL	Unpublished 2 (bases 1 to 29802)		onavirus in Chinese Bats ublished		
AUTHORS	Hu.D.		(bases 1 to 29732)		
JOURNAL	Direct Submission Submitted (05-JAN-2018) Institute of Military Medicine Nanjing Command, Nanjing, Institute of Military Medicine Nanjing Command, Nanjing, NO. 293 East Zhongshan Road, Nanjing, JangSu 210002, China	JOURNAL Subr	D. ect Submission mitted (05-JAN-2018) Institute of Military Medicine Nanjing mand, Nanjing, Institute of Military Medicine Nanjing Command,		
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FEATURES	##Assembly-Data-END## Location/Qualifiers		uencing Technology :: Sanger dideoxy sequencing ssembly-Data-END##		
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Pic. 4

Pic. 5

command (Pic. 4-5).

11 Jan 2020, China CDC released the full genome sequence of 2019 nCoV, and it was upload to GenBank of NIH on 12 Jan (Wuhan seafood market pneumonia virus isolate Wuhan-Hu-1, accession number MN908947.1). 14 Jan, MN908947.1 was replaced by China CDC without announced (accession number MN908947.2). 17 Jan, MN908947.2 was replaced by them for unknown reasons (accession number MN908947.3) (*pic. 6-7*).

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	seafood market pneumonia virus isolate Wuhan-Hu-1, o	complete genome
A CONTRACTOR OF	MN908947.2	
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ACCESSION	genome. MN968947	
VERSION	MN908947.2	
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ORGANISM	Wuhan seafood market pneumonia virus	
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	Orthocoronavirinae; Betacoronavirus; unclassified Betacoronavirus.	
REFERENCE	1 (bases 1 to 29875)	
AUTHORS	Zhang,YZ., Wu,F., Chen,YM., Pei,YY., Xu,L., Wang,W., Zhao,S.,	
	Yu,B., Hu,Y., Tao,ZW., Song,ZG., Tian,JH., Zhang,YL.,	
	Liu,Y., Zheng,JJ., Dai,FH., Wang,QM., She,JL. and Zhu,TY.	
TITLE	A novel coronavirus associated with a respiratory disease in Wuhan	
JOURNAL	of Hubei province, China Unpublished	
REFERENCE	2 (bases 1 to 29875)	
AUTHORS	Zhang, YZ., Wu, F., Chen, YM., Pei, YY., Xu, L., Wang, W., Zhao, S.,	
HOTTORS	Yu,B., Hu,Y., Tao,ZW., Song,ZG., Tian,JH., Zhang,YL.,	
	Liu,Y., Zheng,JJ., Dai,FH., Wang,QM., She,JL. and Zhu,TY.	
TITLE	Direct Submission	
JOURNAL	Submitted (05-JAN-2020) Department of Zoonoses, National Institute	
	of Communicable Disease Control and Prevention, Chinese Center for	
	Disease Control and Prevention, Changping Liuzi 5, Beijing 102206,	
	China	
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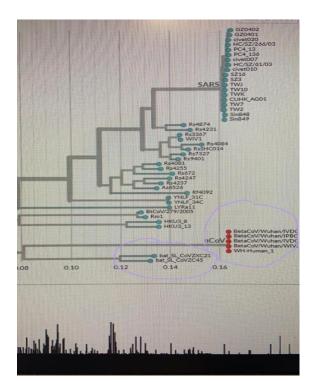
Pic. 6

