

**FAO/OIE Reference Laboratory Report
January - March 2006**

Foot-and-Mouth Disease

FMD Trends

Summary

No outbreaks were officially reported in FMD-free countries that did not practice vaccination. FMD remained largely confined to traditionally infected areas between January and March 2006.

A new strain of serotype A FMDV appeared in Turkey late in 2005 and became widespread, entering the European buffer zone of Turkish Thrace in January 2006. The strain involved had been detected earlier in 2005 in Iran and also spread to Saudi Arabia. In vitro vaccine matching by serology suggests that the A Iran 96 type vaccine used in Turkey, including Turkish Thrace, will not offer good protection against the new strain. Emergency vaccination in Thrace has therefore been completed during March using A22 vaccine. Although A22 is not closely related to the new strain genetically, it appears to give a moderate antigenic match to it. So far, there have been no indications of further westward spread of the strain into Greece or Bulgaria, but this possibility remains a serious concern.

Outbreaks of FMDV type A were reported from Egypt in February 2006, a country where previously only type O was sporadically reported. There was suspicion of multiple serotype involvement, but only type A was confirmed at WRL. The origin of the virus appears to be North East Africa and may be related to cattle imports from there. It is not connected to the outbreaks in Turkey and Saudi Arabia. Commercially available vaccines do not seem to offer a good match to the Egyptian strains, although A Eritrea 98 from Merial may prove to be appropriate once post-vaccination antisera are available for testing. Monovalent antisera to A Eritrea 98 are being prepared at WRL to enable the vaccine to be matched to the Egyptian isolates.

Recent outbreaks of FMDV from Israel and the Palestine Autonomous Authority have been of type O.

WRLFMD received 75 FMDV isolates and samples for vesicular virus isolation from Africa and the Middle East during the period January to March 2006 (Annex 1, Table A and B). These specimens originated from Egypt, Israel, Kenya, Rwanda, Saudi Arabia, Senegal and Turkey. No FMDV was detected in 24 of these samples.

Among 51 field isolates and clinical samples, FMD virus serotypes O, A, SAT 1 and SAT 2 were detected (Annex 1; Table A, B). From the Middle-East, FMDV serotype O was detected in clinical samples collected in Israel and Turkey, while serotype A was detected in Saudi Arabia and Turkey (including Turkish Thrace). African samples collected in Kenya belonged to FMDV serotypes O, A, SAT 1 and SAT 2. A single isolation of serotype O was made from samples from Senegal. Serotype A was found in Egypt.

Four partial VP1 sequences (152 nt at the 3' end of VP1) of FMDV A were submitted by the SAP Institute, Ankara, Turkey. Complete VP1 sequences for three FMDV O and four FMDV A isolates from Thailand were submitted by the Regional Reference Laboratory, Pakchong, Thailand. This laboratory also submitted two complete VP1 sequences of FMDV Asia 1 viruses from Vietnam. Three complete VP1 sequences of FMDV Asia 1 were submitted by the All-Russian Research Institute for Animal Health, Vladimir, Russian Federation, from outbreaks in Amursky (December 2005), Khabarovsk (December 2005) and Chita (January 2006).

Middle East/southern Asia

FMDV serotype A

The complete VP1 sequences of A/SAU/15 & 16/2005 were determined and were shown to be closely related to a new strain recently found in Iran (Annex 2; Fig. 1). Similarly, complete VP1 sequences of three FMDV A isolates from Turkish Thrace were determined (A/TUR/1 to 3/2006). These were closely related to recent Iranian isolates and to the two isolates from Saudi Arabia (Annex 2; Fig. 1). Partial VP1 sequences sent from the SAP Institute, Turkey, indicate that this lineage was found in various parts of Turkey during 2005 (Annex 2; Fig. 2). Thus it appears that a new strain, first seen in Iran in 2003, has swept across Turkey reaching Thrace early in 2006. Work on complete VP1 sequencing of further isolates collected in Anatolia during 2005 is ongoing.

Asia

FMDV serotype Asia 1

FMDV Asia 1 VP1 sequences received from ARRIAH (from Amursky, Khabarovsk and Chita) were compared to the database and found to be closely related to previous outbreak viruses in the region (Annex 2; Fig. 3). The sequences of two isolates from Vietnam (received from the Thailand RRL) were most closely related to viruses from Southeast Asia (from Thailand and Myanmar) but not to the virus circulating in the China/Russia/Mongolia region (Annex 2; Fig. 4).

Africa

Egypt - Serotype A

Complete VP1 sequences from various provinces in Egypt were determined. They were all closely related to each other and most closely related to older viruses from East Africa (e.g. Kenya/98) (Annex 2; Fig. 5). They were not closely related to the recent type A viruses from the Middle East (Iran, Saudi Arabia and Turkey).

Senegal - Serotype O

The complete VP1 sequence of a single isolate of type O (O/SEN/8/2006) was obtained and compared to the WRLFMD database. It was most closely related to other isolates from West Africa indicating that it is probably a virus indigenous to the region (Annex 2; Fig. 6).

Work on the complete VP1 sequencing of type O isolates from Israel, Turkey and Kenya is on-going.

The follow are preliminary analyses of large batches of samples received during this or the last reporting period and which work is still on-going.

Ethiopia

Serotype O: Preliminary VP1 sequence analysis was performed on 15 type O viruses from Ethiopia. These sequences fell into three genetic groups which correlated with place of isolation (Arsi, Robe - O/ETH/54, 56, 57, 63, 64, 65, 66 & 67/2005; Gubalafto, North Wello - O/ETH/48, 49, 51, 52, 53, 61 & 62/2005; Mizan Terefi, Maji - O/ETH/58, 59 & 60/2005 (data not shown). The relationship of these viruses to other type O's remains to be determined.

Serotype C: The complete VP1 sequences of two isolates were determined. One was said to originate from 1983, but no collection date was specified for the other. Both were essentially identical to each other and to a virus (vaccine strain?) received from Ethiopia in 1971 (C/ETH/1/71) (data not shown).

Cameroon

Serotype O: Preliminary VP1 sequence analysis was performed on seven type O viruses from the Cameroon. All were closely related differing by no more than 5% (data not shown). Relationships to other type O's in Africa remain to be determined.

Serotype SAT 2: 19 VP1 sequences were obtained and all found to be closely related to each other; they differed by no more than 4% (data not shown).

Kenya

Serotype A: The VP1 sequence of a single isolate, A/KEN/12/2005, from Nakuru, Rift Valley province was not closely related to any other type A sequence held on our database; the closest match was A/K49/84 at over 13% different.

Serotype SAT 1: Seven VP1 sequences were obtained (data not shown). Preliminary analysis shows that they fall into three groups which correlate with geographic location: Nairobi - SAT1/KEN/11/2005; Meru South (Eastern Province) - SAT1/KEN/21/2004; and Rift Valley - SAT1/KEN/13, 15, 16 & 17/2005.

Serotype SAT 2: Five VP1 sequences were obtained (data not shown). They fell into two groups, i) Central Province - SAT2/KEN/7/2005 and ii) Central Province - SAT2/KEN/13/2005, Eastern Province - SAT2/ETH/17/2004 and Rift Valley Province - SAT2/KEN/22/2004 & SAT2/KEN/8/2005.

Vaccine matching

FMD isolates of serotype A or O collected in Asia (Israel, Malaysia, Saudi Arabia, Turkey) or Africa (Cameroon, Egypt, Ethiopia, Kenya) between 2005 and 2006 were further characterized by VNT and/or ELISA (Annex 1; TABLE C). This confirmed the utility of O₁ Manisa to all serotype O isolates tested (Israel and Malaysia), except for an isolate from Israel (ISR/1/2005). Preliminary sequence analysis of this isolate, both at Pirbright and in Israel, suggests a relatively close relationship with other isolates circulating in the Middle East (Turkey/Lebanon/Israel) in 2003 and 2004; further investigations are necessary to resolve this antigenic anomaly.

The best match, by VNT, for the type A viruses from the 2006 outbreak in Egypt was an antiserum to a bivalent vaccine containing A/Eri/98 and A/Irn/99. However, by ELISA, a good match against A/Irn/2001 was also observed. A/MAY/5/2005 reacted well with antiserum to A/May/97 by VNT. The A/SAU/2005 and A/TUR/2006 isolates could possibly be covered by A22 or A 5925 as judged by VNT and ELISA.

