

The Complete Genomic Sequence of the Modified Vaccinia Ankara Strain: Comparison with Other Orthopoxviruses

G. Antoine, F. Scheifflinger, F. Dorner, and F. G. Falkner¹

Biomedical Research Center, Hyland-Immuno, Uferstrasse 15, A-2304 Orth/Donau, Austria

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The complete genomic DNA sequence of the highly attenuated vaccinia strain modified vaccinia Ankara (MVA) was determined. The genome of MVA is 178 kb in length, significantly smaller than that of the vaccinia Copenhagen genome, which is 192 kb. The 193 open reading frames (ORFs) mapped in the MVA genome probably correspond to 177 genes, 25 of which are split and/or have suffered mutations resulting in truncated proteins. The left terminal genomic region of MVA contains four large deletions and one large insertion relative to the Copenhagen strain. In addition, many ORFs in this region are fragmented, leaving only eight genes structurally intact and therefore presumably functional. The inserted DNA codes for a cluster of genes that is also found in the vaccinia WR strain and in cowpox virus and includes a highly fragmented gene homologous to the cowpox virus host range gene, providing further evidence that a cowpox-like virus was the ancestor of vaccinia. Surprisingly, the central conserved region of the genome also contains some fragmented genes, including ORF F5L, encoding a major membrane protein, and ORFs F11L and O1L, encoding proteins of 39.7 and 77.6 kDa, respectively. The right terminal genomic region carries three large deletions: all classical poxviral immune evasion genes and all ankyrin-like genes located in this region are fragmented except for those encoding the interleukin-1 β receptor and the 68-kDa ankyrin-like protein B18R. Thus, the attenuated phenotype of MVA is the result of numerous mutations, particularly affecting the host interactive proteins, including the ankyrin-like genes, but also involving some structural proteins. © 1998 Academic Press

INTRODUCTION

The members of the poxvirus family have large double-stranded DNA genomes encoding several hundred proteins (review: Moss, 1996). Several members of the poxviridae have been sequenced recently, including the vaccinia virus Copenhagen (CPN) strain (Goebel *et al.*, 1990) encompassing 192 kb, the variola (VAR) strains Bangladesh (Massung *et al.*, 1994) and India (Shchelkunov *et al.*, 1993d) encompassing 186 kb, and the human tumorigenic poxvirus mollusum contagiosum virus (Senkevich *et al.*, 1996) encompassing 190 kb. Sequence analysis of poxvirus genomes has increased our knowledge of the structure and function of poxviral genes and increased our understanding of host–virus interactions. Due to the complexity of poxviral genomes and the complex viral life cycle, questions concerning immunogenicity, virulence, and host range of poxvirus strains have been answered only partially for the respective virus strain. It was therefore of interest to determine the genomic sequence of the highly attenuated vaccinia strain modified vaccinia Ankara (MVA) (Mayr *et al.*, 1978), which cannot grow in most mammalian cells and which is a good candidate for a recombinant vaccine vector (Sutter and Moss, 1992; Sutter *et al.*, 1994). This strain has been passaged over 570 times in chicken embryo

fibroblasts, during which six major deletions relative to the parental wild-type strain Ankara, accompanied by a severe restriction in host range, have occurred (Meyer *et al.*, 1991). Precise restriction maps have been established (Meyer *et al.*, 1991) and two of the deletions have been characterized by sequence analysis (Altenburger *et al.*, 1989; Antoine *et al.*, 1996). In a first step to elucidate the genetic basis for the high degree of attenuation of MVA, the nucleotide sequence of its genomic DNA was determined and the open reading frames were compared to the entries of current sequence databases.

RESULTS

Basic genome data

The sequence of the linear, double-stranded DNA molecule totals 177,923 bp and the G+C content is 33.4%, exactly corresponding to the G+C content of the CPN strain. Translational analysis allowed the mapping of 192 ORFs specifying potential proteins ≥ 65 amino acids. As in other orthopoxviruses, the ORF encoding the RNA polymerase subunit rpo7, G5.5R (MVA083R), is 63 amino acids in size (Amegadzie *et al.*, 1992). Eight duplicated ORFs ≥ 65 amino acids that are located in the repeat regions within the terminal 5.5 kb of the inverted terminal repeats (ITRs) were not listed in Table 1 because they presumably do not represent functional genes. Translation of these ORFs resulted in a family of related proteins with repeat

¹ To whom correspondence and reprint requests should be addressed. Fax: 43-2212-2716. E-mail: falknef@baxter.com.

TABLE 1

Features and Homologies of Open Reading Frames of the Vaccinia MVA Strain

ORF ^a	START STOP	AA ^b	kDa ^c	name / (putative) function / homologies ^e	BLAST ^d expect	BLAST ^c AA id	HSS ^f (%)	references
left terminal region:								
001L/ 193R^h <i>C23L</i>	6822 6412	136	14.9	35k major secr. protein chemokine receptor (f') VAC (<i>C23L/B29R</i>)				(Patel <i>et al.</i> , 1990) (Graham <i>et al.</i> , 1997) (Goebel <i>et al.</i> , 1990)
		244		VAR-I ^l G3R	6.0e-57	41/42	97	(Goebel <i>et al.</i> , 1990)
		253		VAR-I ^l G3R	8.9e-51	46/49	93	(Shchelkunov <i>et al.</i> , 1995)
		246		CPX ORF B	5.6e-49	40/42	95	(Hu <i>et al.</i> , 1994)
		258		SPV T1 protein	2.5e-20	23/42	54	(Upton <i>et al.</i> , 1987)
		260		Myxoma virus T1/35kDa	1.5e-14	21/42	50	(Graham <i>et al.</i> , 1997)
002L/ 192R^h	7784 7254	176 355	19.7	secr. TNF receptor (f) CPX crmB	5.1e-71	76/83	91	(Upton <i>et al.</i> , 1991a) (Hu <i>et al.</i> , 1994)
		348		VAR-BSH G2R	1.0e-66	73/83	87	(Shchelkunov <i>et al.</i> , 1995)
		326		Myxoma virus T2	4.9e-30	21/37	56	(Upton <i>et al.</i> , 1991a)
		325		Rabbit fibroma Virus T2	1.8e-28	17/36	47	(Upton <i>et al.</i> , 1987)
		202		CPX C4L	8.7e-15	30/51	58	(Safronov <i>et al.</i> , 1996)
		346		^h HS TNF receptor protein	1.9e-08	14/26	53	(Heller <i>et al.</i> , 1990)
<i>C19L</i>		259		VAC (<i>C19L/B25R</i>)	0.00026	16/19	84	(Goebel <i>et al.</i> , 1990)
		277		human CD40L receptor	0.0015	11/24	45	(Stamencovic <i>et al.</i> , 1989)
				30 matches to TNF receptors and surface proteins	<0.39			
003L/ 191R^h <i>C17L</i>	8780 8472	102	12.1	45k ank^k-like protein (f1) VAC C17L/B23R				(Goebel <i>et al.</i> , 1990)
		386		VAC C17L/B23R	1.3e-39	62/63	98	(Goebel <i>et al.</i> , 1990)
004L/ 190R^h <i>C17L</i> <i>D1L</i>	9558 8857	233	26.9	45k ank-like protein (f2) VAC (C17L/B23R)				(Goebel <i>et al.</i> , 1990)
		386		VAC (C17L/B23R)	6.2e-159	110/110	100	(Goebel <i>et al.</i> , 1990)
		91		VAR-BSH	9.1e-31	46/49	93	(Shchelkunov <i>et al.</i> , 1995)
		669		CPX host range	1.1e-13	22/50	44	(Spehner <i>et al.</i> , 1988)
		452		VAR-I D6L (BSH:D8L)	1.7e-11	21/50	42	(Shchelkunov <i>et al.</i> , 1995)
		574		VAR-I B19R (BSH: B16R)	1.2e-05	22/73	30	(Shchelkunov <i>et al.</i> , 1995)
		574		VAC B18R (WR: B17R)	8.6e-05	22/73	30	(Goebel <i>et al.</i> , 1990)
		634		VAC C9L	0.00011	11/24	45	(Kotwal and Moss, 1988a)
		585		VAR-I G1R	0.00013	22/74	29	(Shchelkunov <i>et al.</i> , 1995)
		516		orf virus	0.0088	15/49	30	(Sullivan <i>et al.</i> , 1995b)
		153		VAR-I D7L (BSH:D10L)	0.014	12/28	42	(Shchelkunov <i>et al.</i> , 1995)
005R <i>C11R</i> <i>D2R</i>	10203 10625	140	15.5	Growth factor (EGF receptor binding) VAC				(Twardzik <i>et al.</i> , 1985) (Stroobant <i>et al.</i> , 1985)
		142		VAC	2.9e-82	99/104	95	(Goebel <i>et al.</i> , 1990)
		140		VAR-I (BSH:D4R)	3.6e-74	106/140	75	(Shchelkunov <i>et al.</i> , 1995)
		138		CPX D5R	3.4e-95	101/114	88	(Safronov <i>et al.</i> , 1996)
		169		human epiregulin	2.2e-14	29/78	37	D30783
				100 matches to growth factor like sequences	<0.10			
006L <i>C10L</i>	11758 10778	326 331	37.9	37.9k protein VAC				(Venkatesan <i>et al.</i> , 1982) (Goebel <i>et al.</i> , 1990)
		331		CPX D6L	1.7e-235	264/268	98	(Safronov <i>et al.</i> , 1996)
		330		VAR-BSH (I: D3L)	7.7e-235	264/268	98	(Safronov <i>et al.</i> , 1996)
<i>D5L</i>		330		VAR-BSH (I: D3L)	3.6e-233	169/171	97	(Shchelkunov <i>et al.</i> , 1995)
		316		VAR-I D11L (BSH:D14L)	1.7e-94	34/68	44	(Shchelkunov <i>et al.</i> , 1995)
		316		VAC C4L	1.8e-92	30/68	54	(Goebel <i>et al.</i> , 1990)
		315		CPX D16L	2.3e-92	31/68	45	(Safronov <i>et al.</i> , 1996)
		82		Ectromelia 42K protein	1.2e-50	78/82	95	(Senkevich <i>et al.</i> , 1993a)
		418		FPV BamHI ORF1	3.0e-11	13/41	31	(Tomley <i>et al.</i> , 1988)
007R <i>D4R</i>	12263 12538	91 242	10.6	28k virulence factor (f) CPX D7R				(Senkevich <i>et al.</i> , 1993a) (Safronov <i>et al.</i> , 1996)
		184		VAC-WR 21.7k protein	1.5e-51	42/47	89	(Kotwal and Moss, 1988a)
		242		VAR-I (BSH:D6R)	5.3e-51	41/47	87	(Shchelkunov <i>et al.</i> , 1995)
		241		Ectromelia 28k secreted virulence factor	3.7e-50	41/47	87	(Shchelkunov <i>et al.</i> , 1995) (Senkevich <i>et al.</i> , 1993a)
008L <i>D7L</i>	13414 13052	120 126	13.7	13.7k protein VAR-BSH (I:D5L)				(Shchelkunov <i>et al.</i> , 1995)
		138		Ectromelia 16k protein	1.9e-83	57/64	89	(Senkevich <i>et al.</i> , 1993a)
		124		CPX D8L	7.8e-81	58/60	96	(Safronov <i>et al.</i> , 1996)
		68		7.8k protein (VAC-WR)	3.2e-67	49/60	81	(Kotwal and Moss, 1988a)
					1.3e-34	53/64	82	
009L <i>D6L</i>	13745 13473	90 669	10.7	77k CPX hr protein (f1) CPX host range gene				(Spehner <i>et al.</i> , 1988) (Safronov <i>et al.</i> , 1996)
		634		VAC C9L	2.7e-46	43/52	82	(Goebel <i>et al.</i> , 1990)
010L <i>D6L</i>	14186 13758	142 669	16.1	77k CPX hr protein (f2) CPX host range gene				(Goebel <i>et al.</i> , 1990) (Spehner <i>et al.</i> , 1988)
		634		VAC C9L	2.2e-91	133/142	93	(Safronov <i>et al.</i> , 1996)
		452		VAR-I (BSH: D8L)	9.2e-21	26/63	41	(Goebel <i>et al.</i> , 1990)
		150		VAC C18L/B24R	4.5e-13	27/29	93	(Shchelkunov <i>et al.</i> , 1995)
		439		AT ankyrin repeat protein	1.3e-11	19/52	36	(Goebel <i>et al.</i> , 1990)
		558		VAR-I B6R (BSH:B5R)	9.5e-07	23/59	38	(Zhang <i>et al.</i> , 1992)
				30 matches with ankyrin repeat containing proteins	4.0e-05	28/113	24	(Shchelkunov <i>et al.</i> , 1995)
					2.7e-05 to 0.016			
011L <i>D6L</i>	14682 14275	135 669	15.8	77k CPX hr protein (f3) CPX host range gene				(Spehner <i>et al.</i> , 1988) (Safronov <i>et al.</i> , 1996)
		452		VAR-I (BSH: D8L)	7.6e-80	54/64	84	(Shchelkunov <i>et al.</i> , 1995)
012L	15183	90	10.3	77k CPX hr protein (f4)	9.2e-78	52/64	81	(Shchelkunov <i>et al.</i> , 1995) (Spehner <i>et al.</i> , 1988)

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) / homologies ^e	BLAST ^d expect	BLAST ^c AA id	HSS ^f (%)	references
left	terminal	region:							
D6L	14911	452		VAR-I (BSH: D8L)		2.2e-52	80/85	94	(Shchelkunov <i>et al.</i> , 1995)
		669		CPX host range gene		8.1e-51	77/85	90	(Spehner <i>et al.</i> , 1988)
		153		VAR-I D7L (BSH: D10L)		2.9e-17	19/45	42	(Shchelkunov <i>et al.</i> , 1995)
		634		VAC C9L		1.3e-13	19/45	42	(Goebel <i>et al.</i> , 1990)
		1161		C. botulinum NTN protein		0.00019	6/12	50	(Hutson <i>et al.</i> , 1996)
		202		Capripox		0.00058	15/58	25	(Cao <i>et al.</i> , 1995)
		895		UDP glucose dehydrogenase		0.00051	6/19	31	(Bult <i>et al.</i> , 1996)
		516		orf virus ank-like		0.0064	16/49	32	(Sullivan <i>et al.</i> , 1995b)
		673		rabbit fibroma 77.2k protein		0.0072	12/30	40	(Massung <i>et al.</i> , 1992)
013L	15420	71	8.5	77k CPX hr protein (f5)					(Spehner <i>et al.</i> , 1988)
D6L	15205	669		CPX host range gene		5.2e-44	68/69	98	(Safronov <i>et al.</i> , 1996)
		452		VAR (BSH: D8L)		7.9e-42	64/67	95	(Shchelkunov <i>et al.</i> , 1995)
		673		rabbit fibroma 77.2k protein		0.0052	8/26	30	(Massung <i>et al.</i> , 1992)
		386		VAC C17L/B23R		0.018	14/33	42	(Goebel <i>et al.</i> , 1990)
		202		Capripox		0.023	10/19	52	(Sullivan <i>et al.</i> , 1995b)
		574		VAC B18R (WR: B17R)		0.71	12/28	42	(Goebel <i>et al.</i> , 1990)
		574		VAR B19R (BSH:B16R)		0.71	12/28	42	(Shchelkunov <i>et al.</i> , 1995)
014L	16205	109	13.1	75k ank-like gene (f1)					(Kotwal and Moss, 1988a)
C9L	15876	634		VAC		3.9e-73	109/109	100	(Goebel <i>et al.</i> , 1990)
		614		CPX D11L		1.6e-70	105/108	97	(Safronov <i>et al.</i> , 1996)
		91		VAR (I: D6.5L)		1.2e-52	78/91	85	(Shchelkunov <i>et al.</i> , 1995)
		437		CPX D1L		3.7e-19	28/67	41	(Safronov <i>et al.</i> , 1996)
D9L		673		rabbit fibroma 77.2K protein		0.021	5/16	31	(Massung <i>et al.</i> , 1992)
									(Kotwal and Moss, 1988a)
									(Goebel <i>et al.</i> , 1990)
									(Safronov <i>et al.</i> , 1996)
015L	16786	96	11.2	75k ank-like gene (f2)					(Kotwal and Moss, 1988a)
C9L	16496	634		VAC		4.0e-53	80/80	100	(Goebel <i>et al.</i> , 1990)
		614		CPX D11L		3.9e-25	48/80	60	(Safronov <i>et al.</i> , 1996)
		437		CPX D1L		9.6e-12	14/36	38	(Safronov <i>et al.</i> , 1996)
		172		VAR-Garcia 1966 B11L		0.0001	17/17	100	(Massung <i>et al.</i> , 1996)
D7L		141		integrase (simian foamy v.)		0.033	10/24	41	(Schweizer and Neumann, 1995)
		669		CPX host range gene		0.043	9/17	52	(Spehner <i>et al.</i> , 1988)
									(Kotwal and Moss, 1988a)
									(Goebel <i>et al.</i> , 1990)
016L	17759	297	35.0	75k ank-like gene (f3)					(Kotwal and Moss, 1988a)
C9L	16866	634		VAC		3.4e-208	291/294	98	(Goebel <i>et al.</i> , 1990)
		614		CPX D11L		1.4e-130	90/126	71	(Safronov <i>et al.</i> , 1996)
		153		VAR-I (BSH:D10L)		8.4e-68	84/109	77	(Shchelkunov <i>et al.</i> , 1995)
		669		CPX host range gene		4.5e-17	24/61	39	(Spehner <i>et al.</i> , 1988)
D8L		452		CPX D9L		2.2e-16	23/61	37	(Safronov <i>et al.</i> , 1996)
		668		VAR-BSH (I:D6L)		3.3e-16	21/61	34	(Shchelkunov <i>et al.</i> , 1995)
		386		VAC C17L/B23R		2.9e-08	11/24	45	(Goebel <i>et al.</i> , 1990)
		833		CPX D3L		0.0085	13/58	22	(Safronov <i>et al.</i> , 1996)
D8L		574		VAC B18R (WR:B17R)		0.012	13/40	32	(Goebel <i>et al.</i> , 1990)
		202		Capripox virus		0.084	11/29	37	(Sullivan <i>et al.</i> , 1995b)
		574		VAR-I B19R (BSH:B16R)		0.090	13/40	32	(Shchelkunov <i>et al.</i> , 1995)
017L	18335	177	20.8	20.8k protein					(Kotwal and Moss, 1988a)
C8L	17802	184		VAC		1.2e-125	125/129	96	(Goebel <i>et al.</i> , 1990)
		182		CPX D12L		5.0e-118	119/126	94	(Safronov <i>et al.</i> , 1996)
		182		VAC B7R		8.3e-06	16/67	23	(Goebel <i>et al.</i> , 1990)
		795		VAC H4L (RAP94)		0.60	12/45	26	(Goebel <i>et al.</i> , 1990)
018L	18859	150	18.0	host range protein					(Perkus <i>et al.</i> , 1991)
C7L	18407	150		VAC		1.6e-106	150/150	100	(Kotwal and Moss, 1988a)
		150		VAR-BSH (I:D8L)		4.2e-106	149/150	99	(Shchelkunov <i>et al.</i> , 1995)
		185		Swinepox virus ORF SwF8a		3.4e-35	31/82	37	(Schnitzlein and Tripathy, 1991)
		197		Capripox virus ORF CF8a		1.4e-31	29/87	33	(Gershon and Black, 1989a)
		170		CPX D4L		3.5e-17	19/60	31	(Safronov <i>et al.</i> , 1996)
		158		Myxoma virus ORF MF8		5.6e-13	16/43	37	(Jackson and Bults, 1992)
		128		VAR-BSH D3L (I:D1.5L)		5.4e-06	18/60	30	(Shchelkunov <i>et al.</i> , 1995)
019L	19541	157	18.2	18.2k protein					(Kotwal and Moss, 1988a)
C6L	19068	151		VAC		7.6e-104	151/151	100	(Goebel <i>et al.</i> , 1990)
		156		VAR (BSH: D12L)		1.6e-99	145/150	96	(Shchelkunov <i>et al.</i> , 1995)
		156		CPX D14L		1.3e-96	141/150	94	(Safronov <i>et al.</i> , 1996)
		159		Capripox virus ORF T3a		4.4e-07	24/76	31	(Gershon and Black, 1989a)
		151		Rabbit fibroma virus T3Aa		0.0047	16/46	34	(Upton <i>et al.</i> , 1987)
		181		VAC C16L/B22R		0.2	12/46	26	(Goebel <i>et al.</i> , 1990)
		149		VAR C4R		0.29	8/13	61	(Shchelkunov <i>et al.</i> , 1995)
		149		VAC-WR K7R		0.40	8/13	61	(Kotwal and Moss, 1988a)
020L	20025	113	13.2	14k virulence factor, secreted protein (f)					(Kotwal and Moss, 1988a)
N1L	19684	117		VAC		2.6e-60	92/102	90	(Kotwal and Moss, 1988b)
		117		CPX PIL		7.3e-58	85/102	83	(Goebel <i>et al.</i> , 1990)
		117		VAR-BSH, virokinase		6.6e-56	88/102	86	(Safronov <i>et al.</i> , 1996)
		107		Rabbit fibroma virus		0.015	10/17	58	(Massung <i>et al.</i> , 1992)
021L	20656	170	20.3	alpha-amanitin sensitive protein					(Tamin <i>et al.</i> , 1991)
N2L	20144	175		CPX P2L		3.0e-118	138/142	97	(Kotwal and Moss, 1988a)
		175		VAC		6.1e-118	137/142	96	(Safronov <i>et al.</i> , 1996)
		177		VAR		9.7e-115	135/142	95	(Goebel <i>et al.</i> , 1990)
									(Shchelkunov <i>et al.</i> , 1995)
022L	20981	98	11.0	33k host range gene (f)					(Gillard <i>et al.</i> , 1986)
K1L	20685	284		VAC		1.8e-56	86/88	97	(Altenburger <i>et al.</i> , 1989)
		284		CPX MIL		2.3e-56	86/88	97	(Safronov <i>et al.</i> , 1996)
		66		VAR		2.0e-39	63/66	95	(Shchelkunov <i>et al.</i> , 1995)
		65		human NOTCH 2		0.00036	17/41	41	(Katsanis <i>et al.</i> , 1996)