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LOCUS	MN908947 29903 bp ss-RNA linear VRL 17-JAN-2020	
DEFINITION	Wuhan seafood market pneumonia virus isolate Wuhan-Hu-1, complete genome.	
ACCESSION	Benome	
VERSION	MN908947.3	
KEYWORDS		
SOURCE	Wuhan seafood market pneumonia virus	
ORGANISM		
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REFERENCE	1 (bases 1 to 29903)	
AUTHORS	Wu,F., Zhao,S., Yu,B., Chen,YM., Wang,W., Hu,Y., Song,ZG.,	
	Tao,ZW., Tian,JH., Pei,YY., Yuan,M.L., Zhang,YL.,	
	Dai,FH., Liu,Y., Wang,QM., Zheng,JJ., Xu,L., Holmes,E.C. and	
TITLE	Zhang,YZ. A novel coronavirus associated with a respiratory disease in Wuhan	
TITLE	of Hubei province, China	
JOURNAL	Unpublished	
EFERENCE	2 (bases 1 to 29903)	
AUTHORS	Wu,F., Zhao,S., Yu,B., Chen,YM., Wang,W., Hu,Y., Song,ZG.,	
	Tao,ZW., Tian,JH., Pei,YY., Yuan,M.L., Zhang,YL., Dai,FH., Liu,Y., Wang,QM., Zheng,JJ., Xu,L., Holmes,E.C. and	
	Zhang,YZ.	
TITLE	Direct Submission	
JOURNAL	Submitted (05-JAN-2020) Shanghai Public Health Clinical Center &	
	School of Public Health, Fudan University, Shanghai, China	
OMMENT	On Jan 17, 2020 this sequence version replaced <u>MN908947.2</u> .	
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	Sequencing Technology :: Illumina	
FATURES	##Assembly-Data-END##	
EATURES	Location/Qualifiers	

The blast results based on full genome of MN908947.2 and MN908947.3 shown that ZS bat-CoV is the most closed known coronavirus to 2019 nCoV via online blast tool-NIH (per Identity is 88.65-89.12%, MG772933.1 and MG772934.1) (*pic. 8*). According to analysis of virus evolution tree, ZS bat-CoV is the most closed relative to 2019 nCoV (<u>https://nextstrain.org/groups/blab/sars-like-cov</u>) (*pic. 9*). To note, when blast MN908947.1 at that time, there were some error in the sequence which affected the results (no picture recorded).

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Pic.9

Further blast results for the most critical proteins and segments between 2019 nCoV and all the other known coronavirus in Genbank, still show the most significant similarity to ZS bat-CoV, which is much higher than compared with any others. The similarity is Spike protein 80.32-81.00% (S protein) (*pic. 10-12*) and Nucleocapsid protein 94.03% (*pic. 13-15*) to two strains of ZS bat-CoV (MG772933.1 and MG772934.1), while Envelop protein **100%** (E protein) (*pic. 16-18*), ORF8 segment

94.21% (*pic. 19-20*), and Membrane glycoprotein 98.65% (*pic. 21-22*) to MG772933.1, as well as RdRp gene 95.75% (*pic. 23-24*) to MG772934.1.

