

SUZANE RAMOS DA SILVA

Patobiologia do Herpesvírus associado ao Sarcoma de Kaposi / Herpesvírus Humano Tipo-8: Genotipagem de isolados virais em lesões de sarcoma de Kaposi e imunoevasão dependente da inibição da síntese e modulação da degradação da proteína viral LANA-1.

Tese apresentada ao Programa de pós-graduação em Patologia da Faculdade de Medicina de Botucatu, Universidade Estadual Paulista – UNESP, para obtenção do título de Doutor.

Orientador: Prof. Dr. Deilson Elgui de Oliveira

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(São Francisco de Assis)

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"Para ser grande, sê inteiro:
nada teu exagera ou exclui.
Sê todo em cada coisa.
Põe quanto és no mínimo que fazes.
Assim em cada lago a lua toda
Brilha, porque alta vive."

Ricardo Reis (heterônimo de Fernando Pessoa)

14/2/1933

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Principais siglas utilizadas

AIDS: Síndrome da imunodeficiência adquirida (*Acquired Immunodeficiency Syndrome*)

CMV: Citomegalovírus (*Cytomegalovirus*)

CR: Repetição central (*Central Repeat*)

EBNA: Antígeno nuclear do EBV (*EBV Nuclear Antigen 1*)

EBV: Vírus de Epstein-Barr (*Epstein-Barr Virus*)

FLICE: Enzima associada ao FAS, com domínio de morte-símile, convertora de interleucina 1 β (*FAS-associated death domain-like interleukin-1 β converting enzyme*)

FLIP: Proteína semelhante à proteína inibidora de FLICE (*FLICE-like inhibitory protein*)

GAr: Repetições de glicina e alanina (*Glycine-Alanine repeats*)

GPCR: Receptor acoplado a proteína G humana (*G-Protein Coupled Receptor*)

GSK3- β : glicogênio-sintetase quinase (*Glycogen Synthase Kinase 3- β*)

HAART: Terapia anti-retroviral combinada de alta potência (*Highly active antiretroviral therapy*)

HCV: vírus da hepatite C (*Hepatitis C Virus*)

HIV: Vírus da Imunodeficiência Humana (*Human Immunodeficiency Virus*)

HHV-8: Herpesvirus humano tipo 8 (*Human Herpesvirus 8*)

HPV: Vírus do papiloma humano (*Human papillomavirus*)

HVS: Herpesvírus saimiri (*Herpesvirus Saimiri*)

HVS-2: Herpesvírus simples 2 (*Herpesvirus Simplex 2*)

IL-6: Interleucina 6 (*Interleukin 6*)

vIRF: Fator regulador de interferon viral (*viral Interferon Regulatory Factor*)

KSHV: Herpesvirus associado ao sarcoma de Kaposi (*Kaposi's Sarcoma-associated Herpesvirus*)

LANA: Antígeno nuclear associado à latência (*Latency Associated Nuclear Antigen*)

MCD: Doença Multicêntrica de Castleman (*Multicentric Castleman Disease*)

MHC: Complexo principal de histocompatibilidade (*Major Histocompatibility Complex*)

vMIP: Proteínas inflamatórias de macrófagos viral (*viral Macrophage Inflammatory Protein*)

ORF: Sequência aberta para leitura (*Open Read Frame*)

PBMC: Células mononucleares do sangue periférico (*Peripheral Blood Mononuclear Cells*)

PCR: Reação em cadeia da polimerase (*Polymerase Chain Reaction*)

PEL: Linfoma de efusão primária (*Primary Effusion Lymphoma*)

RFLP: Análise de polimorfismos de tamanho de fragmentos de restrição (*Restriction Fragment Length Polymorphisms*)

SDS-PAGE: *Sodium Dodecyl Sulfate - Polyacrylamide Gel Electrophoresis*

SK: Sarcoma de Kaposi

SK-AIDS: Sarcoma de Kaposi associado a AIDS

hTERT: subunidade catalítica da telomerase humana (*human Telomerase Reverse Transcriptase*)

TNF: Fator de necrose tumoral (*Tumor Necrosis Factor*)

TNFr: Receptor do fator de necrose tumoral (*Tumor Necrosis Factor receptor*)

TR: Repetição terminal (*Terminal Repeat*)

UDIs: Usuários de drogas injetáveis

VEGF: Fator para crescimento do endotélio vascular (*Vascular Endothelial Growth Factor*)

REVISÃO DA LITERATURA

1. Aspectos gerais do sarcoma de Kaposi

O sarcoma de Kaposi (SK) é uma doença angioproliferativa que freqüentemente se apresenta como lesões cutâneas, podendo envolver também cavidade oral, trato respiratório, trato gastrointestinal e nódulos linfáticos (IOACHIM et al., 1995, WHELAN & SCADDEN, 2000). Certos aspectos sobre o caráter neoplásico do SK ainda são controversos na literatura, e alguns autores sugerem que as lesões inicialmente são policlonais e evoluem para um processo clonal (GILL et al., 1998, JUDDE et al., 2000, DUPREZ et al., 2007).

A forma clássica da doença (descrita em 1872 por Moritz Kaposi) é rara e acomete predominantemente indivíduos do sexo masculino com mais de 40 anos, notadamente os de etnia judaica de regiões do Mediterrâneo e Leste Europeu (KAPOSI, 1872). O SK clássico se caracteriza pelo aparecimento de placas ou nódulos cutâneos em pequeno número. Apresenta evolução indolente e raramente é observado o envolvimento de vísceras e mucosas, que ocorre em até 10% dos pacientes (ANTMAN & CHANG, 2000, HENGGE et al., 2002a).

Além do SK clássico, três outras formas clínico-epidemiológicas dessa doença são atualmente reconhecidas: o SK endêmico, o SK iatrogênico, e o SK associado à síndrome de imunodeficiência adquirida (*Acquired Immunodeficiency Syndrome* – Aids; SK-Aids). Nas quatro diferentes formas, as lesões do SK evoluem de máculas e placas até os tumores propriamente ditos, histologicamente constituídos por espaços neovasculares anormais e proliferação de células fusiformes com características de diferenciação endotelial (IOACHIM et al., 1995).

A forma endêmica do SK foi descrita no início dos anos 60, período em que se verificava 12,8% de prevalência da doença em regiões da África próximas ao deserto do Saara. O SK endêmico é restrito à África Central e pode ser dividido em

quatro grupos, de acordo com o curso clínico: 1) lesão cutânea benigna nodular, semelhante ao SK clássico, que atinge principalmente indivíduos jovens do sexo masculino; 2) doença cutânea agressiva que invade tecidos e ossos, podendo ser fatal entre 5 e 7 anos; 3) doença mucocutânea e visceral e 4) linfadenopatia fulminante, que acomete crianças jovens (HENGGE et al., 2002a). Sua distribuição se sobrepõe a áreas de alta incidência de infecção pelo vírus de Epstein-Barr (*Epstein-Barr Virus* - EBV) (KEMPF & ADAMS, 1996).

O SK iatrogênico ocorre em pacientes submetidos à imunossupressão terapêutica pós-transplante. Em alguns casos, as lesões podem regredir com a retirada da imunossupressão (FRIEDMAN-KIEN & SALTZMAN, 1990a, SARID et al., 2002), fato que indica importante papel da resposta imunitária no desenvolvimento do SK. Essa hipótese é reiterada pela elevada frequência de SK em indivíduos infectados pelo vírus da imunodeficiência humana (*Human Immunodeficiency Virus* - HIV): em indivíduos portadores do HIV, a incidência de SK é 20.000 vezes maior do que na população geral, e cerca de 300 vezes maior que em indivíduos com outros tipos de imunossupressão (BERAL et al., 1990). O SK-Aids é polimórfico, disseminado, com grande agressividade biológica e atinge quase que exclusivamente homossexuais e bissexuais masculinos (HENGGE et al., 2002a). Indivíduos co-infectados com o HIV-1 e o KSHV/HHV-8 apresentam um aumento de 60% a cada ano transcorrido de infecção pelo HIV-1 na probabilidade de desenvolvimento de SK (JACOBSON et al., 2000). Na década de 1990 o SK foi definido pelo dramaturgo Tony Kushner como “O beijo violeta do anjo da morte”, devido a sua íntima associação com o desenvolvimento da aids (MCALLISTER & MOSES, 2007).

Após a introdução da terapia antiretroviral combinada de alta potência (*Highly active antiretroviral therapy* - HAART), na década de 1990, foi observada uma

redução significativa na incidência de SK-Aids, notadamente em países desenvolvidos (LEDERGERBER et al., 1999, International collaboration on HIV and cancer, 2000, STEBBING et al., 2003). Apesar dos recentes avanços, o SK continua sendo uma das neoplasias malignas mais comumente observada nos pacientes portadores do HIV (MOCROFT et al., 2004), além de ser o câncer mais relatado em alguns países da África (DEDICAT & NEWTON, 2003).

Ao exame histopatológico, o SK é basicamente constituído por células endoteliais, células fusiformes e infiltrado inflamatório (KEMPF & ADAMS, 1996) (Figura 1). As células fusiformes representam a neoplasia propriamente dita. Assim como as células endoteliais, secretam fator de crescimento de endotélio vascular (*Vascular Endothelial Growth Factor* - VEGF) e são estimuladas pelo mesmo, o que contribui para a exuberante angiogênese observada no tumor (BOSHOF, 1998).

Lesões mucocutâneas precoces podem ter forma de placas, enquanto a doença avançada se caracteriza pela formação de nódulos (FRIEDMAN-KIEN & SALTZMAN, 1990b). As lesões aparecem mais freqüentemente em membros inferiores (onde podem exibir confluência circunferencial), palmas das mãos e em face. A história natural do SK demonstra heterogeneidade de evolução, pois há indivíduos que apresentam regressão espontânea e aqueles nos quais ocorre progressão fatal da doença (WHELAN & SCADDEN, 2000).

Em seus estágios iniciais, o SK pode ser clinicamente reconhecido pelo aparecimento de máculas eritematosas ou violáceas, cuja histologia revela células tumorais dispersas na derme. No estágio de placa observa-se lesão saliente, cujo exame microscópico caracteristicamente revela a presença de agrupamentos de células neoplásicas confluentes. Freqüentemente, há aumento do grau de vascularização e pode ser observado acúmulo de hemossiderina no tumor. O estágio nodular pode ser identificado macroscopicamente pelo surgimento de lesão

tumoral, histologicamente constituída por elevada densidade de células fusiformes e número variável dos demais componentes, como células endoteliais, células inflamatórias e eritrócitos (WHELAN & SCADDEN, 2000).

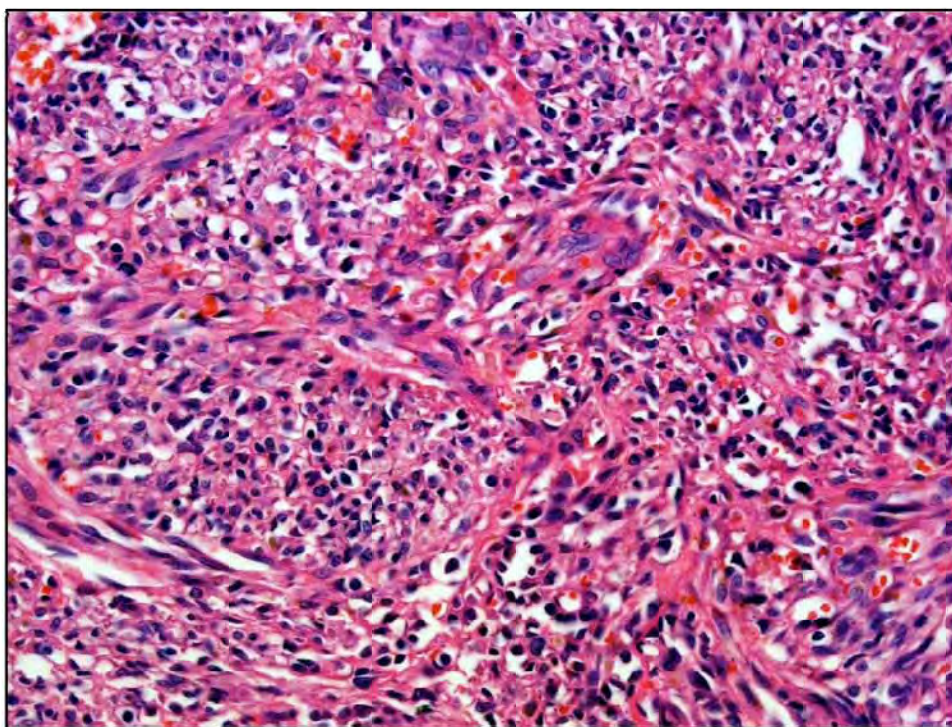


FIGURA 1 - Histopatologia do sarcoma de Kaposi em estágio tumoral. Nota-se abundante proliferação de células neoplásicas fusiformes, contribuindo para vascularização anômala e exuberante do tumor (H&E, 200x).