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) / homologies ^e	BLAST ^d expect	BLAST ^c AA id	HSS ^f (%)	references
left	terminal	region:							
023L	22296 21187	369	42.3	serpin SPI-3, cell-cell fusion mutation					(Boursnell <i>et al.</i> , 1988)
<i>K2L</i>		369		VAC		1.2e-258	365/369	98	(Altenburger <i>et al.</i> , 1989)
<i>C2L</i>		373		CPX M2L		1.2e-256	331/337		(Goebel <i>et al.</i> , 1990)
		373		VAR-BSH		9.9e-249	321/337	95	(Safronov <i>et al.</i> , 1996)
		373		Ectromelia virus H14-B		6.5e-244	312/337		(Shchelkunov <i>et al.</i> , 1995)
		386		HS plasminogen activator inhibitor 1		1.1e-35	30/68	44	U67964
		58		CPX SPI 3 protein		8.2e-33	57/58	98	(Loskutoff <i>et al.</i> , 1987)
		369		Myxoma virus MAP1 gene		7.3e-32	33/131	25	gi:1168082
		397		mouse protease nexin		1.5e-29	31/67	46	(Upton <i>et al.</i> , 1990a)
		397		humane glia derived neurite-promoting factor		8.7e-27	30/65	46	(Vassalli <i>et al.</i> , 1993)
		320		Swinepox SPI like protein		3.6e-21	20/70	28	A03911
		417		a-1 antitrypsin, human		2.2e-20	26/66	39	(Massung <i>et al.</i> , 1993)
		383		Corticosteroid-binding protein (rabbit)		9.0e-20			(Ciliberto <i>et al.</i> , 1985)
		390		squamous cell carcinoma antigen		1.9e-17			(Seralini <i>et al.</i> , 1989)
									(Schneider <i>et al.</i> , 1995)
024L	22612 22346	88	10.5	IFN resistance, eIF-2a homolog					(Beattie <i>et al.</i> , 1991)
		88		CPX M3L		2.6e-61	88/88	100	(Davies <i>et al.</i> , 1992)
<i>K3L</i>		88		VAC		1.4e-60	87/88	98	(Safronov <i>et al.</i> , 1996)
<i>C3L</i>		88		VAR-I		1.0e-52	73/88	82	(Goebel <i>et al.</i> , 1990)
		86		SPV C8 protein		4.1e-22	20/44	45	(Shchelkunov <i>et al.</i> , 1995)
				translation initiation factor 2 family		1.2e-08/ 0.45			(Massung <i>et al.</i> , 1993)
025L	23938 22664	424	48.9	phospholipase D-like protein					(Cao <i>et al.</i> , 1997)
<i>K4L</i>		424		VAC		1.5e-306	423/424	99	(Goebel <i>et al.</i> , 1990)
		424		CPX M4L		2.1e-303	416/424	98	(Safronov <i>et al.</i> , 1996)
		437		human HU-K4		2.8e-135	53/95	55	U60644
		372		D. discoideum		2.5e-91	28/47	59	(Giorda <i>et al.</i> , 1989)
		516		C. elegans		6.6e-89	31/61	50	gi: 2435624
		2327		C. elegans		2.8e-52	36/60	60	gi: 2291241
		635		C. elegans		1.1e-24	19/53	35	(Wilson <i>et al.</i> , 1994)
		377		FPV major envelope protein		2.9e-23	19/61	31	(Calvert <i>et al.</i> , 1992)
		371		Myxoma virus env protein		3.6e-22	18/51	35	U43549
		378		Orf virus env protein B2L		1.2e-21	21/71	29	(Sullivan <i>et al.</i> , 1994)
<i>MC021L</i>		388		MCV subtype 1 env protein		3.2e-21	20/63	31	(Senkevich <i>et al.</i> , 1997)
<i>C17L</i>		372		VAR-BSH		4.6e-19	15/52	28	(Shchelkunov <i>et al.</i> , 1995)
		372		VAC F13L		4.9e-17	15/52	28	(Goebel <i>et al.</i> , 1990)
026L	24478 23966	170	19.1	lysophospholipase-like protein (f1)					(Upton & Buller, unpub.)
		276		CPX M5L		2.6e-110	161/170	94	(Safronov <i>et al.</i> , 1996)
<i>K5L</i>		277		Ectromelia virus H14-E		2.7e-109	160/170	94	X94355 U67964
		136		VAC		5.5e-69	107/108	99	(Goebel <i>et al.</i> , 1990)
		134		VAC-WR		8.3e-63	98/101	97	(Boursnell <i>et al.</i> , 1988)
		313		HS lysophospholipase		3.3e-35	35/105	33	U67963
		323		homolog		1.2e-13	30/94	31	Z97050
				poss. oxidoreductase M. tuberculosis		3.1e-5	13/58	22	U95973
		313		Lysophospholipase isolog A. thaliana		0.047	13/30	43	U32747
				H. influenza probable lysophospholipase L2					
027L	24694 24500	64	7.0	lysophospholipase-like protein (f2)					(Upton & Buller, unpub.)
<i>K6L</i>		81		VAC		5.3e-42	63/63	100	(Boursnell <i>et al.</i> , 1988)
		276		CPX M5L		2.4e-36	57/58	98	(Safronov <i>et al.</i> , 1996)
		277		Ectromelia virus H14-E		2.4e-36	57/58	98	U67964
		313		HS lysophospholipase homolog		9.1e-23	34/53	64	U67963
		323		hyp. oxidoreductase M. tuberculosis		9.9e-14	22/54	40	Z97050
		530		dihydrotestosterone/androsta nediol UDP-glucuronosyl-transferase		7.0e-05	6/17	35	A48633
central	conserved	region:							
028R	24864	149	17.5	17.5k protein					(Goebel <i>et al.</i> , 1990)
<i>K7R</i>	25313	149		VAC		6.1e-105	149/149	100	(Goebel <i>et al.</i> , 1990)
		161		CPX M6R		1.6e-101	144/149	96	(Safronov <i>et al.</i> , 1996)
<i>C4R</i>		149		VAR		4.9e-101	143/149	100	(Shchelkunov <i>et al.</i> , 1995)
		236		Swinepox (sc76)		0.00017	19/49	95	(Massung <i>et al.</i> , 1993)
029L	26046	222	25.9	25.9k protein					(Roseman and Slabaugh, 1990)
<i>F1L</i>	25378	226		VAC		2.7e-158	208/211	98	(Goebel <i>et al.</i> , 1990)
		238		CPX GIL		7.0e-148	166/189	87	(Safronov <i>et al.</i> , 1996)
<i>C5L</i>		251		VAR-I		6.6e-147	184/200	92	(Shchelkunov <i>et al.</i> , 1995)
030L	26501 26058	147	16.2	dUTPase					(Roseman and Slabaugh, 1990)
		147		VAC		2.9e-102	147/147	100	(Roseman <i>et al.</i> , 1996)
<i>F2L</i>		147		CPX G2L		8.2e-100	144/147	97	(Goebel <i>et al.</i> , 1990)
<i>C6L</i>		147		VAR		1.1e-97	142/147	96	(Safronov <i>et al.</i> , 1996)
		164		human dUTPase		4.1e-61	49/69	71	(Shchelkunov <i>et al.</i> , 1995)
									(Ladner <i>et al.</i> , 1996)

TABLE 1—Continued

ORF ^a	START STOP	AA ^b region:	kDa ^c	name / function	(putative) / homologies ^e	BLAST ^d expect	BLAST ^c AA id	HSS ^f (%)	references
			142	Swinepox virus		8.0e-56	43/70	61	(Massung <i>et al.</i> , 1993)
			159	orf virus		1.5e-49	45/69	65	(Mercer <i>et al.</i> , 1989)
			178	avian adenovirus		6.6e-49	40/70	57	(Akopian <i>et al.</i> , 1992)
			1124	FIV pol polyprotein		1.5e-26	49/117	41	(Talbot <i>et al.</i> , 1989)
				dUTPase pyrophosphatase family		>4.2e-06			
031L	27955	476	55.3	kelch-like protein					(Senkevich <i>et al.</i> , 1993b)
	26525								(Roseman and Slabaugh, 1990)
<i>F3L</i>		480		VAC		0.0	292/294	99	(Goebel <i>et al.</i> , 1990)
		485		CPX G3L		0.0	287/293	97	(Safronov <i>et al.</i> , 1996)
<i>C7L</i>		179		VAR-I		1.9e-124	166/179	92	(Shchelkunov <i>et al.</i> , 1995)
		500		Swinepox virus protein C13		4.4e-46	39/133	29	(Massung <i>et al.</i> , 1993)
		564		VAC A55R		2.8e-21	17/51	33	(Goebel <i>et al.</i> , 1990)
		689		kelch protein D.melanogaster		5.3e-18	21/65	32	(Xue and Cooley, 1993)
		512		CPX D18L		1.4e-16	15/33	45	(Safronov <i>et al.</i> , 1996)
		512		VAC C2L		1.6e-16	15/33	45	(Goebel <i>et al.</i> , 1990)
		625		T27E9.4 C. elegans		3.7e-14	15/59	25	Z82059
		624		human KIAA0132 protein		1.9e-13	13/60	21	D50922 o.k
		817		R09A8.3 (C. elegans)		1.1e-12	17/45	37	(Wilson <i>et al.</i> , 1994)
		611		C47D12.7 (C. elegans)		2.4e-12	22/91	24	(Wilson <i>et al.</i> , 1994)
		530		Swinepox virus		3.0e-09	14/58	24	(Massung <i>et al.</i> , 1993)
		589		M.M ^m actin binding protein		1.9e-09	18/88	20	U65079
		521		CPX C3L		1.2e-08	15/37	40	(Safronov <i>et al.</i> , 1996)
		509		Myxoma virus MT-9		2.5e-08	17/58	29	(Upton <i>et al.</i> , 1990a)
		202		Murine IAP-promoted placenta (MIPP) expressed protein		4.3e-08	17/56	30	(Chang-Yeh <i>et al.</i> , 1991)
		326				3.9e-06	22/80	27	Z99708
		559		A. thaliana hyp. protein		9.0e-6	12/31	38	(Senkevich <i>et al.</i> , 1993b)
		916		Ectromelia virus p65		0.00016	13/42	30	(Way <i>et al.</i> , 1995)
		172		β-scrutin (L. polyphemus)		0.018	15/36	41	(Shchelkunov <i>et al.</i> , 1995)
				VAR-I J8R (BSH: J6R)					
032L	28925	319	37.0	ribonucleotide reductase (small subunit)					(Slabaugh <i>et al.</i> , 1988)
	27966								(Roseman and Slabaugh, 1990)
		319		CPX G4L		2.3e-231	317/319	99	(Safronov <i>et al.</i> , 1996)
<i>F4L</i>		319		VAC		3.5e-231	317/319	99	(Goebel <i>et al.</i> , 1990)
<i>C8L</i>		333		VAR-BSH		4.1e-228	313/319	98	(Shchelkunov <i>et al.</i> , 1995)
				ribonucleotide reductase family		>2.2e-10			
033L	29250	97	11.1	36.5k major membrane protein precursor (f1)					(Roseman and Slabaugh, 1990)
	28957								
<i>C9L</i>		348		VAR-BSH		1.9e-36	51/53	96	(Shchelkunov <i>et al.</i> , 1995)
		323		CPX G5L		2.4e-19	47/77	61	(Safronov <i>et al.</i> , 1996)
<i>F5L</i>		321		VAC		3.3e-19	42/70	60	(Goebel <i>et al.</i> , 1990)
		1584		non-receptor tyrosin kinase (Dictyostelium discoideum)		0.00038	15/35	42	(Tan and Spudich, 1990)
034L	29875	218	24.8	36.5k major membrane protein precursor (f2)					(Roseman and Slabaugh, 1990)
	29219								
		323		CPX G5L		8.2e-155	215/217	99	(Safronov <i>et al.</i> , 1996)
<i>F5L</i>		321		VAC		6.4e-155	215/217	99	(Goebel <i>et al.</i> , 1990)
<i>C9L</i>		348		VAR-BSH		6.8e-141	186/210	88	(Shchelkunov <i>et al.</i> , 1995)
035L	30129	74	8.6	8.6k protein					(Roseman and Slabaugh, 1990)
<i>F6L</i>	29905	74		VAC		5.5e-47	74/74	100	(Goebel <i>et al.</i> , 1990)
<i>C10L</i>		72		VAR		2.3e-38	62/70	88	(Shchelkunov <i>et al.</i> , 1995)
036L	30387	80	9.4	9.4k protein					(Roseman and Slabaugh, 1990)
<i>C11L</i>	30145	79		VAR		2.9e-44	34/43	79	(Shchelkunov <i>et al.</i> , 1995)
<i>F7L</i>		92		VAC		1.9e-43	65/65	100	(Goebel <i>et al.</i> , 1990)
037L	30731	65	7.9	7.9k protein					(Roseman and Slabaugh, 1990)
<i>F8L</i>	30534	65		VAC		5.1e-43	63/65	96	(Goebel <i>et al.</i> , 1990)
<i>C12L</i>		65		VAR-I		3.1e-41	61/65	93	(Shchelkunov <i>et al.</i> , 1995)
038L	31429	212	23.8	23.8k protein					(Roseman and Slabaugh, 1990)
<i>F9L</i>	30791	212		VAC		7.1e-148	212/212	100	(Goebel <i>et al.</i> , 1990)
<i>C13L</i>		212		VAR		1.2e-144	207/212	97	(Shchelkunov <i>et al.</i> , 1995)
		215		Swinepox virus		8.1e-72	39/93	41	(Massung <i>et al.</i> , 1993)
<i>MC016L</i>		213		MCV subtype 1		2.8e-62	71/152	46	(Senkevich <i>et al.</i> , 1996)
		225		Orf virus		5.1e-39	27/84	32	(Mercer <i>et al.</i> , 1995)
		243		FPV protein FP2		2.8e-17	26/58	44	(Binns <i>et al.</i> , 1988)
		243		MCV subtype 1 MC069R		7.7e-12	23/58	39	(Senkevich <i>et al.</i> , 1996)
		250		VAC L1R		1.1e-07	20/58	34	(Goebel <i>et al.</i> , 1990)
		250		VAR M1R		1.1e-07	20/58	34	(Shchelkunov <i>et al.</i> , 1995)
039L	32735	439	52.1	serine/threonine kinase 2					(Lin and Broyles, 1994)
	31416								(Wang and Shuman, 1995)
<i>F10L</i>		439		VAC		0.0	429/439	97	(Goebel <i>et al.</i> , 1990)
<i>C14L</i>		439		VAR-BSH		0.0	424/439	96	(Shchelkunov <i>et al.</i> , 1995)
		440		Swinepox virus		2.2e-233	151/214	70	(Massung <i>et al.</i> , 1993)
<i>MC017L</i>		443		MCV subtype 1		2.3e-198	178/282	63	(Senkevich <i>et al.</i> , 1996)
		498		orf virus		2.2e-162	198/366	54	(Mercer <i>et al.</i> , 1995)
040L	33012	84	9.6	39.7k protein (f1)					(Shchelkunov <i>et al.</i> , 1995)
<i>C15L</i>	32758	354		VAR		6.6e-27	50/64	78	(Goebel <i>et al.</i> , 1990)
<i>F11L</i>		354		VAC		9.1e-27	50/64	78	
041L	33771	100	11.4	39.7k protein (f2)					

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) / homologies ^e	BLAST ^d expect	BLAST ^c AA id	HSS ^f (%)	references
left	terminal	region:							
F11L C15L	33469	354 354		VAC VAR		3.8e-62 8.8e-58	95/95 90/95	100 94	(Goebel <i>et al.</i> , 1990), (Shchelkunov <i>et al.</i> , 1995)
042L F12L C16L	35721 33814	635 635 635	73.1	73.1k protein VAC VAR-I		0.0 0.0	629/635 607/635	99 95	(Goebel <i>et al.</i> , 1990), (Shchelkunov <i>et al.</i> , 1995)
MC019L		352		Myxoma virus		3.6e-84	28/66	42	U43549
		663		MCV subtype 1		4.0e-60	29/82	35	(Senkevich <i>et al.</i> , 1996)
		640		orf virus		4.8e-39	19/61	31	U34774
		630		FPV F12 homolog		2.3e-15	19/67	28	(Ogawa <i>et al.</i> , 1993)
043L	36866 35748	372	41.8	37k major EEV antigen IMCBH sensitive protein palmitoylprotein					(Hirt <i>et al.</i> , 1986) (Schmutz <i>et al.</i> , 1991) (Grosenbach <i>et al.</i> , 1997)
F13L C17L		372 372		VAC VAR-BSH		2.1e-268 8.9e-265	369/372 364/372	99 97	(Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995)
MC021L		371		Myxoma virus		2.5e-115	110/200	55	U43549
		378		orf virus		7.6e-108	83/194	42	(Sullivan <i>et al.</i> , 1994)
		388		MCV subtype 1		6.1e-98	44/113	38	(Senkevich <i>et al.</i> , 1996)
		377		FPV major env protein		2.8e-88	47/112	41	(Calvert <i>et al.</i> , 1992)
		251		pigeonpox virus		1.8e-62	47/112	41	S27933
		424		CPX M4L		2.1e-18	16/52	30	(Safronov <i>et al.</i> , 1996)
		424		VAC K4L		1.7e-17	14/35	40	(Goebel <i>et al.</i> , 1990)
		372		D. discoideum		1.4e-16	28/84	33	(Giorda <i>et al.</i> , 1989)
		437		HU-K4 (homo sapiens)		1.5e-11	25/94	26	U60644
044L F14L C18L	37105 36884	73 73 73	8.3	8.3k protein VAC VAR		2.3e-44 2.1e-35	72/73 57/73	98 78	(Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995)
045L F15L C19L MC025L	378533 37377	158 158 161 148 148	18.6	18.6k protein VAC VAR MCV subtype 1 Myxoma virus		2.3e-112 1.4e-107 3.5e-54 5.4e-50	157/158 150/153 52/113 48/112	99 98 46 42	(Goebel <i>et al.</i> , 1990), (Shchelkunov <i>et al.</i> , 1995) (Senkevich <i>et al.</i> , 1996) U43549
046L F16L C20L MC029L	38555 37860	231 231 209 230	26.5	26.5k protein VAC VAR Myxoma virus MCV subtype 1		3.3e-159 5.6e-157 8.3e-48 6.9e-45	227/231 222/231 26/58 16/61	98 96 44 26	(Goebel <i>et al.</i> , 1990), (Shchelkunov <i>et al.</i> , 1995) U43549 (Senkevich <i>et al.</i> , 1996)
047R F17R C21R MC030R	38619 38924	101 101 102 92 46	11.3	11k DNA binding phosphoprotein VAC VAR MYX MCV subtype 1 orf virus		3.0e-69 9.7e-67 6.6e-26 1.5e-20 1.3e-06	100/101 99/101 45/92 33/53 16/29	99 98 98 48 62	(Bertholet <i>et al.</i> , 1985) (Kao and Bauer, 1987) (Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995) U43549 (Senkevich <i>et al.</i> , 1997) (Mercer <i>et al.</i> , 1995)
048L E1L E1L MC031L	40360 38921	479 479 479 470	55.6	poly(A) polymerase catalytic subunit VAC VAR-I MCV subtype 1		0.0 0.0 1.5e-177	478/479 472/479 114/173	99 98 65	(Gershon <i>et al.</i> , 1991) (Goebel <i>et al.</i> , 1990), (Shchelkunov <i>et al.</i> , 1995) (Senkevich <i>et al.</i> , 1997)
049L E2L E2L MC032L	42570 40357	737 737 737 748	85.9	85.9k protein VAC VAR-I MCV subtype 1		0.0 0.0 8.3e-127	735/737 731/737 59/198	99 99 29	(Ahn <i>et al.</i> , 1990a) (Goebel <i>et al.</i> , 1990), (Shchelkunov <i>et al.</i> , 1995) (Senkevich <i>et al.</i> , 1997)
050L E3L E3L	43269 42697	190 192 1175 1226 551	21.5	dsRNA dependent PK inhibitor, host range VAC VAR-BSH dsRNA specific ADA (rat) dsRNA specific ADA (human) human protein kinase p68 INF inducible kinase family		1.4e-129 8.6e-126 7.2e-12 2.8e-09 3.8e-05 >0.00099	188/190 111/114 22/47 21/47 22/42	98 97 46 44 52	(Chang <i>et al.</i> , 1992) (Chang <i>et al.</i> , 1995b) (Goebel <i>et al.</i> , 1990), (Shchelkunov <i>et al.</i> , 1995) (O'Connell <i>et al.</i> , 1995) (Kim <i>et al.</i> , 1994) (Meurs <i>et al.</i> , 1990)
051L E4L E4L MC034L	44103 43324	259 259 444 39 243	29.8	RNA polymerase subunit rpo30, VITF-1 VAC VAR-BSH MCV subtype 1 orf virus African swine fever virus TFIIS family		1.6e-182 3.2e-180 1.2e-84 6.7e-10 0.00034 <0.0096	258/259 255/259 107/171 21/39 17/36	99 98 62 53 47	(Ahn <i>et al.</i> , 1990a) (Broyles and Pennington, 1990) (Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995) (Senkevich <i>et al.</i> , 1996) (Mercer <i>et al.</i> , 1995) (Vydelingum <i>et al.</i> , 1993)
052R ESR ESR	44180 45175	331 331 341 332 329 319 256 276	39.1	39.1k protein VAC VAR Taterapox Camelpox Cowpox Ectromelia MCV subtype 1		1.2e-235 3.1e-223 7.1e-225 1.4e-221 1.5e-202 3.8e-153 8.3e-109	329/331 312/331 300/314 206/220 271/303 218/245 94/152	99 94 95 93 89 88 61	(Goebel <i>et al.</i> , 1990) (Goebel <i>et al.</i> , 1990) (Shchelkunov <i>et al.</i> , 1995) (Douglas and Dumbell, 1996) (Douglas and Dumbell, 1996) (Douglas and Dumbell, 1996) (Douglas and Dumbell, 1996) (Senkevich <i>et al.</i> , 1997)
053R	45312	567	66.7	66.7k protein					(Goebel <i>et al.</i> , 1990)