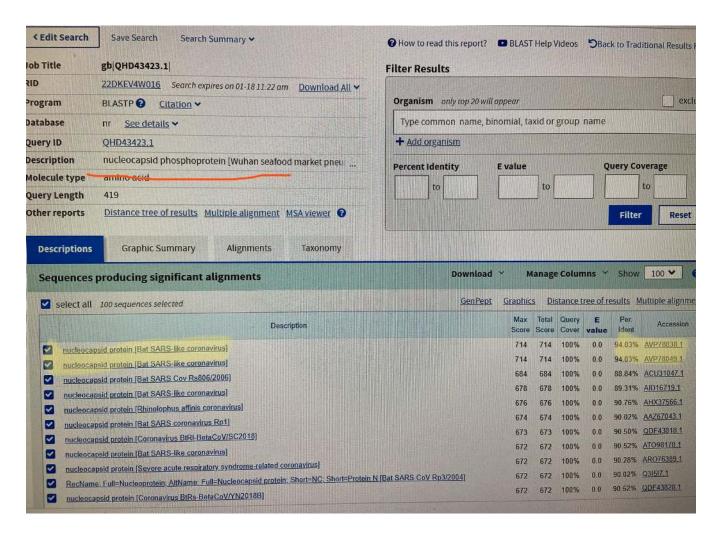
Sequences producing significant alignments Download 🐃 Manage Columns 🐃 Show 🔤 100 🕶 🕻							
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Description		Max Score	Total Score	Query Cover	E value	Per. Ident	Accession
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spike protein [Bat SARS-like coronavirus]		2066	4133	100%	0.0	77.07%	AT098205.
spike protein [Bat SARS-like coronavirus]		2066	4132	100%	0.0	76.92%	AT098157
spike protein [SARS-like coronavirus WIV16]		2065	2065	100%	0.0	77.07%	ALK02457.
spike glycoprotein [recombinant coronavirus]		2054	4108	100%	0.0	77.38%	ACJ60703
spike protein (Bat SARS-like coronavirus RsSHC014)		2050	4100	99%	0.0	77.31%	AGZ48806
spike protein (Bat SARS-like coronavirus)		2049	4099	99%	0.0	77.23%	AT098132
spike glycoprotein [SARS coronavirus GZ02]		2048	4096	100%	0.0	76.27%	AAS00003
spike protein [Bat SARS-like coronavirus]		2046	2046	99%	0.0	77.00%	AT098218
spike glycoprotein S [SARS coronavirus GD01]		2045	2045	100%	0.0	76.19%	AAP51227
spike protein [Bat SARS-like coronavirus WIV1]		2045	2045	99%	0.0	77.07%	AGZ48828
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spike glycoprotein [Coronavirus BtRs-BetaCoV/YN2018B]		2044	2044	99%	0.0	76.92%	QDF43825
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spike glycoprotein [SARS coronavirus PC4-137]		2042	4085	100%	0.0	76.12%	AAV49720
putative E2 glycoprotein precursor [SARS coronavirus CUHK-W1]		2042	4085	100%	0.0	76.12%	AAP13567
spike glycoprotein precursor [SARS coronavirus ExoN1]		2041	2041	100%	0.0		ACZ71976
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spike glycoprotein [SARS coronavirus civet020]		2040			0.0		AAU0466



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REFERENCE	1 (residues 1 to 1245)
AUTHORS	Hu,D.
TITLE	Genomic Characterization and Infectivity of A Novel SARS-like
	coronavirus in Chinese Bats
JOURNAL	Unpublished
REFERENCE	2 (residues 1 to 1245)
AUTHORS	Hu,D.
JOURNAL	Direct Submission Submitted (05-JAN-2018) Institute of Military Medicine Nanjing
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REFERENCE	1 (residues 1 to 1246)
AUTHORS	Hu,D.
TITLE	Genomic Characterization and Infectivity of A Novel SARS-like coronavirus in Chinese Bats
JOURNAL	Unpublished
REFERENCE	2 (residues 1 to 1246)
AUTHORS	Hu,D.
TITLE	Direct Submission
JOURNAL	Submitted (05-JAN-2018) Institute of Military Medicine Nanjing
	Command, Nanjing, Institute of Military Medicine Nanjing Command,
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	/name="S"
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	/note="Spike glycoprotein N-terminal domain; pfam16451"
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Pic. 11



Pic. 13

nucleocapsid protein [Bat SARS-like coronavirus] GenBank: AVP78038.1 Identical Proteins FASTA Graphics				
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VERSION DBSOURCE KEYWORDS	AVP78038.1 accession <u>MG772933.1</u>			
SOURCE	Bet SARS-like coronavirus <u>Bat SARS-like coronavirus</u> Viruses; ssRNA viruses; ssRNA positive-strand viruses, no DNA stage; Nidovirales; Coronaviridae; Coronavirinae; Betacoronavirus.			
AUTHORS	1 (residues 1 to 419) Hu.D.			
TITLE	Genomic Characterization and Infectivity of A Novel SARS-like coronavirus in Chinese Bats			
JOURNAL REFERENCE AUTHORS	Unpublished 2 (residues 1 to 419) Hu.D.			
TITLE JOURNAL	Direct Submission Submitted (05-JAN-2018) Institute of Military Medicine Nanjing Command, Nanjing, Institute of Military Medicine Nanjing Command, Nanjing, No. 293 East Zhongshan Road, Nanjing, JangSu 210002, China			
FEATURES source	Location/Qualifiers 1419 /organism="Bat SARS-like coronavirus"			