Publication of data to the scientific community and the industry

FMD papers published in the reporting period from the Pirbright Laboratory (Pirbright authors underlined):

- Bordeleau ME, Mori A, Oberer M, Lindqvist L, Chard LS, Higa T, Belsham GJ, Wagner G, Tanaka J, Pelletier J. (2006). Functional characterization of IRESes by an inhibitor of the RNA helicase eIF4A. *Nat Chem Biol.* 2(4):213-20.
- Chard LS, Bordeleau ME, Pelletier J, Tanaka J, Belsham GJ. (2006). Hepatitis C virus-related internal ribosome entry sites are found in multiple genera of the family Picornaviridae. *J Gen Virol.* 87(Pt 4):927-36.
- Chard LS, Kaku Y, Jones B, Nayak A, Belsham GJ. (2006). Functional analyses of RNA structures shared between the internal ribosome entry sites of hepatitis C virus and the picornavirus porcine teschovirus 1 Talfan. *J Virol.* 80(3):1271-9.
- Cox SJ, Voyce C, Parida S, Reid SM, Hamblin PA, Hutchings G, Paton DJ, Barnett PV. (2006). Effect of emergency FMD vaccine antigen payload on protection, sub-clinical infection and persistence following direct contact challenge of cattle. *Vaccine*. [Epub ahead of print]
- King DP, Ferris NP, Shaw AE, Reid SM, Hutchings GH, Giuffre AC, Robida JM, Callahan JD, Nelson WM, Beckham TR (2006) Detection of foot-and-mouth disease virus: comparative diagnostic sensitivity of two independent real-time reverse transcription-polymerase chain reaction assays. *Journal of Veterinary Diagnostic Investigation* 18: 93-97.
- Ko Y-J, Choi K-S, Nah J-J, Paton DJ, Oem J-K, Wilsden G, Kang S-Y, Jo N-I, Kim J-H, Lee H-W, Park J-M. (2005). Noninfectious virus-like particle antigen for detection of swine vesicular disease virus antibodies in pigs by enzyme linked immunosorbent assay. *Clinical and Diagnostic Laboratory Immunology* 12 (8), 922-929.
- Parida S, Oh Y, Reid SM, Cox SJ, Statham RJ, Mahapatra M, Anderson J, Barnett PV, Charleston B, Paton D.J. (2006). Interferon- γ production in vitro from whole blood of foot-and-mouth disease virus (FMDV) vaccinated and infected cattle after incubation with inactivated FMDV. *Vaccine* 24, 964-9.
- Parida S, Anderson J, Cox SJ, Barnett PV, Paton DJ. (2006). Secretory IgA as an indicator of oro-pharyngeal foot-and-mouth disease virus replication and as a tool for post vaccination surveillance. *Vaccine* 24, 1107-1116.
- Paton DJ, Valarcher J-F, Bergmann I, Matlho OG, Zakharov VM, Palma EL, Thomson GR. (2005). Selection of foot-and-mouth disease vaccine strains – a review. *OIE Sci et Tech Rev.* 24 (3), 981-993.
- Reid SM, Parida S, King DP, Hutchings GH, Shaw AE, Ferris NP, Zhang Z, Hillerton JE, Paton DJ. (2006). Utility of automated real-time RT-PCR for the detection of foot-and-mouth disease virus excreted in milk. *Veterinary Research* 37, 121-132
- Wernery U, Nagy P, Amaral-Doel CM, Zhang Z, Alexandersen S. (2006). Lack of susceptibility of the dromedary camel (*Camelus dromedarius*) to foot-and-mouth disease virus serotype O. *Vet Rec.*, 158(6):201-3.
- Zhang Z., J. Bashiruddin, C. Doel, J. Horsington, S. Durand and S. Alexandersen (2006) Cytokine and Toll-like receptor mRNAs in the nasal-associated lymphoid tissues of cattle during foot-and-mouth disease virus infection. *J. Comp. Path.* 134:60-6.

**Table A: Summary of clinical sample diagnostics made by the WRL
Between January to March 2006**

Country	WRL for FMD Sample Identification	Animal	Date of Collection	Results		
				VI/ELISA	RT-PCR	Final report
ISRAEL	ISR 7/2004	Cattle	17.01.04	O	Positive	O
	ISR 8/2004	Cattle	26.01.04	O	Positive	O
	ISR 9/2004	NK	08.02.04	O	Positive	O
	ISR 10/2004	Sheep	11.02.04	O	Positive	O
	ISR 11/2004	Cattle	18.03.04	O	Positive	O
	ISR 1/2005	Cattle	19.12.05	O	Positive	O
	ISR 2/2005	Cattle	22.12.05	O	Positive	O
KENYA	KEN 13/2004	Cattle	13.01.04	SAT 2	Positive	SAT 2
	KEN 14/2004	Cattle	20.01.04	NVD	Positive	FMDV GD
	KEN 15/2004	Cattle	06.02.04	NVD	Positive	FMDV GD
	KEN 16/2004	Cattle	18.02.04	NVD	Negative	NVD
	KEN 17/2004	Cattle	16.03.04	SAT 2	Positive	SAT 2
	KEN 18/2004	Cattle	22.03.04	NVD	Positive	FMDV GD
	KEN 19/2004	Cattle	25.05.04	NVD	Positive	FMDV GD
	KEN 20/2004	Cattle	26.05.04	NVD	Positive	FMDV GD
	KEN 21/2004	Cattle	11.06.04	SAT 1	Positive	SAT 1
	KEN 22/2004	Cattle	18.06.04	SAT 2	Positive	SAT 2
	KEN 23/2004	Cattle	08.07.04	O	Positive	O
	KEN 24/2004	Cattle	30.07.04	O	Positive	O
	KEN 25/2004	Cattle	18.08.04	NVD	Negative	NVD
	KEN 26/2004	Cattle	23.08.04	NVD	Positive	FMDV GD
	KEN 27/2004	Cattle	09.09.04	NVD	Positive	FMDV GD
	KEN 28/2004	Cattle	19.10.04	NVD	Negative	NVD
	KEN 29/2004	Cattle	21.10.04	O	Positive	O
	KEN 30/3004	Cattle	24.12.04	O	Positive	O
	KEN 2/2005	Cattle	11.01.05	NVD	Positive	FMDV GD
	KEN 3/2005	Cattle	20.01.05	NVD	Positive	FMDV GD
	KEN 4/2005	Cattle	26.01.05	O	Positive	O
	KEN 5/2005	Cattle	22.02.05	NVD	Positive	FMDV GD
	KEN 6/2005	Cattle	01.03.05	O	Positive	O
	KEN 7/2005	Cattle	22.03.05	SAT 2	Positive	SAT 2
	KEN 8/2005	Cattle	19.04.05	SAT 2	Positive	SAT 2
	KEN 9/2005	Cattle	NK	NVD	Positive	FMDV GD
	KEN 10/2005	Cattle	13.06.05	O	Positive	O
	KEN 11/2005	Cattle	15.07.05	SAT 1	Positive	SAT 1
	KEN 12/2005	Cattle	15.07.05	A	Positive	A
	KEN 13/2005	Cattle	19.07.05	SAT 1	Positive	SAT 1
	KEN 14/2005	Cattle	21.07.05	O	Positive	O
	KEN 15/2005	Cattle	28.07.05	NVD	Positive	FMDV GD
	KEN 16/2005	Cattle	25.11.05	SAT 1	Positive	SAT 1
KEN 17/2005	Cattle	11.12.05	SAT 1	Positive	SAT 1	
KEN 18/2005	Cattle	13.12.05	SAT 1	Positive	SAT 1	
KEN 19/2005	Cattle	15.12.05	SAT 1	Positive	SAT 1	

RWANDA	RWA 1/2005	Cattle	26.10.05	NVD	Negative	NVD
SAUDI ARABIA	SAU 15/2005	Cattle	27.12.05	A	Positive	A
	SAU 16/2005	Cattle	27.12.05	A	Positive	A
EGYPT	EGY 1/2006	Cattle	09.02.06	A	Positive	A
	EGY 2/2006	Cattle	09.02.06	A	Positive	A
	EGY 3/2006	Cattle	09.02.06	A	Positive	A
	EGY 4/2006	NK	00.02.06	A	Positive	A
	EGY 5/2006	NK	00.02.06	A	Positive	A
SENEGAL	SEN 1/2006	Cattle	00.01.06	NVD	Negative	NVD
	SEN 2/2006	Cattle	00.01.06	NVD	Negative	NVD
	SEN 3/2006	Cattle	00.01.06	NVD	Negative	NVD
	SEN 4/2006	Cattle	00.01.06	NVD	Negative	NVD
	SEN 5/2006	Cattle	00.01.06	NVD	Negative	NVD
	SEN 6/2006	Cattle	00.01.06	NVD	Negative	NVD
	SEN 7/2006	Cattle	00.01.06	NVD	Negative	NVD
	SEN 8/2006	Cattle	00.01.06	O	Negative	O
	SEN 9/2006	Cattle	23.01.06	NVD	Negative	NVD
TURKEY	TUR 1/2005	Cattle	15.07.05	O	Positive	O
	TUR 2/2005	Cattle	11.08.05	O	Positive	O
	TUR 3/2005	Cattle	15.09.05	O	Positive	O
	TUR 4/2005	Cattle	16.09.05	O	Positive	O
	TUR 5/2005	Cattle	25.09.05	O	Positive	O
	TUR 6/2005	Cattle	18.11.05	A	Positive	A
	TUR 7/2005	Cattle	26.11.05	A	Positive	A
	TUR 8/2005	Cattle	07.12.05	A	Positive	A
	TUR 9/2005	Cattle	13.12.05	A	Positive	A
	TUR 10/2005	Cattle	20.12.05	A	Positive	A
	TUR 11/2005	Cattle	23.12.05	A	Positive	A
	TUR 12/2005	Cattle	27.12.05	A	Positive	A
	TUR 1/2006	Cattle	31.01.06	A	Positive	A
	TUR 2/2006	Cattle	01.02.06	A	Positive	A
	TUR 3/2006	Cattle	05.02.06	A	Positive	A