2. Vírus associado ao sarcoma de Kaposi / Herpesvírus Humano Tipo-8

A partir da observação de que indivíduos infectados pelo HIV apresentam risco aumentado para o desenvolvimento do SK, diversos vírus foram apontados como possíveis agentes etiológicos dessa neoplasia, incluindo o citomegalovírus (*Cytomegalovirus* - CMV), os herpesvírus humanos tipos 6 e 7 e o vírus do papiloma humano (*Human papillomavirus* - HPV) (KEMPF & ADAMS, 1996). Em 1994, Chang e colaboradores identificaram um novo herpesvírus em espécimes biológicos de pacientes com aids, que foi originalmente denominado herpesvírus associado ao sarcoma de Kaposi (*Kaposi's sarcoma-associated herpesvirus* - KSHV) (CHANG et

al., 1994). Atualmente o KSHV, ou herpesvírus humano tipo 8 (*Human Herpesvirus type 8* - HHV-8), já foi detectado em todas as formas de SK, independente da associação com o HIV.

O KSHV/HHV-8 é um vírus de DNA, cujo material genético é mantido na forma episomal na latência, mas que está linearizado durante a montagem do vírion e a replicação viral (JARVILUOMA & OJALA, 2006). Pertence à família *Herpesviridae*, subfamília *Gammaherpesvirinae*, da qual também fazem parte o vírus de Epstein-Barr (*Epstein-Barr virus* - EBV) e o herpesvírus saimiri (*Herpesvirus Saimiri* - HVS). Assim como o HVS, o KSHV/HHV-8 faz parte do gênero *Rhadnovirus*; entretanto, é o primeiro membro conhecido desse gênero que infecta humanos (CESARMAN et al., 1996, KIEFF & SHENK, 1998, JENNER & BOSHOFF, 2002). Os herpesvírus gama são linfotrópicos e promovem o aparecimento de células linfóides atípicas com elevada capacidade de proliferação celular. Além disso, em indivíduos co-infectados com KSHV/HHV-8 e HIV, sem apresentações clínicas de doenças associadas ao KSHV/HHV-8, as células B positivas para o KSHV/HHV-8 presentes nos nódulos linfáticos funcionam como reservatório, contribuindo para a persistência viral (CAMPBELL et al., 2005).

O genoma do KSHV/HHV-8 possui tamanho aproximado de 180Kb e 96 seqüências abertas para leitura (*Open Reading Frame* - ORF) descritas. Destas, 13 codificam produtos homólogos a proteínas humanas envolvidas na regulação do ciclo celular, transdução de sinais e inibição de apoptose (CESARMAN & KNOWLES, 1999, JARVILUOMA & OJALA, 2006). Além do SK, o KSHV/HHV-8 já foi identificado em distúrbios linfoproliferativos, incluindo a doença multicêntrica de Castleman (*Multicentric Castleman Disease* - MCD) (SOULIER et al., 1995, GESSAIN et al., 1996), linfomas de cavidades corpóreas (*Primary Effusion*

Lymphoma - PEL) e alguns linfomas não-Hodgkin de células B, freqüentemente com co-infecção por EBV (CESARMAN et al., 1995).

Embora o KSHV/HHV-8 seja encontrado em apenas 1-6% das células endoteliais em cultura, ensaios *in vitro* demonstraram que a infecção viral interfere significativamente na sobrevivência das células, estendendo-a e promovendo o crescimento independente de ancoragem (FLORE et al., 1998).

2.1 Principais produtos do KSHV/HHV-8

2.1.1 Proteínas de ciclo lítico

Dentre as proteínas líticas do KSHV/HHV-8, a proteína rta (codificada pela ORF-50) merece destaque em virtude de sua expressão ser necessária e suficiente para ativação do ciclo lítico do KSHV/HHV-8. O ciclo lítico viral é elemento importante na patogênese das doenças associadas ao KSHV/HHV-8, pois possibilita a produção de partículas virais e sua dispersão para infecção de novas células susceptíveis (SUN et al., 1999, STAUDT & DITTMER, 2007).

A proteína codificada pela ORF-K2, homóloga a interleucina 6 humana (IL-6), tem sua expressão restrita a distúrbios linfoproliferativos associados ao KSHV/HHV-8, como MDC e PEL (DENG et al., 2002, DENG et al., 2007). A vIL-6 contribui para a progressão tumoral pelo estímulo à secreção do VEGF, proporcionando angiogênese (NICHOLAS et al., 1997, AOKI et al., 1999). A vIL-6 e a IL-6 endógena interagem com diferentes receptores celulares; adicionalmente, vIL-6 não é inibida pelo mecanismo de regulação negativa que regula sua contraparte celular. Como resultado, a expressão de vIL-6 gera estímulos positivos para proliferação de células KSHV/HHV-8-positivas e células adjacentes não-infectadas (CHATTERJEE et al., 2002, MOORE & CHANG, 2003).

Outro importante produto viral é a proteína homóloga ao receptor acoplado a proteína G humana (*G-Protein Coupled Receptor* - GPCR), codificada pela ORF-74 (SCHULZ, 1998). vGPCR atua na regulação do ciclo celular, indução de angiogênese (assim como a vIL-6, favorece a produção de VEGF) e inflamação (MONTANER et al., 2003, CANNON, 2007). Em indivíduos infectados pelo HIV-1, a vGPCR pode contribuir para patogenicidade do KSHV/HHV-8 por meio de sua interação com a proteína tat do HIV-1, resultando em ativação das vias NF- κ B e NF-AT (GUO et al., 2004).

O KSHV/HHV-8 é capaz de evadir o sistema imunitário graças à interação de proteínas celulares e virais. O fator regulador de interferon viral (*viral Interferon Regulatory Factor* - vIRF), codificado pela ORF-K9; bloqueia atividade de IRF-1 que resulta na alteração da transcrição de diversos genes celulares IRF-1-dependentes (OFFERMANN, 2007). A proteína codificada pela ORF-45, por sua vez, interage com o IRF-7, inibindo a resposta anti-viral do hospedeiro (ZHU et al., 2002, ZHU et al., 2005).

O próprio KSHV/HHV-8 contribui para o descontrole do sistema imunitário. Produtos codificados pelas ORF-K3 e ORF-K5 aumentam a internalização e endocitose de moléculas de classe I do complexo principal de histocompatibilidade (*Major Histocompatibility Complex* – MHC), impedindo o reconhecimento das células infectadas, por linfócitos T citotóxicos (COSCOY & GANEM, 2000, ISHIDO et al., 2000, LORENZO et al., 2001). Além disso, recentemente foi descrito que as proteínas virais K3 e K5 inibem a resposta imunitária mediada por citocinas, pois promovem a degradação de IFN- γ (LI et al., 2007).

Curiosamente, proteínas do KSHV/HHV-8 homólogas às proteínas inflamatórias de macrófagos (*viral Macrophage Inflammatory Protein* – vMIP) celulares atuam em alguns co-receptores utilizados pelo HIV-1. A vMIP-I (codificada na ORF-

K6 do KSHV/HHV-8) liga-se a CCR5 e inibe a entrada e a replicação das variantes CCR-5-dependentes do HIV-1 (MOORE et al., 1996). A vMIP-II (codificada pela ORF-K4), por sua vez, dificulta a infecção de linfócitos T CD₄⁺ pelo HIV-1, ainda que de maneira mais eficaz em células que expressam CCR3 em comparação às que expressam CXCR4 ou CCR5 (BOSHOF et al., 1997). Além de favorecer a resposta Th2 em detrimento de Th1 (LINDOW et al., 2003). A vMIP-III, codificada pela ORFK4.1, possui propriedades agonistas em receptores CCR4, atuando como agente quimiotático para linfócitos T do sangue periférico que expressam citocinas do perfil Th2, o que potencializa a resposta imunitária humoral em detrimento da celular (STINE et al., 2000).

2.1.2 Proteínas de ciclo latente

Assim como outros herpesvírus, o KSHV/HHV-8 apresenta infecção latente na maioria das células infectadas e os genes expressos durante essa fase desempenham funções importantes para a transformação celular (KATANO et al., 1999).

A proteína LANA-1 (*Latency-associated Nuclear Antigen-1* - LANA-1), codificada pela ORF-73, é uma das principais proteínas de latência, juntamente com os produtos das ORFs -71 e -72 (RAINBOW et al., 1997, CESARMAN & MESRI, 2007). A ORF-71 codifica a vFLIP (*FLICE-like inhibitory protein*), proteína semelhante à proteína inibidora de FLICE (*FAS-associated death domain-like interleukin-1 β converting enzyme*), i.e., a FLIP celular. Por sua vez, a ciclina viral (vCyc), codificada pela ORF-72, é homóloga à ciclina D humana. LANA-1, vFLIP e vCyc são transcritas a partir de uma mesma região que produz um RNA mensageiro (RNAm) tricistrônico (DITTMER et al., 1998, CESARMAN & MESRI, 2007). Por meio de processamento alternativo, dois transcritos são gerados: um com 5,4Kb, que codifica LANA, vCyc e vFLIP, e um com 1,7Kb, que codifica apenas vCyc e vFLIP

(DITTMER et al., 1998). O promotor da proteína LANA é bi-direcional e controla a expressão dos genes de latência ORF-71, ORF-72 e ORF-73, localizados à esquerda do promotor, e os líticos ORF-K14 e ORF-74, à direita do promotor (VERMA et al., 2007).

A primeira atividade atribuída à proteína vFLIP foi a regulação da apoptose desencadeada pela família de receptores do fator de necrose tumoral (*Tumor Necrosis Factor receptor* - TNFr) e bloqueio de ativação de caspases (SCHULZ, 1998, NEIPEL & FLECKENSTEIN, 1999). Entretanto, mais tarde percebeu-se que as principais atividades dessa proteína viral estão relacionadas à ativação de NF- κ B, pela interação de vFLIP com o complexo I κ B quinase, mediada por TRAF-2 (GUASPARRI et al., 2006). A ativação de NF- κ B por vFLIP ocasiona a transcrição de genes celulares anti-apoptóticos dependentes de NF- κ B, tais como cFLIP, cIAP-1 e cIAP-2 (GUASPARRI et al., 2004), e bloqueia apoptose desencadeada por ausência de fatores de crescimento (SUN et al., 2003).

Assim como as ciclinas endógenas, vCyc atua na regulação do ciclo celular, mas possui algumas peculiaridades em relação à sua homóloga celular - a ciclina D2. vCyc interage preferencialmente com Cdk-6; adicionalmente, o complexo vCyc-Cdk-6 é menos susceptível aos inibidores p16^{Ink4A} e proteínas Cip/Kip. A expressão de vCyc induz passagem da fase G1 para S, desregulando a mitose e induzindo síntese de DNA. Essas atividades favorecem a proliferação de células KSHV/HHV-8-positivas e, conseqüentemente, a propagação viral (VERSCHUREN et al., 2004, KOOPAL et al., 2007).

Pela análise das funções exercidas pelos produtos do KSHV/HHV-8 é possível perceber as diferentes estratégias desenvolvidas pelo vírus para modulação de diferentes fenômenos, incluindo proliferação celular, apoptose e evasão do

sistema imunitário. Produtos do KSHV/HHV-8 não apenas usufruem da maquinaria celular, como também regulam proteínas celulares e mimetizam suas funções.

2.2 LANA-1: proteína multifuncional

A proteína LANA-1 possui 1.162 aminoácidos e tamanho estimado de 135kDa (RUSSO et al., 1996, KEDES et al., 1997). Em gel de SDS-PAGE (*Sodium Dodecyl Sulfate - Polyacrylamide Gel Electrophoresis*), entretanto, é encontrada com 222-234kDa em células BC-1. Essa diferença no tamanho estimado é o verificado em linhagens de células infectadas pelo KSHV/HHV-8 provavelmente está relacionado à presença de uma região de repetição altamente ácida na sequência de aminoácidos, além de modificações na estrutura primária da proteína (RAINBOW et al., 1997).

A proteína LANA-1 é dividida nas regiões amino-terminal, carboxi-terminal e uma região de repetição central (*Central Repeat - CR*). Esta última é ainda composta por 3 sub-regiões: CR1/DED (321-428aa), região de repetição de ácido aspártico (D) e ácido glutâmico (E), CR2/QED (430-768aa), região rica em glutamina (Q), ácido glutâmico, ácido aspártico, e CR3 (769-937aa), que comporta um domínio de zíper de leucina (RUSSO et al., 1996).

