Betapolyomavirus

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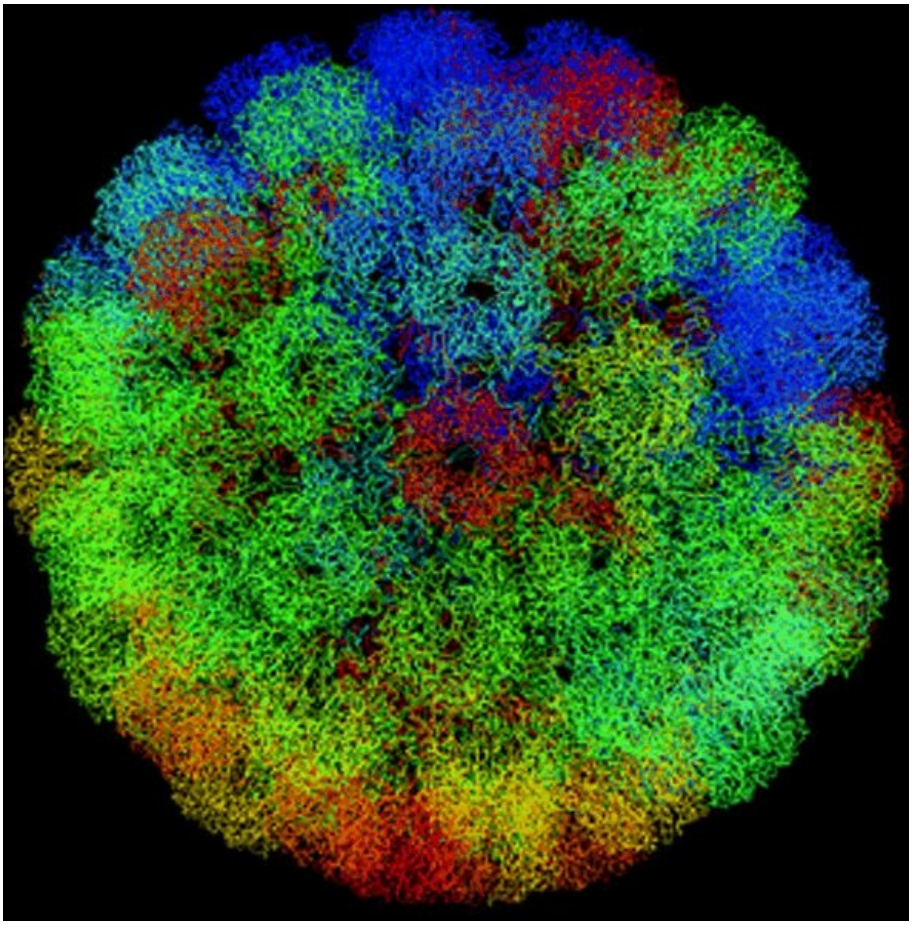
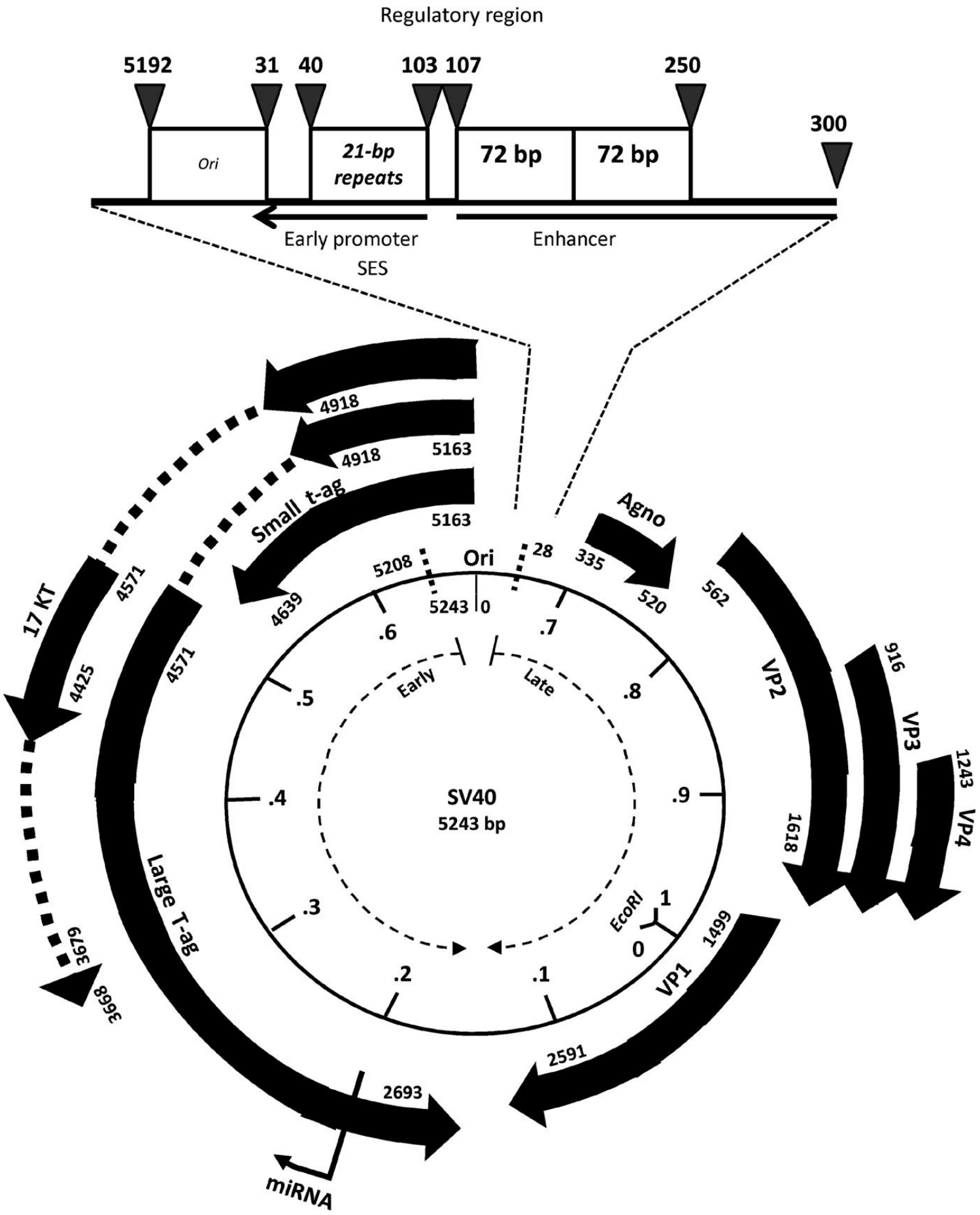
Virion