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REFERENCE AUTHORS TITLE JOURNAL	1 (residues 1 to 419) Hu,D. Genomic Characterization and Infectivity of A Novel SARS-like coronavirus in Chinese Bats Unpubliched			
REFERENCE AUTHORS TITLE JOURNAL	2 (residues 1 to 419) HujD. Direct Submission Submitted (05-JAN-2018) Institute of Military Medicine Nanjing Command, Nanjing, Institute of Military Medicine Nanjing Jangsu 210002, China Manjing, No. 293 East Zhongshan Road, Nanjing, Jangsu 210002, China			
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Pic. 14

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Description	envelope protein [Wuhan seafood market pneumonia virus]	Percent Identity	E value		Query	Coverage
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LOCUS	AVP78033 75 aa linear VRL 28-MAR-2018
DEFINITION	envelope protein [Bat SARS-like coronavirus].
ACCESSION	AVP78033
VERSION	AVP78033.1
DBSOURCE	accession MG772933.1
KEYWORDS	
SOURCE	Bat SARS-like coronavirus
ORGANISM	Bat SARS-like coronavirus
	Viruses; ssRNA viruses; ssRNA positive-strand viruses, no DNA
	stage; Nidovirales; Coronaviridae; Coronavirinae; Betacoronavirus.
REFERENCE	1 (residues 1 to 75)
AUTHORS	Hu,D.
TITLE	Genomic Characterization and Infectivity of A Novel SARS-like
	coronavirus in Chinese Bats
JOURNAL	Unpublished
REFERENCE	2 (residues 1 to 75)
AUTHORS	Hu,D.
TITLE	Direct Submission
JOURNAL	Submitted (05-JAN-2018) Institute of Military Medicine Nanjing
	Command, Nanjing, Institute of Military Medicine Nanjing Command,
Constant of the states	Nanjing, NO. 293 East Zhongshan Road, Nanjing, JangSu 210002, China
FEATURES	Location/Qualifiers
source	175

Protein	Protein
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LOCUS	QHD43418 75 aa linear VRL 17-JAN-2020
DEFINITION	envelope protein [Wuhan seafood market pneumonia virus].
ACCESSION	QHD43418
VERSION	QHD43418.1
DBSOURCE KEYHORDS	accession MN908947.3
SOURCE	Wuhan seafood market pneumonia virus
ORGANISM	
	Viruses; Riboviria; Nidovirales; Cornidovirineae; Coronaviridae;
	Orthocoronavirinae; Betacoronavirus; unclassified Betacoronavirus.
REFERENCE	1 (residues 1 to 75)
AUTHORS	Wu,F., Zhao,S., Yu,B., Chen,YM., Wang,W., Hu,Y., Song,ZG., Tao,ZW., Tian,JH., Pei,YY., Yuan,M.L., Zhang,YL.,
	<pre>lao,2w., lian,JH., Pel,YY., Yuan,M.L., Zhang,YL., Dai,FH., Liu,Y., Wang,QM., Zheng,JJ., Xu,L., Holmes,E.C. and</pre>
	Zhang,YZ.
TITLE	A novel coronavirus associated with a respiratory disease in Wuhan
	of Hubei province, China
JOURNAL	Unpublished
REFERENCE	2 (residues 1 to 75)
AUTHORS	Wu,F., Zhao,S., Yu,B., Chen,YM., Wang,W., Hu,Y., Song,ZG., Tao,ZW., Tian,JH., Pei,YY., Yuan,M.L., Zhang,YL.,
	Dai,FH., Liu,Y., Wang,QM., Zheng,JJ., Xu,L., Holmes,E.C. and
	Zhang, YZ.
TITLE	Direct Submission
JOURNAL	Submitted (05-JAN-2020) Shanghai Public Health Clinical Center &
	School of Public Health, Fudan University, Shanghai, China
COMMENT	##Assembly-Data-START## Assembly Method :: Megahit v. V1.1.3
	Assembly Method :: Meganit V. VI.I.S Sequencing Technology :: Illumina
	##Assembly-Data-END##