A marcação de LANA-1 pela técnica de imunofluorescência revela sinal de aspecto puntiforme e localização nuclear (LENNETTE et al., 1996). Embora apenas a região N-terminal apresente um sinal de localização nuclear já identificado, em análises de citolocalização das diferentes porções de LANA-1, ambas as regiões N- e C-terminais são encontradas no núcleo (VERMA et al., 2007).

LANA-1 apresenta múltiplas funções e é capaz de interagir com diversas proteínas celulares e virais. Sua primeira atividade descrita foi a manutenção do epissoma viral (BALLESTAS et al., 1999): LANA-1 possibilita a persistência

epissomal e sua adequada segregação pela interação da região C-terminal da proteína com a região de repetição terminal (*Terminal Repeat* - TR) do KSHV/HHV-8 (BALLESTAS & KAYE, 2001). Além disso, a região N-terminal de LANA-1 interage com as histonas H2A e H2B, o que também contribui para a manutenção do epissoma (BARBERA et al., 2006). A região de zíper de leucina é o sítio de ligação com a p53, e a interação de LANA-1 com essa proteína supressora tumoral inibe sua atividade transcricional, dificultando a expressão de genes relacionados ao reparo de DNA e deflagração da apoptose (FRIBORG et al., 1999). Assim, LANA-1 favorece a sobrevivência da célula infectada pelo KSHV/HHV-8, essencial para a disseminação do vírus.

Os aminoácidos de 5 a 13 da região N-terminal de LANA-1 são necessários para associação da proteína com os cromossomos, replicação do DNA do KSHV/HHV-8 e persistência epissomal (BARBERA et al., 2004). Por outro lado, a porção C-terminal possui destacada importância para homodimerização de LANA-1 (VERMA et al., 2007). Adicionalmente, a porção C-terminal de LANA-1 se liga à proteína Rta do KSHV/HHV-8, de modo a inibir simultaneamente seu próprio promotor e a atividade de Rta, conferindo à proteína papel no controle do ciclo lítico viral (LAN et al., 2004).

A via de sinalização Wnt pode ser modulada pela ação de LANA-1, que é capaz de interagir com a glicogênio-sintetase quinase (*Glycogen Synthase Kinase 3- β* - GSK3- β) de modo a alterar sua distribuição intracelular proporcionando seu acúmulo no núcleo. Essa interação ocasiona liberação de β -catenina, que atua induzindo a expressão de diferentes genes, incluindo *MYC*, *JUN* e *CCDN1* (FUJIMURO & HAYWARD, 2003, FUJIMURO et al., 2005, CESARMAN & MESRI, 2007). Via interação com o fator de transcrição Sp1, LANA-1 também é capaz de transativar o promotor da subunidade catalítica da telomerase humana (*human*

Telomerase Reverse Transcriptase – hTERT) (KNIGHT et al., 2001, VERMA et al., 2004). Embora a interação de Sp-1 com a região N-terminal seja essencial para essa atividade, a região C-terminal da proteína aumenta a atividade transcricional de Sp-1 (VERMA et al., 2004).

Embora a região CR seja pouco estudada, principalmente com relação à interação com proteínas, recentemente foi demonstrado que essa região possui características similares à CR do antígeno nuclear do EBV (*EBV Nuclear Antigen 1* - EBNA-1), que possui uma região constituída por repetições de glicina e alanina (*Glycine-Alanine repeats* - GAR). Assim como EBNA-1, LANA-1 é capaz de inibir o processamento antigênico *in cis* e, dessa maneira, contribui para a evasão do sistema imunitário (ZALDUMBIDE et al., 2007).

2.3 Epidemiologia Molecular do KSHV

2.3.1 Transmissão e Fatores ambientais associados ao KSHV/HHV-8

A prevalência de infecção pelo KSHV/HHV-8 em indivíduos imunocompetentes usualmente não se correlaciona com o risco de desenvolvimento do SK. Entretanto, países como Itália, Grécia e Israel apresentam altos índices de soroprevalência de KSHV/HHV-8 na população em geral, (WHITBY et al., 1998, DAVIDOVICI et al., 2001, SCHULZ et al., 2002) e os maiores índices de incidências de SK clássico na Europa são reportados na ilhas italianas da Sardenha e Sicília (ISCOVICH et al., 2000).

Diferentes aspectos da transmissão do KSHV/HHV-8 ainda são debatidos na literatura. Na população adulta, há relatos que destacam a importância da via sexual (MELBYE et al., 1998, RENWICK et al., 2002, PIERROTTI et al., 2005, CATERINO-DE-ARAUJO et al., 2007). A transmissão do KSHV/HHV-8 predominantemente por via sexual foi sugerida em estudo analisando a associação

de infecção pelo KSHV/HHV-8 e pelo herpesvírus simples 2 (*Herpesvirus Simplex 2* - HSV-2) entre 784 prisioneiros italianos (SARMATI et al., 2007). Entretanto, também é relevante a transmissão pelo compartilhamento de seringas e agulhas no uso de drogas injetáveis (ABLASHI et al., 2002, ATKINSON et al., 2003). Adicionalmente, o risco de soroconversão para o KSHV/HHV-8 é maior em pacientes receptores de sangue soropositivo para o vírus quando comparados com os pacientes que receberam sangue soronegativo (HLADIK et al., 2006). É curioso notar que o SK raramente ocorre em indivíduos que adquiriram o HIV-1 por via parenteral, como usuários de drogas injetáveis (UDIs) e hemofílicos (WEISS, 1999).

Outros estudos dedicam maior atenção à veiculação do vírus pela saliva (LADUCA et al., 1998, COOK et al., 2002). O KSHV/HHV-8 já foi detectado na orofaringe de homossexuais masculinos sem HIV (CASPER et al., 2007), nas células epiteliais de mucosa oral de indivíduos portadores do HIV (sem relação com progressão clínica do SK, estágio da lesão ou sobrevida) (WIDMER et al., 2006) e na mucosa bucal e palato de indivíduos que receberam transplante renal (AL-OTAIBI et al., 2007).

A transmissão vertical do KSHV/HHV-8 foi demonstrada por Mantina e colaboradores (2001), que encontraram DNA viral em dois neonatos. Contudo, os autores enfatizam que não pôde ser determinado se a infecção ocorreu *in utero* ou *intrapartum*, mas a infecção pós-natal foi descartada devido à impossibilidade de detecção do DNA no pós-natal imediato (MANTINA et al., 2001).

Duas hipóteses são discutidas quanto ao contágio de pacientes transplantados, notadamente os que desenvolvem SK iatrogênico: a infecção pelo KSHV/HHV-8 pode ser prévia ao transplante, ou o vírus é adquirido a partir do enxerto (LUPPI et al., 2000, HENGGE et al., 2002b, a, MARCELIN et al., 2007). No primeiro caso documentado de soroconversão, pós-transplante renal, para o

KSHV/HHV-8, a paciente desenvolveu MCD e SK em um período de 27 meses após a cirurgia (PARRAVICINI et al., 1997).

A despeito de a prevalência de infecção pelo KSHV/HHV-8 ser igual entre indivíduos do sexo masculino e feminino na África, o risco de desenvolver SK é maior entre os homens. Essa diferença não pôde ser atribuída a mudanças na resposta imunológica, contagem de linfócitos CD₄⁺ ou carga viral do KSHV/HHV-8. Por esse motivo, é cogitada a contribuição de fatores ambientais na etiopatogênese do SK. (MEDITZ et al., 2007). O solo vulcânico de regiões com alta prevalência do SK endêmico contém elevadas quantidades de ferro mineral. Alguns estudos referem que, nestas regiões, óxidos de ferro e argila podem penetrar pela pele de membros inferiores de trabalhadores do campo através de micro-lesões causadas pelo quartzo, também presente no solo. Nesse contexto, a resposta inflamatória crônica à agressão dermo-linfática pode contribuir para o desenvolvimento de SK (ZIEGLER et al., 2001, SIMONART, 2006).

Assim, embora os mecanismos ainda não estejam adequadamente elucidados, fatores ambientais e sócio-econômicos devem contribuir no desenvolvimento do SK. Também o uso de inalantes de nitritos já foi associado com maior risco de infecção pelo HIV e pelo KSHV/HHV-8 (BUCHBINDER et al., 2005). Por outro lado, é descrito papel inibitório da fumaça de tabaco concentrada na infecção do KSHV/HHV-8, supostamente por proporcionar alterações nos níveis de citocinas que influenciam a patogênese do SK (FORD et al., 2005).

Outros estudos sugerem que artrópodes hematófagos podem fomentar a transmissão do KSHV/HHV-8, particularmente em comunidades menos favorecidas em termos sócio-econômicos. Por outro lado, especula-se que a infecção pode ser veiculada pela saliva humana aplicada no local da picada com a finalidade de aliviar a irritação (SIMONART, 2006). Outros fatores relacionados com baixas condições

sócio-econômicas referem-se ao uso de água não-encanada: pouca disponibilidade de água está intimamente relacionada com baixas condições de higiene, e em alguns países da África é trivial o hábito de limpar o rosto de crianças com saliva. Nestas regiões, crianças soro-positivas para o KSHV/HHV-8 comumente têm mães também soro-positivas (MBULAITEYE et al., 2005).

2.3.2 Genotipagem do KSHV/HHV-8

Os genótipos A, B e C do KSHV/HHV-8 foram descritos com base na análise de segmentos das ORFs 25/26, e 75 (ZONG et al., 1997). Entretanto, Fouchard e colaboradores (2000) demonstraram discrepâncias entre os resultados de genotipagem obtidos pela análise das ORFs 26 e 75 (FOUCHARD et al., 2000). Em 1999, estudos publicados por Zong e Meng demonstraram o uso da região ORF-K1 viral para genotipagem do KSHV/HHV-8 (MENG et al., 1999, ZONG et al., 1999). A variabilidade na ORF-K1, que codifica uma proteína viral transmembrana, revelou-se mais adequada para análise filogenética de isolados de KSHV/HHV-8 em comparação às ORFs 26 e 75. Adicionalmente, o estudo das regiões hipervariáveis VR1 e VR2 da proteína K1 permite a análise da filogenia equivalente àquelas obtidas com as seqüências completas da respectiva ORF viral (Figura 2) (MENG et al., 1999).

MENG et al. verificaram que indivíduos norte-americanos (independente de infecção pelo HIV e presença do SK) apresentavam dois genótipos do KSHV/HHV-8, denominados I (ou A) e II (ou C). Um novo genótipo, denominado III (ou D), foi identificado em amostras da Austrália, e o genótipo IV (ou B) e uma variante do genótipo I (ou A) (MENG et al., 1999) foram identificados em amostras da Uganda. O genótipo D é restrito ao Japão, Austrália, Taiwan, Nova Zelândia e

Polinésia (DUPREZ et al., 2006). Por outro lado, foi descrito o genótipo E em ameríndios brasileiros (BIGGAR et al., 2000).

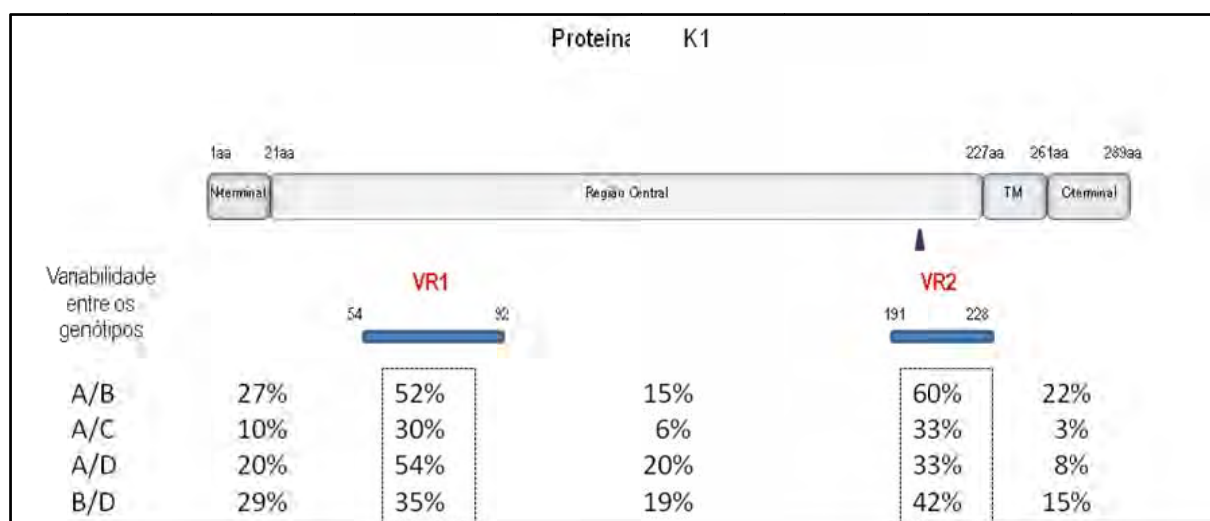


FIGURA 2 - Estrutura geral da proteína da ORF-K1. Domínios N-terminal, região central (que inclui as regiões hipervariáveis VR1 e VR2), domínio transmembrana (TM) e a porção C-terminal, que corresponde à calda citoplasmática da proteína. A variabilidade entre os três genótipos descritos é apresentada em cada região. Há elevada variação nas regiões VR1 e VR2 entre os diferentes genótipos. ▴ - região em que há duas deleções nos genótipos A e C, e uma em B. (Adaptado de ZONG et al. (1999)).