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) / homologies ^e	BLAST ^d expect	BLAST ^e AA id	HSS ^f (%)	references
left	terminal	region:							
E6R		567		VAR		0.0	555/567	97	(Shchelkunov <i>et al.</i> , 1995)
MC037R		565		MCV subtype 1		7.2e-247	258/451	57	(Senkevich <i>et al.</i> , 1997)
054R	47082	166	19.5	17k myristylprotein					(Martin <i>et al.</i> , 1997)
E7R	47582	166		VAC		9.7e-116	166/166	100	(Goebel <i>et al.</i> , 1990)
E7R		60		VAR-I (BSH: E6.5R)		2.7e-36	53/60	88	(Shchelkunov <i>et al.</i> , 1995)
055R	47695	273	31.9	31.9k protein					(Earl <i>et al.</i> , 1986)
E8R	48516	273		VAC		4.5e-195	272/273	99	(Goebel <i>et al.</i> , 1990)
E8R		273		VAR		9.9e-192	266/273	99	(Shchelkunov <i>et al.</i> , 1993a)
MC038R		276		MCV subtype 1		8.3e-109	94/152	97	(Senkevich <i>et al.</i> , 1997)
056L	51543	1006	116.9	DNA polymerase					(Earl <i>et al.</i> , 1986)
E9L	48523	1006		VAC		0.0	1005/10	99	(Goebel <i>et al.</i> , 1990)
E9L		1005		VAR BSH		0.0	06	98	(Shchelkunov <i>et al.</i> , 1995)
		1008		Orf virus		0.0	598/608	51	(Mercer <i>et al.</i> , 1996)
		988		FPV		0.0	199/388	60	(Binns <i>et al.</i> , 1987)
MC039L		1004		MCV subtype 1		0.0	179/294	58	(Senkevich <i>et al.</i> , 1997)
		964		C. biennis poxvirus		2.6e-77	175/297	34	(Mustafa and Yuen, 1991)
				DNA polymerase family		>6.0e-06	28/82		
057R	51575	95	10.9	10.9k protein					(Goebel <i>et al.</i> , 1990)
E10R	51862	95		VAC		1.2e-65	93/95	97	(Goebel <i>et al.</i> , 1990)
E10R		95		VAR		3.1e-64	90/95	100	(Shchelkunov <i>et al.</i> , 1993a)
MC040R		101		MCV subtype 1		5.2e-44	58/95	94	(Senkevich <i>et al.</i> , 1997)
058L	52246	129	14.9	14.9k protein					(Goebel <i>et al.</i> , 1990)
E11L	51857	129		VAC		3.3e-89	129/129	100	(Goebel <i>et al.</i> , 1990)
E11L		129		VAR		4.2e-87	125/129	96	(Shchelkunov <i>et al.</i> , 1995)
MC041L		132		MCV subtype 1		1.8e-30	31/96	32	(Senkevich <i>et al.</i> , 1997)
059L	52691	152	17.6	77.6k protein (f1)					(Goebel <i>et al.</i> , 1990)
O1L	52233	666		VAC		6.9e-101	151/152	99	(Goebel <i>et al.</i> , 1990)
Q1L		666		VAR-BSH		3.4e-92	137/152	90	(Shchelkunov <i>et al.</i> , 1995)
MC042L		783		MCV subtype 1		1.5e-22	39/105	37	(Senkevich <i>et al.</i> , 1997)
				leu zipper, bipartite nuclear targeting sequence					(Goebel <i>et al.</i> , 1990)
060L	54189	405	47.4	77.6k protein (f2)					(Goebel <i>et al.</i> , 1990)
O1L	52972	666		VAC		5.8e-277	399/400	99	(Goebel <i>et al.</i> , 1990)
Q1L		666		VAR-I		1.7e-269	383/400	95	(Shchelkunov <i>et al.</i> , 1995)
MC042L		783		MCV subtype 1		2.7e-51	38/104	36	(Senkevich <i>et al.</i> , 1997)
061L	54555	108	12.4	glutaredoxin 1					(Ahn and Moss, 1992a)
	54229								(Johnson <i>et al.</i> , 1991)
O2L		108		VAC		2.0e-74	108/108	100	(Goebel <i>et al.</i> , 1990)
Q2L		108		VAR		4.9e-72	104/108	96	(Shchelkunov <i>et al.</i> , 1995)
		106		human glutaredoxin		3.2e-31	49/106	46	(Fernando <i>et al.</i> , 1994)
				glutaredoxin family		>9.0e-05			
062L	55639	312	35.9	35.9k protein					(Schmitt and Stunnenberg, 1988)
I1L	54701	312		VAC		4.7e-208	310/312	99	(Goebel <i>et al.</i> , 1990)
K1L		312		VAR-BSH		4.8e-205	305/312	97	(Shchelkunov <i>et al.</i> , 1995)
MC044L		310		MCV subtype 1		3.8e-110	163/307	53	(Senkevich <i>et al.</i> , 1996)
		1451		transcription initiation protein (S. cerevisiae)		0.029	10/28	35	(Hansen <i>et al.</i> , 1996)
063L	55867	73	8.5	8.5k protein					(Schmitt and Stunnenberg, 1988)
I2L	55646	73		VAC		5.5e-50	73/73	100	(Goebel <i>et al.</i> , 1990)
K2L		73		VAR		5.5e-50	73/73	100	(Shchelkunov <i>et al.</i> , 1995)
MC045L		72		MCV subtype 1		3.5e-18	20/33	60	(Senkevich <i>et al.</i> , 1996)
		887		hypothetical yeast protein		8.1e-05	9/24	37	S48422
064L	56677	269	30.0	DNA binding phospho-protein (F4L interacting)					(Schmitt and Stunnenberg, 1988)
	55868								(Davis and Mathews, 1993)
I3L		269		VAC		2.1e-173	267/269	99	(Goebel <i>et al.</i> , 1990)
K3L		269		VAR		2.5e-172	265/269	98	(Shchelkunov <i>et al.</i> , 1995)
MC046L		288		MCV subtype 1		9.6e-66	61/149	40	(Senkevich <i>et al.</i> , 1996)
		209		FPV I3 protein		8.4e-35	23/66	34	A48563
065L	59075	771	87.8	ribonucleotide reductase (large subunit)					(Schmitt and Stunnenberg, 1988)
	56760								(Tengelsen <i>et al.</i> , 1988)
I4L		771		VAC		0.0	771/771	100	(Goebel <i>et al.</i> , 1990)
K4L		771		VAR		0.0	761/771	98	(Shchelkunov <i>et al.</i> , 1995)
				ribonucleotide red. family		>1.8e-05			
066L	59342	79	8.8	8.8k protein					(Schmitt and Stunnenberg, 1988)
I5L	59103	79		VAC		6.3e-49	79/79	100	(Goebel <i>et al.</i> , 1990)
K5L		79		VAR		1.2e-47	76/79	96	(Shchelkunov <i>et al.</i> , 1995)
MC047L		82		MCV subtype 1		2.6e-17	27/73	36	(Senkevich <i>et al.</i> , 1996)
		81		FPV 9.1k protein		1.4e-12	13/38	34	(Binns <i>et al.</i> , 1988)
		321		formate dep. nitrit reductase protein (H. influenzae)		0.00022	7/18	38	(Fleischmann <i>et al.</i> , 1995)
		496		permease (b. subtilis)		0.00031	12/43	27	gi:2415386
067L	60509	382	43.5	43.5k protein					(Schmitt and Stunnenberg, 1988)
I6L	59361	382		VAC		8.6e-268	382/382	100	(Goebel <i>et al.</i> , 1990)
K6L		382		VAR		3.1e-267	380/382	99	(Shchelkunov <i>et al.</i> , 1995)
MC048L		406		MCV subtype 1		2.1e-99	44/119	36	(Senkevich <i>et al.</i> , 1996)

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) / homologies ^d	BLAST ^d expect	BLAST ^e AA id	HSS ^f (%)	references
	left	terminal	region:						
			390	FPV I6 protein		1.4e-86	50/136	36	E48563, P12925 (Goebel <i>et al.</i> , 1990)
				mitochondrial energy transfer proteins signature					
068L	61773 60502	423	49.0	core protein, topoisomerase II					(Schmitt and Stunnenberg, 1988) (Kane and Shuman, 1993)
I7L		423		VAC		0.0	420/423	99	(Goebel <i>et al.</i> , 1990)
K7L		423		VAR		1.5e-306	419/423	99	(Shchelkunov <i>et al.</i> , 1995)
MC049L		515		MCV subtype I		1.9e-199	126/207	60	(Senkevich <i>et al.</i> , 1996)
		421		FPV I7 protein		8.1e-180	185/340	54	F48563
		464		Amsacta moorei poxvirus		3.2e-14	14/47	29	(Hall and Moyer, 1991)
069R	61776 63809	676	77.6	NPH-II, NTPase, RNA helicase					(Shuman, 1992), (Koonin and Senkevich, 1992)
I8R		676		VAC		0.0	674/676	99	(Goebel <i>et al.</i> , 1990)
K8R		676		VAR		0.0	665/676	98	(Shchelkunov <i>et al.</i> , 1995)
MC050R		684		MCV subtype I		7.6e-227	144/272	52	(Senkevich <i>et al.</i> , 1997)
		682		FPV virus I8FPV		4.2e-206	98/178	55	(Binns <i>et al.</i> , 1988)
				61 matches mainly to RNA helicase family		<0.38			
070L	65588 63813	591	68.0	68k protein					(Schmitt and Stunnenberg, 1988)
G1L		591		VAC		0.0	590/591	99	(Goebel <i>et al.</i> , 1990)
H1L		591		VAR-I		0.0	582/591	98	(Shchelkunov <i>et al.</i> , 1995)
MC056L		593		MCV subtype I		1.2e-217	183/361	50	(Senkevich <i>et al.</i> , 1997)
		341		FPV		9.4e-75	45/101	44	H48563
071L	65920 65585	111	12.8	12.8k protein					(Schmitt and Stunnenberg, 1988) (Meis and Condit, 1991)
G3L		111		VAC		7.6e-74	111/111	100	(Goebel <i>et al.</i> , 1990)
H3L		111		VAR		2.4e-71	108/111	97	(Shchelkunov <i>et al.</i> , 1995)
MC057L		108		MCV subtype I		0.00012	15/45	33	(Senkevich <i>et al.</i> , 1997)
072R	65914 66576	220	25.8	IBT-dependent protein					(Meis and Condit, 1991)
G2R		220		VAC		1.9e-155	220/220	100	(Goebel <i>et al.</i> , 1990)
H2R		220		VAR		1.1e-151	214/220	97	(Shchelkunov <i>et al.</i> , 1995)
MC058R		246		MCV subtype I		2.7e-36	42/135	31	(Senkevich <i>et al.</i> , 1997)
073L	66920 66546	124	14.0	glutaredoxin 2 membrane protein					(Gvakharia <i>et al.</i> , 1996) (Jensen <i>et al.</i> , 1996)
H4L		124		VAR		4.0e-83	123/124	99	(Shchelkunov <i>et al.</i> , 1995)
G4L		124		VAC		7.5e-83	123/124	99	(Goebel <i>et al.</i> , 1990)
MC059L		126		MCV subtype I		1.1e-21	21/51	41	(Senkevich <i>et al.</i> , 1997)
074R	66923 68227	434	49.9	49.8k protein					(Goebel <i>et al.</i> , 1990)
G5R		434		VAC		1.6e-305	432/434	99	(Goebel <i>et al.</i> , 1990)
H5R		434		VAR		1.9e-299	423/434	97	(Shchelkunov <i>et al.</i> , 1995)
MC60R		437		MCV subtype I		1.0e-55	56/119	47	(Senkevich <i>et al.</i> , 1997)
		1300		HSV CGI protein		0.015	22/82	26	(Print <i>et al.</i> , 1994)
075R	68235 68426	63	7.3	RNA polymerase subunit rpo7					(Amegadzie <i>et al.</i> , 1992), (Meis and Condit, 1991)
G5.5R		63		VAC		1.1e-40	63/63	100	(Goebel <i>et al.</i> , 1990)
H5.5R		63		VAR		1.1e-39	61/63	96	(Shchelkunov <i>et al.</i> , 1995)
MC061R		63		MCV subtype I		9.3e-27	41/63	65	(Senkevich <i>et al.</i> , 1997)
				35 matches mainly to RNA polymerases		<0.54			
076R	68428 68925	165	19.0	18.9k protein					(Goebel <i>et al.</i> , 1990)
G6R		165		VAC		3.8e-116	162/165	98	(Goebel <i>et al.</i> , 1990)
H6R		165		VAR		1.5e-116	164/165	99	(Shchelkunov <i>et al.</i> , 1995)
MC062R		195		MCV subtype I		3.0e-32	27/57	47	(Senkevich <i>et al.</i> , 1997)
077L	70005 68890	371	42.0	42.0k protein					(Schmitt and Stunnenberg, 1988)
G7L		371		VAC		5.2e-255	370/371	99	(Goebel <i>et al.</i> , 1990)
H7L		371		VAR		7.1e-255	369/371	99	(Shchelkunov <i>et al.</i> , 1995)
MC065L		402		MCV subtype I		2.0e-109	69/145	47	(Senkevich <i>et al.</i> , 1997)
078R	70036 70818	260	29.9	VLTF-1, late transcription factor					(Keck <i>et al.</i> , 1990) (Wright <i>et al.</i> , 1991)
G8R		260		VAC		8.6-184	259/260	99	(Goebel <i>et al.</i> , 1990)
H8R		260		VAR-I		3.1e-183	258/260	99	(Shchelkunov <i>et al.</i> , 1995)
MC067R		260		MCV subtype I		8.5e-136	185/260	71	(Senkevich <i>et al.</i> , 1997)
		260		FPV virus FPO		3.3e-129	175/250	67	(Binns <i>et al.</i> , 1988)
079R	70838 71860	340	38.9	37k myristylprotein					(Martin <i>et al.</i> , 1997)
G9R		340		VAC		3.7e-237	317/319	99	(Goebel <i>et al.</i> , 1990)
H9R		340		VAR		9.1e-236	315/319	98	(Shchelkunov <i>et al.</i> , 1995)
MC068R		342		MCV subtype I		4.8e-79	59/127	46	(Senkevich <i>et al.</i> , 1997)
		336		FPV virus FP1		3.9e-65	59/124	47	(Binns <i>et al.</i> , 1988)
080R	71861 72613	250	27.3	25k myristylprotein IMV virion protein					(Franke <i>et al.</i> , 1990) (Martin <i>et al.</i> , 1997)
L1R		250		VAC		1.8e-175	250/250	100	(Goebel <i>et al.</i> , 1990)
M1R		250		VAR		6.4e-170	249/250	99	(Shchelkunov <i>et al.</i> , 1995)
MC069R		243		MCV subtype I		6.5e-103	145/243	59	(Senkevich <i>et al.</i> , 1997)
		243		FPV virus FP2		6.2e-95	128/243	52	(Binns <i>et al.</i> , 1988)
		212		VAC F9L		1.6e-07	20/58	34	(Goebel <i>et al.</i> , 1990)
		212		VAR C13L		3.1e-07	20/58	34	(Shchelkunov <i>et al.</i> , 1995)

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) homologies ^d	BLAST ^e expect	BLAST ^c AA id	HSS ^f (%)	references
left	terminal	region:							
		213		MCV subtype 1	MC016L	1.6e-0.7	13/57	22	(Senkevich <i>et al.</i> , 1997)
		215		swinepox		3.3e-0.5	15/51	29	(Massung <i>et al.</i> , 1993)
081R	72645	87	10.3	10.3k protein					(Plucienniczak <i>et al.</i> , 1985)
<i>L2R</i>	72908	87		VAC		3.9e-57	87/87	100	(Goebel <i>et al.</i> , 1990)
<i>M2R</i>		87		VAR		4.0e-56	85/87	97	(Shchelkunov <i>et al.</i> , 1995)
<i>MC070R</i>		93		MCV subtype 1		0.064	18/80	22	(Senkevich <i>et al.</i> , 1997)
		504		Na ⁺ dependent phosphate transporter	<i>C. elegans</i>	6.9e-05	10/39	25	(Wilson <i>et al.</i> , 1994)
		233		ATPase subunit	<i>T. cruzi</i>	0.013	16/44	36	U38184
		2336		Ca ²⁺ channel	rat	5.2e+0.2	6/25	24	(Dubel <i>et al.</i> , 1992)
		2238		Ca ²⁺ channel	mouse	7.1e+0.2	6/25	24	(Coppola <i>et al.</i> , 1994)
		1559		ABC transporter	yeast	0.40	12/40	30	X97560
082L	73950	350	40.6	40.6k protein					(Plucienniczak <i>et al.</i> , 1985)
<i>L3L</i>	72898	350		VAC		2.2e-251	346/350	98	(Goebel <i>et al.</i> , 1990)
<i>M3L</i>		349		VAR		1.5e-241	296/306	96	(Shchelkunov <i>et al.</i> , 1995)
<i>MC072L</i>		310		MCV subtype 1		1.5e-88	64/136	47	(Senkevich <i>et al.</i> , 1997)
		301		FPV F4 protein		1.1e-80	58/134	43	(Binns <i>et al.</i> , 1988)
083R	73975	251	28.5	core protein VP8					(Yang and Bauer, 1988)
	74730			DNA/RNA binding protein					(Baylis and Smith, 1997)
<i>L4R</i>		251		VAC		5.6e-170	251/251	100	(Goebel <i>et al.</i> , 1990)
<i>M4R</i>		251		VAR		3.7-169	250/251	99	(Shchelkunov <i>et al.</i> , 1995)
<i>MC073R</i>		254		MCV subtype 1		1.7e-76	36/59	61	(Senkevich <i>et al.</i> , 1997)
		253		FPV virus FP5		6.4e-55	29/57	50	(Binns <i>et al.</i> , 1988)
084R	74740	128	15.1	15.1k protein					
<i>L5R</i>	75126	128		VAC 14.0k protein		2.9e-89	127/128	99	(Goebel <i>et al.</i> , 1990)
<i>M5R</i>		128		VAR		2.0-87	125/128	97	(Shchelkunov <i>et al.</i> , 1995)
-		129		FPV FP6		8.1e-16	19/45	42	(Drillien <i>et al.</i> , 1987)
<i>MC074R</i>		146		MCV subtype 1		0.073	10/18	55	(Senkevich <i>et al.</i> , 1997)
		152		melatonin receptor	<i>D. rerio</i>	0.44	15/66	222	(Reppert <i>et al.</i> , 1995)
085R	75083	153	17.9	dimeric virion protein					(Holzer & Falkner, unpubl.)
<i>J1R</i>	75544	153		VAC		6.0e-103	152/153	99	(Goebel <i>et al.</i> , 1990)
<i>L1R</i>		159		VAR-I		1.4e-101	149/153	97	(Shchelkunov <i>et al.</i> , 1995)
		147		capripox CF7		6.5e-54	53/90	58	(Gershon and Black, 1989b)
		148		myxoma MF7		4.8e-51	54/93	58	(Jackson and Bults, 1992)
		183		MCV subtype 1		1.9e-47	47/93	50	(Senkevich <i>et al.</i> , 1997)
<i>MC075R</i>		148		FPV FP7		1.3e-35	37/84	44	(Drillien <i>et al.</i> , 1987)
086R	75560	177	20.0	thymidine kinase					(Hruby and Ball, 1982)
	76093								(Weir and Moss, 1983)
<i>J2R</i>		177		VAC		5.7e-125	175/177	98	(Goebel <i>et al.</i> , 1990)
<i>L2R</i>		177		VAR		2.7e-122	170/177	96	(Shchelkunov <i>et al.</i> , 1995)
				38 matches mainly to thymidine kinase family		<0.18			
087R	76159	333	38.9	poly(A) polymerase su, 2'methyl transferase					(Gershon <i>et al.</i> , 1991)
	77160								(Gershon and Moss, 1993)
<i>J3R</i>		333		VAC		8.7e-136	330/333	99	(Goebel <i>et al.</i> , 1990)
<i>L3R</i>		333		VAR-BSH		9.8e-233	326/333	97	(Shchelkunov <i>et al.</i> , 1995)
		338		myxoma		5.7e-288	247/333	74	(Jackson and Bults, 1990)
<i>MC076R</i>		343		MCV subtype 1		1.4e-135	79/144	54	(Senkevich <i>et al.</i> , 1997)
		308		FPV VP39		1.7e-96	125/267	46	(Binns <i>et al.</i> , 1988)
088R	77075	185	21.3	RNA pol subunit rpo22					(Broyles and Moss, 1986)
<i>J4R</i>	77632	185		VAC		1.2e-125	185/185	100	(Goebel <i>et al.</i> , 1990)
<i>L4R</i>		185		VAR-BSH		7.9e-125	182/185	98	(Shchelkunov <i>et al.</i> , 1995)
		185		myxoma		1.5e-86	124/185	67	(Jackson and Bults, 1990)
<i>MC077R</i>		187		MCV subtype 1		1.9e-76	73/132	55	(Senkevich <i>et al.</i> , 1997)
		186		FPV		2.1e-73	72/135	53	(Binns <i>et al.</i> , 1988)
089L	78101	133	15.2	15.2k protein					(Plucienniczak <i>et al.</i> , 1985)
<i>J5L</i>	77700	133		VAC		2.4e-95	133/133	100	(Goebel <i>et al.</i> , 1990)
<i>L5L</i>		133		VAR-I		2.4e-94	131/133	98	(Shchelkunov <i>et al.</i> , 1995)
<i>MC078L</i>		134		MCV subtype 1		5.7e-45	60/127	47	(Senkevich <i>et al.</i> , 1997)
		137		FPV		1.4e-43	60/130	46	(Drillien <i>et al.</i> , 1987)
		377		VAR-I A16L (BSH:A17L)		0.049	7/28	25	(Shchelkunov <i>et al.</i> , 1995)
		378		VAC A16L		0.049	7/28	25	(Goebel <i>et al.</i> , 1990)
090R	78207	1286	146.9	RNA pol subunit rpo147					(Broyles and Moss, 1986)
<i>J6R</i>	82067	1286		VAC		0.0	1283/1286	99	(Goebel <i>et al.</i> , 1990)
<i>L6R</i>		1286		VAR		0.0	1275/1286	99	(Shchelkunov <i>et al.</i> , 1995)
<i>MC079R</i>		1289		MCV subtype 1		0.0	556/760	73	(Senkevich <i>et al.</i> , 1997)
				100 matches to RNA pol (large subunit) family		<3.7e-07			
091L	82579	171	19.7	protein tyrosine/serine phosphatase					(Rosel <i>et al.</i> , 1986)
	82064								(Guan <i>et al.</i> , 1991)
<i>H1L</i>		171		VAC		2.0e-117	170/171	99	(Goebel <i>et al.</i> , 1990)
<i>I1L</i>		171		VAR		1.1e-114	166/171	97	(Shchelkunov <i>et al.</i> , 1995)
		171		racoonpox		6.0e-111	157/171	91	B47452
		172		myxoma virus		1.5e-77	83/138	60	(Mossman <i>et al.</i> , 1995a)
		173		rabbit fibroma virus		1.8e-77	46/80	57	(Mossman <i>et al.</i> , 1995a)
<i>MC082L</i>		169		MCV subtype 1		1.4e-65	60/114	52	(Senkevich <i>et al.</i> , 1997)
				protein phosphatase family		>2.8e-05			