TOTAL: 318

* Institute for Animal Health, Pirbright Laboratory, Woking, Surrey GU24 0NF

FMDV foot-and-mouth disease virus

VI/ELISA FMDV serotype identified following virus isolation in cell culture and antigen detection ELISA

RT-PCR reverse transcription polymerase chain reaction for FMD or SVD viral genome

NVD no foot-and-mouth disease, swine vesicular disease or vesicular stomatitis virus detected

GD genome detected

TABLE B: Samples received in 2005

Country	No. of samples	Virus isolation in cell culture/ELISA								RT-PCR for FMD (or SVD) virus		
		FMD virus serotypes						SVD	NVD	Positive	Negative	
		O	A	C	SAT 1	SAT 2	SAT 3	Asia 1	virus			
BOTSWANA	8	-	-	-	-	8	-	-	-	-	8	-
BURKINA FASO	10	-	-	-	-	-	-	-	-	10	-	10
CAMEROON	119 ^a	25	3	-	-	54	-	-	-	38	19	100
CHINA (HONG KONG)	16	7	-	-	-	-	-	8	-	1	16	-
COTE D'IVOIRE	6	-	-	-	-	-	-	-	-	6	-	6
ETHIOPIA	68 ^b	22	9	4	-	-	-	-	-	36	45	23
GAMBIA	5	-	-	-	-	-	-	-	-	5	1	4
GHANA	4	-	-	-	-	-	-	-	-	4	-	4
IRAN	55	20	20	-	-	-	-	-	-	15	42	13
IRELAND	11	-	-	-	-	-	-	-	-	11	-	11 ^d
ITALY	4	-	-	-	-	-	-	-	4	-	4 ^c	-
KENYA	1	-	-	-	1	-	-	-	-	-	1	-
MALAYSIA	8	7	1	-	-	-	-	-	-	-	8	-
MALI	4	3	-	-	-	-	-	-	-	1	4	-
PAKISTAN	26 ^c	19	-	-	-	-	-	2	-	7	25	1
PHILIPPINES	10	3	-	-	-	-	-	-	-	7	3	7
SAUDI ARABIA	14	11	-	-	-	-	-	-	-	3	10	4
SENEGAL	3	-	-	-	-	-	-	-	-	3	-	3
SUDAN	3	3	-	-	-	-	-	-	-	-	2	1
TOGO	16	4	1	-	-	-	-	-	-	11	3	13
VIETNAM	5	5	-	-	-	-	-	-	-	-	5	-
ZAMBIA	2	-	-	-	2	-	-	-	-	-	2	-
TOTAL	398	129	34	4	3	62	-	10	4	158	198	200

- * Institute for Animal Health, Pirbright Laboratory, Woking, Surrey GU24 0NF
- VI/ELISA FMD (or SVD) virus serotype identified following virus isolation in cell culture and antigen detection ELISA
- FMD foot-and-mouth disease
- SVD swine vesicular disease
- NVD no FMD, SVD or vesicular stomatitis virus detected
- RT-PCR reverse transcription polymerase chain reaction for FMD (or SVD) viral genome
- ^a one sample from Cameroon contained a mixture of FMD virus serotypes O and SAT 2
- ^b two samples from Ethiopia contained a mixture of FMD virus serotypes - one of A and C and one of O, A and C
- ^c two samples from Pakistan contained a mixture of FMD virus serotypes O and Asia 1
- ^d negative by RT-PCR for both FMD and SVD viral genome
- ^e positive by RT-PCR for SVD viral genome

The following samples were additionally received by the OIE/FAO World Reference Laboratory for Foot and Mouth Disease in 2005 :

Country	Sample year	No. of samples	ELISA/Virus isolation in cell culture							RT-PCR for FMD (or SVD) virus			
			FMD virus serotypes			SVD	NVD	Positive		Negative			
			O	A	C	SAT 1	SAT 2	SAT 3	Asia 1	virus			
CHINA (HONG KONG)	2004	1	1	-	-	-	-	-	-	-	1	-	
IRAN	2004	12	-	2	-	-	-	-	3	-	7	4	8
ITALY	2004	6	-	-	-	-	-	-	-	6	-	6 ^a	-
KENYA	2003	2	-	2	-	-	-	-	-	-	-	2	-
	2004	12	-	-	1	-	7	-	-	-	4	12	-
LAOS	2003	1	-	1	-	-	-	-	-	-	-	1	-
MALI	2004	16	-	1	-	-	-	-	-	-	15	-	16
MYANMAR	2004	4	4	-	-	-	-	-	-	-	-	4	-
PAKISTAN	2004	2	-	-	-	-	-	-	-	-	2	2	-
THAILAND	2004	9	1	2	-	-	-	-	-	-	6	9	-
TOGO	2004	1	1	-	-	-	-	-	-	-	-	-	1
ZAMBIA	2004	16	-	-	-	6	-	-	-	-	10	7	9
TOTAL		82	7	8	1	6	7	-	3	6	44	48	34

* Institute for Animal Health, Pirbright Laboratory, Woking, Surrey GU24 0NF

VI/ELISA FMD (or SVD) virus serotype identified following virus isolation in cell culture and antigen detection ELISA

FMD foot-and-mouth disease

SVD swine vesicular disease

NVD no foot-and-mouth disease, swine vesicular disease or vesicular stomatitis virus detected

RT-PCR reverse transcription polymerase chain reaction for FMD (or SVD) viral genome

^a positive by RT-PCR for SVD viral genome

NPF, 23 January 2006

TABLE C: Antigenic characterisation of FMD field isolates by matching with vaccine strains. rValues were obtained by VNT or ELISA

FMD 'r' values Jan-Mar 06

Strain	A22		A Irn96	A May97	A 5925		A Sau95		A Irn 01		A Eri98/ Irn99	A 4164	A Irn99	A Irn87	A Ken 35/80
	vnt	elisa	vnt	vnt	elisa	vnt	elisa	vnt	elisa	vnt	elisa	elisa	elisa	elisa	elisa
A Car 036/05	0.29		0.21	0.16											
A Car 115/05	0.22		0.30	0.08											
A Car 116/05	0.22		0.30	0.08											
A Egy 01/06	0.23	0.17	0.25	0.21	0.06		0.32	0.42	0.3	0.83	0.60	<0.17	0.21	0.23	0.38
A Egy 02/06	0.24	0.14	0.16	0.20	<0.03		0.30	0.50	0.2	1.00	0.95	0.25	0.23	0.14	0.38
A Eth 16/05	0.13		0.21	0.22											
A Ken 12/05	0.13		0.30	0.33											
A May 5/05	0.12		0.19	0.58											
A Sau 15/05	0.29	>0.88	0.12	0.16	0.17	0.50	0.35	>1.0				>0.89			
A Sau 16/05	0.25	>0.88	0.12	0.17	0.15	0.58	0.39	>1.0				>1.0			
A Tur 01/06	0.42	0.21	0.08	0.11		0.41	0.32	0.21	0.26			0.29			
A Tur 2/06	0.36	0.29	0.07	0.18		0.48	0.56	0.20	0.50			0.30			
A Tur 3/06	0.39		0.09	0.13		0.48									
O Manisa															
vnt															
O Isr 01/05	0.07														
O Isr 11/04	>1.0														
O May 04/06	>1.0														
O May 06/06	>1.0														
C Ober															
vnt															
elisa															
C Eth 6/05	0.44	0.19	0.75	0.56	0.14										
C Eth 7/05	0.39	0.13	0.59	0.30	0.10										
C Ken 267/67															
elisa															
C Noville															
elisa															
C Phi 7/84															
elisa															

Interpretation of r_1 values

In the case of ELISA:

$r_1 = 0.4-1.0$. Suggests that there is a close relationship between field isolate and vaccine strain. A potent vaccine containing the vaccine strain is likely to confer protection.