Em estudo com 70 indivíduos infectados pelo KSHV/HHV-8 provenientes de Israel, Coréia do Sul, Sicília, Escandinávia, Brasil, Uganda, África do Sul, e EUA, Zong e colaboradores (2002) encontraram mais de 135 genomas distintos do vírus, agrupados em sete genótipos, de acordo com a análise das ORFs K1 e K15: A/P, B/P, C/P, D/P, M, N, e Q. Importante destacar que a análise do genoma do KSHV/HHV-8 obtido de SK proveniente de Israel revelou que o genótipo A1', resultado da análise da ORF-K1, foi predominante entre judeus *Ashkenazi* imigrantes da Rússia, enquanto as variantes C2 e C6 predominaram nos judeus *Sephardi* do norte da África (ZONG et al., 2002).

Para o entendimento da evolução do vírus, os três ramos A/C, B e D foram mapeados de acordo com as migrações de populações humanas: o ramo B se correlaciona às primeiras migrações pela África sub-Saara há 100.000 anos, o D foi

para o sul da Ásia, Austrália, Taiwan e Ilhas do Pacífico há 60.000-70.000 anos e o terceiro para a Europa e norte da Ásia há 35.000 anos (A e C), com expansão para Américas e norte da Europa no fim da era glacial (HAYWARD, 1999). COOK e colaboradores (1999) demonstraram que os genótipos de isolados do leste e do oeste da África estão filogeneticamente relacionados, mas distantes daqueles observados na Europa. Os autores sugerem que a variabilidade da região K1 do KSHV/HHV-8 possa ter sido influenciada pela seleção, não apresentando correlação com as diferentes doenças associadas ao KSHV/HHV-8, e nem com os locais onde há predominância de SK endêmico (COOK et al., 1999).

Um estudo publicado em 2001 analisou as ORFs-K1 e -K15 do KSHV/HHV-8 em isolados obtidos de indivíduos do sul do Texas, local em que 60-80% da população é hispânica, com ancestrais mexicanos. Os isolados de genótipo M estavam presentes em amostras de todos os pacientes com SK clássico, fato que poderia sugerir sua existência na população antes do advento da AIDS. Por outro lado, todos os casos de SK-Aids apresentavam o genótipo P, dado que demonstra sua propagação preferencial durante epidemia de aids (ZHANG et al., 2001).

A grande variedade genotípica do KSHV/HHV-8 encontrada nas regiões endêmicas africanas não está restrita aos adultos. Em crianças com e sem infecção pelo HIV, embora o genótipo predominante seja K1-A₅ (LACOSTE et al., 2000), foram encontrados os genótipos K1-A₂, A₃, B e C₃; K12-B₁ ou B₂ e K14.1/15 P ou M (KASOLO et al., 2007). Elevada diversidade também foi encontrada entre diferentes tribos indígenas na região Amazônica do Brasil. Foram encontrados genótipos C na tribo Zo'e e E na comunidade Tiriyo. A prevalência de KSHV/HHV-8 foi maior entre os ameríndios quando comparados aos indivíduos da área urbana de Belém, PA. O genótipo B foi encontrado entre pacientes portadores do HIV da área urbana, fato

que pode ser explicado pela ascendência africana da população (ISHAK et al., 2007).

Em populações com baixas taxas de miscigenação, como na Rússia, não é relatada diversidade de genótipos do KSHV/HHV-8 nas diferentes formas de SK, prevalecendo os grupos A e C (KADYROVA et al., 2003). Em amostras provenientes de Okinawa (Japão), Kamiyama e colaboradores (2005) relataram que o único caso de SK-Aids avaliado apresentava isolado de genótipo A, enquanto o genótipo C foi verificado nos isolados de três casos de SK clássico (KAMIYAMA et al., 2004).

Embora sejam raros os dados sobre a genotipagem do KSHV/HHV-8 em casos SK no Brasil, é descrito que os genótipos B e C identificados são similares àqueles que circulam na Europa, Estados Unidos e África (CATERINO-DE-ARAUJO, 1998). Nos 33 indivíduos analisados com SK-Aids da cidade de São Paulo, SP, Nascimento e colaboradores (2005) encontraram isolados de genótipos virais dos grupos A, B e C nas frequências de 48%, 21% e 30%, respectivamente. Segundo os autores, a presença dos genótipos A₅ e B em indivíduos descendentes de caucasianos e de ameríndios indicam que uma linhagem ancestral do KSHV/HHV-8 foi introduzida na América durante o tráfico de escravos e posteriormente houve sua distribuição pela população brasileira (NASCIMENTO et al., 2005).

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CAPÍTULO 1:

**KSHV/HHV-8 Genotypes in Kaposi's
sarcoma lesions from patients infected
or not by the human
immunodeficiency virus**

KSHV/HHV-8 Genotypes in Kaposi's sarcoma lesions from patients infected or not by the human immunodeficiency virus*

** De acordo com as normas da J Gen Virol*

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1. Summary

Kaposi's sarcoma-associated herpesvirus/Human herpesvirus 8 (KSHV/HHV-8) plays a role in the pathogenesis of Kaposi's sarcoma (KS) and some lymphoproliferative diseases, mainly in patients infected by the human immunodeficiency virus (HIV). Worldwide, geographic and ethnic factors impact the distribution of KSHV/HHV-8 genotypes in human populations. Moreover, it is not known whether distinct viral genotypes have a predominant association with specific KSHV/HHV-8-associated diseases. As Brazil has many racially mixed inhabitants, viral genotypes are expected to be highly diverse in KS specimens in the Brazilian population. Thus, the present study aimed to retrospectively evaluate the genotype of KSHV/HHV-8 isolated from KS lesions in patients with or without infection of human immunodeficiency virus (HIV) from Brazil. KSHV/HHV-8 genotyping was performed by Polymerase Chain Reaction / Restriction Fragment Length Polymorphisms (PCR-RFLP), as well as DNA sequencing and phylogenetic analysis of viral ORF-K1. Fifty KS cases were evaluated, 22 (44.0%) from HIV-positive and 14 (28.0%) from HIV-negative patients; the HIV status was not available in the remaining 14 (28.0%) patients. The mean ages of HIV-positive and HIV-negative patients were, respectively, 37.9 and 60.5 years. The most frequently detected viral genotypes were A (25/50; 50.0%) and C (24/50; 48.0%); the B genotype was isolated in one case only (2.0%). There was a preferential distribution of viral A genotype among HIV-positive patients, whereas C genotype was found mostly in the HIV-negative setting. This result suggests that distinct viral genotypes may have unique biological properties that impact their distribution in KSHV/HHV-8-associated diseases, as observed in KS.

2 Introduction

Kaposi's sarcoma associated herpesvirus (KSHV), also known as Human herpesvirus type-8 (HHV-8), is the most recently described human gammaherpesvirus (Chang *et al.*, 1994). KSHV/HHV-8 is the causal agent of Kaposi's sarcoma (KS), an angioproliferative neoplastic disease. It is also associated with Multicentric Castleman Disease (MCD) (Gessain *et al.*, 1996; Karcher & Alkan, 1995; Soulier *et al.*, 1995) and primary effusion lymphoma (PEL) (Cesarman *et al.*, 1995), notably in patients also harboring the Human immunodeficiency virus (HIV).

Besides the classic KS, the disease can be classified as AIDS-associated KS, iatrogenic KS or endemic KS according to its clinical and epidemiological features (Schwartz, 2004). The classic form of KS (described by Moritz Kaposi in 1872) affects predominantly elderly men from the Mediterranean, mainly Jews of eastern European descent (Kaposi, 1872). Patients usually present one or a few small and indolent lesions in lower limbs (Antman & Chang, 2000). Conversely, AIDS-associated KS more frequently affects homosexual and bisexual men and it is characterized by multiple and fast-growing lesions (Hengge *et al.*, 2002). Iatrogenic KS is commonly found in patients receiving post-transplant immunosuppressive therapy, whereas endemic KS affects children and young adults in equatorial Africa (Friedman-Kien & Saltzman, 1990; Sarid *et al.*, 2002). All KS forms share the same histological features, and the lesions evolves from patch to tumoral lesions, which are commonly associated with advanced stages of the disease (Ioachim *et al.*, 1995; Whelan & Scadden, 2000).

Using several molecular approaches, in the last decade, the KSHV/HHV-8 genome was detected in all types of KS specimens (Curreli *et al.*, 2003; Kuhara *et al.*, 2008; Lock *et al.*, 1997; Mendez *et al.*, 1998; White & Campbell, 2000). The

analysis of the viral DNA has generated valuable data to clarify the molecular epidemiology of KSHV/HHV-8 infection and associated diseases (Zong *et al.*, 2007). After analysis of viral ORFs 25/26 and ORF-75, three distinct forms of the KSHV/HHV-8 genome were originally described: the so-called viral genotypes A, B and C (Alagiozoglou *et al.*, 2000; Zong *et al.*, 1997). It was reported that A genotypes were more commonly isolated from classic KS, whereas B and C were more often found among African cases of the disease (Hayward & Zong, 2007). Because of the low variation in nucleotide sequences of viral ORFs -25, -26 and -75, other regions in the KSHV/HHV-8 genome have been evaluated in order to identify a better target for genotyping (Fouchard *et al.*, 2000; Meng *et al.*, 1999b; Zong *et al.*, 1999).

Currently, the molecular genotyping of KSHV/HHV-8 is usually based on the analysis of viral ORF-K1, which encodes a transmembrane glycoprotein that shares homology with human receptors of the immunoglobulin superfamily. The K1 glycoprotein is composed of three domains: the extracellular, the transmembrane and the cytoplasmatic domains (Zong *et al.*, 1999). Viral ORF-K1 shows the highest variability in the nucleotide sequence compared to other regions in the KSHV/HHV-8 genome. A and C genotypes, as defined by viral ORF-K1 analysis, differ by 39 amino acids (15%), whereas A and B have a variation of 85 amino acids (29%). The K1 extracellular domain is the most variable region in the protein; it consists of two hypervariable regions, VR1 and VR2, whose analyses provide valuable data for KSHV/HHV-8 genotyping (Meng *et al.*, 1999b; Zong *et al.*, 1999).

Besides A, B and C genotypes, D genotypes were isolated from South Pacific inhabitants (Meng *et al.*, 1999b), and E genotypes were isolated from Brazilian Amerindians in an endemic area of KSHV/HHV-8 infection; remarkably, no cases of KS were reported in this population (Biggar *et al.*, 2000). Therefore, five major

KSHV/HHV-8 genotypes are currently described: A, B, C, D and E. They are distributed in human populations according to geographic localization and ethnicity: overall, A and C genotypes are found in Europe, the USA and Asia; B genotypes and the A₅ variant are found in Africa and French Guiana; D is usually found in Taiwan, Australia and some islands in the South Pacific; finally, E genotypes are isolated from Brazilian Amerindians (Hayward & Zong, 2007; Meng *et al.*, 1999a).

Among the relevant available information in the literature, there are only a few studies on the distribution of KSHV/HHV-8 genotypes in Brazil (Biggar *et al.*, 2000; Caterino-de-Araujo, 1998; Ishak *et al.*, 2007; Nascimento *et al.*, 2005; Zong *et al.*, 2002). European immigration, African slavery and interracial breeding in the Brazilian territory have given rise of a population with high ethnic diversity. Research on KSHV genotypes in Brazil is of special importance, and may provide crucial information for a better understanding of the dynamics of KSHV/HHV-8 distribution in humans. On the other hand, it is unknown whether different KSHV/HHV-8 genotypes have distinct biological properties that could influence the development and evolution of KSHV/HHV-8-associated diseases. Therefore, the present study aimed to retrospectively assess the frequency of KSHV/HHV-8 genotypes in KS specimens from HIV-positive and HIV-negative patients, as well as to evaluate the genotype distribution with the data available for the KS cases studied.