ORF ^a	START STOP	AA ^b	kDa ^c	name / (putative) function / homologies ^d	BLAST ^d expect	BLAST ^c AA id	HSS ^e (%)	references
left	terminal	region:						
092R	82593	189	21.5	21.5k protein				(Rosel <i>et al.</i> , 1986)
<i>H2R</i>	83162	189		VAC	5.2e-134	188/189	99	(Goebel <i>et al.</i> , 1990)
<i>I2R</i>		189		VAR	1.4e-133	188/189	99	(Shchelkunov <i>et al.</i> , 1995)
MC083R		191		MCV subtype 1	1.4e-71	95/181	52	(Senkevich <i>et al.</i> , 1997)
		142		myxoma	1.3e-65	93/142	65	(Jackson and Bults, 1990)
093L	84139	324	37.5	immunodominant env protein p35; IMV membrane-associated				(Rosel <i>et al.</i> , 1986)
	83165			VAC				(Chertov <i>et al.</i> , 1991)
<i>H3L</i>		324		VAC	3.3e-231	322/324	99	(Takahashi <i>et al.</i> , 1994)
<i>I3L</i>		325		VAR-BSH	1.7e-225	311/320	97	(Shchelkunov <i>et al.</i> , 1995)
MC084L		298		MCV subtype 1	1.1e-36	38/117	32	(Senkevich <i>et al.</i> , 1996)
094L	86527	795	93.6	RAP 94 (RNA-pol assoc. transcr. spec. factor)				(Ahn and Moss, 1992b)
	84140			VAC				(Kane and Shuman, 1992)
<i>H4L</i>		795		VAC	0.0	791/795	99	(Goebel <i>et al.</i> , 1990)
<i>I4L</i>		795		VAR	0.0	780/795	98	(Shchelkunov <i>et al.</i> , 1995)
MC085L		791		MCV subtype 1	0.0	327/546	59	(Senkevich <i>et al.</i> , 1996)
		804		Orf virus	0.0	96/131	73	(Fleming <i>et al.</i> , 1993)
		484		FPV L1L protein	2.4e-181	91/176	51	2209386A
095R	86713	203	22.3	late transcription factor VLTF-4				(Kovacs and Moss, 1996)
	87324			VAC				(Rosel <i>et al.</i> , 1986)
<i>H5R</i>		203		VAC	1.8e-128	202/203	99	(Goebel <i>et al.</i> , 1990)
<i>I5R</i>		221		VAR	5.1e-102	91/97	93	(Shchelkunov <i>et al.</i> , 1995)
		227		orf virus F3R	3.1e-14	29/69	42	(Fleming <i>et al.</i> , 1993)
		220		MCV subtype 1	3.1e-09	28/64	43	(Senkevich <i>et al.</i> , 1997)
		705		nucleolin Xenopus	0.00041	18/57	31	(Messmer and Dreyer, 1993)
				31 matches to glu/asp rich proteins	E<0.52			
096R	87325	314	36.7	DNA topoisomerase I				(Shuman and Moss, 1987)
	88269			VAC				(Rosel <i>et al.</i> , 1986)
<i>H6R</i>		314		VAC	0.0	314/314	100	(Goebel <i>et al.</i> , 1990)
<i>I6R</i>		314		VAR-BSH	9.5e-220	312/314	99	(Shchelkunov <i>et al.</i> , 1995)
		314		shope fibroma virus	8.5e-141	119/170	70	(Upton <i>et al.</i> , 1990b)
		318		orf virus	5.2e-128	82/138	59	(Fleming <i>et al.</i> , 1993)
MC087R		323		MCV subtype 1	1.6e-121	111/202	54	(Senkevich <i>et al.</i> , 1997)
		316		FPV L3R	2.9e-113	159/303	52	(Zantinge <i>et al.</i> , 1996)
				21 matches to topoisomerase family				
097R	88306	146	17.0	17.0k protein				(Rosel <i>et al.</i> , 1986)
<i>H7R</i>	88746	146		VAC	2.1e-98	144/146	98	(Goebel <i>et al.</i> , 1990)
<i>I7R</i>		146		VAR	6.7e-96	141/146	96	(Shchelkunov <i>et al.</i> , 1995)
MC088R		143		MCV subtype 1	4.3e-30	45/115	39	(Senkevich <i>et al.</i> , 1997)
098R	88790	844	96.8	mRNA capping enzyme, large subunit				(Morgan <i>et al.</i> , 1984)
	91324			VAC				(Niles <i>et al.</i> , 1986)
<i>D1R</i>		844		VAC	0.0	842/844	99	(Goebel <i>et al.</i> , 1990)
<i>F1R</i>		844		VAR-BSH	0.0	830/844	98	(Shchelkunov <i>et al.</i> , 1995)
MC090R		950		MCV subtype 1	0.0	322/64	64	(Senkevich <i>et al.</i> , 1997)
		836		shope fibroma virus	0.0	243/305	79	(Upton <i>et al.</i> , 1991b)
		868		ASV NP868R	0.0033	17/55	30	(Pena <i>et al.</i> , 1993)
099L	91723	146	16.9	structural protein				(Niles <i>et al.</i> , 1986)
	91283			VAC				(Dyster and Niles, 1991)
<i>D2L</i>		146		VAC	5.9e-98	146/146	100	(Goebel <i>et al.</i> , 1990)
<i>F2L</i>		146		VAR (BSH; F3L)	1.5e-97	145/146	99	(Shchelkunov <i>et al.</i> , 1995)
		143		Rabbit fibroma virus	2.0e-27	13/33	39	(Upton <i>et al.</i> , 1991b)
MC091L		170		MCV subtype 1	1.1e-20	19/41	46	(Senkevich <i>et al.</i> , 1996)
100R	91716	233	27.6	27k structural protein				(Dyster and Niles, 1991)
<i>D3R</i>	92417	237		VAC	3.8-167	136/142	95	(Goebel <i>et al.</i> , 1990)
<i>F2R</i>		237		VAR I:F3R	1.5e-162	131/142	92	(Shchelkunov <i>et al.</i> , 1995)
		241		shope fibroma virus	9.3e-20	27/100	27	(Upton <i>et al.</i> , 1991b)
MC092R		268		MCV subtype 1	3.5e-18	16/39	41	(Senkevich <i>et al.</i> , 1997)
		206		rabbit fibroma virus C3	1.6e-09	26/96	27	(Strayer <i>et al.</i> , 1991)
101R	92417	218	25.1	uracil DNA glycosylase				(Upton <i>et al.</i> , 1993)
<i>D4R</i>	93073	218		VAC	1.4e-157	217/218	99	(Goebel <i>et al.</i> , 1990)
<i>F4R</i>		218		VAR-BSH	5.1e-157	216/218	99	(Shchelkunov <i>et al.</i> , 1995)
		218		shope fibroma virus	1.5e-117	151/218	69	(Upton <i>et al.</i> , 1993)
MC093R		226		MCV subtype 1	8.4e-91	65/113	57	(Senkevich <i>et al.</i> , 1997)
		218		FPV FPD4	3.1e-88	116/216	53	(Tartaglia <i>et al.</i> , 1990)
		297		uracil DNA glycosylase UL2 gallid herpesvirus 1	0.019	8/14	57	L34064
102R	93105	785	90.4	90.4k ATP/GTP binding protein				(Niles <i>et al.</i> , 1986)
	95462			VAC				(Shchelkunov <i>et al.</i> , 1993c)
<i>D5R</i>		785		VAC	0.0	780/785	99	(Goebel <i>et al.</i> , 1990)
<i>F5R</i>		785		VAR	0.0	774/785	98	(Shchelkunov <i>et al.</i> , 1995)
		786		shope fibroma C5	0.0	283/450	62	(Strayer <i>et al.</i> , 1991)
		791		MCV subtype 1	0.0	184/334	55	(Senkevich <i>et al.</i> , 1997)
		791		FPV virus FPD5	0.0	170/345	49	(Tartaglia <i>et al.</i> , 1990)
MC094R		942		C29E6.4 C. elegans	0.72	16/56	28	(Wilson <i>et al.</i> , 1994)
103R	95503	637	73.9	early transcription factor VETF-1				(Broyles and Fesler, 1990)
	97416							(Gershon and Moss, 1990)

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) / homologies ^e	BLAST ^d expect	BLAST ^e AA id	HSS ^f (%)	references
left	terminal	region:							
D6R		637		VAC		0.0	635/637	99	(Goebel <i>et al.</i> , 1990)
F6R		637		VAR-I		0.0	633/637	99	(Shchelkunov <i>et al.</i> , 1995)
		635		shope fibroma virus		0.0	212/262	80	(Strayer <i>et al.</i> , 1991)
MC095R		635		MCV subtype 1		0.0	199/263	75	(Senkevich <i>et al.</i> , 1997)
		605		FPV		0.0	188/263	71	(Binns <i>et al.</i> , 1990)
									(Tartaglia <i>et al.</i> , 1990)
		648		Choristoneura biennis EPV		2.7e-08	24/72	33	(Yuen <i>et al.</i> , 1991)
		648		Amsacta moorei EPV		4.2e-06	24/77	31	(Hall and Moyer, 1991)
		706		African swine fever virus		1.5e-05	13/38	34	(Yanez <i>et al.</i> , 1993)
104R	97443 97928	161	17.9	RNA polymerase subunit rpo18					(Ahn <i>et al.</i> , 1990b)
									(Quick and Broyles, 1990)
D7R		161		VAC		1.4e-108	160/161	99	(Goebel <i>et al.</i> , 1990)
F7R		161		VAR		2.2e-106	156/161	96	(Shchelkunov <i>et al.</i> , 1995)
		163		rabbit fibroma C8		3.4e-76	108/161	67	(Strayer <i>et al.</i> , 1991)
MC097R		161		MCV subtype 1		4.0e-70	99/158	62	(Senkevich <i>et al.</i> , 1997)
		161		FPV D7		5.4e-66	95/160	59	(Binns <i>et al.</i> , 1990)
105L	98805 97891	304	35.4	virion transmembrane protein, carbonic anhydrase-like					(Niles and Seto, 1988)
									(Niles <i>et al.</i> , 1986)
									(Maa <i>et al.</i> , 1990)
D8L		304		VAC		2.3e-212	297/304	97	(Goebel <i>et al.</i> , 1990)
F8L		304		VAR		2.5e-209	291/304	95	(Shchelkunov <i>et al.</i> , 1995)
		304		Camelpox virus		1.1e-207	290/304	95	X97857
		303		Ectromelia virus		2.2e-207	195/207	94	X97856
		304		Monkeypox virus		3.0e-207	287/304	94	X97855
		304		Cowpox virus		9.8e-206	285/304	93	X97858
				Carbonic anhydrase family		>4.9e-13			
106R	98847 99488	213	25.0	25k mutT-like protein					(Koonin, 1993)
									(Niles <i>et al.</i> , 1986)
D9R		213		VAC		1.6e-146	212/213	99	(Goebel <i>et al.</i> , 1990)
F9R		213		VAR		5.3e-145	209/213	98	(Shchelkunov <i>et al.</i> , 1995)
		218		rabbit fibroma		1.7e-75	105/203	51	(Strayer <i>et al.</i> , 1991)
MC098R		212		MCV subtype 1		5.3e-67	54/111	48	(Senkevich <i>et al.</i> , 1997)
		78		FPV D9		2.0e-13	25/51	49	(Tartaglia <i>et al.</i> , 1990)
MC099R		229		MCV subtype 1		0.0041	13/31	41	(Senkevich <i>et al.</i> , 1997)
		248		VAR-I F10R		0.018	14/32	43	(Shchelkunov <i>et al.</i> , 1995)
		225		FPV D10		0.14	15/34	44	(Tartaglia <i>et al.</i> , 1990)
		248		VAC D10R		0.23	11/26	42	(Goebel <i>et al.</i> , 1990)
107R	99485 100231	248	28.9	29k mutT-like protein					(Koonin, 1993)
									(Niles <i>et al.</i> , 1986)
D10R		248		VAC		7.4e-173	245/248	98	(Goebel <i>et al.</i> , 1990)
F10R		248		VAR-I		5.4e-173	245/248	98	(Shchelkunov <i>et al.</i> , 1995)
		260		shope fibroma D10		3.8e-72	96/202	47	(Strayer <i>et al.</i> , 1991)
MC099R		229		MCV subtype 1		1.4e-54	44/100	44	(Senkevich <i>et al.</i> , 1997)
		225		FPV D10		1.1e-45	45/102	44	(Binns <i>et al.</i> , 1990)
		218		shope fibroma D9		1.9e-06	19/54	35	(Strayer <i>et al.</i> , 1991)
		212		MCV subtype 1 MC098R		0.13	12/21	57	(Senkevich <i>et al.</i> , 1997)
		136		mutator Synechocystis		0.23	12/27	44	D90899
		213		VAC D9R		0.24	11/26	42	(Goebel <i>et al.</i> , 1990)
		213		VAR F9R		0.24	11/26	42	(Shchelkunov <i>et al.</i> , 1995)
		169		mutator M. jannaschii		0.39	13/25	52	(Bult <i>et al.</i> , 1996)
108L	102127 100232	631	72.4	nucleoside triphosphate phosphohydrolase I, DNA helicase					(Broyles and Moss, 1987)
									(Rodriguez <i>et al.</i> , 1986)
									(Koonin and Senkevich, 1992)
D11L		631		VAC		0.0	629/631	99	(Goebel <i>et al.</i> , 1990)
N1L		631		VAR		0.0	626/631	99	(Shchelkunov <i>et al.</i> , 1995)
MC100R		634		MCV subtype 1		7.3e-286	392/627	62	(Senkevich <i>et al.</i> , 1996)
		637		FPV protein 5		2.8e-275	214/357	59	S42251
		370		Rabbit fibroma C14 protein		1.8e-176	244/368	66	F36819
		648		AmEPV		6.0e-142	81/159	50	(Hall and Moyer, 1991)
		648		Choristoneura biennis EPV		1.1e-136	81/158	51	(Yuen <i>et al.</i> , 1991)
		89		Swinepox virus		1.2e-34	60/89	67	(Massung <i>et al.</i> , 1993)
		1098		ASF		1.6e-13	26/89	29	(Baylis <i>et al.</i> , 1993)
		1085		RAD26 (yeast)		5.1e-05	16/45	35	(Huang <i>et al.</i> , 1994)
		769		HS transcription activator		0.00093	10/22	45	(Okabe <i>et al.</i> , 1992)
				NTase family		>5.1e-5			
109L	103025 102162	287	33.3	mRNA capping enzyme, transcription initiation factor VITF					(Niles <i>et al.</i> , 1989)
									(Weinrich and Hruby, 1986)
									(Vos <i>et al.</i> , 1991)
D12L		287		VAC		2.0e-198	285/287	99	(Goebel <i>et al.</i> , 1990)
N2L		287		VAR		9.8e-198	284/287	99	(Shchelkunov <i>et al.</i> , 1995)
-		287		Swinepox virus		4.1e-160	220/287	76	(Massung <i>et al.</i> , 1993)
MC101L		295		MCV subtype 1		5.8e-126	171/279	61	(Senkevich <i>et al.</i> , 1996)
		289		FPV protein 6		3.4e-113	114/215	53	S42252
110L	104711 103056	551	61.9	rifampicin resistance gene, IMV protein					(Tartaglia and Paoletti, 1985)
									(Weinrich and Hruby, 1986)
D13L		551		VAC		0.0	551/551	100	(Goebel <i>et al.</i> , 1990)
N3L		551		VAR		0.0	547/551	99	(Shchelkunov <i>et al.</i> , 1995)
		551		Swinepox virus		4.5e-286	357/506	70	(Massung <i>et al.</i> , 1993)
MC102L		547		MCV subtype 1		5.4e-248	298/494	60	(Senkevich <i>et al.</i> , 1996)
		552		FPV protein 7		6.6e-223	182/305	59	S42253
		584		Heliothis armigera EPV		9.5e-51	54/107	50	(Osborne <i>et al.</i> , 1996)