Pic. 17

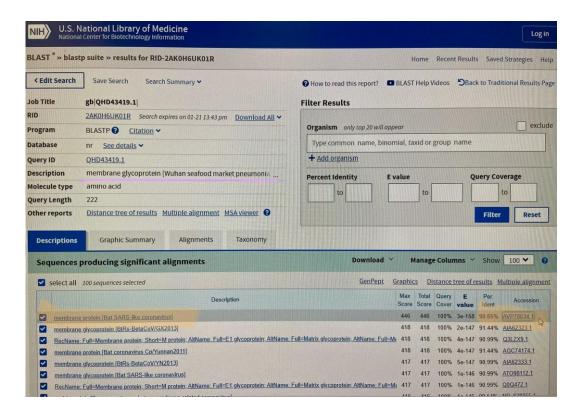
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Pic. 19

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hypothe	etical protein [Bat SARS-like coronavirus]
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LOCUS	AVP78037 121 aa linear VRL 28-MAR-2018
DEFINITION	hypothetical protein [Bat SARS-like coronavirus].
ACCESSION VERSION	AVP78037 AVP78037.1
DBSOURCE	accession <u>MG772933.1</u>
KEYWORDS	accession (07/2333.1
SOURCE	Bat SARS-like coronavirus
ORGANISM	Bat SARS-like coronavirus
	Viruses; ssRNA viruses; ssRNA positive-strand viruses, no DNA
	stage; Nidovirales; Coronaviridae; Coronavirinae; Betacoronavirus.
REFERENCE	1 (residues 1 to 121)
AUTHORS	Hu,D.
TITLE	Genomic Characterization and Infectivity of A Novel SARS-like coronavirus in Chinese Bats
JOURNAL	Unpublished
REFERENCE	2 (residues 1 to 121)
AUTHORS	Hu,D.
TITLE	Direct Submission
JOURNAL	Submitted (05-JAN-2018) Institute of Military Medicine Nanjing
	Command, Nanjing, Institute of Military Medicine Nanjing Command,
	Nanjing, NO. 293 East Zhongshan Road, Nanjing, JangSu 210002, China
FEATURES	Location/Qualifiers
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	/organism="Bat SARS-like coronavirus"
	/isolate="bat-SL-CoVZC45" /host="Rhinolophus sinicus"
	/db xref="taxon:1508227"
	/country="China"
	/collection date="Feb-2017"
Protei	
	/product="hypothetical protein"
	/name="protein 10b"
Region	
	/region_name="Corona_NS8"
	/note="Coronavirus NS8 protein; pfam12093"
CDS	/db_xref="CDD: <u>152528</u> " 1121

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Protein	Protein Advanced
GenPept -	
GenBank: A	ane protein [Bat SARS-like coronavirus] VP78034.1 eins FASTA Graphics
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REFERENCE AUTHORS TITLE JOURNAL REFERENCE AUTHORS TITLE	1 (residues 1 to 222) Hu,D. Genomic Characterization and Infectivity of A Novel SARS-like coronavirus in Chinese Bats Unpublished 2 (residues 1 to 222) Hu,D. Direct Submission
JOURNAL	Submitted (05-JAN-2018) Institute of Military Medicine Nanjing Command, Nanjing, Institute of Military Medicine Nanjing Command, Nanjing, NO. 293 East Zhongshan Road, Nanjing, JangSu 210002, China