3 Methods

This study was approved by the Research Ethics Committee (#352/2005) at Botucatu Medical School, Sao Paulo State University (UNESP). Sixty-eight KS cases were selected from the files of the Pathology Department at Botucatu Medical School, UNESP, and three private Surgical Pathology Laboratories in Sao Paulo State, Brazil. Cases were previously evaluated for KSHV/HHV-8 infection by molecular and immunohistochemical techniques (Ramos da Silva *et al.*, 2007). DNA samples were extracted from paraffin-embedded formalin-fixed tissues (FFPET) as previously described (Ramos-da-Silva S *et al.*, 2006), and submitted for viral genotyping by Polymerase Chain Reaction and Restriction Fragment Length Polymorphism (PCR-RFLP), as well as automated DNA sequencing and phylogenetic analysis.

3.1 KSHV/HHV-8 Genotyping

KSHV/HHV-8 genotyping was performed through viral ORF-K1 amplification by nested-PCR followed by RFLP, as previously proposed (Caterino-de-Araujo & Moreira, 2002). The forward and reverse primers used were K1inn5 (CCC TGG AGT GAT TTC AAC GC) and K1inn6 (ACA TGC TGA CCA CAA GTG AC) for the first PCR, and K1-1 (GAG TGA TTT CAA CGC CTT AC) and K1-N (TGC TGA CCA CAA GTG ACT GT) for the second (nested) PCR. These primers amplify 255bp and 247bp long segments of KSHV/HHV-8 ORF-K1 in the first and second PCR round, respectively. In all assays, reactions were set up with PCR buffer (Tris-Cl 100mM pH 8.8/750Mm KCl), 3.0mM of MgCl₂, 0.2 mM of each dNTP, 0.5µM of each primer, 1.25U Taq DNA polymerase and DNA template. The PCR profile was 35 cycles at 94°C 30s, 57°C for 30 s, and 72°C for 1 min in the first reaction; and 94°C for 30 sec, 55°C for 30 sec, and 72°C for 1 min in the nested-PCR. PCR products were

evaluated in 2% agarose gels stained with ethidium bromide. Afterwards, RFLP was performed with single digestion by the enzymes Hinf I, Taq I, Hae III, Nsi I, Mse I (Tru I). In order to define the KSHV/HHV-8 genotype, digestion patterns were interpreted using the key presented in Figure 1.

Automated DNA sequencing was performed for validation of genotyping results by PCR-RFLP, and for phylogenetic analysis of KSHV/HHV-8 isolates obtained. After the nested-PCR, ORF-K1 amplicons were purified with the GFX PCR DNA System and Gel Band Purification Kit (GE Healthcare - Little Chalfont Buckinghamshire, UK, England), following the manufacturer's instructions. Purified amplicons were quantified in a 2% agarose gel loaded with Low DNA Mass Ladder (Invitrogen - Carlsbade, CA, USA). Sequencing reactions were performed in the MegaBACE 1000 sequencer using the DYEnamic ET Dye Terminator and Thermo Sequenase™ II DNA Polymerase System (both from GE Healthcare, Little Chalfont Buckinghamshire, UK, England). Sequences were initially analyzed with the Sequence Analyzer utilizing Base Caller Cimarron 3.12 software. The M13 plasmid was sequenced as a control for DNA sequencing reactions using the primers provided with the sequencing reagents.

After analysis of both strands of KSHV/HHV-8 ORF-K1 amplicons, consensus sequences were generated for each viral isolate. Consensus sequences and sequences from KSHV/HHV-8 prototype isolates in the GenBank (National Institutes of Biological Information, USA) were used to produce ORF-K1 DNA and polypeptide phylogenetic trees using the Mega 3.1 package software (Kumar *et al.*, 2004) with the neighbor-joining algorithm (500 bootstrap replicas). Visual analysis of the phylogenetic trees was employed to validate the results of KSHV/HHV-8 genotyping by PCR-RFLP.

All clinicopathological data available for the KS cases studied were evaluated using descriptive statistical analysis. ANOVA was performed to assess the statistical significance in age differences between individuals with and without HIV infection. Furthermore, the Bonferroni test was used for multiple comparisons among groups of KS arising in HIV-positive patients, KS in HIV-negative patients and KS not otherwise specified. Fisher's test was used to compare the frequency of viral genotypes in KS cases, as well as to evaluate the frequency of genotypes identified in relation to the stage of KS lesions. Associations were considered statistically significant when $\alpha \leq 0.05$.

4. Results

4.1 Kaposi's sarcoma casuistic characterization

Fifty out of sixty-eight cases (73.5%) studied could be evaluated for frequency of KSHV/HHV-8 genotypes in KS lesions. Male patients were 44/50 (88.0%) cases, while 6/50 (12.0%) were female. Overall, the mean age of KS patients was 50.5 years (16 to 87 years old). Patients harboring HIV were 22/50 (44.0%), whereas 14/50 (28.0%) were HIV-negative; 14/50 (28.0%) cases were classified as KS not otherwise specified (NOS), since the HIV status was not available. Male patients were predominant in all KS groups; and no significant difference was observed in male/female ratios. The mean ages for HIV-positive and HIV-negative patients were 37.9 and 60.5 years old, respectively. HIV-positive patients with KS were younger compared to HIV-negative patients or patients with KS NOS ($p < 0.01$; Bonferroni's test) (Table 1).

Advanced disease was verified by histopathological analysis in 30/50 (60.0%) patients with KS: 23/50 (46.7%) had nodular or tumoral lesions, whereas disease in esophagus, stomach or lymph nodes was found in 7/50 (14.0%) cases. Conversely, 20/50 (40.0%) patients had early stage KS, mostly plaque lesions (14/50; 28.0%).

4.2 Genotyping and KSHV/HHV-8 Phylogenetic Analysis

In the present study, KSHV/HHV-8 isolates obtained from KS lesions were indicated by the prefix BRBtu/SK followed by KS case index. Based exclusively on PCR-RFLP, viral isolates were mostly the A_P variant (22/50 cases; 44.0%) and the C genotype (18/50 cases; 36.0%). Only one isolate with B genotype was identified, and no D or E genotypes were found. The PCR-RFLP analysis revealed that 3/50 (6.0%) KSHV/HHV-8 isolates had digestion patterns that match the one expected for the A_M

variant. Thus, taking the PCR-RFLP results into account, the total number of KSHV/HHV-8 A genotypes found in this study was 25/50 (50.0%).

In 6/50 KS cases (12.0%), digestion patterns obtained after PCR-RFLP had not been described previously (Caterino-de-Araujo & Moreira, 2002). One non-described pattern was shared by isolates BRBtu/SK03, BRBtu/SK13, BRBtu/SK36, BRBtu/SK69 and BRBtu/SK75, whereas BRBtu/SK50 showed a unique one. Among isolates with A genotype, 20/25 (80.0%) were obtained from KS lesions arising in male patients, whilst 5/25 (20.0%) were obtained from lesions in female patients. On the other hand, all isolates of the C genotype came from KS lesions of male patients (n=18). Figure 2 shows examples of digestion patterns observed after KSHV/HHV-8 genotyping by PCR-RFLP as performed in the present study.

The distribution of KS cases according to HIV status and the viral genotypes identified is shown in Table 2. A high frequency of A-genotype isolates was found in HIV-positive patients (15/22; 68.2%); conversely, the majority of KS isolates from HIV-negative patients had C genotypes (10/14; 71.4%). The difference in proportions between A and C genotypes within HIV-positive and negative patients was statistically significant ($p=0.026$; Fisher's exact test).

KSHV/HHV-8 isolates from early stage KS lesions presented the A genotype more often (11/20; 55.0%), while late stage lesions showed predominantly C genotype (15/29; 51.7%) (Table 3). Moreover, this difference achieved no statistical significance, and it might be biased by the proportions of early and late stage KS lesions in HIV-positive and negative patients, which have predominantly A and C genotypes, respectively. In addition, no significant differences between the mean ages of KS patients infected by A or C genotypes of KSHV/HHV-8 were observed (Table 4).

In general, there was good correlation between results for KSHV/HHV-8 by PCR-RFLP and the phylogenetic analysis of viral ORF-K1 sequences after DNA sequencing. Exceptions were isolates BRBtu/SK03, BRBtu/SK13, BRBtu/SK36, BRBtu/SK50, BRBtu/SK69, BRBtu/SK75, which showed non-described banding patterns after digestion with the set of enzymes used for RFLP analysis of viral ORF-K1.

Phylogenetic trees based on nucleotide sequences of KSHV/HHV-8 ORF-K1 (Figure 3) and predicted polypeptide chains were equivalent (data not shown). All isolates with non-described digestion patterns (BRBtu/SK03, BRBtu/SK13, BRBtu/SK36, BRBtu/SK69, BRBtu/SK75, and BRBtu/SK50) clustered under the branch of the KSHV/HHV-8 C genotype. Figure 4 displays the phylogenetic relationships among isolates in the present study, other isolates from Brazil, and KSHV/HHV-8 prototype isolates previously described in the literature.

5. Discussion

At least to some extent, ethnic and geographical variation in the frequency of KSHV/HHV-8-associated disease, including KS, may result from exposure of human populations to different viral genotypes. For this reason, efforts to evaluate the distribution of KSHV/HHV-8 genotypes in different settings have been conducted worldwide (Biggar *et al.*, 2000; Duprez *et al.*, 2006a; Duprez *et al.*, 2006b; Meng *et al.*, 2001; Meng *et al.*, 1999a; Nascimento *et al.*, 2005; Szalai *et al.*, 2005; Zhang *et al.*, 2000; Zong *et al.*, 1999; Zong *et al.*, 1997).

Data on the emergence of distinct viral genotypes provide important clues on the evolutionary history of KSHV/HHV-8. It was estimated that A and C genotype strains emerged about 35,000 years ago in Europe and northern Asia, B strains about 100,000 years ago in Africa, whereas D strains originated about 60,000 years ago on the Pacific Islands (Zong *et al.*, 1999). In accord with this scenario, KSHV/HHV-8 A and C strains are predominant in the New World and Europe, whereas B strains are commonly found in Africa, and D are more frequent in the South Pacific and Australia (Hayward & Zong, 2007). Although the classic viral genotypes A, B, C and D are the most commonly studied worldwide, the analysis of ORF-K1 in addition to ORF-K15 allows KSHV/HHV-8 isolates to be divided into at least seven genotypes: A/P, B/P, C/P, D/P, M, N, and Q (Zong *et al.*, 2002).

The Brazilian population is highly heterogeneous, composed mostly of European and African immigrants, in addition to South American natives. For this reason, high diversity among KSHV/HHV-8 genotypes is expected to be found in Brazil. Currently, only a few studies on KSHV/HHV-8 infection in Brazilian populations are found in the literature, with a small number of viral isolates usually

described (Biggar *et al.*, 2000; Caterino-de-Araujo, 1998; Ishak *et al.*, 2007; Nascimento *et al.*, 2005; Zong *et al.*, 2002).

In 1998, Caterino-de-Araujo *et al.* reported that KSHV/HHV-8 B and C genotypes found in 7 AIDS-associated KS cases were similar to viral isolates from Europe, the USA and Africa (Caterino-de-Araujo, 1998). In 2005, Nascimento *et al.* evaluated specimens from 33 individuals with KS-AIDS from Sao Paulo city, SP, Brazil, and found that frequencies for viral A, B and C genotypes were 48%, 21% and 30%, respectively (Nascimento *et al.*, 2005). Interestingly, the KSHV/HHV-8 A₅ variant, which is detected in Africa and in African descendents from French Guiana (Hayward & Zong, 2007), was identified among viral isolates from Caucasian and Amerindian descendents (Nascimento *et al.*, 2005). The authors claim that the presence of A₅ or B genotypes in such a racially mixed population indicates that an ancestral KSHV/HHV-8 strain might have been introduced in South America during the era of the transatlantic slave trade, and its distribution in the Brazilian population occurred more recently (Nascimento *et al.*, 2005).

High diversity was also observed among different Indian tribes in the Brazilian Amazon region. Genotype C was found in the Zo'e tribe, and the genotype E in the Tiriyo tribe. The prevalence of the KSHV/HHV-8 was higher among Amerindians compared to individuals in the urban area of Belem, PA, Brazil. Furthermore, the B genotype was found in HIV-infected individuals in this urban area, which could be explained by the African heritage of this population (Ishak *et al.*, 2007).

In the present study, KS cases evaluated were basically classic and AIDS-associated forms of the disease. The majority of patients were male, and viral isolates found in KS lesions were almost always A and C genotypes (50.0% and 48.0%, respectively). Interestingly, there was a predominance of KSHV/HHV-8 A

genotypes in HIV-positive patients, whereas C genotypes were more frequently found in HIV-negative individuals with KS. As far as we could verify, this association has not been consistently described in the literature before, and strengthens the hypothesis that specific KSHV/HHV-8 genotypes may have unique properties that cause its preferential association with specific biological settings.