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) / homologies ^e	BLAST ^d expect	BLAST ^c AA id	HSS ^f (%)	references
left	terminal	region:							
111L	105187 104735	150	16.9	late gene	trans-activator, VLTf-2				(Weinrich and Hruby, 1986)
<i>A1L</i>		150		VAC		6.8e-103	149/150	99	(Keck <i>et al.</i> , 1993)
<i>A1L</i>		150		VAR		6.8e-103	149/150	99	(Goebel <i>et al.</i> , 1990)
<i>MC103L</i>		169		MCV subtype 1		6.3e-54	74/147	50	(Shchelkunov <i>et al.</i> , 1995)
		154		FPV protein 8		2.8e-50	50/87	57	(Senkevich <i>et al.</i> , 1996)
									S42254
112L	105882 105208	224	26.3	late gene	trans-activator				(Weinrich and Hruby, 1986)
<i>A2L</i>		224		VAC					(Passarelli <i>et al.</i> , 1996)
<i>A2L</i>		224		VAR		1.3e-158	224/224	100	(Goebel <i>et al.</i> , 1990)
<i>MC104L</i>		224		MCV subtype 1		1.3e-158	224/224	100	(Shchelkunov <i>et al.</i> , 1995)
		228		orf virus		6.4e-127	172/222	77	(Senkevich <i>et al.</i> , 1996)
		606				6.8e-30	43/66	65	(Mercer <i>et al.</i> , 1995)
113L	106109 105879	76	8.9	8.9k protein					
		76		VAC-WR		1.6e-47	73/76	96	(Weinrich and Hruby, 1986)
<i>A3L</i>		76		VAR-BSH (I: A2.5L)		2.1e-47	71/76	93	(Shchelkunov <i>et al.</i> , 1995)
<i>MC105L</i>		70		MCV subtype 1		9.8e-12	26/63	41	(Senkevich <i>et al.</i> , 1996)
114L	108058 106124	644	72.6	major core protein P4b					(Rosel and Moss, 1985)
<i>A3L</i>		644		VAC		0.0	643/644	99	(Goebel <i>et al.</i> , 1990)
<i>A4L</i>		644		VAR-BSH (I: A3L)		0.0	636/644	98	(Shchelkunov <i>et al.</i> , 1995)
<i>MC106L</i>		675		MCV subtype 1		8.9e-272	227/357	63	(Senkevich <i>et al.</i> , 1996)
		657		FPV Major core protein P4b		9.1e-220	169/299	56	(Binns <i>et al.</i> , 1989)
115L	108929 108111	272	29.9	membrane associated core protein					(Demkowicz <i>et al.</i> , 1992)
<i>A4L</i>		281		VAC		1.1e-145	180/187	96	(Cudmore <i>et al.</i> , 1996)
<i>A5L</i>		271		VAR-BSH (I: A4L)		1.1e-112	165/178	92	(Goebel <i>et al.</i> , 1990)
		268		Thermoproteus phage 1		1.9e-09	38/127	29	(Shchelkunov <i>et al.</i> , 1995)
		5179		human mucin		4.5e-07	34/139	24	(Neumann and Zillig, 1990)
				many matches to Pro-rich proteins					(Gum <i>et al.</i> , 1994)
116R	108967 109461	164	19.0	RNA pol subunit rpo19					(Ahn <i>et al.</i> , 1992)
<i>A5R</i>		164		VAC		5.8e-110	164/164	100	(Goebel <i>et al.</i> , 1990)
<i>A5R</i>		164		VAR-I (BSH:A6R)		7.0e-109	162/164	98	(Shchelkunov <i>et al.</i> , 1995)
<i>MC108R</i>		165		MCV subtype 1		3.3e-51	82/151	53	(Senkevich <i>et al.</i> , 1997)
		167		FPV		3.3e-51	72/161	44	(Kumar and Boyle, 1990)
				54 matches/glu-rich proteins		<0.51			
117L	110576 109458	372	43.1	43.1k protein					
<i>A6L</i>		372		VAC		1.2e-248	371/372	99	(Goebel <i>et al.</i> , 1990)
<i>A7L</i>		372		VAR-BSH (I: A6L)		1.1e-244	364/372	97	(Shchelkunov <i>et al.</i> , 1995)
<i>MC109L</i>		461		MCV subtype 1		4.0e-99	132/367	35	(Senkevich <i>et al.</i> , 1996)
		339		FPV ORF 2 protein		1.9e-95	111/279	39	B60013
118L	112732 110600	710	82.3	VETf 82k subunit					(Gershon and Moss, 1990)
<i>A7L</i>		710		VAC		0.0	708/710	99	(Goebel <i>et al.</i> , 1990)
<i>A8L</i>		710		VAR-BSH (I: A7L)		0.0	700/710	98	(Shchelkunov <i>et al.</i> , 1995)
<i>MC110L</i>		707		MCV subtype 1		0.0	240/374	64	(Senkevich <i>et al.</i> , 1996)
119R	112786 113652	288	33.6	33.6k protein					(Van Meir and Wittek, 1988)
<i>A8R</i>		288		VAC		5.3e-198	287/288	99	(Goebel <i>et al.</i> , 1990)
<i>A8R</i>		288		VAR-I (BSH:A9R)		3.1e-195	284/288	98	(Shchelkunov <i>et al.</i> , 1995)
<i>MC111R</i>		435		MCV subtype 1		4.4e-94	100/169	59	(Senkevich <i>et al.</i> , 1997)
120L	113929 113645	94	10.5	10.5k protein					(Van Meir and Wittek, 1988)
<i>A10L</i>		95		VAR-BSH (I: A9L)		9.0e-59	78/79	98	(Shchelkunov <i>et al.</i> , 1995)
<i>A9L</i>		99		VAC		9.4e-55	82/91	90	(Goebel <i>et al.</i> , 1990)
<i>MC112L</i>		128		MCV subtype 1		1.0e-29	47/71	66	(Senkevich <i>et al.</i> , 1996)
		69		orf virus		3.0e-16	27/45	60	(Mercer <i>et al.</i> , 1995)
121L	116605 113930	891	102.2	major core protein P4a					(Van Meir and Wittek, 1988)
<i>A10L</i>		891		VAC		0.0	883/891	99	(Vanslyke <i>et al.</i> , 1991)
<i>A11L</i>		892		VAR-BSH (I: A10L)		0.0	442/463	95	(Goebel <i>et al.</i> , 1990)
<i>MC113L</i>		889		MCV subtype 1		5.8e-289	99/177	55	(Shchelkunov <i>et al.</i> , 1995)
									(Senkevich <i>et al.</i> , 1996)
122R	116620 117576	318	36.1	36.1k protein					(Goebel <i>et al.</i> , 1990)
<i>A11R</i>		318		VAC		3.5e-212	318/318	100	(Goebel <i>et al.</i> , 1990)
<i>A11R</i>		319		VAR-I (BSH: A12R)		2.7e-154	242/277	87	(Shchelkunov <i>et al.</i> , 1995)
<i>MC114R</i>		304		MCV subtype 1		2.9e-98	92/154	59	(Senkevich <i>et al.</i> , 1997)
		148		FPV 4a gene		1.9e-13	18/32	56	A20158
123L	118141 117578	187	20.0	virion protein					(Takahashi <i>et al.</i> , 1994)
<i>A12L</i>		192		VAC		4.8e-127	127/128	99	(Goebel <i>et al.</i> , 1990)
<i>A13L</i>		189		VAR-BSH (I: A12L)		5.9e-64	101/144	70	(Shchelkunov <i>et al.</i> , 1995)
<i>MC115L</i>		178		MCV subtype 1		5.9e-37	39/83	46	(Senkevich <i>et al.</i> , 1996)
124L	118377 118165	70	7.6	structural protein					(Takahashi <i>et al.</i> , 1994)
		70		IMV membrane protein					(Jensen <i>et al.</i> , 1996)
<i>A13L</i>		68		p 8		2.4e-42	66/69	95	(Goebel <i>et al.</i> , 1990)
<i>A14L</i>				VAC		4.1e-20	37/64	57	(Shchelkunov <i>et al.</i> , 1995)
				VAR-BSH (I: A13L)					
125L	118757 118485	90	10.0	structural protein					(Takahashi <i>et al.</i> , 1994)
				IMV membrane protein					(Jensen <i>et al.</i> , 1996)
				p 16					

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) / homologies ^e	BLAST ^d expect	BLAST ^c AA id	HSS ^f (%)	references
left	terminal	region:							
A14L		90		VAC		5.3e-62	90/90	100	(Goebel <i>et al.</i> , 1990)
A15L		90		VAR-BSH (I: A14L)		5.3e-61	88/90	97	(Shchelkunov <i>et al.</i> , 1995)
MC118L		94		MCV subtype 1		7.3e-22	31/72	43	(Senkevich <i>et al.</i> , 1996)
		125		human interferon inducible protein		0.23	15/49	30	(Deblandre <i>et al.</i> , 1995)
126L	119209	94	11.0	11k protein					
A15L	118925	94		VAC		4.1e-63	94/94	100	(Goebel <i>et al.</i> , 1990)
A16L		94		VAR-BSH (I:A15L)		1.0e-61	92/94	97	(Shchelkunov <i>et al.</i> , 1995)
MC120L		96		MCV subtype 1		6.7e-08	17/51	33	(Senkevich <i>et al.</i> , 1996)
127L	120326	377	43.4	35k myristylprotein					(Martin <i>et al.</i> , 1997)
A16L	119193	378		VAC		6.3e-288	327/327	100	(Goebel <i>et al.</i> , 1990)
A17L		377		VAR-BSH (I:A16L)		1.5e-283	368/377	97	(Shchelkunov <i>et al.</i> , 1995)
MC121L		364		MCV subtype 1		6.5e-110	45/115	39	(Senkevich <i>et al.</i> , 1996)
128L	120940	203	23.0	IMV membrane protein morphogenesis factor					(Krijnse-Locker <i>et al.</i> , 1996)
	120329								(Rodriguez <i>et al.</i> , 1995)
									(Wolffe <i>et al.</i> , 1996)
A17L		203		VAC		1.0e-141	201/203	99	(Goebel <i>et al.</i> , 1990)
A18L		203		VAR-BSH (I:A17L)		1.0e-141	201/203	99	(Shchelkunov <i>et al.</i> , 1995)
MC122L		179		MCV subtype 1		1.4e-47	36/81	44	(Senkevich <i>et al.</i> , 1996)
129R	120955	493	56.8	DNA helicase					(Koomin and Senkevich, 1992)
	122436			DNA dependent ATPase					(Bayliss and Condit, 1995)
A18R		493		VAC		0.0	488/493	98	(Goebel <i>et al.</i> , 1990)
A18R		493		VAR-I (BSH:A19R)		0.0	478/493	96	(Shchelkunov <i>et al.</i> , 1995)
MC123R		694		MCV subtype 1		5.3e-167	203/403	50	(Senkevich <i>et al.</i> , 1997)
		450		Bacteriophage T5 D10 helicase-like protein		0.0066	13/36	36	P11107
130L	122650	77	8.3	8.3kb protein					(Goebel <i>et al.</i> , 1990)
A19L	122417	77		VAC		2.9e-50	77/77	100	(Goebel <i>et al.</i> , 1990)
A19L		76		VAR-I (BSH: A20L)		1.2e-34	54/64	84	(Shchelkunov <i>et al.</i> , 1995)
MC124L		78		MCV subtype 1		1.5e-13	14/37	37	(Senkevich <i>et al.</i> , 1996)
		1721		HS RIZ, zink finger protein		0.0060	7/16	43	(Buyse <i>et al.</i> , 1995)
131L	123004	117	13.6	13.6k protein					(Goebel <i>et al.</i> , 1990)
A21L	122651	117		VAC		5.3e-83	117/117	100	(Goebel <i>et al.</i> , 1990)
A22L		117		VAR-BSH (I: A20L)		7.2e-82	115/117	98	(Shchelkunov <i>et al.</i> , 1995)
MC125L		114		MCV subtype 1		2.8e-28	23/41	56	(Senkevich <i>et al.</i> , 1996)
132R	123003	426	49.1	49.1k protein					(Goebel <i>et al.</i> , 1990)
A20R	124283	426		VAC		7.6e-298	423/426	99	(Goebel <i>et al.</i> , 1990)
A21R		426		VAR		1.6e-294	418/426	98	(Shchelkunov <i>et al.</i> , 1995)
MC126R		476		MCV subtype 1		3.2e-95	34/131	25	(Senkevich <i>et al.</i> , 1997)
		1118		Pichia klyveri DNA pol		0.069	12/54	22	Y11606
133R	124213	187	21.9	21.9k protein					(Goebel <i>et al.</i> , 1990)
A22R	124776	187		VAR-I (BSH:A23R)		1.1e-126	182/187	97	(Shchelkunov <i>et al.</i> , 1995)
A22R		176		VAC		1.2e-122	174/176	98	(Goebel <i>et al.</i> , 1990)
MC127R		282		MCV subtype 1		5.8e-43	35/85	41	(Senkevich <i>et al.</i> , 1997)
134R	124796	382	44.6	44.6k protein					(Goebel <i>et al.</i> , 1990)
A23R	125944	382		VAC		4.2e-269	382/382	100	(Goebel <i>et al.</i> , 1990)
A23R		382		VARI (BSH:A24R)		1.7e-265	377/382	98	(Shchelkunov <i>et al.</i> , 1995)
MC128R		383		MCV subtype 1		3.5e-136	83/143	58	(Senkevich <i>et al.</i> , 1997)
135R	125966	1155	132.4	RNA pol subunit rpo132					(Hooda-Dhingra <i>et al.</i> , 1990)
	129436								(Amegadzie <i>et al.</i> , 1991b)
A24R		1164		VAC		0.0	794/796	99	(Goebel <i>et al.</i> , 1990)
		1164		CPX rpo132		0.0	794/795	99	(Patel and Pickup, 1989)
A25R		1164		VAR-BSH (I:A24R)		0.0	789/795	99	(Shchelkunov <i>et al.</i> , 1995)
MC129R		1165		MCV subtype 1		0.0	441/565	78	(Senkevich <i>et al.</i> , 1997)
		1162		orf virus		0.0	166/258	64	U33419
				101 matches to RNA pol beta subunit family		<0.036			
right	terminal	region:							
136L	129638	65	7.5	150k CPX-ATI (f)					(Funahashi <i>et al.</i> , 1988)
A25L	129441	65		VAC		1.3e-41	64/65	98	(Goebel <i>et al.</i> , 1990)
		1284		Cowpox (CPX-ATI)		3.2e-15	28/30	93	(Funahashi <i>et al.</i> , 1988)
137L	130916	230	27.1	27.1k protein (f)					(Amegadzie <i>et al.</i> , 1991a)
A30L	130224	498		VAR-BSH (I: A29L)		3.1e-158	216/227	95	(Shchelkunov <i>et al.</i> , 1995)
A26L		322		VAC (ATI flanking protein)		5.6e-142	195/197	98	(Goebel <i>et al.</i> , 1990)
MC131L		513		MCV subtype 1		2.1e-12	19/59	32	(Senkevich <i>et al.</i> , 1996)
MC133L		546		MCV subtype 1		4.2e-11	12/40	30	(Senkevich <i>et al.</i> , 1996)
MC130L		451		MCV subtype 1		2.3e-10	14/40	35	(Senkevich <i>et al.</i> , 1996)
		702		VAR-I A28L (BSH:A29L)		0.0021	12/37	32	(Shchelkunov <i>et al.</i> , 1995)
		726		Camelpox		0.051	11/37	29	(Meyer and Rziha, 1993)
138L	131298	110	12.5	14k membrane protein EEV protein fusion protein					(Rodriguez and Esteban, 1987)
	130966								(Rodriguez and Smith, 1990)
									(Gong <i>et al.</i> , 1990)
A27L		110		VAC		3.3e-70	108/110	98	(Goebel <i>et al.</i> , 1990)
A31L		110		VAR-BSH (I: /A30L)		1.1e-69	107/110	97	(Shchelkunov <i>et al.</i> , 1995)
		117		Camelpox virus		1.5e-69	106/110	96	(Meyer <i>et al.</i> , 1994)
		110		Cowpox virus		1.6e-69	107/110	97	(Meyer <i>et al.</i> , 1994)

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) / homologies ^e	BLAST ^d expect	BLAST ^c AA id	HSS ^f (%)	references
	left	terminal	region:						
		110		Ectromelia virus		6.7e-68	105/110	95	(Meyer <i>et al.</i> , 1994)
		110		Monkeypox virus		8.3e-67	103/110	93	(Meyer <i>et al.</i> , 1994)
		89		Orf virus		4.8e-15	22/57	38	(Naase <i>et al.</i> , 1991)
		188		Myxoma virus		2.5e-12	18/33	54	(Jackson <i>et al.</i> , 1996)
MC133L		546		MCV subtype 1		1.5e-11	26/58	44	(Senkevich <i>et al.</i> , 1996)
		148		Capripox virus HM2 protein		2.6e-10	21/42	50	(Gershon <i>et al.</i> , 1989)
MC131L		513		MCV subtype 1		1.5e-05	18/58	31	(Senkevich <i>et al.</i> , 1996)
139L	131739	146	16.3	16.3k protein					(Amegadzie <i>et al.</i> , 1991a)
A28L	131299	146		VAC		1.7e-103	146/146	100	(Goebel <i>et al.</i> , 1990)
A31.5L		146		VAR-BSH (I: A31L)		2.9e-100	141/146	96	(Shchelkunov <i>et al.</i> , 1995)
		140		Myxoma virus		1.3e-55	30/52	57	(Jackson <i>et al.</i> , 1996)
		140		Capripox virus HM3 protein		3.3e-55	30/49	61	(Gershon <i>et al.</i> , 1989)
MC134L		141		MCV subtype 1		1.0e-53	31/52	59	(Senkevich <i>et al.</i> , 1996)
		143		Amsacta moorei poxvirus		2.0e-14	16/36	44	(Hall and Moyer, 1991)
140L	132657	305	35.4	RNA pol subunit rpo35					(Amegadzie <i>et al.</i> , 1991a)
A29L	131740	305		VAC		3.6e-215	304/305	99	(Goebel <i>et al.</i> , 1990)
A32L		305		VAR-BSH		7.5e-211	297/303	97	(Shchelkunov <i>et al.</i> , 1995)
MC135L		303		MCV subtype 1		7.0e-98	51/103	49	(Senkevich <i>et al.</i> , 1996)
		126		Capripox virus		2.2e-54	46/61	75	(Gershon <i>et al.</i> , 1989)
141L	132853	77	8.7	8.7k protein					(Amegadzie <i>et al.</i> , 1991a)
A30L	132620	77		VAC		5.5e-48	77/77	100	(Goebel <i>et al.</i> , 1990)
A33L		77		VAR		5.5e-48	77/77	100	(Shchelkunov <i>et al.</i> , 1995)
MC136L		67		MCV subtype 1		9.2e-16	18/40	45	(Senkevich <i>et al.</i> , 1996)
142R	133013	125	14.4	14.4k protein					(Smith <i>et al.</i> , 1991)
A31R	133390	124		VAC		2.0e-84	118/124	95	(Goebel <i>et al.</i> , 1990)
A34R		140		VAR		1.6e-79	111/114	97	(Shchelkunov <i>et al.</i> , 1995)
MC138R		117		MCV subtype 1		6.2e-24	39/98	39	(Senkevich <i>et al.</i> , 1997)
143L	134169	269	30.8	30.8k protein					(Smith <i>et al.</i> , 1991)
	133360			ATP/GTP binding motif A					(Koonin <i>et al.</i> , 1993)
A32L		300		VAC		6.4e-190	268/269	99	(Goebel <i>et al.</i> , 1990)
A35L		270		VAR		1.6e-186	263/269	97	(Shchelkunov <i>et al.</i> , 1995)
MC140L		249		MCV subtype 1		7.6e-95	58/94	61	(Senkevich <i>et al.</i> , 1996)
144R	134287	185	20.6	EEV glycoprotein					(Roper <i>et al.</i> , 1996)
A33R	134844	185		VAC		2.1e-124	182/185	98	(Goebel <i>et al.</i> , 1990)
A36R		184		VAR		1.8e-121	103/112	91	(Shchelkunov <i>et al.</i> , 1995)
		185		Ectromelia		2.8e-113	165/185	89	(Roper <i>et al.</i> , 1996)
145R	134868	168	19.6	EEV glycoprotein					(Duncan and Smith, 1992a)
	135374			virulence factor					(McIntosh and Smith, 1996)
				actin microvilli inducer					(Wolffe <i>et al.</i> , 1997)
A34R		168		VAC		1.2e-117	165/168	98	(Goebel <i>et al.</i> , 1990)
A37R		168		VAR-I		1.7e-117	164/168	97	(Shchelkunov <i>et al.</i> , 1995)
		167		FPV ORFs BamHI 2,8,11 hepatic		<0.056	16/66	24	(Tomley <i>et al.</i> , 1988)
		199		lectins homologs					
				HS early T-cell activation		0.0038	12/38	31	(Hamann <i>et al.</i> , 1993)
				antigen CD69					
MC143R		159		MCV subtype 1		0.080	12/48	25	(Senkevich <i>et al.</i> , 1997)
				17 matches to lectins					
146R	135418	176	20.0	20.0k protein					(Smith <i>et al.</i> , 1991)
A35R	135948	176		VAC		1.4e-126	176/176	100	(Goebel <i>et al.</i> , 1990)
A38R		60		VAR-I		2.9e-37	57/60	95	(Shchelkunov <i>et al.</i> , 1995)
MC145R		233		MCV subtype 1		1.2e-07	18/55	32	(Senkevich <i>et al.</i> , 1997)
147R	136015	208	23.8k	EEV membrane protein					(Parkinson and Smith, 1994)
	136641			virulence factor					(Smith <i>et al.</i> , 1991)
A36R		221		VAC		2.8e-143	140/141	99	(Goebel <i>et al.</i> , 1990)
A39R		216		VAR		2.1e-89	138/177	77	(Shchelkunov <i>et al.</i> , 1995)
				19 matches to asn/ser-rich proteins		<0.41			
148R	136705	263	29.8	29.8k protein					(Smith <i>et al.</i> , 1991)
A37R	137496	263		VAC		6.8e-183	261/262	99	(Goebel <i>et al.</i> , 1990)
A40R		68		VAR		4.9e-37	61/67	91	(Shchelkunov <i>et al.</i> , 1995)
149L	138589	277	31.5	31.5k protein					(Amegadzie <i>et al.</i> , 1991a)
A38L	137756	277		VAC		9.3e-198	274/277	98	(Goebel <i>et al.</i> , 1990)
A41L		277		VAR		1.6e-187	259/277	93	(Shchelkunov <i>et al.</i> , 1995)
		303		Rattus norvegicus CD47		3.9e-24	23/86	26	(Nishiyama <i>et al.</i> , 1997)
		324		MM integrin assoc. protein		1.0e-21	23/86	26	(Lindberg <i>et al.</i> , 1993)
		323		human CD47 precursor		5.0e-19	28/86	32	(Campbell <i>et al.</i> , 1992)
150R	138606	83	9.4	semaphorin-like protein					(Kolodkin <i>et al.</i> , 1993)
	138857			(f1)					
A39R		403		VAC		8.0e-46	73/76	96	(Goebel <i>et al.</i> , 1990)
A42R		74		VAR-I		8.6e-44	67/71	94	(Shchelkunov <i>et al.</i> , 1995)
151R	139163	210	23.9	semaphorin-like protein					(Kolodkin <i>et al.</i> , 1993)
	139795			(f2)					
A39R		403		VAC		3.0e-147	209/210	99	(Goebel <i>et al.</i> , 1990)
A43R		139		VAR (I:A44R)		1.8e-68	91/105	86	(Shchelkunov <i>et al.</i> , 1995)
		653		semaphorin-like protein		1.7e-20	29/79	36	(Ensser and Fleckenstein, 1995)
				Alcelaphine herpesvirus					
				37 matches to semaphorin					