$r_1 = 0.2-0.39$, Suggests that the field isolate is antigenically related to the vaccine strain. The vaccine strain might be suitable for use if no closer match can be found provided that a potent vaccine is used and animals are preferably immunised more than once.

$r_1 = <0.2$. Suggests that the field isolate is so different from the vaccine strain that the vaccine is unlikely to protect

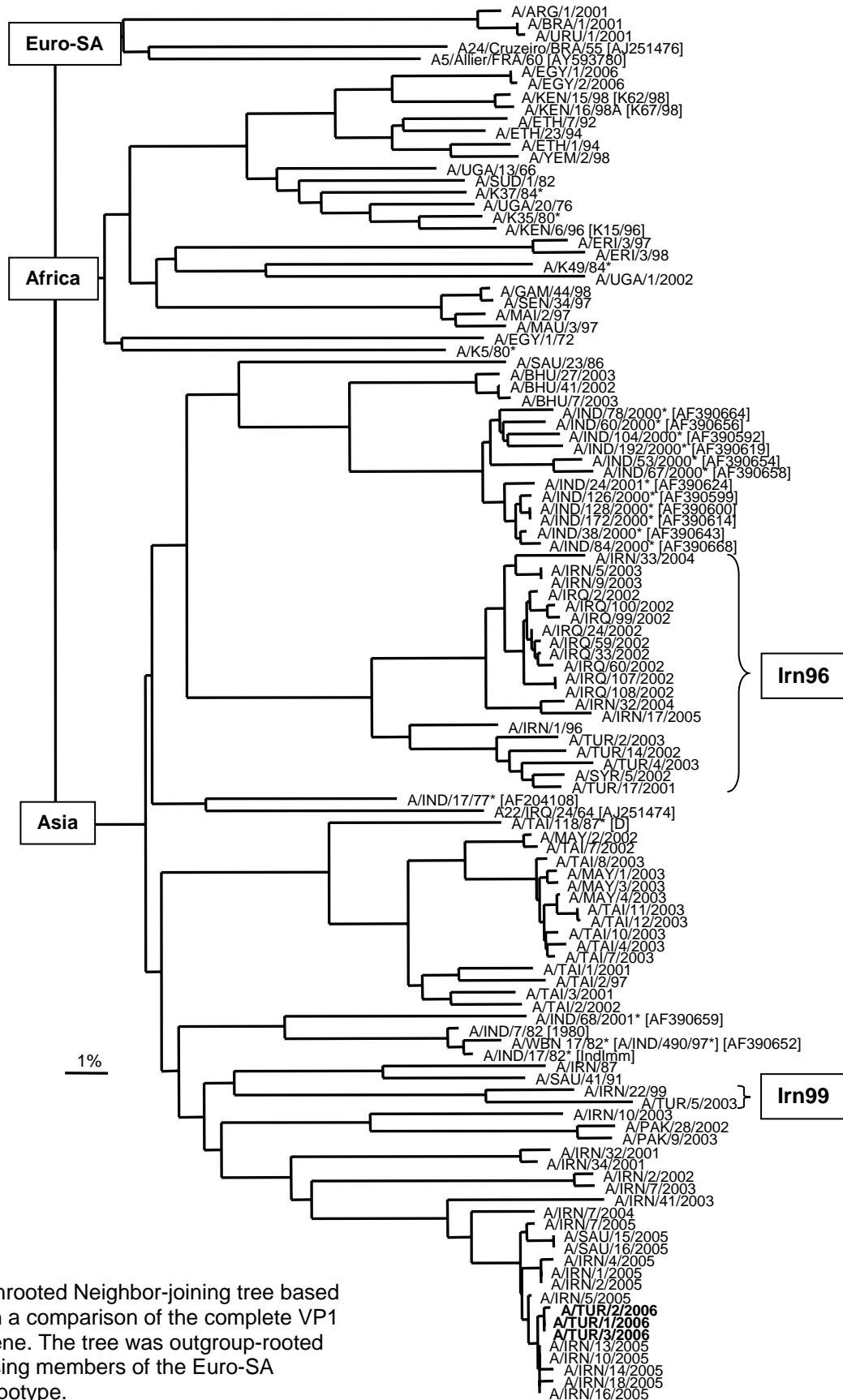
In the case of neutralisation:

$r_1 = \geq 0.3$. Suggests that there is a close relationship between field isolate and vaccine strain. A potent vaccine containing the vaccine strain is likely to confer protection.

$r_1 = < 0.3$. Suggests that the field isolate is so different from the vaccine strain that the vaccine is unlikely to protect.

Annex 2

Fig. 1: Report on FMD serotype A collected in Turkey in 2006.



Unrooted Neighbor-joining tree based on a comparison of the complete VP1 gene. The tree was outgroup-rooted using members of the Euro-SA toptype.

N.J. Knowles, J. Smith & K. Swabey, 23 February 2006

Fig. 2: Report on FMD serotype A collected in Turkey, 2005-6 (partial VP1 sequences).