Sample isolates BRBtu/SK03, BRBtu/SK13, BRBtu/SK36, BRBtu/SK69, BRBtu/SK50 and BRBtu/SK75 in the present study showed digestion patterns that had not been described previously (Caterino-de-Araujo & Moreira, 2002). After phylogenetic analysis, all these isolates were classified as C genotypes. The non-described digestion patterns found indicate that caution must be taken whenever evaluating KSHV/HHV-8 genotypes based solely on the PCR-RFLP approach used in the present study, since KSHV/HHV-8 variants of C genotype could be misclassified as other viral genotypes. The PCR-RFLP protocol for KSHV/HHV-8 genotyping, however, is suitable for screening of the most common viral genotypes, since its results match those obtained by DNA sequencing and phylogenetic analysis. Remarkably, DNA sequencing is mandatory for correct identification of some C-genotype isolates, as well as for confirming results of isolates of rare genotypes, including the E genotype found in South America.

After phylogenetic analysis, KSHV/HHV-8 isolates from KS lesions found in the present study clustered with the prototype isolates of the same genotype described in the literature, as well as other isolates previously identified in Brazil. Isolates with unpredicted digestion patterns were found to be KSHV/HHV-8 C genotype. This group is known to be highly diverse. Indeed, Duprez et al. (2006) identified at least four distinct variants of C genotype (C3, C7, C" and C5) in 35 samples evaluated

from 28 Moroccan individuals with classic KS (n=17), AIDS-associated KS (n=10) and iatrogenic KS (n=1) (Duprez *et al.*, 2006b).

In summary, KSHV/HHV-8 A genotypes demonstrated preferential distribution among viral isolates from HIV-positive patients, whereas C genotypes were found predominantly in HIV-negative patients. These data may stimulate new studies focused on discriminating among biological properties of different KSHV/HHV-8 genotypes, and the results may clarify whether the differences have a role in the KS pathogenesis in patients with or without HIV infection.

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TABLE 1 – Age and sex for KS patients studied.

KS groups (n)	M/F Ratio	Age						
		Mean (years)	SD (years)	CV (%)	P ₂₅	P ₇₅	Median (years)	Range (years)
KS HIV-positive (22)*	21:1	37.9	12.6	33.3	30.5	42.8	34.0 [†]	16-62
KS HIV-negative (14)	3.7:1	60.5	17.6	29.1	48.0	75.0	63.5 [†]	21-83
KS N.O.S. (14) ¹	6:1	59.9	18.1	30.2	40.8	74.8	64.0 [†]	34-87
Total (50)	7.3:1	50.5	19.0	37.7	34.0	67.0	46.5	16-87

* There is no age information for one patient. [†]p < 0.001 (ANOVA); KS HIV-positive < KS HIV-negative/KS HIV-positive < KS NOS (p < 0.01; Bonferroni test). KS: Kaposi's sarcoma; N.O.S.: not otherwise specified; SD: standard deviation; CV: coefficient of variation; P25: 25th percentile; P75: 75th percentile.

TABLE 2- KSHV/HHV-8 genotypes isolated from 50 cases of Kaposi's sarcoma.

Groups (n)	KSHV/HHV-8 genotypes		
	A (%)	B (%)	C (%)
HIV-negative KS (14)*	3.0 (21.4)	1.0 (7.1)	10.0 (71.4) [†]
HIV-positive KS (22)	15.0 (68.2) [†]	0.0	7.0 (31.8)
KS N.O.S. (14)	7.0 (50.0)	0.0	7.0 (50.0)
Total (50)	25.0 (100)	1.0 (100)	24.0 (100)

KS: Kaposi's sarcoma, N.O.S.: not otherwise specified; * Includes classic KS, iatrogenic KS, and KS from other HIV-negative patients (clinical-serological status); † p= 0.026 (Fisher's exact test).

TABLE 3– Distribution of KSHV/HHV-8 A and C genotypes in Kaposi's sarcoma according to stage of the disease.

Kaposi's sarcoma	A (%)	C (%)	Total (%)
<i>Early stages</i>	11.0/20.0 (55.0)	9.0/20.0 (45.0)	20.0/49.0 (40.8)
Patch	3.0/11.0 (27.3)	3.0/9.0 (33.3)	6.0/20.0 (30.0)
Plaque	8.0/11.0 (72.7)	6.0/9.0 (66.7)	14.0/20.0 (70.0)
<i>Late stages</i>	14.0/29.0 (48.3)	15.0/29.0 (51.7)	29.0/49.0 (59.2)
Tumoral	11.0/14.0 (78.6)	11.0/15.0 (73.3)	22.0/29.0 (75.9)
Lymph node	2.0/14.0 (14.3)	1.0/15.0 (6.7)	3.0/29.9 (10.3)
Visceral	1.0/14.0 (7.1)	3.0/15.0 (20.0)	4.0/29.0 (13.8)
<i>Total (%)</i>	25.0 (100.0)	24.0 (100)	49.0 (100)

TABLE 4 – Analysis of age in patients with Kaposi's sarcoma infected with KSHV/HHV-8 A and C genotypes.

Genotypes (n)	Age						
	Mean (years)	SD (years)	CV (%)	P ₂₅	P ₇₅	Median (years)	Range (years)
A (25)	48.2	22.0	45.6	30.5	71.8	41.0	16-87
C (24)	52.5	15.4	29.3	39.0	65.0	49.0	32-78
Total (49)	50.2	19.1	36.4	34.0	68.0	45.0	16-87

SD: standard deviation; CV: coefficient of variation; P25: 25th percentile; P75: 75th percentile

Hinf I															
Yes												No			
A _M ''	A _M (A3)	B _M	B _M (B2)	B _M (B3)	B _P	D ₁	D ₂	D ₃	Hok 1	Hok 2		A _M '	A _P	C	E _P
147/100	203/44	173/74	173/74	168/79	173/74	173/74	143/74/30	147/100	126/121	155/92		247	247	247	247
Taq I															
Yes												No			
A _M ''	A _M (A3)	B _M	B _M (B3)	D ₁	D ₃	Hok 1	Hok 2	D ₂	B _M (B2)	B _P		A _M '	A _P	C	E _P
158/89	158/89	130/117	166/81	161/86	161/86	142/115	153/94	247	247	247		158/89	158/89	158/89	105/86/56
Hae III															
Yes												No			
B _M	D ₁	D ₃	Hok 1	Hok 2	A _M ''	A _M (A3)	B _M (B3)	B _M (B2)	B _P	No		Yes		Ap	E _P
155/92-156/91	153/94	149/98	154/93	133/114	247	247	247	155/92	156/91	D ₂	D ₂	149/98	247	247	247
Nsi I												Nsi I			
Yes												No			
D ₁	D ₃	Hok 1	Hok 2	B _M	A _M ''	A _M (A3)	B _M (B3)	B _M (B2)	B _P	Yes	No	Yes		C	E _P
203/44	203/44	174/73	195/52	247	203/44	247	247	247	203/44	247	203/44	203/44	203/44	203/44	247
Mse I												Mse I			
Y		N	Y	N	Y	Y	N	Y	N	Y	N	Y	N	Y	N
Hok-1 / Hok-2 ⁽¹⁾	D ₁ / D ₃ ⁽²⁾	✗	✗	B _M	✗	B _M (B3)	A _M (A3)	B _M (B2)	B _P	✗	D ₂	✗	✗	A _P	C

FIGURE 1 - Key for KSHV/HHV-8 genotyping using PCR-RFLP as performed in the present study. Yes (Y) or No (N) refers to digestion or lack of digestion, respectively, using the enzymes indicated. Bands observed are supposed to match the predicted size of fragments after digestion (base-pairs values below genotypes).. Digestion not expected to occur are indicated by ✗. (1) For discrimination between Hok1 and Hok2, size of fragments should be considered in each digestion. (2) For discrimination between D1 and D3, the size of fragments obtained after Hinf I digestion should be analyzed (D₁: 173/74bp; D₃: 147/100bp).

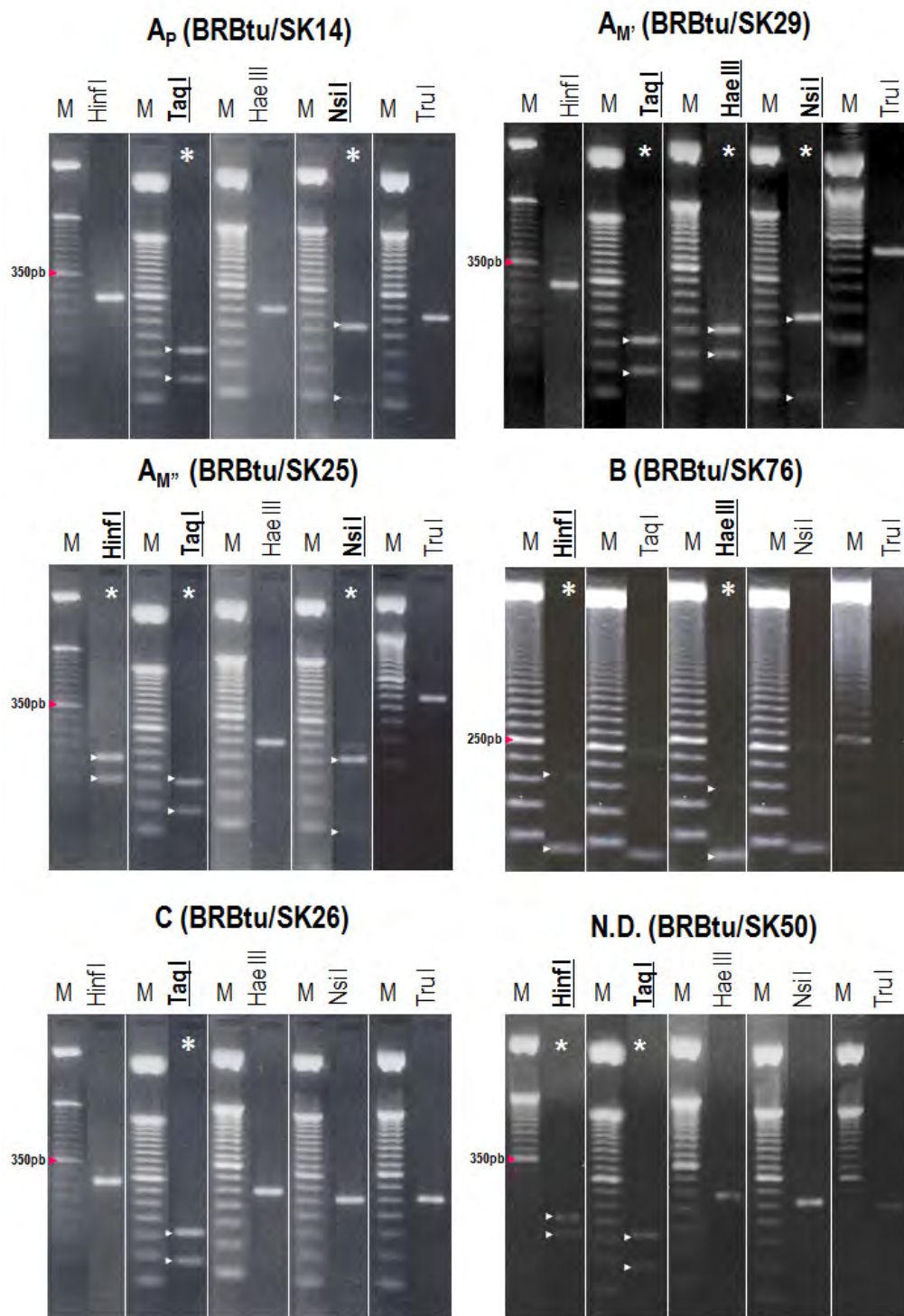


FIGURE 2 - Representative examples of digestion patterns obtained after KSHV/HHV-8 genotyping by PCR-RFLP. Genotypes shown are A_P (BRBtu/SK14), A_M (BRBtu/SK29 and BRBtu/SK25), B (BRBtu/SK76), and C (BRBtu/SK26). The digestion pattern for BRBtu/SK50 was not described previously (Moreira, 2003). Reactions where digestion was observed are indicated by (*). Shaded arrowheads indicate the reference band of the molecular weight marker. White arrowheads indicate bands for fragments generated after enzymatic digestion. N.D.; non-described pattern.