Pic. 21



Protein	Protein	
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non struc	tural polyprotein 1ab [Bat SARS-like coronavirus]	
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GenBank: AVP	8041.1	
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	P78041 7070 aa linear VRL 28-MAR-2018	
DEFINITION no ACCESSION AV	n-structural polyprotein 1ab [Bat SARS-like coronavirus].	
	P78041 P78041.1	
	cession MG772934.1	
KEYWORDS .		
	t SARS-like coronavirus	
	t SARS-like coronavirus	
Vi	ruses; ssRNA viruses; ssRNA positive-strand viruses, no DNA	
	age; Nidovirales; Coronaviridae; Coronavirinae; Betacoronavirus. (residues 1 to 7070)	
	.D.	
	nomic Characterization and Infectivity of A Novel SARS-like	
	ronavirus in Chinese Bats	
JOURNAL Un	published	
	(residues 1 to 7070)	
AUTHORS Hu		
TITLE Di	rect Submission mitted (05-JAN-2018) Institute of Military Medicine Nanjing	
JOURNAL Su	mmand, Nanjing, Institute of Military Medicine Nanjing Command,	5
Na	njing, NO. 293 East Zhongshan Road, Nanjing, JangSu 210002, China	
FEATURES	Location/Qualifiers	
source	17070	
	/organism="Bat SARS-like coronavirus"	
	/isolate="bat-SL-CoVZXC21"	
	/host="Rhinolophus sinicus" /db xref="taxon: <u>1508227</u> "	
	/country="China"	
	/collection_date="Jul-2015"	
Protein	17070	
	/product="non-structural polyprotein lab"	
Region	13127	
	/region_name="Nsp1"	
	/note="Non structural protein Nsp1; pfam11501"	
	/db_xref="CDD: <u>288369</u> "	
Region	920985	
	/region_name="DUF3655" /note="Protein of unknown function (DUF3655); pfam12379"	
	/db xref="CDD:289172"	
Site	order(1017,1035,1042,10441045,1123,11251127)	
	/site type="other"	

Pic. 23

					11111	0
		Total score	Query cover		Ident	Accession
	1045	1045	97%	0.0	95.75%	AVP78041.1
	887	887	97%	0.0	80.31%	AGC74164.1
	886	886	97%	0.0	80.31%	AIA62309.1
ider protein; C	884	884	97%	0.0	79.92%	P0C6F5.1
ider protein; C	884	884	97%	0.0	80.58%	P0C6F8.1



As mentioned in Nanjing military paper(1), from homology analyses of different

ORFs, ORF8 fragments in ZS bat-CoV showed the lowest homology, presenting only 60% identity with its closest relatives (**while 94.21% to 2019 nCoV**) (*pic. 25*). As well, analysis of the RNA-dependent RNA polymerase (RdRp) gene showed that the genomic sequences of bat CoV samples obtained from different parts of the world shared 80–90% identity among themselves and exhibited 87–92% identity with the SARS-CoVs extracted from human or civet sources (**while 95.75% to 2019 nCoV**).

Compared with high mutant S protein, E protein is more conserved (2). However, undergoing a natural evolution, the possibility of 100% identical E protein between the cross-species 2019 nCoV and ZS bat-CoV is almost impossible. It was simlply confirmed by using another online tool-Cluster Omega, which shows that the E protein of one strain of ZS bat-CoV (AVP78033.1, belong to MG772933.1) is more identical (100%) to 2019 nCoV, rather than another ZS bat-CoV (AVP78044.1,

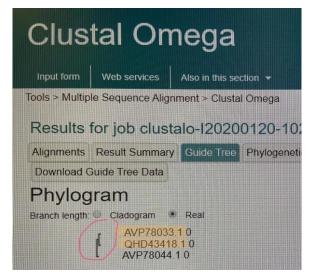
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(ORFs) similar to the HKU3-1 strain. The two new bat SL-CoVs shared 97% genomic sequence identity among themselves. The overall nucleotide sequence identity of these two genomes with civet SARS-CoV (SZ3 strain) was 81%, which was lower than the previously reported observations associated with bat SL-CoVs collected from China (88–92%). From homology analyses of different ORFs, ORF8 fragments showed the lowest homology with the reported SL-CoV homology data²⁴, presenting a shared identity of only 60% with its closest relatives.

Pic. 25

belong to MG772934.1) (pic. 26).