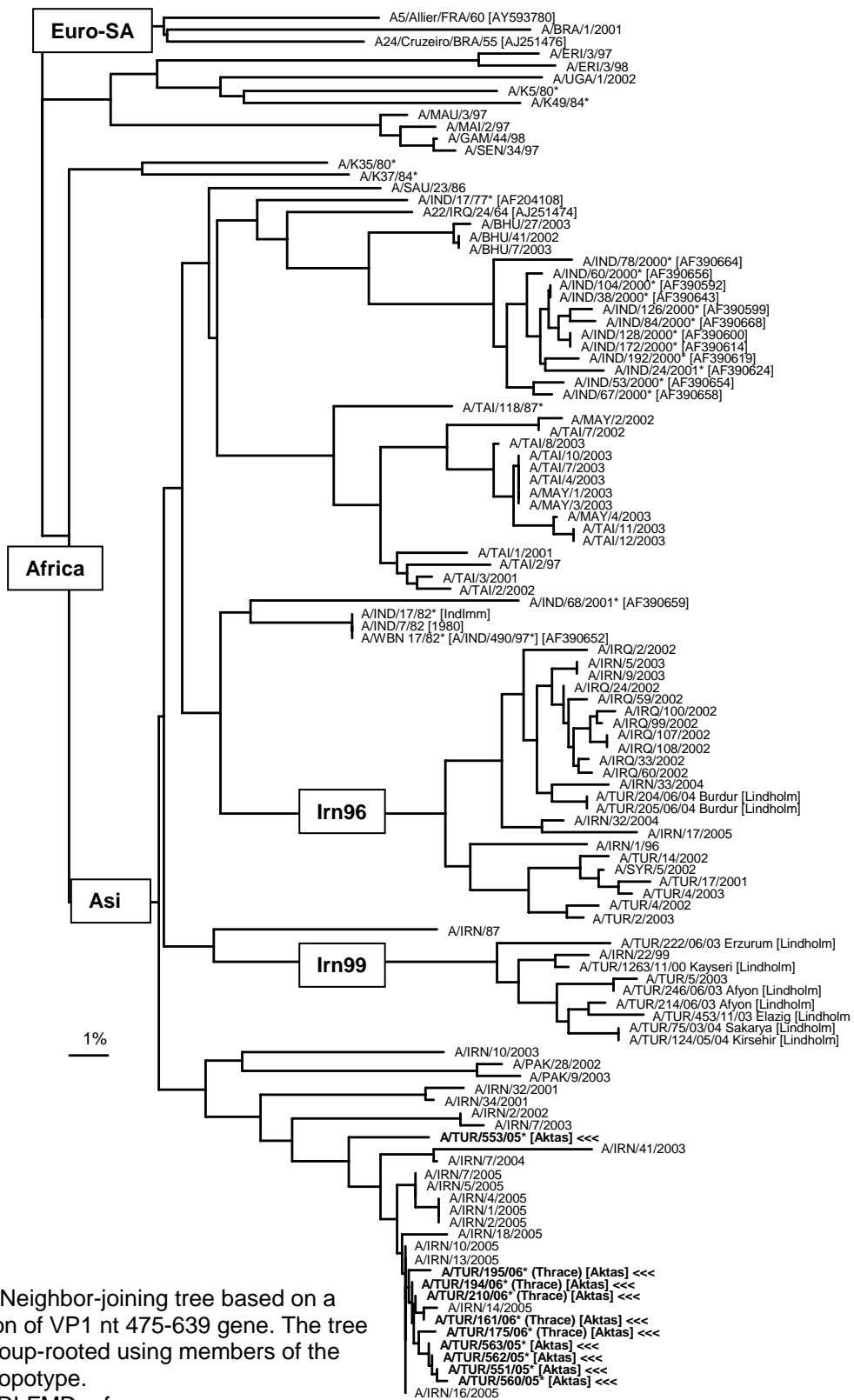
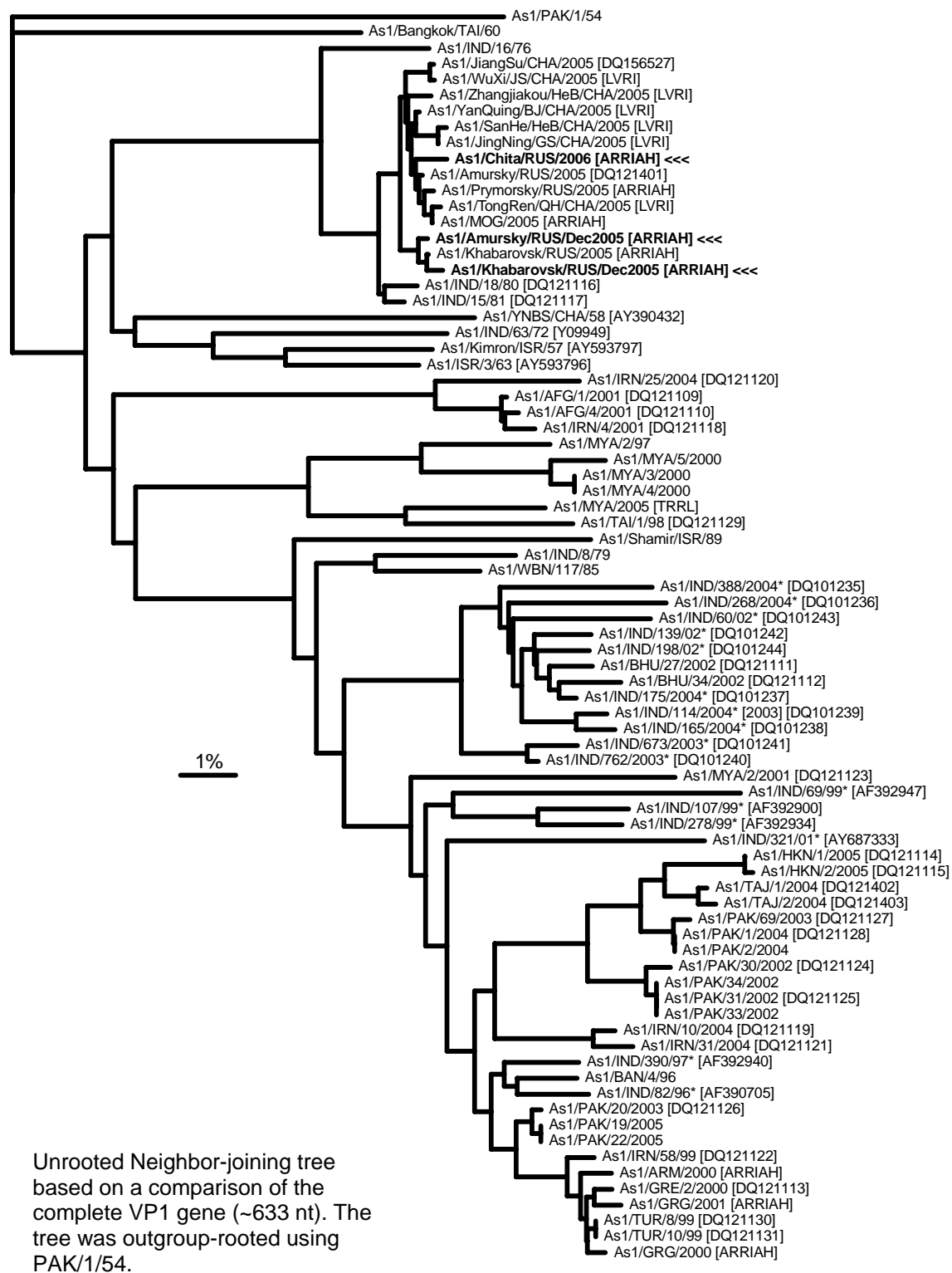
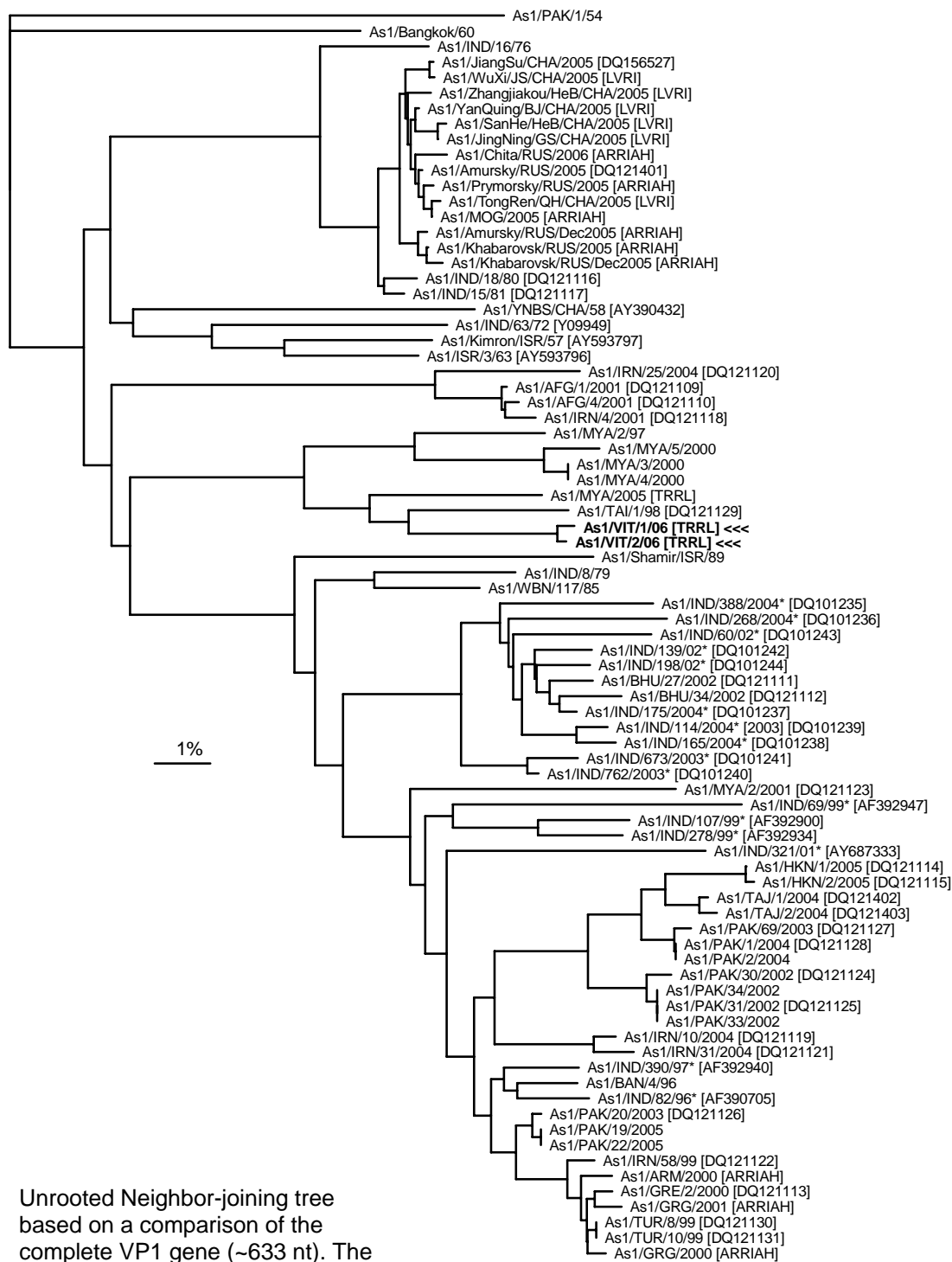


Fig. 3: Report on FMD serotype Asia 1 collected in the Russian Federation in 2005-06.



N.J. Knowles, 31 January 2006

Fig. 4: Report on FMD serotype Asia 1 collected in the Vietnam in 2006.