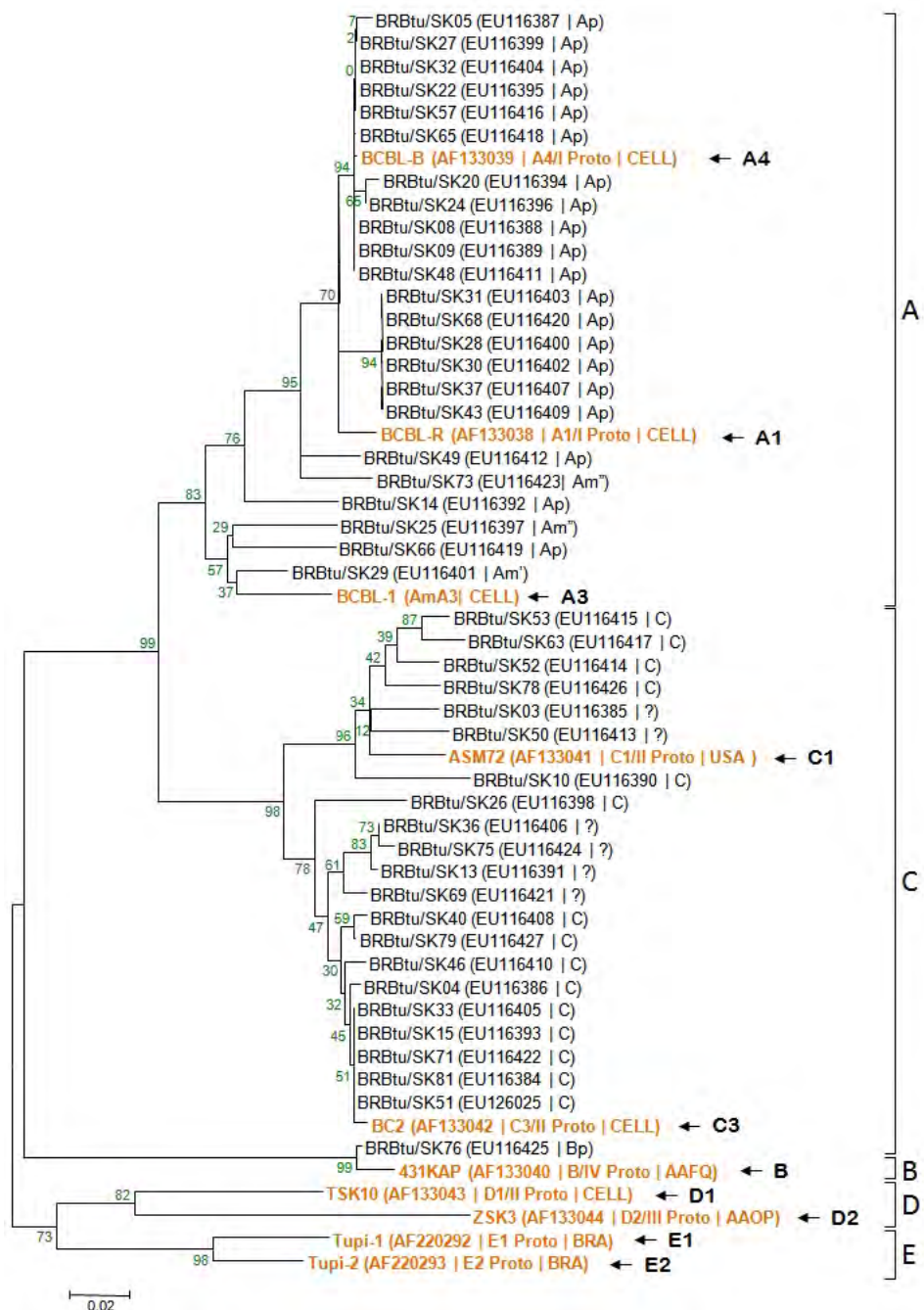


FIGURE 3 - Phylogenetic tree of KSHV/HHV-8 ORF-K1 DNA sequences constructed with the neighbor-joining algorithm (500 replicates) using MEGA 3.1 software package (Kumar *et al.*, 2004). Relationships between KSHV/HHV-8 isolates identified in the present study and prototype isolates in the literature are shown. Within the brackets, the GenBank accession number for the sequence and the KSHV/HHV-8 genotyping result by PCR-RFLP are provided. Question marks indicate isolates with digestion pattern not described previously (Caterino-de-Araujo & Moreira, 2002). For prototype isolates, the viral genotype was indicated as the description given by their authors, the country of the samples (ISO 3166 alpha-3 code) or geographic origin of the samples (AAFQ – African Continent; AAOP - Australia, New Zealand and Pacific Islands). CELL indicates KSHV/HHV-8-positive cell lines.

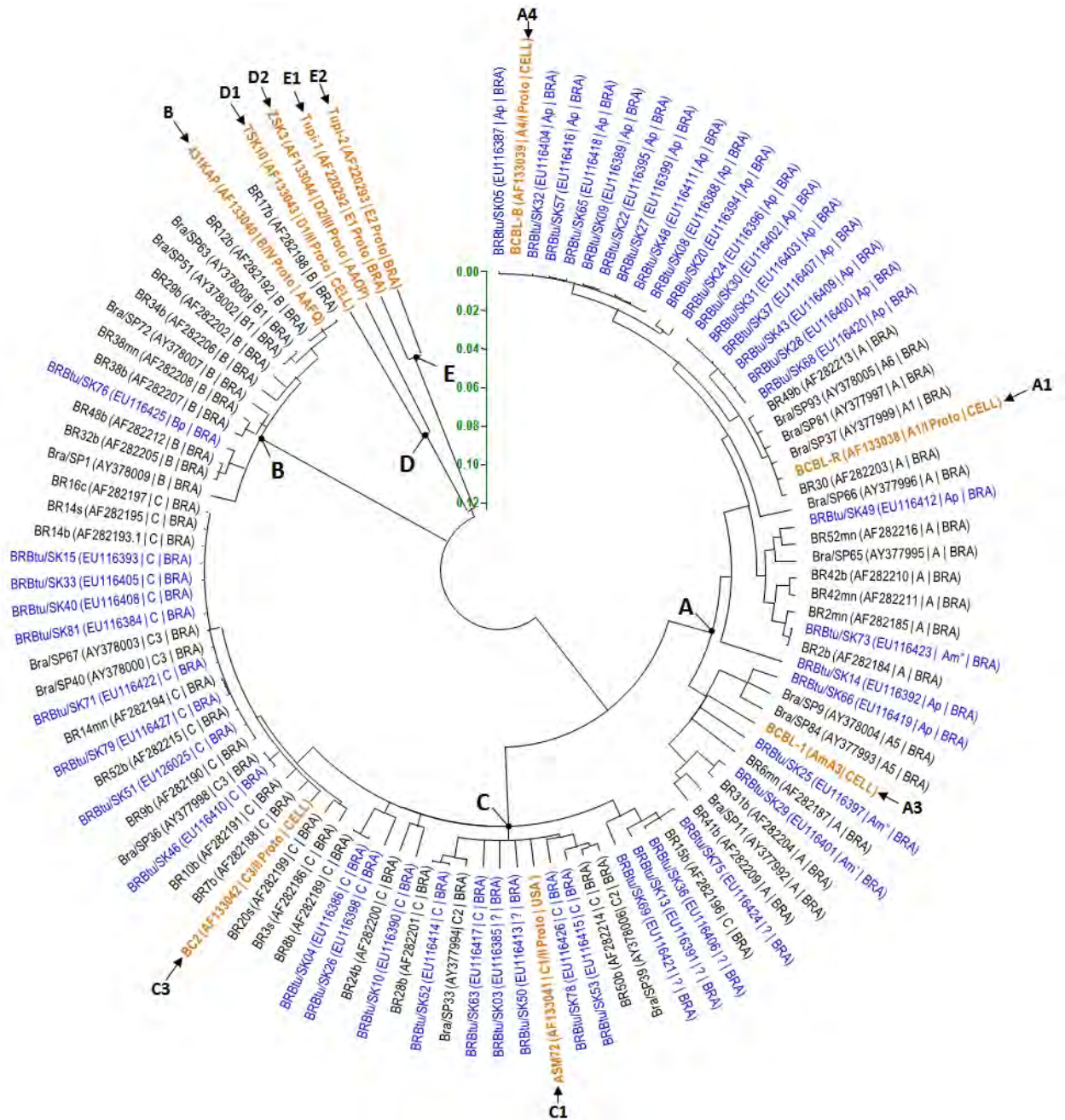


FIGURE 4 - Phylogenetic tree of KSHV/HHV-8 ORF-K1 DNA sequences constructed with the neighbor-joining algorithm (500 replicates) using MEGA 3.1 software package (Kumar *et al.*, 2004). Relationships among KSHV/HHV-8 isolates identified in the present study (BRBtu/SK isolates), other viral isolates from Brazil, and prototype isolates in the literature (arrows) are shown. Within the brackets, the GenBank accession number for the sequence and the KSHV/HHV-8 genotyping result by PCR-RFLP are provided. Question marks indicate isolates with digestion pattern not described previously (Caterino-de-Araujo & Moreira, 2002). For prototype isolates, the viral genotype was indicated as the description given by their authors, the country of the samples (ISO 3166 alpha-3 code) or geographic origin of the samples (AAFQ – African Continent; AAOP - Australia, New Zealand and Pacific Islands). CELL indicates KSHV/HHV-8-positive cell lines.

ANEXOS

LOCUS EU126025 232 bp DNA linear VRL 18-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK51 K1 (K1) gene, partial cds.
ACCESSION EU126025
VERSION EU126025.1 GI:157165878
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 232)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 232)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (29-AUG-2007) Pathology, Botucatu School of Medicine -
Sao Paulo State University - UNESP, Faculdade de Medicina de
Botucatu (UNESP) - Patologia - Rubiao Junior, s/n, Botucatu, Sao
Paulo 18618-000, Brazil
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arising in a 39 year old HIV-positive male patient"
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61 ctcggcttct ccgactgacg cagcaaacat tcaactgttg cacccttata tgcaatttta
121 gttgtgtggg acaatctggg catcgacaca gcctttggat tacatgggtat ccacaacctg
181 tcttacaac cttgtgtgga caaccatcaa acacagtcac ttgtggtcag ca//

LOCUS EU116427 240 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK79 K1 protein (K1) gene,
partial cds.
ACCESSION EU116427
VERSION EU116427.1 GI:157057832
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 240)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 240)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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121 caattttagt tgtgtgggac aatctgggca tcgacacagc ctttggatta catggtatcc
181 acaacctgtc ttacaaacct tgtgtggaca accatcaaac acagtcactt gtggtcagca
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LOCUS EU116426 234 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK78 K1 protein (K1) gene,
partial cds.
ACCESSION EU116426
VERSION EU116426.1 GI:157057830
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 234)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 234)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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/country="Brazil"
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121 tgcaattttt cttgtgtggg acaatctggg catcgacaca gcctttggat gacatgggtct
181 gcacaacctg tcttacaaac cttgtgtgga caaccatcaa acacagtcac ttgt//

LOCUS EU116425 221 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK76 K1 protein (K1) gene,
partial cds.
ACCESSION EU116425
VERSION EU116425.1 GI:157057828
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 221)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 221)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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121 gcaattttac ttgtatgaca acatctgggc ctacacacag catttggatt gaatggtata
181 cacaacctgt cttacaaacc ttgtgtgcac agccatcaaa c//

LOCUS EU116424 244 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK75 K1 protein (K1) gene,
partial cds.
ACCESSION EU116424
VERSION EU116424.1 GI:157057826
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 244)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 244)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
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181 tccacaacct gtcttataaa cttgtgtgtg acaaccatca aacacagtca cttgtggtca
241 gcaa//

LOCUS EU116423 232 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK73 K1 protein (K1) gene,
partial cds.
ACCESSION EU116423
VERSION EU116423.1 GI:157057824
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 232)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 232)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
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121 ttacttgtgt ggaacaatct gggcatcgac agagcatttg gattacatgg catgcacaac
181 ctgtcttaca aaccttgtgt gcacagccat caaacacagt cacttgtggt ca//