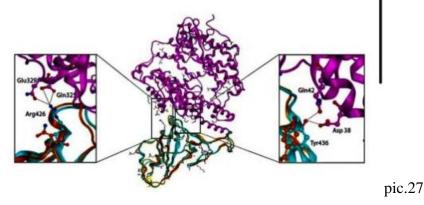
21 Jan, the first paper studied 2019 nCoV is published in a journal under Chinese Academy of Sciences, from Beijing Institute of Pharmacology and Toxicology (belonging to military) and Chinese Academy of Sciences (3). In that paper, they mentioned that the natural host of 2019 nCoV may be certain bat (not directly mentioned ZS bat-CoV). In their official Chinese introduction for this paper, they stressed the key point of their finding as: **"To be surprised"**, compared with SARS CoV, 4 of 5 amino acid changed in the receptor binding domain (RBD) of S protein in 2019 nCoV, but still maintains the core structure to support strong interaction with human ACE2 molecules **"in a very perfect way"**. It means 2019 nCoV could infect human respiratory epithelial cells in the same way as what SARS CoV did (*pic. 27*).



Pic. 26



为了分析清楚这个问题, 文章作者利用分子结构模拟 的计算方法,对武汉冠状病毒S=蛋白和人ACE2蛋白 进行了结构对接研究,获得了令人 惊讶的 结果。虽然 武汉冠状病毒S-蛋白中与ACE2蛋白结合的5个关键 氨基酸有<u>4</u>个发生了变化,但变化后的氨基酸,却整 体性上非常完美的维持了SARS病毒S-蛋白与ACE2 蛋白互作的原结构构象。尽管武汉新型冠状病毒的新 结构与ACE2蛋白互作能力,由于丢失的少数氢键有 所下降(相比SARS病毒S-蛋白与ACE2的作用有下 降),但仍然达到很强的结合自由能(-50.6 这一结果说明武汉冠状病毒是通过Skcal/met) 人ACE2互作的分子机制,来感染人的呼吸道 上皮细胞。研究成果预测了武汉冠状病毒有很强的对 人感染能力,为科学防控,制定防控策略和开发检 测/干预技术手段奠定了科学理论基础。



To noted, 23 Jan, another paper with similar content was upload to BioRxiv, which is from famous bat and SARS CoV investigator Zheng-li Shi's team (4).

There are also a lot of official news and poor-quality academic articles from end of last Dec show that no evidence about wild animals in Huanan seafood market as intermediate host for 2019 nCoV (which can be explained in a detail way later). Hence, one hypothesis of lab-made 2019 nCoV is recombined with SARS RBD of S

protein (to human ACE2 gene), based on ZS bat-CoV (esp. MG772933.1), going through in vitro and in vivo adaptation and amplification in a limited range in the lab, generated an ideal strain (2019 nCoV) with effective RBD, while the other comparable conserved sequence did not change much, or even without any change (E protein). Since stock virus kept in culture media at -80 °C, slowly thaw it on ice could help the virus released in the environment better.

According to Mr. Miles Guo, thymosin is out of stock in commercial market in China. Thymosin is potential therapeutic in the treatment of severe SARS and MERS (5).

PS. More evidence from official media and government response along the time in 2019 nCoV crisis is not written in this brief report.

1. Hu D, Zhu C, Ai L, He T, Wang Y, Ye F, et al. Genomic characterization and infectivity of a novel SARS-like coronavirus in Chinese bats. Emerg Microbes Infect. 2018;7(1):154.

2. Schoeman D, Fielding BC. Coronavirus envelope protein: current knowledge. Virology journal. 2019;16(1):69.

3. Xu X, Chen, P., Wang, J., Feng, J., Zhou, H., Li, X., Zhong, W., and Hao, P. . Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. Sci China Life Sci. 2020.

4. Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. bioRxiv. 2020:2020.01.22.914952.

5. Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, et al. From SARS to MERS, Thrusting Coronaviruses into the Spotlight. Viruses. 2019;11(1).