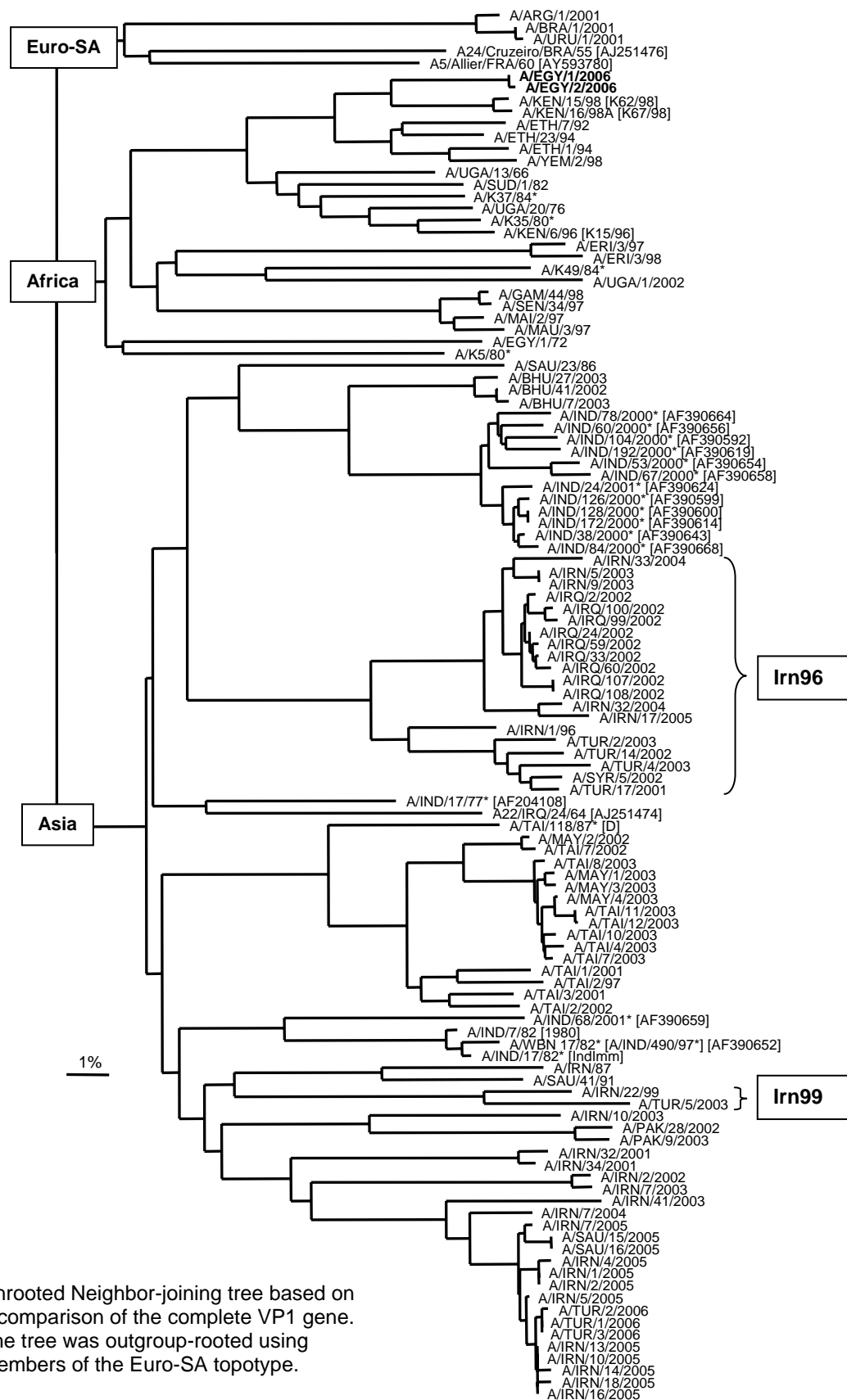


Unrooted Neighbor-joining tree based on a comparison of the complete VP1 gene (~633 nt). The tree was outgroup-rooted using PAK/1/54.

* Not a WRLFMD reference number.

N.J. Knowles, 6 February 2006

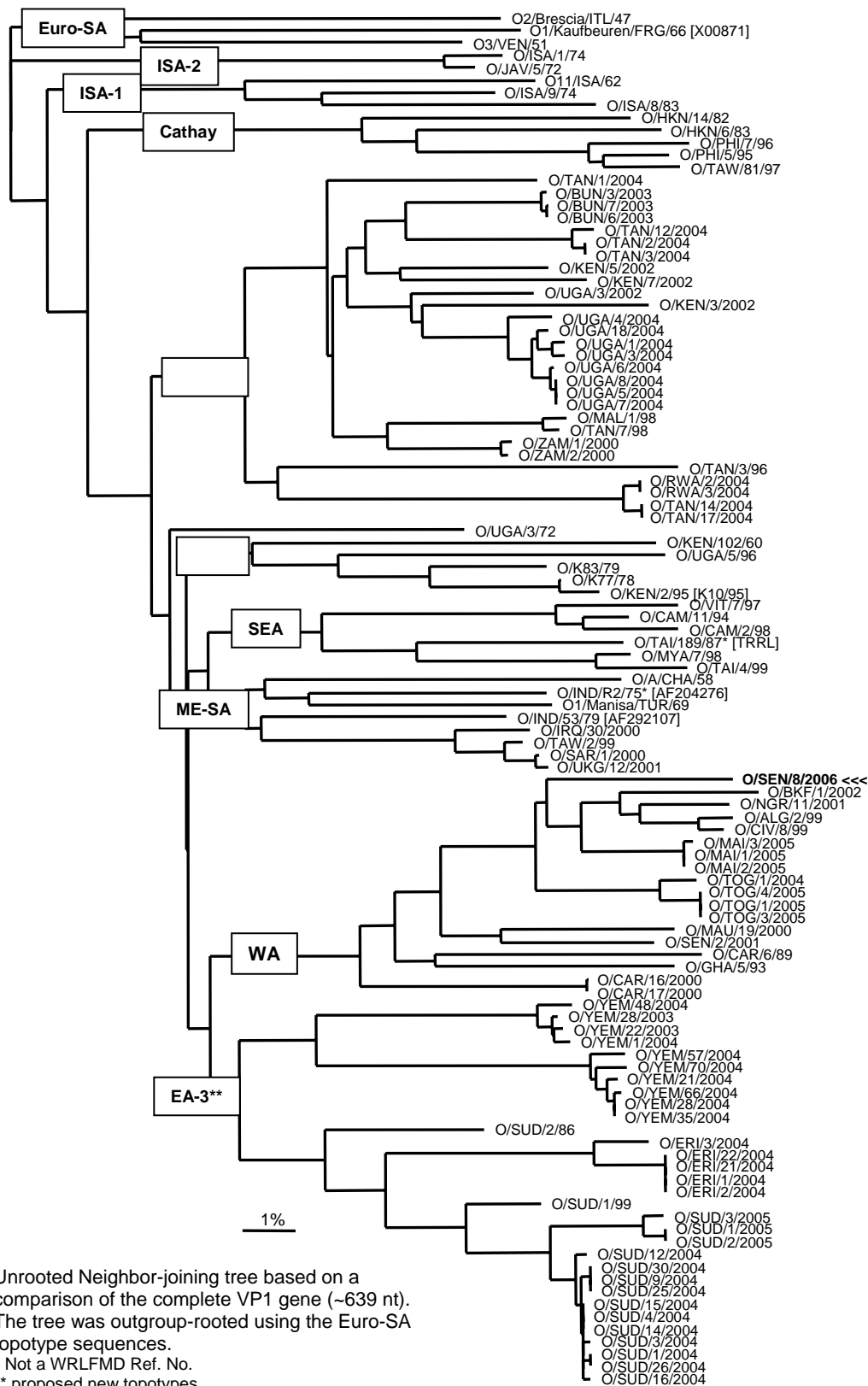
Fig. 5: Report on FMD serotype A collected in Egypt in 2006.



Unrooted Neighbor-joining tree based on a comparison of the complete VP1 gene. The tree was outgroup-rooted using members of the Euro-SA toptype.

N.J. Knowles, J. Smith & K. Swabey, 23 February 2006

Fig. 6: Report on FMD serotype O collected in Senegal in 2006.