Morphology	Icosahedral
Envelope	No
Diameter (nm)	45
Length (nm)	-
Structural Components	Capsid, minichromosome
Buoyant Density (g/ml)	1.34
Additional Information	Composed of 72 pentameric capsomers; T = 7

Genome


Regulatory region
5192
31
40
103
107
250
300
Ori
21-bp repeats
72 bp
72 bp
Early promoter
SES
Enhancer
4918
4918
5163
Small t-ag
5163
Agno
17 KT
4571
4425
4639
5208
Ori
28
335
520
562
5243
0
.6
.7
.5
.8
Early
Late
VP2
916
VP3
1243
VP4
1618
.4
.9
SV40
5243 bp
4571
Large T-ag
EcoRI
1
0
.3
.2
.1
1499
VP1
3679
3668
2591
2693
miRNA

Nucleic Acid	DNA
Strandedness	Double-stranded
Polarity	-
Configuration	Circular
Segments	1
Size (kb)	5.3
G+C Content (%)	47.3
mRNA Transcripts	7
Additional Information	Genome is nonsegmented, closed circular, supercoiled; viral minichromosome within virions is complexed with histones H2A, H2B, H3, and H4, but lacks H1

Replication

Entry Mechanism	Caveolae- or clathrin-mediated endocytosis
Site of Transcription	Nucleus
Transcriptase	Host cell RNA polymerase II and its accessory proteins
Site of Genome Replication	Nucleus
Replicase	SV40 large tumor antigen, DNA pol alpha-primase, DNA pol delta/RFC/PCNA
Replication Intermediate	Unknown
Site of Virion Assembly	Nucleus
Egress Mechanism	Virus release occurs by cytolysis; cytoplasmic vesicles also transport some virions to cell surface
Additional Information	Ganglioside GM1 is cell-surface receptor for SV40; MHC class I proteins may be co-receptors. Virions taken up in caveosomes, transported to smooth ER, enter nucleus via nuclear pore by recognition of nuclear localization signal in viral protein VP3