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) homologies ^e	BLAST ^d expect	BLAST ^c AA id	HSS ^f (%)	references
left	terminal	region:							
				/collapsin gene family					
152R	139821 140327	168	19.4	NK cell receptor homolog lectin-like protein					(Scheifflinger et al., unpubl.) (Smith et al., 1991)
<i>A40R</i>		168		VAC		6.6e-97	134/137	97	(Goebel et al., 1990)
<i>A45R</i>		61		VAR-I (BSH: A43.5R)		9.6e-36	54/59	91	(Shchelkunov et al., 1995)
		233		HS natural killer (NK) cell protein group 2-A, B		4.5e-11	20/74	27	(Houchins et al., 1991)
		240		HS type II membrane protein		6.9e-11	16/36	44	(Adamkiewicz et al., 1994)
		182		MM NK cell receptor		5.5e-09	16/36	44	(Giorda et al., 1992)
		179		HS CD 94		1.7e-07	11/29	37	(Chang et al., 1995a)
				127 matches to lectins including NK cell surface proteins and snake venoms					
153L	141025	219	25.1	25.1k protein					(Smith et al., 1991)
<i>A41L</i>	140366	219		VAC		1.9e-158	218/219	99	(Goebel et al., 1990)
<i>A44L</i>		218		VAR-BSH (I:A46L)		1.4e-152	152/159	95	(Shchelkunov et al., 1995)
		244		VAC B29R/C23L		0.0076	12/53	22	(Goebel et al., 1990)
		258		Rabbit fibroma virus T1		0.057	13/49	26	(Upton et al., 1987)
154R	141197 141583	128	14.5	profilin-like protein					(Blasco et al., 1991)
<i>A42R</i>		133		VAC		1.2e-87	85/87	97	(Smith et al., 1991)
<i>A47R</i>		133		VAR-I (BSH:A45R)		1.4e-85	82/87	94	(Goebel et al., 1990)
		140		HS profilin		2.2e-23	19/45	42	(Shchelkunov et al., 1995)
				10 matches profilin family					
155R	141621 142193	190	22.1	class I membrane glycoprotein					(Smith et al., 1991)
<i>A43R</i>		194		VAC		1.5e-137	162/164	98	(Duncan and Smith, 1992b)
<i>A48R</i>		195		VAR-I (BSH:A46R)		1.9e-128	101/109	92	(Goebel et al., 1990)
		51		HS leukocyte antigen		0.096	7/23	30	(Shchelkunov et al., 1995)
				X79517					
156R	142201 142437	78	8.8	8.8k protein					(Smith et al., 1991)
		78		VAC-WR SalF6R		3.9e-45	78/78	100	(Smith et al., 1991)
		258		rabbit myosin heavy chain		0.00048	13/39	33	A02985
				144 matches to various asp/glu/lys-rich proteins					
157L	143577 142537	346	39.4	3β-hydroxysteroid dehydrogenase (3β-HSD)					(Moore and Smith, 1992)
<i>A44L</i>		346		VAC		4.5e-249	342/346	98	(Blasco et al., 1991)
<i>A47L</i>		210		VAR-BSH (I: A49L)		1.1e-136	185/195	94	(Goebel et al., 1990)
<i>MC152R</i>		354		MCV subtype I		8.2e-104	123/272	45	(Shchelkunov et al., 1995)
		369		FPV		3.1e-83	33/85	38	(Senkevich et al., 1996)
				matches to dihydroflavonol reductases, cholesterol dehydrogenases, UDP- galactose-4-epimerases					
				>2.8e-05					
158R	143624 143989	121	13.3	superoxide dismutase-like protein					(Blasco et al., 1991)
<i>A45R</i>		125		VAC		2.1e-82	94/96	97	(Smith et al., 1991)
<i>A51R</i>		125		VAR-I BSH A48R		1.1e-82	93/96	96	(Goebel et al., 1990)
				117 matches with superoxide dismutase family					
				<0.027					
159R	143979	241	27.6	27.6k protein					(Smith et al., 1991)
<i>A46R</i>	144701	214		VAC		9.6e-167	238/240	99	(Goebel et al., 1990)
<i>A52R</i>		240		VAR-I (BSH: A49R)		5.6e-164	233/240	97	(Shchelkunov et al., 1995)
160L	145465	238	27.6	27.6k protein					(Goebel et al., 1990)
<i>J1L</i>	144749	244		VAR		5.1e-146	114/127	89	(Shchelkunov et al., 1995)
<i>A47L</i>		244		VAC		8.2e-135	121/127	95	(Goebel et al., 1990)
				integrin lipid binding motif					
				(Smith et al., 1991)					
161R	145564	204	23.2	thymidylate kinase					(Smith et al., 1991)
<i>A48R</i>	146178	204		VAC		5.2e-140	204/204	100	(Goebel et al., 1990)
<i>J2R</i>		205		VAR		1.1e-137	161/165	97	(Shchelkunov et al., 1995)
				16 matches to thymidylate kinase family					
				<0.49					
162R	146202	162	18.8	18.8k protein					(Smith et al., 1991)
<i>A49R</i>	146690	162		VAC		6.0e-106	159/162	98	(Goebel et al., 1990)
<i>J3R</i>		162		VAR		2.4e-103	154/162	95	(Shchelkunov et al., 1995)
163R	146722	552	63.5	DNA ligase					(Kerr and Smith, 1989)
<i>A50R</i>	148380	552		VAC		0.0	547/552	99	(Goebel et al., 1990)
<i>J4R</i>		552		VAR-I		0.0	537/552	97	(Shchelkunov et al., 1995)
		922		HS DNA ligase III		2.1e-235	102/165	61	(Wei et al.,)
		559		shope fibroma ligase		9.9e-213	95/200	47	(Parks et al., 1994)
		564		FPV ligase		3.0e-195	101/170	59	(Skinner et al., 1994)
				31 matches mainly to DNA ligase family					
				<0.029					
164R	148426	310	34.9	34.9k protein					(Antoine et al., 1996)
<i>A51R</i>	149358	334		VAC		1.5e-217	267/274	97	(Goebel et al., 1990)
<i>J5R</i>		334		VAR		9.1e-208	251/274	91	(Shchelkunov et al., 1995)

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) / homologies ^e	BLAST ^d expect	BLAST ^c AA id	HSS ^f (%)	references
left	terminal	region:		fusion of <i>A51R/A55R</i> ORFs					(Antoine <i>et al.</i> , 1996)
165R	149416	315	34.8	hemagglutinin					(Shida, 1986)
<i>A56R</i>	150363	315		VAC		1.8e-211	312/315	99	(Goebel <i>et al.</i> , 1990)
<i>J9R</i>		313		VAR-I (BSH:J7R)		4.3e-178	183/238	76	(Shchelkunov <i>et al.</i> , 1995)
		310		raccoonpox		1.5e-91	74/104	71	(Cavallaro and Esposito, 1992)
				124 matches to various proteins		<0.34			
166R	150659	97	11.4	guanylate kinase (f)					(Smith <i>et al.</i> , 1991)
<i>A57R</i>	150952	151		VAC		3.2e-62	94/97	96	(Goebel <i>et al.</i> , 1990)
<i>J10R</i>		151		VAR (BSH:J8R)		2.2e-57	88/97	90	(Shchelkunov <i>et al.</i> , 1995)
		198		MM guanylate kinase		4.3e-24	39/91	42	(Brady <i>et al.</i> , 1996)
		197		HS guanylate kinase		2.8e-20	35/91	38	(Brady <i>et al.</i> , 1996)
				21 matches mainly to guanylate kinases		<0.20			
167R	151103	300	34.3	serine/threonine protein kinase					(Howard and Smith, 1989)
	152005								(Banham and Smith, 1992)
									(Lin <i>et al.</i> , 1992)
<i>B1R</i>		300		VAC		7.1e-215	298/300	99	(Goebel <i>et al.</i> , 1990)
<i>B1R</i>		300		VAR-I		2.7e-210	289/300	96	(Shchelkunov <i>et al.</i> , 1995)
		283		VAC B12R		4.9e-49	27/53	50	(Goebel <i>et al.</i> , 1990)
				100 matches mainly to protein kinase family		<0.00031			
168R	152144	96	11.5	24.6k protein (f1)					
<i>B2R</i>	152434	219		VAC		8.5e-38	54/60	90	(Goebel <i>et al.</i> , 1990)
		149		histone H2A pea		0.59	16/50	32	P40281
169R	152289	143	16.1	24.6k protein (f2)					(Goebel <i>et al.</i> , 1990)
<i>B2R</i>	152720	219		VAC		5.7e-86	124/128	96	(Goebel <i>et al.</i> , 1990)
170R	152917	179	20.9	20.9k protein (f)					
<i>B3R</i>	153456	124		VAC		8.2e-33	51/56	91	(Goebel <i>et al.</i> , 1990)
		167		VAC WR		5.3e-45	51/56	91	(Smith <i>et al.</i> , 1991)
		92		VAR-GAR H5R		3.4e-06	19/28	67	U18339
171R	153683	177	21.4	65k ank-like protein virulence factor (f1)					(Howard <i>et al.</i> , 1991)
	154216			VAC		8.5e-107	151/154	98	(Mossman <i>et al.</i> , 1996)
<i>B4R</i>		558		VAR-I (BSH:B5R)		1.7e-98	140/154	90	(Goebel <i>et al.</i> , 1990)
<i>B6R</i>		558							(Shchelkunov <i>et al.</i> , 1995)
172R	154107	409	47.7	65k ank-like protein virulence factor (f2)					(Howard <i>et al.</i> , 1991)
	155336			VAC		2.4e-283	195/201	97	(Mossman <i>et al.</i> , 1996)
<i>B4R</i>		558		VAR-I (BSH:B5R)		2.3e-270	185/201	92	(Goebel <i>et al.</i> , 1990)
<i>B6R</i>		558		MYX M-T5 protein		5.5e-10	19/57	33	(Shchelkunov <i>et al.</i> , 1995)
		483		MM ankryrin 3		9.7e-10	22/54	40	(Mossman <i>et al.</i> , 1996)
		1765		orf virus		9.7e-10	22/54	40	(Peters <i>et al.</i> , 1995)
		516		VAC B18R		1.8e-09	16/47	34	U34774
		574		VAR-I B19R		3.3e-09	11/23	47	(Goebel <i>et al.</i> , 1990)
		574		HS KIAA0379		3.6e-09	19/72	26	(Shchelkunov <i>et al.</i> , 1995)
		882		CPX host range gene		5.1e-09	20/52	38	AB002377
		668		VAC WR hr gene		1.7e-08	14/47	29	(Spehner <i>et al.</i> , 1988)
		237		VAC MIL		2.8e-08	15/47	31	(Kotwal and Moss, 1988a)
		472		CPX OIL		5.1e-07	23/81	28	(Goebel <i>et al.</i> , 1990)
		474		VAR OIL		8.7e-07	22/61	36	(Safronov <i>et al.</i> , 1996)
		446		CPX DIL		8.8e-07	23/81	28	(Shchelkunov <i>et al.</i> , 1995)
		437		VAC C9L		1.7e-06	8/27	29	(Safronov <i>et al.</i> , 1996)
		634		159 matches including ankryrin proteins		7.8e-05			(Goebel <i>et al.</i> , 1990)
173R	155424	317	35.1	ps/hr protein/EEV gp42					(Takahashi-Nishimaki <i>et al.</i> , 1991)
	156377			complement control protein					(Engelstad <i>et al.</i> , 1992)
<i>B5R</i>		317		VAC		1.6e-232	312/317	98	(Isaacs <i>et al.</i> , 1992)
<i>B7R</i>		317		VAR-I (BSH:B6R)		7.1e-220	294/316	93	(Goebel <i>et al.</i> , 1990)
		259		CPX D17L		2.1e-12	16/52	30	(Shchelkunov <i>et al.</i> , 1995)
				186 matches to complement control protein family		<7.7e-05			(Safronov <i>et al.</i> , 1996)
174R	156474	173	20.2	20.2k protein					
<i>B6R</i>	156995	173		VAC		1.5e-121	173/173	100	(Goebel <i>et al.</i> , 1990)
<i>B7R</i>		65		VAR-BSH (I:B8R)		6.0e-40	62/65	95	(Shchelkunov <i>et al.</i> , 1995)
		685		NAD-protein ADP ribosyl-transferase phage T4		0.56	17/56	30	SXBPT4
175R	157033	177	20.7	20.7k protein					
<i>B7R</i>	157566	182		VAC		7.8e-129	95/108	87	(Goebel <i>et al.</i> , 1990)
		184		VAC C8L		0.16	9/44	20	(Goebel <i>et al.</i> , 1990)
		182		CPX D12L		0.49	8/36	22	(Safronov <i>et al.</i> , 1996)
				EF-hand calcium-binding domain					
176R	157621	226	26.0	31k interferon-gamma receptor (f)					(Upton <i>et al.</i> , 1992)
	158301			VAC		3.3e-164	116/123	94	(Alcami and Smith, 1995)
<i>B8R</i>		272		VAR-BSH (I:B9R)		3.0e-153	111/123	90	(Goebel <i>et al.</i> , 1990)
<i>B8R</i>		266		BCT		2.6e-151	110/123	89	(Shchelkunov <i>et al.</i> , 1995)
		266		swinepox C6		3.2e-09	12/31	38	(Mossman <i>et al.</i> , 1995b)
		274							(Massung <i>et al.</i> , 1993)

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) / homologies ^d	BLAST ^d expect	BLAST ^c AA id	HSS ^f (%)	references
left terminal region:									
177R	158458	72	8.3	8.3k protein					
<i>B9R</i>	158676	77		VAC		3.0e-49	60/60	100	(Goebel <i>et al.</i> , 1990)
		240		capripox T4 protein		1.2e-09	16/44	36	M28823
		237		shope fibroma virus		0.0057	15/50	30	F43692
178R	158639	158	17.9	17.9k protein					
<i>B10R</i>	159115	166		VAC		4.7e-110	146/146	100	(Goebel <i>et al.</i> , 1990)
		530		swinepox VC04		0.040	13/42	30	(Massung <i>et al.</i> , 1993)
		689		kelch protein D. melanogaster		0.14	12/54	27	(Xue and Cooley, 1993)
									(Senkevich <i>et al.</i> , 1993b)
179R	159187	74	8.5	8.5k protein					
<i>B11R</i>	159411	88		VAC		9.2e-43	70/73	95	(Goebel <i>et al.</i> , 1990)
				177 matches to glu/asn rich proteins					
180R	159478	283	33.3	protein kinase					(Howard and Smith, 1989)
<i>B12R</i>	160329	283		VAC		1.8e-207	282/283	99	(Goebel <i>et al.</i> , 1990)
<i>B12R</i>		134		VAR-I		8.7e-26	31/54	57	(Shchelkunov <i>et al.</i> , 1995)
		300		VAC B1R		1.7e-54	26/53	49	(Goebel <i>et al.</i> , 1990)
		300		VAR-I B1R		7.7e-53	25/53	47	(Shchelkunov <i>et al.</i> , 1995)
				120 matches mainly to protein kinase family		<0.34			
181R	160437	116	13.0	ICE inhibitor / SPI-2 (f1)					(Kotwal and Moss, 1989)
	160787								(Smith <i>et al.</i> , 1989)
<i>B13R</i>				VAC					(Ray <i>et al.</i> , 1992)
<i>B13R</i>		116		VAR-I (BSH:B12R)		3.0e-72	111/116	95	(Goebel <i>et al.</i> , 1990)
		344		CPX crmA		2.7e-69	105/114	92	(Shchelkunov <i>et al.</i> , 1995)
		341		VAC C12L (SPI-1)		2.8e-39	66/100	66	(Pickup <i>et al.</i> , 1986)
		353		Ectromelia serpin		2.1e-23	25/34	73	(Goebel <i>et al.</i> , 1990)
		344		rabbitpox SPI-1		9.2e-23	24/34	70	(Senkevich <i>et al.</i> , 1993b)
		357		CPX SPI-1		5.5e-22	25/34	73	(Ali <i>et al.</i> , 1994)
		355		VAR-I B25R (BSH:B21R)		1.4e-21	25/36	69	(Ali <i>et al.</i> , 1994)
		372		CPX serpin-like protein		1.7e-21	25/34	73	(Shchelkunov <i>et al.</i> , 1995)
		372		135 matches mainly to serpins		1.7e-36	25/36	69	(Ali <i>et al.</i> , 1994)
						<0.12			
182R	160762	222	24.9	ICE inhibitor/SPI-2 (f2)					see above
<i>B14R</i>	161430	222		VAC		6.2e-158	218/222	98	(Goebel <i>et al.</i> , 1990)
		345		VAC WR		9.4e-156	215/221	97	(Kotwal and Moss, 1989)
		345		rabbit pox SPI-2		1.6e-153	211/221	95	(Ali <i>et al.</i> , 1994)
		341		CPX crmA		4.5e-148	203/220	92	(Pickup <i>et al.</i> , 1986)
<i>B13R</i>		344		VAR-I (BSH:B12R)		1.5e-146	203/220	92	(Shchelkunov <i>et al.</i> , 1995)
				309 matches see above		<1.3e-21			
183R	161506	143	16.7	16.7k protein					(Smith and Chan, 1991)
<i>B15R</i>	161937	149		VAC		3.6e-105	97/98	98	(Goebel <i>et al.</i> , 1990)
<i>B14R</i>		149		VAR-I (BSH:B13R)		9.1e-104	95/98	96	(Shchelkunov <i>et al.</i> , 1995)
		153		VAR-I D1L (BSH:D2L)		8.8e-31	25/52	48	(Shchelkunov <i>et al.</i> , 1995)
		181		VAC C16L/B22R		1.0e-26	25/52	48	(Goebel <i>et al.</i> , 1990)
		159		capripox T3A		1.4e-17	17/42	40	(Gershon and Black, 1989a)
		151		rabbit fibroma T3A		2.6e-07	17/44	38	(Upton <i>et al.</i> , 1987)
		190		VAC A52R		0.073	10/28	35	(Goebel <i>et al.</i> , 1990)
		149		VAC WR K7R		0.21	7/22	31	(Boursnell <i>et al.</i> , 1988)
		149		VAR-1C4R		0.30	7/22	31	(Shchelkunov <i>et al.</i> , 1995)
		161		CPX M6R		0.51	7/22	31	(Safronov <i>et al.</i> , 1996)
184R	162021	326	36.6	interleukin-1B receptor (IL-1B R)					(Alcami and Smith, 1992)
	163001								(Spriggs <i>et al.</i> , 1992)
		326		VAC-WR B15R		2.8e-229	323/326	99	(Smith <i>et al.</i> , 1991)
		326		CPX B16		2.3e-217	306/326	93	(Spriggs <i>et al.</i> , 1992)
<i>B16R</i>		290		VAC		4.4e-202	287/290	98	(Goebel <i>et al.</i> , 1990)
<i>B17R</i>		69		VAR-I (BSH:deleted)		8.1e-38	59/68	86	(Shchelkunov <i>et al.</i> , 1995)
		296		HS type II IL-1 receptor		1.7e-36	28/75	37	U64094
				271 matches mainly to IL-1 receptors, growth factor receptors and Ig family proteins		<0.011			
185L	164069	340	39.6	39.6k protein					
<i>B17L</i>	163047	340		VAC		4.8e-248	335/340	98	(Goebel <i>et al.</i> , 1990)
<i>B15L</i>		340		VAR-BSH (I:B18L)		2.7e-241	325/340	95	(Shchelkunov <i>et al.</i> , 1995)
186R	164209	574	68.0	68k ank-like protein					(Smith <i>et al.</i> , 1991)
<i>B18R</i>	165933	574		VAC		0.0	560/574	97	(Goebel <i>et al.</i> , 1990)
<i>B19R</i>		574		VAR-I (BSH:B16R)		0.0	539/574	93	(Shchelkunov <i>et al.</i> , 1995)
				100 matches mainly to poxvirus ankyrin proteins		<0.53			
187R	165999	234	27.5	surface antigen, IFN-alpha/beta receptor (f)					(Ueda <i>et al.</i> , 1990)
	166703								(Symons <i>et al.</i> , 1995)
									(Colamonici <i>et al.</i> , 1995)
<i>B19R</i>		353		VAC (WR:B18R)		1.4e-163	218/233	93	(Goebel <i>et al.</i> , 1990)
<i>B20R</i>		354		VAR-I (BSH:B17R)		1.53-149	111/133	83	(Shchelkunov <i>et al.</i> , 1995)
		569		HS interleukin-1 receptor		0.0051	15/43	34	(McMahan <i>et al.</i> , 1991)
				28 matches mainly to IL-1 receptors		<0.53			
188R	167202	70	8.2	8.2k protein (f)					