N.J. Knowles, J. Smith & K.G. Swabey, 18 April 2006

Annex 3. FMD Publications cited by PubMed dated from January 2006

- Garcia-Briones M, Rosas MF, Gonzalez-Magaldi M, Martin-Acebes MA, Sobrino F, Armas-Portela R. Differential distribution of non-structural proteins of foot-and-mouth disease virus in BHK-21 cells. *Virology*. 2006 Apr 17; [Epub ahead of print]
- Biswas S, Sanyal A, Hemadri D, Tosh C, Mohapatra JK, Manoj Kumar R, Bandyopadhyay SK. Sequence analysis of the non-structural 3A and 3C protein-coding regions of foot-and-mouth disease virus serotype Asia1 field isolates from an endemic country. *Vet Microbiol*. 2006 Apr 16; [Epub ahead of print]
- Hole K, Clavijo A, Pineda LA. Detection and serotype-specific differentiation of vesicular stomatitis virus using a multiplex, real-time, reverse transcription-polymerase chain reaction assay. *J Vet Diagn Invest*. 2006 Mar;18(2):139-46.
- Jinding C, Mingqiu Z, Hui KH, Leung FC. Molecular Characterization of Foot-and-mouth Disease Virus in Hong Kong During 2001-2002. *Virus Genes*. 2006 Apr;32(2):139-43.
- Poulin MC, Christianson WT. On-farm eradication of foot-and-mouth disease as an alternative to mass culling. *Vet Rec*. 2006 Apr 8;158(14):467-72.
- King DP, Ferris NP, Shaw AE, Reid SM, Hutchings GH, Giuffre AC, Robida JM, Callahan JD, Nelson WM, Beckham TR. Detection of foot-and-mouth disease virus: comparative diagnostic sensitivity of two independent real-time reverse transcription-polymerase chain reaction assays. *J Vet Diagn Invest*. 2006 Jan;18(1):93-7.
- Borrego B, Fernandez-Pacheco P, Ganges L, Domenech N, Fernandez-Borges N, Sobrino F, Rodriguez F. DNA vaccines expressing B and T cell epitopes can protect mice from FMDV infection in the absence of specific humoral responses. *Vaccine*. 2006 Mar 3; [Epub ahead of print]
- Reynolds D. Vigilance for classical swine fever and FMD. *Vet Rec*. 2006 Mar 18;158(11):383. No abstract available.
- Chinnasamy D, Milsom MD, Shaffer J, Neuenfeldt J, Shaaban AF, Margison GP, Fairbairn LJ, Chinnasamy N. Multicistronic lentiviral vectors containing the FMDV 2A cleavage factor demonstrate robust expression of encoded genes at limiting MOI. *Virol J*. 2006 Mar 15;3(1):14 [Epub ahead of print]
- Chen W, Liu M, Jiao Y, Yan W, Wei X, Chen J, Fei L, Liu Y, Zuo X, Yang F, Lu Y, Zheng Z. Adenovirus-mediated RNA interference against foot-and-mouth disease virus infection both in vitro and in vivo. *J Virol*. 2006 Apr;80(7):3559-66.
- Iakovleva AS, Shcherbakov AV, Kan'shina AV, Mudrak NS, Fomina TA. [Recombinant non-structural 3A, 3B and 3AB proteins of foot-and-mouth disease virus: use for differentiation of vaccinated and infected cattle] *Mol Biol (Mosk)*. 2006 Jan-Feb;40(1):165-71. Russian.
- de Avila Botton S, Brum MC, Bautista E, Koster M, Weiblen R, Golde WT, Grubman MJ. Immunopotential of a foot-and-mouth disease virus subunit vaccine by interferon alpha. *Vaccine*. 2006 Apr 24;24(17):3446-56. Epub 2006 Feb 20.
- Brown JK, McAleese SM, Thornton EM, Pate JA, Schock A, Macrae AI, Scott PR, Miller HR, Collie DD. Integrin- α v β 6, a Putative Receptor for Foot-and-Mouth Disease Virus, Is Constitutively Expressed in Ruminant Airways. *J Histochem Cytochem*. 2006 Mar 3; [Epub ahead of print]
- Tildesley MJ, Savill NJ, Shaw DJ, Deardon R, Brooks SP, Woolhouse ME, Grenfell BT, Keeling MJ. Optimal reactive vaccination strategies for a foot-and-mouth outbreak in the UK. *Nature*. 2006 Mar 2;440(7080):83-6.

- Cox SJ, Voyce C, Parida S, Reid SM, Hamblin PA, Hutchings G, Paton DJ, Barnett PV. Effect of emergency FMD vaccine antigen payload on protection, sub-clinical infection and persistence following direct contact challenge of cattle. *Vaccine*. 2006 Apr 12;24(16):3184-90. Epub 2006 Jan 30.
- Knowles NJ, Samuel AR, Davies PR, Midgley RJ, Valarcher JF. Pandemic strain of foot-and-mouth disease virus serotype O. *Emerg Infect Dis*. 2005 Dec;11(12):1887-93.
- Diaz-San Segundo F, Salguero FJ, de Avila A, de Marco MM, Sanchez-Martin MA, Sevilla N. Selective lymphocyte depletion during the early stage of the immune response to foot-and-mouth disease virus infection in swine. *J Virol*. 2006 Mar;80(5):2369-79.
- Wernery U, Nagy P, Amaral-Doel CM, Zhang Z, Alexandersen S. Lack of susceptibility of the dromedary camel (*Camelus dromedarius*) to foot-and-mouth disease virus serotype O. *Vet Rec*. 2006 Feb 11;158(6):201-3. No abstract available.
- Rasmussen TB, Uttenthal A, Aguero M. Detection of three porcine vesicular viruses using multiplex real-time primer-probe energy transfer. *J Virol Methods*. 2006 Feb 9; [Epub ahead of print]
- Gu CJ, Zheng CY, Zhang Q, Shi LL, Li Y, Qu SF. An antiviral mechanism investigated with ribavirin as an RNA virus mutagen for foot-and-mouth disease virus. *J Biochem Mol Biol*. 2006 Jan 31;39(1):9-15.
- Rivas AL, Kunsberg B, Chowell G, Smith SD, Hyman JM, Schwager SJ. Human-mediated foot-and-mouth disease epidemic dispersal: disease and vector clusters. *J Vet Med B Infect Dis Vet Public Health*. 2006 Feb;53(1):1-10.
- Ferrer-Orta C, Arias A, Agudo R, Perez-Luque R, Escarmis C, Domingo E, Verdaguer N. The structure of a protein primer-polymerase complex in the initiation of genome replication. *EMBO J*. 2006 Feb 22;25(4):880-8. Epub 2006 Feb 2.
- Dukes JP, King DP, Alexandersen S. Novel reverse transcription loop-mediated isothermal amplification for rapid detection of foot-and-mouth disease virus. *Arch Virol*. 2006 Feb 2; [Epub ahead of print]
- Lee F, Jong MH, Yang DW. Presence of antibodies to non-structural proteins of foot-and-mouth disease virus in repeatedly vaccinated cattle. *Vet Microbiol*. 2006 Jan 27; [Epub ahead of print]
- de Los Santos T, de Avila Botton S, Weiblen R, Grubman MJ. The leader proteinase of foot-and-mouth disease virus inhibits the induction of beta interferon mRNA and blocks the host innate immune response. *J Virol*. 2006 Feb;80(4):1906-14.
- Chowell G, Rivas AL, Smith SD, Hyman JM. Identification of case clusters and counties with high infective connectivity in the 2001 epidemic of foot-and-mouth disease in Uruguay. *Am J Vet Res*. 2006 Jan;67(1):102-13.
- Zhang Z, Bashiruddin JB, Doel C, Horsington J, Durand S, Alexandersen S. Cytokine and Toll-like receptor mRNAs in the nasal-associated lymphoid tissues of cattle during foot-and-mouth disease virus infection. *J Comp Pathol*. 2006 Jan;134(1):56-62.
- Yoon H, Wee SH, Stevenson MA, O'leary BD, Morris RS, Hwang IJ, Park CK, Stern MW. Simulation analyses to evaluate alternative control strategies for the 2002 foot-and-mouth disease outbreak in the Republic of Korea. *Prev Vet Med*. 2006 Jan 16; [Epub ahead of print]
- Wang F, He XW, Jiang L, Ren D, He Y, Li DA, Sun SH. Enhanced immunogenicity of microencapsulated multi-epitope DNA vaccine encoding T and B cell epitopes of foot-and-mouth disease virus in mice. *Vaccine*. 2006 Mar 15;24(12):2017-26. Epub 2005 Dec 1.
- Savill NJ, Shaw DJ, Deardon R, Tildesley MJ, Keeling MJ, Woolhouse ME, Brooks SP, Grenfell BT. Topographic determinants of foot and mouth disease transmission in the UK 2001 epidemic. *BMC Vet Res*. 2006 Jan 16;2:3.