History

Year	Event	Reference
1960	Detection of simian vacuolating agent 40 (SV40) as a contaminant of poliovaccines	Sweet BH, Hilleman MR (1960) Proc Soc Exp Biol Med 105:420-427
1962	SV40 plaque assay	Stinebaugh S, Melnick J (1962) Virology 16:348-349
1962	Discovery that SV40 is oncogenic in hamsters	Eddy BE et al (1962) Virology 17:65-75; Girardi AJ et al (1962) Proc Soc Exp Biol Med 109:649-660
1964	Detection of SV40 T-antigen expression in SV40 tumor cells and infected cells	Black PH et al (1963) Proc Natl Acad Sci USA 50:1148-1156; Rapp F, Butel JS, Melnick JL (1964) Proc Soc Exp Biol Med 116:1131-1135; Rapp F et al (1964) Proc Natl Acad Sci USA 52:1138; Rapp F et al (1964) Proc Natl Acad Sci USA 52:1138-1142
1968	SV40 DNA is integrated in transformed cells	Sambrook J et al (1968) Proc Natl Acad Sci USA 60:1288-1295
1971	Replicating SV40 genomes contain closed circular DNAs	Jaenisch R, Mayer A, Levine A (1971) Nat New Biol 233:72-75
1971	Cleavage of SV40 DNA by restriction enzyme and first physical map of a DNA molecule	Danna K, Nathans D (1971) Proc Natl Acad Sci USA 68:2913-2917; Morrow JF, Berg P (1972) Proc Natl Acad Sci USA 69:3365-3369
1972	First artificial ligation of foreign DNA into SV40: Lambda phage genes and the galactose operon of E. coli are cloned into SV40	Jackson DA, Symons RH, Berg P (1972) Proc Natl Acad Sci USA 69:2904-2909
1972	SV40 DNA replication is bidirectional	Danna KJ, Nathans D (1972) Proc Natl Acad Sci USA 69:3097-3100; Fareed GC, Garon CF, Salzman NP (1972) J Virol 10:484-491
1973	Description of adenovirus-SV40 hybrids	Lewis AM Jr (1973) Biohazards in biological research. Cold Spring Harbor Laboratory Press, New York
1975	Large T-antigen required for maintenance of cell transformation	Brugge JS, Butel JS (1975) J Virol 15:619-635; Tegtmeyer P (1975) J Virol 15:613-618
1975	The SV40 genome exists as a minichromosome	Griffith JD (1975) Science 187:1202-1203
1977	Identification of T-antigen as early gene A product	Rundell K et al (1977) J Virol 21:636-646
1977	SV40 can cause progressive multifocal leukoencephalopathy in rhesus monkeys	Holmberg CA et al (1977) J Infect Dis 136:593-596
1978	Determination of SV40 DNA sequence; first full genomic sequence of a virus that affects eukaryotes	Fiers W et al (1978) Nature 273:113-120; Reddy VB et al (1978) Science 200:494-502
1978	Spliced SV40 messenger RNAs	Berk AJ, Sharp PA (1978) Proc Natl Acad Sci USA 75:1274-1278
1979	SV40 large T-antigen binds p53	Lane DP, Crawford LV (1979) Nature 278:261-263; Linzer DI, Levine AJ (1979) Cell 17:43-52

1980	Propagation of cloned, infectious SV40 DNA in bacteria	Peden KW et al (1980) Science 209:1392-1396
1981	A 72-bp sequence in SV40 is a strong enhancer of transcription	Banerji J, Rusconi S, Schaffner W (1981) Cell 27:299-308; Moreau P et al (1981) Nucleic Acids Res 9:6047-6068
1981	Monoclonal antibodies against SV40 tumor antigens	Deppert W, Gurney EG, Harrison RO (1981) J Virol 37:478-482; Harlow E et al (1981) J Virol 39:861-869
1983	Sp1 binds to the SV40 early promoter	Dynan WS, Tjian R (1983) Cell 32:669-680; Dynan WS, Tjian R (1983) Cell 35:79-87
1983	Repeated GC-rich motifs are in the SV40 promoter	Everett RD, Baty D, Chambon P (1983) Nucleic Acids Res 11:2447-2464
1984	Replication of SV40 DNA in vitro	Li JJ, Kelly TJ (1984) Proc Natl Acad Sci USA 81:6973-6977
1984	Large T-antigen induces tumors in transgenic mice	Brinster RL et al (1984) Cell 37:367-379; Hanahan D (1985) Nature 315:115-122
1984	Discovery of nuclear localization signal on SV40 T-antigen	Kalderon D et al (1984) Nature 311:33-38; Lanford RE, Butel JS (1984) Cell 37:801-813
1988	SV40 large T-antigen binds pRB	DeCaprio JA et al (1988) Cell 54:275-283
1988	Mapping of cytotoxic T cell epitopes on T-antigen	Anderson RW et al (1988) J Virol 62:285-296; Tanaka Y et al (1988) Virology 162:427-436
1989	SV40 T-antigen binds heat shock protein	Sawai ET, Butel JS (1989) J Virol 63:3961-3973
1991	Structure of SV40 virions at 3.8- Å resolution	Liddington RC et al (1991) Nature 354:278-284
1992	Cell surface receptors for SV40 are MHC class I molecules and GM1 ganglioside	Breau WC, Atwood WJ, Norkin LC (1992) J Virol 66:2037-2045; Tsai B et al (2003) EMBO J 22:4346-4355
1992	Association of SV40 DNA with pediatric brain tumors	Bergsagel DJ et al (1992) N Engl J Med 326:988-993
1992	Genetic analysis of SV40 in brains and kidneys of macaque monkeys	Ilyinskii PO et al (1992) J Virol 66:6353-6360
1993	Discovery of 17 kDa SV40 tumor antigen	Zerrahn J et al (1993) EMBO J 12:4739-4746
1994	Association of SV40 DNA with human mesotheliomas	Carbone M et al (1994) Oncogene 9:1781-1790
1996	SV40 enters cells through caveolae	Anderson HA, Chen Y, Norkin LC (1996) Mol Biol Cell 7:1825-1834
1997	Major histocompatibility class I molecules mediate association of SV40 with caveolae	Stang E, Kartenbeck J, Parton RG (1997) Mol Biol Cell 8:47-57
1998	Genetic heterogeneity of SV40 in	Lednicky JA et al (1998) J Virol 72:3980-3990