TABLE 1—Continued

ORF ^a	START STOP	AA ^b	kDa ^c	name / function	(putative) / homologies ^e	BLAST ^d expect	BLAST ^c AA id	HSS ^f (%)	references
left terminal region:									
B22R	167414	1897		VAR-BSH (I:B26R)		9.9e-23	31/38	81	(Shchelkunov <i>et al.</i> , 1995)
189R	167897	188	21.7	21.7k protein					
B22R	168463	181		VAC B22R/C16L		2.9e-111	95/104	91	(Goebel <i>et al.</i> , 1990)
D1L		153		VAR-I (BSH:D2L)		1.2e-88	66/71	92	(Shchelkunov <i>et al.</i> , 1995)
		149		VAC B15R		7.2e-19	25/52	48	(Goebel <i>et al.</i> , 1990)
		159		capripox T3A		8.0e-05	15/45	33	(Gershon and Black, 1989a)
		151		VAC C6L		0.25	12/46	26	(Goebel <i>et al.</i> , 1990)
		156		VAR (I:D9L;BSH:D12L)		0.26	12/46	26	(Shchelkunov <i>et al.</i> , 1995)
190R/004L	168531	233	26.9	45k ank-like protein (f2)					
B23R	169232			VAC (C17L/B23R)		6.2e-159	110/110	100	(Goebel <i>et al.</i> , 1990)
D1L		386		VAR-BSH		9.1e-31	46/49	93	(Shchelkunov <i>et al.</i> , 1995)
		669		CPX host range		1.1e-13	22/50	44	(Spehner <i>et al.</i> , 1988)
		452		VAR-I D6L (BSH:D8L)		1.7e-11	21/50	42	(Shchelkunov <i>et al.</i> , 1995)
		574		VAR-I B19R (BSH: B16R)		1.2e-05	22/73	30	(Shchelkunov <i>et al.</i> , 1995)
		574		VAC B18R (WR: B17R)		8.6e-05	22/73	30	(Goebel <i>et al.</i> , 1990)
		634		VAC C9L		0.00011	11/24	45	(Kotwal and Moss, 1988a)
		585		VAR-I G1R		0.00013	22/74	29	(Shchelkunov <i>et al.</i> , 1995)
		516		orf virus		0.0088	15/49	30	(Sullivan <i>et al.</i> , 1995b)
		153		VAR-I D7L (BSH:D10L)		0.014	12/28	42	(Shchelkunov <i>et al.</i> , 1995)
191R/003L	169309	102	12.1	45k ank-like protein (f1)					
B23R	169617			VAC C17L/B23R		1.3e-39	62/63	98	(Goebel <i>et al.</i> , 1990)
192R/002L	170305	176	19.7	secre. TNF receptor (f)					
G2R	170835	355		CPX crmB		5.1e-71	76/83	91	(Upton <i>et al.</i> , 1991a)
		348		VAR-BSH		1.0e-66	73/83	87	(Hu <i>et al.</i> , 1994)
		326		Myxoma virus T2		4.9e-30	21/37	56	(Shchelkunov <i>et al.</i> , 1995)
		325		Rabbit fibroma Virus T2		1.8e-28	17/36	47	(Upton <i>et al.</i> , 1991a)
		202		CPX C4L		8.7e-15	30/51	58	(Upton <i>et al.</i> , 1987)
B25R		346		HS TNF receptor		1.9e-08	14/26	53	(Heller <i>et al.</i> , 1990)
		259		VAC (C19L/B25R)		0.00026	16/19	84	(Safronov <i>et al.</i> , 1996)
		277		human CD40L receptor		0.0015	11/24	45	(Goebel <i>et al.</i> , 1990)
				30 matches to TNF receptors and surface proteins		<0.39			(Stamenovic <i>et al.</i> , 1989)
193R/001L	171267	136	14.9	35k major secr. protein chemokine receptor (f)					
B29R	171677			VAC (C23L/B29R)		6.0e-57	41/42	97	(Patel <i>et al.</i> , 1990)
G5R		244		VAR-I		8.9e-51	46/49	93	(Graham <i>et al.</i> , 1997)
		253		CPX ORFB		5.6e-49	40/42	95	(Goebel <i>et al.</i> , 1990)
		258		SFV T1 protein		2.5e-20	23/42	54	(Shchelkunov <i>et al.</i> , 1995)
		260		Myxoma virus T1/35kDa		1.5e-14	21/42	50	(Hu <i>et al.</i> , 1994)
									(Upton <i>et al.</i> , 1987)
									(Graham <i>et al.</i> , 1997)

^a Open reading frame coding for at least 65 amino acids (for exceptions see text); minor ORFs located in reverse orientation within large ORFs or ORFs located in the repeat regions of the ITRs (see text) are not listed; the MVA ORFs (boldface), listed consecutively as appearing in the genome, and homologs in the Copenhagen strain (in italics), in the variola strains and in the molluscum contagiosum, are listed in this row. Split ORFs are boxed.

^b Number of deduced amino acids (AA) encoded within an ORF.

^c Predicted M_r (kDa) for the unmodified protein.

^d The lowest Poisson probability determined by the BLAST search (Altschul *et al.*, 1990). The Expect value of 0.0 indicates a probability of zero that an alignment occurs by chance; low Expect values correspond to high homology and vice versa.

^e Amino acid identity (AA id) of first high-scoring segment pair in the BLASTp protocol.

^f Amino acid identity of first high-scoring segment pair (HSS)%.

^g Homologies based on searching PIR and SWISS-PROT databases (BLASTp nr).

^h Duplicated ORFs located in ITRs.

ⁱ Fragment; complete homologous ORF present in related poxvirus (see reference).

^j Variola India (I) or variola Bangladesh (BSH) sequences; in cases where the variola sequences are not identical, the variola strain first appearing in the blast search protocol is listed.

^k ank, ankyrin.

^l HS, homo sapiens.

^m MM, *Mus musculus*.

structures reflecting the natures of their DNA templates (not shown). For this family of hypothetical proteins, no significant homologies were found except for the homology to the ORF G4R, the last ORF present in the repeat region of the right terminus of the Brazilian alastrim variola minor virus strain Garcia-1966 (Masung *et al.*, 1996). Minor ORFs located in the reverse orientation within large ORFs and minor overlapping

ORFs were analyzed but no homologies except for the CPN homologs (Goebel *et al.*, 1990) were found; these ORFs are also not listed in Table 1. Although all MVA ORFs were named systematically according to their appearance in the genome, the established ORF nomenclature of the CPN strain (Goebel *et al.*, 1990) was used in this report for the homologous MVA ORFs unless otherwise indicated.

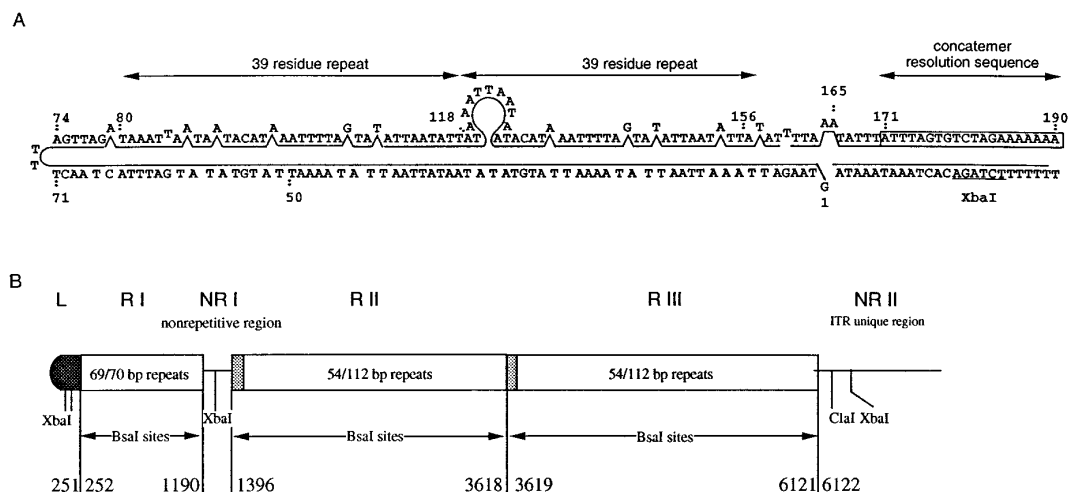


FIG. 1. (A) Structure of the terminal hairpin loops of MVA. The program DNAsis (Hitachi, Inc.) was used to calculate the most stable basepairing. The location of the 39 residue tandem repeats and the concatemer resolution sequence (Merchinsky and Moss, 1989) are indicated by arrows. The G-residue of the first mismatched basepair was defined as residue 1. Thus, the database entry starts with this G-residue and proceeds leftward around the hairpin. (B) Repeat structure of the termini. The 9.8-kb-sized inverted terminal repeat (ITR) consists of six sequence elements, the terminal hairpin loop (L), the repeat regions I–III (RI–RIII), and the nonrepeated regions I and II (NRI–II). Restriction sites critical for cloning and characterization of the repeats (*Clal*, *XbaI*, *BsaI*) are indicated; the recognition sequence of the enzyme *BsaI* is part of the basic repeat unit and thus occurs frequently within the repeat regions. The numbers indicate the positions of the sequence elements within the MVA genomic sequence.

Structure of termini

The linear double-stranded DNA genome of poxviruses has covalently closed termini; the telomeric regions are identical but inverted in sequence (review: Moss, 1996). Within the poxviruses, ITRs are variable in sequence and length; the CPN and the Shope fibrome ITRs, for instance, are 12 kb in size (Cabirac *et al.*, 1985; Goebel *et al.*, 1990) and encode for up to 12 ORFs, while the variola Bangladesh (VAR-BSH) ITR is 725 bp long and does not include ORFs larger than 65 amino acids (Masung *et al.*, 1994). In MVA the ends of the genome contain a 9.8-kb ITR that are identical up to positions 9809 and 168,280.

To characterize the incompletely base-paired terminal hairpin loops, which are characteristic for poxviral ITRs (Moss, 1996), telomeric RNA transcribed from the concatemer resolution sequence (Hu and Pickup, 1991) was converted into cDNA and sequenced. The MVA terminal hairpin loops are 165 residues in size, differing from the usual size of about 100 bases. The loop contains a perfect 39-nucleotide-long tandem repeat at positions 80–118 and 119–156, not present in the CPN strain (Fig. 1A). Similar to the CPN sequence, the first base of the MVA genome was defined to be the first mismatched residue of the hairpin loop (see below). Thus, the database entry, consisting of the upper DNA strand in 5′–3′ orientation, starts with this G-residue and proceeds leftward around the 165 bases of the hairpin (see Fig. 1) and proceeds to the last base 177,923, the junction to the right hairpin loop, that is formally provided by the lower DNA strand and therefore not repeated in the database entry. The left concatemer resolution sequence is located adjacent to the hairpin (positions 171–190; see Fig.

1); the right concatemer resolution sequence is located at positions 177,899–177,918.

The structure of the repeated elements at both ends of the genome are depicted in Fig. 1B. Six segments were identified within the ITR; three regions of tandem repeats (RI, RII, and RIII) are located next to the hairpin loop (L) with an intervening nonrepetitive segment NRI. The inner part of the ITR consists of another nonrepetitive sequence NR II. Adjacent to the hairpin loop, an outer bloc of 13 tandem repeats (RI; Fig. 1B) is located from bases 252 to 1190; the equivalent region in the CPN strain is similarly organized but about three times larger. The RI region is composed of two types of different repeated elements, the 69- and the 70-bp repeat. Southern blot analyses confirmed that this region is responsible for a microheterogeneity of the terminal 1.1-kb *XbaI* fragment (not shown). The outer bloc is followed by the nonrepetitive region NRI (positions 1191 to 1395). Interestingly, a sequence stretch starting at position 1396 is repeated in position 3619 and nowhere else in the genome. Regions RII (positions 1396–3618) and RIII (positions 3619–6121) are very similar to each other and obviously the result of a duplication. Thus, MVA has two inner blocs, RII and RIII, 2.2 and 2.5 kb in length, respectively. The tandem repeats of the RII–RIII region start at base 1500 and end at 6121. RII and RIII contain clusters from one to seven copies of a conserved 54-bp repeat element also found in the CPN strain. Between these clusters, repeat elements similar to the 54-bp repeat element, but with variations in the sequence and length, are found. All repeats in RI, RII, and RIII have a 14-bp sequence (AA-GAGAGAAAGAGA) in common, which is repeated 77

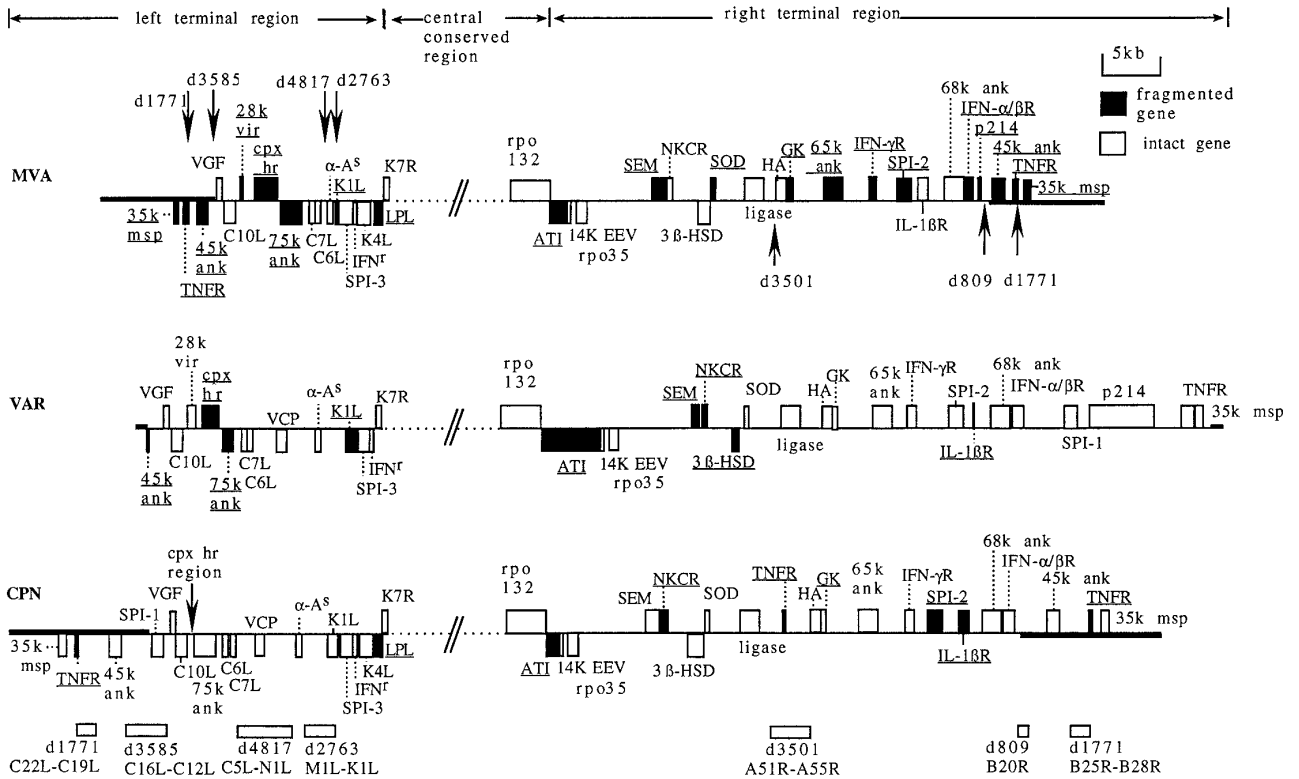


FIG. 2. Maps of the left and right terminal regions of the vaccinia strains MVA and Copenhagen (CPN) and variola virus (VAR). A selection of genes involved in host-virus interaction is shown. Filled boxes indicate fragmented and open boxes structurally intact genes; names of fragmented genes are underlined. Deletion >150 bp in MVA relative to the CPN strain are indicated by bars located below the CPN map; the numbers refer to the size of the deletion (d) in basepairs. Vertical arrows in the MVA map indicate the positions of the deletions. ORFs in the left terminal region: 35k msp, 35-kDa major secreted protein, chemokine receptor (C23L); TNFR, tumor necrosis factor receptor (C22L); 45k ank, 45-kDa ankyrin-like protein (C17L); VGF, vaccinia growth factor (C11R); 28k vir, 28-kDa virulence factor (VAR-BSH D6R); cpx hr, 77-kDa cowpox host range protein (VAR ORFs D5L and D6L); SPI-1, serpin SPI-1 (C12L); 75k ank, 75-kDa ankyrin-like protein (C9L); C6L, 18.2k protein of unknown function; C7L, host range protein; VCP, 35-kDa vaccinia complement control protein (C3L); α -A^s, alpha-amanitin-sensitive protein (N2L); K1L, host range gene; SPI-3, serpin SPI-3 (K2L); IFN^r, interferon resistance (K3L); LPL, lysophospholipase-like gene (K5L). ORFs in the right terminal region: rpo132 (35), 132 (35)-kDa subunit of the RNA polymerase (A24R and A29L); ATI, cowpox A-type inclusion body region (A25L); 14k EEV, 14-kDa extracellular enveloped virus protein (A27L); SEM, semaphorin-like protein (A39R); NKCR, natural killer cell receptor homolog (A40R); 3 β -HSD, 3 β -hydroxysteroid dehydrogenase (A44L); SOD, superoxide dismutase-like protein (A45R); HA, hemagglutinin (A56R); GK, guanylate kinase (A57R); 65k ank, 65-kDa ankyrin-like protein (B4R); IFN- γ R, interferon- γ receptor (B8R); SPI-2, serpin SPI-2 (B13R); IL-1 β R, interleukin-1 β receptor (B16R); 68k ank, 68-kDa ankyrin (B18R); IFN- α/β R, interferon- α/β receptor (B19R); p214, variola 214-kDa protein (VAR B22R). Boldface horizontal lines indicate the extent of the inverted terminal repeats. Dotted lines help to identify the respective gene locus.

times, found for the first time at position 359 and ending the last time at position 5972.

Fragmented and deleted ORFs in the left terminal genomic region

The genomes of orthopoxviruses may be subdivided into a left terminal genomic region, spanning the region from the left hairpin loop to the lysophospholipase (LPL)-like gene (K6L), with the central conserved region including ORFs K7R to A24R (encoding a hypothetical 17.5-kDa protein and the RNA polymerase subunit rpo132, respectively) and the right terminal region extending from the A-type inclusion body (ATI) region (A25L) to the right hairpin loop (Massung *et al.*, 1994). The majority of ORFs in the left terminal genomic region of MVA are deleted, fragmented, or truncated (see Fig. 2 and Table 1). The first gene in the vaccinia CPN strain, C23L encoding the

35-kDa major secreted protein (Patel *et al.*, 1990), recently shown to encode a chemokine binding protein expressed by several orthopoxvirus strains (Graham *et al.*, 1997), is disrupted in MVA. Fragmented ORFs in the left terminal genomic region further include C19L, encoding a tumor necrosis factor receptor (TNFR) homolog (Hu *et al.*, 1994; Upton *et al.*, 1991a), and C17L, coding for the 45-kDa ankyrin-like protein (Goebel *et al.*, 1990). A region common to MVA and the variola Bangladesh (BSH) strain, but absent in CPN, is the highly fragmented cowpox (CPX) virus host range (hr) gene region. This region includes a fragmented ORF (MVA007R) defined as a virulence factor in ectromelia virus, the 28k virulence factor (Senkevich *et al.*, 1993a), which is also structurally intact in variola and CPX (Table 1), and a 13.7-kDa protein (MVA008L) that is homologous to a variola ORF (BSH-D7L) and to a corresponding ectromelia and CPX ORF.

Alignment of the CPX hr gene region with the corresponding sequence in MVA (not shown) confirmed that an MVA homolog to the CPX hr gene is present, but, due to deletions and frameshifts, is split into five ORFs (MVA009L-013L). An interrupted remnant of the CPX hr gene is also present in the vaccinia WR strain (Kotwal and Moss, 1988a) and in the ectromelia strain Moscow (Chen *et al.*, 1992).

Adjacent to the CPX hr gene homolog is the 75-kDa ankyrin-like protein (75k ank, C9L), which is split into three ORFs in MVA (MVA014L-016L). Furthermore, the neighboring C8L ORF has a 21-nucleotide internal deletion and the secreted 14k virulence factor (N1L) is partially deleted. A further potential virulence factor, which is intact in CPX and ectromelia, but split into the ORFs MVA026L and 27L as well as in the corresponding ORFs K5L and K6L in the CPN strain (see Table 1 and Fig. 2), is the vaccinia LPL homolog, which is homologous to human and bacterial lysophospholipases (R. L. Buller & C. Upton, unpublished).