- Liu YC, Huang GS, Wu MC, Hong MY, Hsiung KP. Detection of foot and mouth disease and porcine reproductive and respiratory syndrome viral genes using microarray chip. *Vet Res Commun.* 2006 Feb;30(2):191-204.
- Qing L, Lv J, Li H, Tan Y, Hao H, Chen Z, Zhao J, Chen H. The Recombinant Nonstructural Polyprotein NS1 of Porcine Parvovirus (PPV) as Diagnostic Antigen in ELISA to Differentiate Infected from Vaccinated Pigs. *Vet Res Commun.* 2006 Feb;30(2):175-90.
- Sellers RF. Comparison of different control strategies for foot-and-mouth disease: a study of the epidemics in Canada in 1951/52, Hampshire in 1967 and Northumberland in 1966. *Vet Rec.* 2006 Jan 7;158(1):9.
- Garner MG, Beckett SD. Modelling the spread of foot-and-mouth disease in Australia. *Aust Vet J.* 2005 Dec;83(12):758-66.
- Hietala SK, Crossley BM. Armored RNA as virus surrogate in a real-time reverse transcriptase PCR assay proficiency panel. *J Clin Microbiol.* 2006 Jan;44(1):67-70.
- Niedbalski W. Detection of foot-and-mouth disease virus infection in vaccinated cattle. *Pol J Vet Sci.* 2005;8(4):283-7.
- Fernandez-Miragall O, Ramos R, Ramajo J, Martinez-Salas E. Evidence of reciprocal tertiary interactions between conserved motifs involved in organizing RNA structure essential for internal initiation of translation. *RNA.* 2006 Feb;12(2):223-34. Epub 2005 Dec 22.
- Sharma M, Kadian SK, Sharma R, Rana TS. Kinetics of humoral immune response in pigs vaccinated against foot and mouth disease. *Indian J Exp Biol.* 2005 Dec;43(12):1144-9.
- Domingo E, Gonzalez-Lopez C, Pariente N, Airaksinen A, Escarmis C. Population dynamics of RNA viruses: the essential contribution of mutant spectra. *Arch Virol Suppl.* 2005;(19):59-71. Review.
- Rubel F, Fuchs K. A decision-support system for real-time risk assessment of airborne spread of the foot-and-mouth disease virus. *Methods Inf Med.* 2005;44(4):590-5.
- Bailey C, Convery I, Mort M, Baxter J. Different public health geographies of the 2001 foot and mouth disease epidemic: 'citizen' versus 'professional' epidemiology. *Health Place.* 2006 Jun;12(2):157-66.
- Hutber AM, Kitching RP, Pilipcinec E. Predictions for the timing and use of culling or vaccination during a foot-and-mouth disease epidemic. *Res Vet Sci.* 2006 Aug;81(1):31-6. Epub 2005 Dec 5.
- Reid SM, Parida S, King DP, Hutchings GH, Shaw AE, Ferris NP, Zhang Z, Hillerton JE, Paton DJ. Utility of automated real-time RT-PCR for the detection of foot-and-mouth disease virus excreted in milk. *Vet Res.* 2006 Jan-Feb;37(1):121-32.
- Reigadas S, Pacheco A, Ramajo J, de Quinto SL, Martinez-Salas E. Specific interference between two unrelated internal ribosome entry site elements impairs translation efficiency. *FEBS Lett.* 2005 Dec 19;579(30):6803-8. Epub 2005 Nov 28.
- Mohapatra JK, Sanyal A, Hemadri D, Tosh C, Rasool TJ, Bandyopadhyay SK. A novel genetic lineage differentiating RT-PCR as a useful tool in molecular epidemiology of foot-and-mouth disease in India. *Arch Virol.* 2006 Apr;151(4):803-9. Epub 2005 Dec 5.
- Li Y, Sun M, Liu J, Yang Z, Zhang Z, Shen G. High expression of foot-and-mouth disease virus structural protein VP1 in tobacco chloroplasts. *Plant Cell Rep.* 2006 Apr;25(4):329-33. Epub 2005 Dec 1.
- Chowell G, Rivas AL, Hengartner NW, Hyman JM, Castillo-Chavez C. The role of spatial mixing in the spread of foot-and-mouth disease. *Prev Vet Med.* 2006 Mar 16;73(4):297-314. Epub 2005 Nov 11.
- Grubman MJ. Development of novel strategies to control foot-and-mouth disease: marker

vaccines and antivirals. *Biologicals*. 2005 Dec;33(4):227-34. Epub 2005 Nov 14.

Eble PL, de Bruin MG, Bouma A, van Hemert-Kluitenberg F, Dekker A. Comparison of immune responses after intra-typic heterologous and homologous vaccination against foot-and-mouth disease virus infection in pigs. *Vaccine*. 2006 Feb 27;24(9):1274-81. Epub 2005 Oct 4.

Shirley MD, Rushton SP. Where diseases and networks collide: lessons to be learnt from a study of the 2001 foot-and-mouth disease epidemic. *Epidemiol Infect*. 2005 Dec;133(6):1023-32.

Clavijo A, Hole K, Li M, Collignon B. Simultaneous detection of antibodies to foot-and-mouth disease non-structural proteins 3ABC, 3D, 3A and 3B by a multiplexed Luminex assay to differentiate infected from vaccinated cattle. *Vaccine*. 2006 Mar 6;24(10):1693-704. Epub 2005 Oct 17.

Bergmann IE, Malirat V, Neitzert E. Non-capsid proteins to identify foot-and-mouth disease viral circulation in cattle irrespective of vaccination. *Biologicals*. 2005 Dec;33(4):235-9. Epub 2005 Oct 28.

Song H, Wang Z, Zheng D, Fang W, Li Y, Liu Y, Niu Z, Qiu B. A novel mucosal vaccine against foot-and-mouth disease virus induces protection in mice and swine. *Biotechnol Lett*. 2005 Nov;27(21):1669-74.

Mouchantat S, Haas B, Lutz W, Pohlmeier K, Frolich K. Absence of antibodies to foot-and-mouth disease virus in free-ranging roe deer from selected areas of Germany (2001-2002). *J Wildl Dis*. 2005 Jul;41(3):599-605.

Parida S, Oh Y, Reid SM, Cox SJ, Statham RJ, Mahapatra M, Anderson J, Barnett PV, Charleston B, Paton DJ. Interferon-gamma production in vitro from whole blood of foot-and-mouth disease virus (FMDV) vaccinated and infected cattle after incubation with inactivated FMDV. *Vaccine*. 2006 Feb 13;24(7):964-9. Epub 2005 Oct 4.

Chen L, Shao H. Extract from *Agaricus blazei* Murill can enhance immune responses elicited by DNA vaccine against foot-and-mouth disease. *Vet Immunol Immunopathol*. 2006 Jan 15;109(1-2):177-82. Epub 2005 Oct 6.

Parida S, Anderson J, Cox SJ, Barnett PV, Paton DJ. Secretory IgA as an indicator of oro-pharyngeal foot-and-mouth disease virus replication and as a tool for post vaccination surveillance. *Vaccine*. 2006 Feb 20;24(8):1107-16. Epub 2005 Sep 19.

Vane CH, Trick JK. Evidence of adipocere in a burial pit from the foot and mouth epidemic of 1967 using gas chromatography-mass spectrometry. *Forensic Sci Int*. 2005 Nov 10;154(1):19-23. Epub 2004 Nov 10.

Robiolo B, Seki C, Fondevilla N, Grigera P, Scodeller E, Periolo O, La Torre J, Mattion N. Analysis of the immune response to FMDV structural and non-structural proteins in cattle in Argentina by the combined use of liquid phase and 3ABC-ELISA tests. *Vaccine*. 2006 Feb 13;24(7):997-1008. Epub 2005 Sep 7.

Vosloo W, Bastos AD, Boshoff CI. Retrospective genetic analysis of SAT-1 type foot-and-mouth disease outbreaks in southern Africa. *Arch Virol*. 2006 Feb;151(2):285-98. Epub 2005 Sep 9.

Golde WT, Pacheco JM, Duque H, Doel T, Penfold B, Ferman GS, Gregg DR, Rodriguez LL. Vaccination against foot-and-mouth disease virus confers complete clinical protection in 7 days and partial protection in 4 days: Use in emergency outbreak response. *Vaccine*. 2005 Dec 30;23(50):5775-82. Epub 2005 Aug 8.

Shi XJ, Wang B, Zhang C, Wang M. Expressions of Bovine IFN-gamma and foot-and-mouth disease VP1 antigen in *P. pastoris* and their effects on mouse immune response to FMD antigens. *Vaccine*. 2006 Jan 9;24(1):82-9. Epub 2005 Aug 11.

Zhang HY, Sun SH, Guo YJ, Chen ZH, Huang L, Gao YJ, Wan B, Zhu WJ, Xu GX, Wang JJ. Tissue distribution of a plasmid DNA containing epitopes of foot-and-mouth disease virus in mice. *Vaccine*. 2005 Dec 1;23(48-49):5632-40. Epub 2005 Aug 15.

Nunez JI, Fusi P, Borrego B, Brocchi E, Pacciarini ML, Sobrino F. Genomic and antigenic characterization of viruses from the 1993 Italian foot-and-mouth disease outbreak. *Arch Virol*. 2006 Jan;151(1):127-42. Epub 2005 Aug 12. 1