	immunocompromised monkeys	
1998	Description of the SV40 encapsidation signal (SES)	Gordon-Shaag A et al (1998) J Mol Biol 275:187-195
2001	SV40 regulatory region structural diversity	Lednicky JA, Butel JS (2001) Semin Cancer Biol 11:39-47
2002	SV40 can alter three of five cellular pathways, the disruption of which is necessary for transformation of human cells	Hahn WC et al (2002) Mol Cell Biol 22:2111-2123
2003	Crystal structure of T-antigen helicase domain	Li DW et al (2003) Nature 423:512-518
2004	Phylogenetic grouping of SV40 strains	Forsman ZH et al (2004) J Virol 78:9306-9316
2005	Discovery of SV40 microRNAs	Sullivan CS et al (2005) Nature 435:682-686
2005	Use of SV40-derived gene therapy vectors	Strayer DS et al (2005) Curr Gene Ther 5:151-165
2007	SV40 T/t-antigen signature from transgenic models predictive of human carcinomas with poor prognosis	Deeb KK et al (2007) Cancer Res 67:8065-8080
2008	Influence of viral regulatory region on SV40 tumor induction	Sroller V et al (2008) J Virol 82:871-879
2009	Cell-type specific global gene expression regulated by T-antigen in SV40-transformed mouse cells	Cantalupo PG et al (2009) Virology 386:183-191
2009	Seroepidemiology of polyomaviruses in humans	Kean JM et al (2009) PLoS Pathogens 5:e1000363

Genus Members

Species (Abbreviation) **- Synonyms (Abbreviation)**	**ICTV Status**	**Host Range**
Macaca mulatta polyomavirus 1 - Simian virus 40 (SV40)	type species	Asian macaque, humans
Acerodon celebensis polyomavirus 2	approved	
Artibeus planirostris polyomavirus 1	approved	
Canis familiaris polyomavirus 1	approved	
Cebus albifrons polyomavirus 1	approved	
Cercopithecus erythrotis polyomavirus 1	approved	
Chlorocebus pygerythrus polyomavirus 2	approved	

Desmodus rotundus polyomavirus 1	approved	
Dobsonia moluccensis polyomavirus 2	approved	
Dobsonia moluccensis polyomavirus 3	approved	
Enhydra lutris polyomavirus 1	approved	
Equus caballus polyomavirus 1	approved	
Human polyomavirus 1 - BK polyomavirus (BKPyV)	approved	humans
Human polyomavirus 2 - JC polyomavirus (JCPyV)	approved	humans
Human polyomavirus 3	approved	
Human polyomavirus 4	approved	
Leptonychotes weddellii polyomavirus 1	approved	
Loxodonta africana polyomavirus 1	approved	
Mastomys natalensis polyomavirus 1	approved	
Meles meles polyomavirus 1	approved	
Microtus arvalis polyomavirus 1	approved	
Miniopterus africanus polyomavirus 1	approved	
Mus musculus polyomavirus 2 - Kilham polyomavirus (KPyV) - Mice pneumotropic virus - Murine pneumotropic virus (MPtV)	approved	mouse
Mus musculus polyomavirus 3	approved	
Myodes glareolus polyomavirus 1	approved	
Myotis lucifugus polyomavirus 1	approved	
Pan troglodytes polyomavirus 8	approved	
Papio cynocephalus polyomavirus 2	approved	
Pteronotus davyi polyomavirus 1	approved	
Pteronotus parnellii polyomavirus 1	approved	
Rattus norvegicus polyomavirus 2	approved	
Rousettus aegyptiacus polyomavirus 1	approved	
Saimiri boliviensis polyomavirus 1	approved	