Four large deletions in the MVA left terminal region relative to the CPN sequence, termed d1771, d3585, d4817, and d2763 (the numbers refer to the size of the deletion in basepairs) include totally or partially the ORFs C22L-C19L, C16L-C12L, C5L-N1L, and M1L-K1L (see lower part of Fig. 2). Among them is a potential virulence factor, the vaccinia complement-binding protein (VCP) that modulates complement activation (Kotwal, 1988; Miller *et al.*, 1997), the serpin SPI-1 (C12L), and the host range gene K1L (see also Altenburger *et al.*, 1989), thought to be necessary for growth of vaccinia in human cells.

Structurally intact ORFs in the left terminal genomic region

Only 8 of 27 listed ORFs are structurally intact in the left terminal region of MVA (see Table 1 and Fig. 2) and presumably encode functional proteins. The intact ORFs encode the vaccinia growth factor VGF (C11R), the C10L and C6L proteins of unknown function, the C7L hr protein, the α -amanitin-sensitive protein (N2L), the serpin SPI-3 (K2L), an interferon resistance protein (K3L) and the protein encoded by ORF K4L. The ORF K4L, encoding a major poxvirus envelope antigen present in various poxviruses except for variola, is highly homologous to a human member of the phospholipase D superfamily (Cao *et al.*, 1997). Although structural integrity of an ORF does not mean expression of a functional protein, the eight intact ORFs in the left terminal region of MVA seem to be the minimal requirement of genes necessary for an efficient vaccinia vaccine strain. In summary, the left terminal genomic region of MVA is unique and includes relatively few intact genes, most of which seem to be involved in host-virus interaction. The region has large deletions but also a large insertion relative to the prototype vaccinia CPN sequence. The presence of the large

"cowpox hr-region" and its adjacent genes not present in the CPN strain supports the idea that CPX or a CPX-like virus is the ancestor of vaccinia viruses. This view is further supported by the fact that the vaccinia WR strain (Kotwal and Moss, 1988a) and the ectromelia Moscow strain (Chen *et al.*, 1992; Senkevich *et al.*, 1993a) also harbor a cowpox hr region including the 28k virulence factor and the adjacent 13.7k protein (or remnants thereof) and interrupted versions of the CPX hr gene (see also Safronov *et al.*, 1996). DNA alignments of the CPX hr genes of the CPX Brighton strain, the vaccinia MVA and WR strains, and the ectromelia Moscow strain revealed a closer relationship of the vaccinia and ectromelia sequences compared to the cowpox sequence (data not shown), again arguing for an ancestral CPX or CPX-like virus as an ancestor of vaccinia and ectromelia virus. Although similar, the mutations in the CPX hr genes of the MVA and the WR strain result in different fragmentations on the protein level excluding a closer relationship of the two strains. Since the CPX hr gene is sufficiently divergent between orthopoxviral strains, it seems to be an excellent candidate for establishing phylogenetic relationships.

Fragmented and mutated genes in the central conserved genomic region

As expected, most of the ORFs in the central conserved region are intact, although amino acid changes, compared to the respective homologs in the CPN and VAR strains, are frequent (see also Table 2). Surprisingly, however, three fragmented ORFs F5L, F11L, and O1L, were found in the MVA central region, indicating that these genes are nonessential and constitute potential stable insertion sites for foreign genes. In fact, WR strain-based mutants inactivating the F5L, F11L, and O1L loci could be generated, confirming their nonessential character (F. Scheiflinger, unpublished). The ORF F5L, encoding the 36.5k major membrane precursor (Roseman and Slabaugh, 1990), is split into two ORFs in MVA (MVA033L and MVA034L). An array of small ORFs of unknown function, F6L-F8L (MVA 035L-037L), located downstream of F5L, is present in variola and vaccinia strains. Further analysis of corresponding orthopoxviral sequences would be useful to clarify the question of whether this region is the remnant of one large gene.

The second fragmented ORF of the central region, F11L, encoding a 39.7-kDa protein of unknown function, is split into the ORFs MVA040L and MVA041L. In the orf virus strain NZ2, the F11L homolog is an early gene located near the left terminus in the orf virus genome (Sullivan *et al.*, 1995a).

The third ORF in this region that is split into two parts (MVA059L and MVA060L) is O1L, encoding a 77.6-kDa protein of unknown function. This protein contains a leucine zipper and a bipartite nuclear target sequence (Goebel *et al.*, 1990). Two of the nonessential ORFs also have ho-

TABLE 2

Divergent Homologous ORFs Located in the Central Conserved Region of MVA, CPN, and Variola Virus

ORF name			Amino acids	Deletion/insertion >2aa/function or homology
MVA ^a	CPN	VAR ^b	MVA/CPN/VAR	
029L	F1L	C5L	222/226/237	12nt del; ukn
031L	F3L	C7L	476/480/161	12nt del; envelope antigen
032L	F4L	C8L	319/319/333	Ribonucleotide reductase
033L	F5L	C9L	97/321/348	Frame shift; truncation
034L	F5L	C9L	218/321/348	Membrane protein precursor
036L	F7L	C11L	80/92/79	36nt del (lys-asn repeats)
040L	F11L	C15L	84/354/354	Multiple deletions; truncation
041L	F11L	C15L	100/354/354	ukn
052R	E5R	E5R	331/331/341	30nt del; ukn
054R	E7R	E7R	166/166/60	17k myristylprotein; ukn
055R	E8R	E8R	273/273/273	Deletion in promoter region; ukn
059L	O1L	O1L	152/666/666	19nt, 25nt del; fragmentation
060L	O1L	O1L	405/666/666	Leu-zipper pattern; ukn
085R	J1R	L1R	153/153/159	Dimeric virion protein; ukn
095R	H5R	I5R	203/203/220	VLTF-4
100R	D3R	F2R	233/237/237	12nt del; structural 27k protein
104R	D7R	F7R	161/161/157	RNA pol subunit
115L	A4L	A5L	272/282/271	27nt del; core protein
120L	A9L	A10L	94/99/95	15nt del; ukn
123L	A12L	A13L	187/192/189	15nt del; virion protein
133R	A22R	A23R	187/176/187	ATG mutated in CPN; ukn
135R	A24R	A25R	1155/1164/1164	"Minor" ATG mutated; rpol132

^a Split ORFs are boxed.^b Nomenclature according to Massung *et al.* (1994), ukn, unknown.

mologs in MCV; F11L is the homolog of MCV018L and O1L is homologous to MCV042L. F5L has no counterpart in MCV, consistent with its nonessential character.

Further significant differences (deletion/insertions > 2 amino acids) in homologous genes located in the central conserved regions of MVA, CPN, and variola are summarized in Table 2. An unusual mutation, the partial deletion of the promoter region of the E8R ORF, may influence expression of this gene in MVA. A second mutation of this type is the deletion of the late part of the hemagglutinin gene promoter (Antoine *et al.*, 1996). Furthermore, some genes have suffered small in-frame deletions, resulting in slightly smaller proteins, among them genes encoding an envelope protein (F3L) and a structural 28-kDa protein (D3R). The F7L gene product, encoding a protein with lys-asn repeats, has suffered an internal deletion of 12 amino acids. A further interesting mutation that may affect the stability of MVA virions is the deletion of 9 amino acids in the membrane-associated core protein A4L (Cudmore *et al.*, 1996).

A point mutation in the first of two possible ATGs of the A24R ORF, encoding the large RNA polymerase subunit, has the consequence that only the major primary gene product of 1155 amino acids, the 132-kDa form of the enzyme (Patel and Pickup, 1989), can be synthesized. A second mutation affecting a start codon was noted; the A22R gene in the CPN strain is mutated, resulting in a protein of reduced size. The MVA and variola homologs

share the same initiation codons. Although the functions of many proteins have been elucidated, the majority of genes in the central conserved region have not been characterized in detail.

Deleted and mutated ORFs in the right terminal genomic region

The right terminal region, beginning downstream of the RNA polymerase rpo132 subunit gene (A24R), with the remnants of the CPX A-type inclusion body (ATI) ORF and its flanking regions, is structurally more conserved than the left one. However, three large deletions, termed d3501, d809, and d1771, were found in the right terminal region relative to CPN sequence (Fig. 2). Deletion d3501 has been described previously and includes the ORFs A51R-A55R (Antoine *et al.*, 1996), among them a small ORF (A53R) with homologies to TNFR. Due to d3551, a large new ORF (MVA164R) that is a fusion between ORFs A51R and A55R was formed, resulting in a hybrid gene. The promoter region of the hemagglutinin gene is also affected by d3551, presumably resulting in poor expression of this gene (see also Antoine *et al.*, 1996). Deletion d809 affects the small ORF B20R of unknown function while deletion d1771, located in the ITR, includes the ORFs B25R-B28R, a region fragmented in the CPN strain that corresponds to a large ORF in variola coding for a 69k ankyrin-like gene (BSH-G1R).

An array of more conserved genes, A27L-A38L, is located downstream of the ATI ORFs, including many proteins present in extracellular enveloped virions (EEV). One of them, the 43- to 50-kDa EEV membrane protein encoded by ORF A36R is also a virulence factor and determines plaque size (Parkinson and Smith, 1994). This gene is intact in MVA but two in-frame deletions of 27 and 12 nucleotides result in an altered protein of slightly reduced size, potentially affecting the properties of MVA.

A fragmented ORF that follows this conserved region in MVA is A39R encoding the human semaphorin (SEM) homolog. The semaphorin gene family encodes neural growth cone guidance molecules (see Kolodkin *et al.*, 1993) and was recently also found in lymphoid tissue, including T cells and natural killer cells (Furuyama *et al.*, 1996; Hall *et al.*, 1996). The semaphorin-like genes are structurally intact in CPN but disrupted in the variola strains as well as in MVA. Semaphorins are also present in herpesvirus (Ensser and Fleckenstein, 1995).

The ORF located downstream of the semaphorin homolog, A40R, was originally described as a lectin-like protein (Smith *et al.*, 1991). Recent progress in molecular biology of natural killer (NK) cells (review: Lanier, 1997) allowed the identification of this ORF as the human NK cell receptor (NKCR) homolog; the structures of A40R in various poxviruses and the potential role of this molecule, including MVA immune evasion, is discussed elsewhere (Scheiflinger *et al.*, submitted for publication).

One of the interesting genes downstream of the NK receptor homolog is the profilin homolog A42R (Blasco *et al.*, 1991). This ORF has a 15-nt in-frame deletion in MVA, which may affect the function of the slightly smaller profilin in the microfilament metabolism in which profilins are involved. The adjacent ORF A43R also carries a 12-nt deletion, reducing its size from 194 to 190 amino acids. The 3 β -hydroxysteroid dehydrogenase (3 β -HSD; A44L) is intact in MVA and CPN, while defective in variola. The superoxide dismutase-like ORF (SOD; A45R) carries an internal 12-nt deletion in MVA relative to the CPN and variola sequences.

A hypervariable region begins downstream of the viral ligase gene (Table 1). The guanylate kinase (GK; A57R) is truncated in MVA while intact in the CPN and variola strains. Further fragmented ORFs in the right terminal genomic region include B2R, an ORF of unknown function, split into two small ORFs (MVA168R and MVA169R), and B4R, a 65kDa ankyrin-like protein, split into the ORFs MVA171R and MVA172R. The B4R protein corresponds to the MT-5 protein, which is a strong virulence factor in myxoma virus (Mossman *et al.*, 1996). Many of the classical poxviral immune evasion genes located in the right terminal region, including the interferon- γ receptor (IFN- γ R; B8R), the interleukin converting enzyme inhibitor (SPI-2), the interferon- α/β receptor (IFN- α/β R; B19R) and the TNFR (CPX crmB), are fragmented; the interleukin 1 β receptor (IL1 β -R), however, is intact and highly conserved between MVA, the WR strain, and CPX (see Table 1).

The right terminal genomic region additionally harbors ankyrin-like genes, the structures of which are summarized in Table 3. With the exception of the 68-kDa ank gene (B18R), all genes of this class are either fragmented or deleted in MVA, among them the 65- and the 54-kDa ank genes B4R and M1L, respectively. Interestingly, a small gene fragment, homologous to the largest poxvirus protein identified so far, the variola transmembrane protein (BSH-B22R), is present in the right terminal region (MVA188R). The last ORF in the unique part of the genome (B22R; unknown function) has suffered two deletions relative to the CPN sequence causing frame shifts. The duplicated open reading frames located in the right ITR are described above.

DISCUSSION

Mutated structural and membrane proteins potentially affecting the physical properties of MVA

Although MVA grows efficiently in chicken embryo fibroblasts (Mayr and Malicki, 1966) and also in baby hamster kidney (BHK) cells (Carroll and Moss, 1997), it seems to be unstable upon purification (F. G. Falkner, unpublished). The reasons for these properties are unclear, but may be the results of mutations in structural and membrane proteins. Most genes encoding structural, membrane, and core proteins are highly conserved among orthopoxviruses. However, several exceptions from this rule were found in the MVA sequence. The A36R ORF (MVA147R) has suffered two internal deletions of 9 and 3 amino acids that may affect EEV formation and virulence (see also Parkinson and Smith, 1994). A structural component that carries an internal deletion of 3 amino acids in MVA is the D3R protein, found in a detergent-insoluble fraction of the virion (Dyster and Niles, 1991). A further interesting structural protein carrying an internal deletion of 9 amino acids is the membrane-associated core protein p39 encoded by ORF A4L. This protein most likely interacts with an integral membrane protein of the IMV and possibly functions as a matrix-like linker protein between the core and the innermost of the two membranes surrounding the IMV (Cudmore *et al.*, 1996). Substitution of the D3R or A4L ORFs by their wild-type counterparts may improve the physical properties of MVA.

Host range genes and genes containing ankyrin repeats in MVA

The "classical" host range genes in orthopoxviruses include K1L and C7L, thought to be sufficient for growth of vaccinia in human cells, and the CPX virus hr gene, which extends the vaccinia host range to Chinese hamster ovary cells (review: Perkus *et al.*, 1990). The structures of the hr and ankyrin-like genes are summarized in Table 3. As described previously (Altenburger *et al.*, 1989; Meyer *et al.*, 1991), the hr gene K1L is partially deleted in

TABLE 3

Structure of ORFs of MVA Located in the Terminal Regions Specifying Potential Host Range (hr) Proteins, Including Proteins with Ankyrin (ank) Repeats and their Homologs in Vaccinia Copenhagen and Variola Virus

MVA ^a	CPN	VAR ^b	Amino acids	Putative function/ homology
			MVA/CPN/VAR	
003L	C17L	—	102/386/—	45k ank ^c protein
004L	C17L	D1L	233/386/91	45k ank protein
009L	—	—	90/—/—	77k CPX ^d hr protein
010L	—	D6L	142/—/452	77k CPX hr protein
011L	—	D6L	135/—/452	77k CPX hr protein
012L	—	D6L	90/—/452	77k CPX hr protein
013L	—	D6L	71/—/452	77k CPX hr protein
014L	C9L	D6.5L	109/634/91	75k ank protein
015L	C9L	—	96/634/—	75k ank protein
016L	C9L	D7L	297/634/153	75k ank protein
018L	C7L	D11L	150/150/150	hr protein
—	M1L	O1L	—/472/446	54k ank protein
022L	K1L	O3L	98/284/70+76	Host range
022L	K1L	C1L	98/284/76	Protein
050L	E3L	E3L	190/190/192	dsRNA dep. PKI
171R	B4R	B5R	177/558/558	65k ank protein
172R	B4R	B5R	409/558/558	65k ank protein
173R	B5R	B6R	317/317/317	ps/hr / EEVgp42
186R	B18R	B16R	574/574/574	68k ank protein
190R	B23R	D1L	233/386/91	45k ank protein
191R	B23R	—	102/386/—	45k ank protein

Note. —, deleted in the respective virus.

^{a,b} see Table 2.

^c ankyrin.

^d cowpox host range.

MVA, and, similar to the situation in variola, the CPX hr homolog is split into several separate ORFs. Only C7L is intact (100% identity to C7L of the vaccinia WR strain); nevertheless, MVA does not grow in human cells. A further candidate gene that may affect host range in MVA is the serpin gene SPI-1, the lack of which in rabbit poxvirus (a close relative of vaccinia) resulted in a restricted host range including human cells (Ali *et al.*, 1994). The SPI-1 gene is deleted in MVA.

A class of genes related to and including some hr genes are the ankyrin-like (ank) genes (review: Shchelkunov *et al.*, 1993b). All ank genes are defective or deleted in MVA except for the 68-kDa ank gene (B18R), the function of which is unclear. The 54-kDa ank gene (M1L) is deleted in MVA and the 65-kDa ank gene (B4R) is split into two pieces. A homolog of B4R, the strong myxoma virulence factor M-T5 (Mossman *et al.*, 1996), is involved in attenuation and host range in myxoma virus. Two further ank genes present in variola, the 69k and the 94k ank genes (BSH-B18R and BSH-G1R), are absent in MVA. In summary, despite the presence of an intact human host range gene (C7L), MVA does not grow in most mammalian cell lines; replication of vaccinia in human cells is dependent not only on the configuration of the classical human hr genes, but also on the genetic background of the respective vaccinia strain.

A comparison of MVA with the host range restricted vaccinia strain NYVAC, which harbors 18 engineered deleted ORFs (Tartaglia *et al.*, 1992), revealed that both viruses share common deleted or nonfunctional ORFs including the 6 ORFs of deletion d4817 (C5L-N1L), ORFs B13R and B14R encoding the ICE inhibitor, the ATI remnant ORF A26L, and the K1L host range gene. In contrast to NYVAC, the MVA strain has a functional thymidine kinase gene, an intact C7L host range gene, and intact C6L, A56R (hemagglutinin), and I4L (ribonucleotide reductase) ORFs. Despite similarities, the two potential life vaccine viruses have a clearly different genetic background.

Further ORFs involved in host-virus interaction

Homologies of vaccinia proteins with proteins involved in lipid metabolism were found recently; the vaccinia K4L protein is homologous to the phospholipase D (PLD) gene family (Cao *et al.*, 1997; Sung *et al.*, 1997). Mutation of a crucial motif found in the vaccinia PLD homolog resulted in loss of efficient vaccinia virus cell-to-cell spreading, suggesting that it encodes a lipid modifying or binding activity (Sung *et al.*, 1997). The adjacent ORFs K5L and K6L are fragments of a gene that is intact in cowpox virus and is homologous to human LPL (Table 1).

Lysophosphatidic acid, the product of LPLs, is a multifunctional phospholipid messenger with many biological activities (review: Moolenaar *et al.*, 1997). Lysophospholipases are suspected to be virulence factors in many pathogenic bacteria, such as *Vibrio cholerae* (Whayeb *et al.*, 1996) or *Mycobacterium leprae* (Prabhakaran *et al.*, 1996). The presence of intact PLD homologs (K4L) and the fragmentation of the LPL homologs (K5L and K6L) seem to be markers for attenuated vaccinia viruses. In variola, both proteins are mutated, the K4L homolog is deleted, and the lysophospholipase is fragmented, while in CPX both ORFs are intact.

The role of the semaphorin homologs, further potential host interactive proteins in viruses, is still unclear. Originally identified as molecules expressed in neural tissue (Kolodkin *et al.*, 1993), expression of family members in lymphoid cells was found, suggesting a role in the immune system. It seems reasonable to speculate that an interaction of viral semaphorins with lymphoid, rather than neural, cells occurs. Some semaphorins, such as CD100, interact with the CD40/CD40L B cell signaling system (Hall *et al.*, 1996), which also affects virus replication (Ruby *et al.*, 1995). In T cells and natural killer cells a serine kinase activity is associated with CD100 (Elhabazi *et al.*, 1997). These cell types may be partners for interaction with viral semaphorins. Interestingly, the ORF adjacent to this potential immune modulator is the NK receptor homolog A40R (Table 1). Although key mutations were responsible for the attenuation of MVA (Meyer *et al.*, 1991), numerous genes in MVA that differ only slightly compared to their CPN or BSH counterparts presumably contribute to the properties of MVA. Thus, the highly attenuated phenotype of MVA is the result of numerous mutations including large and small deletions and substitutions, resulting in the deletion and fragmentation of ORFs and the alteration of proteins.

MATERIALS AND METHODS

Sequence analysis of the MVA genome

Prior to sequencing, the MVA strain (obtained from Prof. A. Mayr, University of Munich, Faculty of Veterinary Medicine) was plaque purified once. The DNA from MVA clone M4 was cleaved with *Xba*I and cloned into pUC19 and minipreparations of DNA (QIAprep-8 kit (Qiagen 19047)) were sequenced (Sanger *et al.*, 1977) on an Applied Biosystems Model 373A Sequencer using the cycle sequencing method with dye terminators and AmpliTaq DNA polymerase FS (ABI PRISM Dye Terminator Cycle Sequencing Ready Reaction Kit 402122; Perkin-Elmer, Inc.). Selected regions were sequenced with genomic DNA as template with manually designed primers. Frameshift mutations were confirmed by direct sequencing of the corresponding genomic templates. The sequence of the MVA genome was deposited with GenBank (Accession No. U94848) using the Sequin Program (National Center for Biotechnology Information, NIH).

Open reading frames (ORFs) >65 codons were translated using the MacMolly sequence analysis Software (Softgene, Inc.) and protein sequences were compared with the nonredundant protein sequence database (National Center for Biotechnology Information, NIH) using the program BLASTp (Altschul *et al.*, 1990). Selected proteins were also compared to the protein databases using the BLAST2 program that constructs alignments with gaps (Altschul and Gish, 1996).

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