Saimiri sciureus polyomavirus 1	approved
Vicugna pacos polyomavirus 1	approved
Zalophus californianus polyomavirus 1	approved

Nucleotide Sequences

Genomic Region	Virus Species / Strain	Nucleotides	Accession Number	Reference
Complete genome	SV40, 776	5,243	J02400.1	Fiers W et al (1978) Nature 273:113-120; Reddy VB et al (1978) Science 200:494-502

Proteins

Protein Name	Abbreviation	Amino Acids	Molecular Weight (kDa)	Time of Expression	Accession Number	Additional Information
Agnoprotein	agno; LP1	62	7.9	Late	AAB59920.1	Facilitates virus assembly
Large tumor antigen	T-ag	708	90	Early	AAB59924.1	Major transforming protein; regulates viral transcription; binds key host cell regulators p53 and pRB; initiates viral DNA unwinding and replication
Small tumor antigen	t-ag	174	20	Early	AAB59925.1	Promotes cell transformation by negative regulation of the protein phosphatase 2A family of phosphatases
Tiny tumor antigen	17kT	135	17	Early		Regulates pRB proteins
Viral coat protein 1	VP1	364	45	Late	AAB59923.1	Major structural protein; receptor binding protein
Viral coat protein 2	VP2	352	42	Late	AAB59921.1	Minor structural protein
Viral coat protein 3	VP3	234	30	Late	AAB59922.1	Minor structural protein
Viral coat protein 4	VP4	125	15	Very late		Nonstructural protein; induces lysis of infected cells

Biology

Cytopathic Effect	Virus Species / Strain	Permissive Cells	Tissue Tropism	Additional Information
Cell lysis	SV40	African green monkey kidney cell lines (BSC-	Kidney	Perinuclear vacuolation

		1, CV-1, TC-7)		common
Lytic	SV40	Human renal leiomyoblastoma, G402	Kidney	
Minimal lysis	SV40	Primary human mesothelial cells	Mesothelium	High rate of transformation
None	SV40	Rhesus monkey kidney cell line LLCMK2	Kidney	
Usually none	SV40	Primary rhesus monkey kidney cells	Kidney	

Diseases

Disease Name	Virus Species / Strain	Affected Organisms	Disease Characteristics	Transmission Route / Vector	Treatment	Geographic Distributio
Cancers	SV40	Humans	Brain, bone, lymphomas, mesotheliomas; rare			Etiology not proven
Interstitial pneumonia	SV40	Unhealthy Rhesus monkeys	Pneumonia			Captive Asian macaques
Natural infections	SV40	Rhesus monkeys	Inapparent, persistent in kidneys	Respiratory, fecal/oral, urine/oral		Asian macaques
Neoplasms	SV40	T-ag transgenic mice	Foreign promoters determine tissue-specific hyperplasia, tumors	SC, IP, IV, intrathecal		Laboratory
Neurological lesions	SV40	Immunocompromised Rhesus monkeys	Encephalitis, meningoencephalitis; rare complication			Captive Asian macaques
Progressive multifocal leukoencephalopathy	SV40	Immunocompromised Rhesus monkeys	Destruction of myelin; rare complication			Captive Asian macaques
Renal tubular necrosis	SV40	Immunocompromised Rhesus monkeys	Kidney disease, rare			Captive Asian macaques

Vectors

Vector Name	Backbone Virus Species / Strain	Application	Insertion Capacity (kb)	Additional Information	Reference
pGL4.13(luc2/SV40)	Regulatory region, SV40 strain 776 in ColEI plasmid replication origin	Internal control	N/A	Ampicillin resistance; reporter expressing firefly luciferase	Yamasaki K et al (2009) Invest Ophthalmol Vis Sci

				protein	50:604-613
pRL-SV40	Regulatory region, SV40 strain 776 in ColEI plasmid replication origin	Internal control	N/A	Ampicillin resistance; reporter expressing Renilla reniformis protein	Zhang Y et al (2007) Proc Natl Acad Sci USA 104:10613-10618

Key Literature

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