LOCUS EU116422 231 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK71 K1 protein (K1) gene,
partial cds.
ACCESSION EU116422
VERSION EU116422.1 GI:157057822
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 231)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 231)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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a 48 year old HIV-negative male patient"
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LOCUS EU116421 240 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK69 K1 protein (K1) gene,
partial cds.
ACCESSION EU116421
VERSION EU116421.1 GI:157057820
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 240)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 240)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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LOCUS EU116420 234 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK68 K1 protein (K1) gene,
partial cds.
ACCESSION EU116420
VERSION EU116420.1 GI:157057818
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 234)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 234)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..234
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK68"
/isolation_source="plaque stage Kaposi sarcoma lesion in a
62 year old HIV-positive male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>234
/gene="K1"
CDS <1..>234
/gene="K1"
/codon_start=3
/product="K1 protein"
/protein_id="ABV02897.1"
/db_xref="GI:157057819"
/translation="STPYRLTCLSNASLPISWYCNNTLSRLTERTLFPVTIACNFTC
VEQSGHRQSIWITWHAQPVLQTLCAQPSNTVTC"
ORIGIN
1 tttcaacgcc ttacaggttg acctgtctgt ctaatgcac cttgccaata tcctgggtatt
61 gcaacaatac tcggctttcc cgactgacgg agagaacact ttttcctgtc accattgcct
121 gcaattttac ttgtgtggaa caatctgggc atcgacagag catttggatt acatggcatg
181 cacaacctgt cttacaaacc ttgtgtgcac agccatcaaa cacagtcact tgtg//

LOCUS EU116419 247 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK66 K1 protein (K1) gene,
partial cds.
ACCESSION EU116419
VERSION EU116419.1 GI:157057816
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 247)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 247)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..247
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK66"
/isolation_source="tumoral stage Kaposi sarcoma lesion in
a 80 year old female patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>247
/gene="K1"
CDS <1..>247
/gene="K1"
/codon_start=3
/product="K1 protein"
/protein_id="ABV02896.1"
/db_xref="GI:157057817"
/translation="VISTPYTLTCLSDASLPISWYCNDTRLWRVTDQSFTLANITCNF
TCVEQSGHRQSIWITWNAQPVLQTLCAHPSNTVTCGQ"
ORIGIN
1 gagtgatttc aacgccttac acgttgacct gtctgtctga tgcattccttg ccaatatacct
61 ggtattgcaa cgatactcgg ctttggcgag tgacggacca atcattcact cttgccaaca
121 ttacctgcaa ttttacttgt gtggaacaat ctgggcatcg acagagcatt tggattacat
181 ggaatgcaca acctgtctta caaaccttgt gtgcacaccc atcaaacaca gtcacttggtg
241 gtcagca//

LOCUS EU116418 234 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK65 K1 protein (K1) gene,
partial cds.
ACCESSION EU116418
VERSION EU116418.1 GI:157057814
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 234)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 234)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..234
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK65"
/isolation_source="tumoral stage Kaposi sarcoma lesion in
a 54 year old male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttc aacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>234
/gene="K1"
CDS <1..>234
/gene="K1"
/codon_start=3
/product="K1 protein"
/protein_id="ABV02895.1"
/db_xref="GI:157057815"
/translation="VISTPYKLTCLSNASLPISWYCNDTRLFRLTERTLFPVTIPCNF
TCVEQSGHRQSIWITWHAQPVLQTLCAQPSNTV"
ORIGIN
1 gagtgatttc aacgccttac aagttgacct gtctgtctaa tgcataccttg ccaatatacct
61 ggtattgcaa cgatactcgg cttttccgac tgacggagag aacacttttt cctgtcacca
121 ttccctgcaa ttttacttgt gtggaacaat ctgggcatcg acagagcatt tggattacat
181 ggcatgcaca acctgtctta caaaccttgt gtgcacagcc atcaaacaca gtca//

LOCUS EU116417 225 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK63 K1 protein (K1) gene,
partial cds.
ACCESSION EU116417
VERSION EU116417.1 GI:157057812
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 225)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 225)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..225
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="C"
/isolate="BRBtu/SK63"
/isolation_source="tumoral stage Kaposi sarcoma lesion in
a 64 year old male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>225
/gene="K1"
CDS <1..>225
/gene="K1"
/codon_start=3
/product="K1 protein"
/protein_id="ABV02894.1"
/db_xref="GI:157057813"
/translation="TPYTLTCPSDTSLPTSWYCNDFRLTQGTITVVQLVCNFSCV
GQSGHRHSLWMTWSAQPVLQTLCRQPANTV"
ORIGIN
1 caacgcctta cacgttgacc tgtccgtctg atacatcctt gccaacatcc tggatttgca
61 acgatactcg gcttttccga ctgacgcagg gcacaatcac tgttggtccaa cttgtctgca
121 atttttcttg tgtgggacaa tctgggcacg gacacagcct ttggatgaca tgggtctgcac
181 aacctgtctt acaaaccttg tgtagacaac cagcaaacac agtca//

LOCUS EU116416 237 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK57 K1 protein (K1) gene,
partial cds.
ACCESSION EU116416
VERSION EU116416.1 GI:157057810
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 237)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 237)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..237
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK57"
/isolation_source="tumoral stage Kaposi sarcoma lesion in
a 31 year old HIV-positive male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
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gene <1..>237
/gene="K1"
CDS <1..>237
/gene="K1"
/codon_start=2
/product="K1 protein"
/protein_id="ABV02893.1"
/db_xref="GI:157057811"
/translation="TPYKLTCLSNASLPISWYCNTRLFRLTERTLFVPTIPCNFTCV
EQSGHRQSIWITWHAQPVLQTLCAQPSNTVTGQ"
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1 aacgccttac aagttgacct gtctgtctaa tgcatacctt ccaatatacct ggtattgcaa
61 cgatactcgg cttttccgac tgacggagag aacacttttt cctgtcacca ttccctgcaa
121 ttttacttgt gtggaacaat ctgggcatcg acagagcatt tggattacat ggcattgcaca
181 acctgtctta caaaccttgt gtgcacagcc atcaaacaca gtcacttgtg gtcagca//

LOCUS EU116415 239 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK53 K1 protein (K1) gene,
partial cds.
ACCESSION EU116415
VERSION EU116415.1 GI:157057808
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 239)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 239)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..239
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="C"
/isolate="BRBtu/SK53"
/isolation_source="stomach Kaposi sarcoma lesion in a
HIV-positive male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>239
/gene="K1"
CDS <1..>239
/gene="K1"
/codon_start=1
/product="K1 protein"
/protein_id="ABV02892.1"
/db_xref="GI:157057809"
/translation="ISTPYTLTcpsdtSLPTswyCNDTRLfRLTQGTITVDNLVCNFS
CVGQSGHRHSLWMTWSAQPVLQTLcQPANTVTCG"
ORIGIN
1 atttcaacgc cttacacgtt gacctgtccg tctgatacat ccttgccaac atcctgggtat
61 tgcaacgata ctcggctttt ccgactgacg cagggcaca tcaactgttg caaccttgct
121 tgcaattttt cttgtgtggg acaatctggg catcgacaca gcctttggat gacatggtct
181 gcacaacctg tcttacaac cttgtgtcaa caaccagcaa acacagtcac ttgtggtca//

LOCUS EU116414 233 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK52 K1 protein (K1) gene,
partial cds.
ACCESSION EU116414
VERSION EU116414.1 GI:157057806
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 233)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 233)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..233
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="C"
/isolate="BRBtu/SK52"
/isolation_source="stomach Kaposi sarcoma lesion in a 49
year old male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
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gene <1..>233
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CDS <1..>233
/gene="K1"
/codon_start=2
/product="K1 protein"
/protein_id="ABV02891.1"
/db_xref="GI:157057807"
/translation="STPYTLTcpsdtslptswycndtrlfRLTQEKITVVS LVcNFSC
VGQSGHRHSLWMTWSAQPVLQTLcGQPANTVTC"
ORIGIN
1 ttcaacgcct tacacgttga cctgtccgtc tgatacatcc ttgccaacat cctggatttg
61 caacgatact cggcttttcc gactgacgca ggagaaaatc actgttgtca gccttgctctg
121 caatttttct tgtgtgggac aatctgggca tcgacacagc ctttgatga catgggtctgc
181 acaacctgtc ttacaaacct tgtgtggaca accagcaaac acagtcactt gtg//

LOCUS EU116413 232 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK50 K1 protein (K1) gene,
partial cds.
ACCESSION EU116413
VERSION EU116413.1 GI:157057804
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 232)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 232)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..232
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="C"
/isolate="BRBtu/SK50"
/isolation_source="plaque stage Kaposi sarcoma lesion in a
34 year old male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>232
/gene="K1"
CDS <1..>232
/gene="K1"
/codon_start=2
/product="K1 protein"
/protein_id="ABV02890.1"
/db_xref="GI:157057805"
/translation="ISTPYTLTcpsdtSLPTSWYCNdTRLfRLRQNRFTVLNLSCNFS
CVGQSGHRHSLWMTWSAQpVLQTLcGQPANTVT"
ORIGIN
1 gatttcaacg ctttacacgt tgacctgtcc gtctgataca tccttgccaa catcctggta
61 ttgcaacgat actcggcttt tccgactgag gcagaacaga ttcactgttc tcaaccttag
121 ctgcaatttt tcttgtgtgg gacaatctgg gcatcgacac agcctttgga tgacatggtc
181 tgcacaacct gtcttataaa ccttgtgtgg acaaccagca aacacagtca ct//

LOCUS EU116412 240 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK49 K1 protein (K1) gene,
partial cds.
ACCESSION EU116412
VERSION EU116412.1 GI:157057802
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 240)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 240)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..240
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK49"
/isolation_source="lymph nodes Kaposi sarcoma lesion in a
45 year old HIV-positive male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
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gene <1..>240
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CDS <1..>240
/gene="K1"
/codon_start=2
/product="K1 protein"
/protein_id="ABV02889.1"
/db_xref="GI:157057803"
/translation="ISTPYNLTCLSNASLPISWYCNNTLRLTEKTLLGVNIACNFT
CVEQSGHRQSIWITWHAQPVLQTLCAQPSNTVTCG"
ORIGIN
1 gatttcaacg cttacaatt tgacctgtct gtctaata gca tccttgccaa taccctggta
61 ttgcaacaat actcggcttt tccgactgac ggagaaaaca ctccttggtg tcaacattgc
121 ctgcaatttt acttgtgtgg aacaatctgg gcatcgacag agcatttgga ttacatggca
181 tgcacaacct gtcttataaa ccttgtgtgc acagccatca aacacagtca cttgtggtca
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LOCUS EU116411 242 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK48 K1 protein (K1) gene,
partial cds.
ACCESSION EU116411
VERSION EU116411.1 GI:157057800
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 242)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 242)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..242
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK48"
/isolation_source="plaque stage Kaposi sarcoma lesion in a
32 year old HIV-positive male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
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gene <1..>242
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CDS <1..>242
/gene="K1"
/codon_start=2
/product="K1 protein"
/protein_id="ABV02888.1"
/db_xref="GI:157057801"
/translation="ISTPYKLTCLSNASLPISWYCNDRFLRTERLFPVTIPCNFT
CVEQSGHRQSIWITWHAQPVLQTLCAQPSNTVTCGQ"
ORIGIN
1 gatttcaacg cttacaagt tgacctgtct gtctaata gca tccttgccaa tatcctggta
61 ttgcaacgat actcggcttt tccgactgac ggagagaaca ctttttcctg tcaccattcc
121 ctgcaatttt acttgtgtgg aacaatctgg gcatcgacag agcatttgga ttacatggca
181 tgcacaacct gtcttacaaa ccttgtgtgc acagccatca aacacagtca cttgtgggtca
241 gc//

LOCUS EU116410 240 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK46 K1 protein (K1) gene,
partial cds.
ACCESSION EU116410
VERSION EU116410.1 GI:157057798
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 240)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 240)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..240
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="C"
/isolate="BRBtu/SK46"
/isolation_source="plaque stage Kaposi sarcoma lesion in a
34 year old HIV-positive male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
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gene <1..>240
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CDS <1..>240
/gene="K1"
/codon_start=2
/product="K1 protein"
/protein_id="ABV02887.1"
/db_xref="GI:157057799"
/translation="STPYTLTCPSNTSLPTSWYCNDRLLRLTQQTITVDTLICNFSC
VGQSGHRHSLWITWYPQVPLQTLGQPSNTVTCGQ"
ORIGIN
1 ttcaacgcct tacacgttga cctgtccgtc taatacatcc ttgccaacat cctggatttg
61 caacgatact cggcttctcc gactgacgca gaaacaatc actgttgaca cccttatctg
121 caatttttagt tgtgtgggac aatctgggca tcgacacagc ctttggatta catggtatcc
181 acaacctgtc ttacaaacct tgtgtggaca accatcaaac acagtcactt gtggtcagca
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LOCUS EU116409 231 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK43 K1 protein (K1) gene,
partial cds.
ACCESSION EU116409
VERSION EU116409.1 GI:157057796
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 231)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 231)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..231
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK43"
/isolation_source="lymph nodes Kaposi sarcoma lesion in a
16 year old HIV-positive male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>231
/gene="K1"
CDS <1..>231
/gene="K1"
/codon_start=2
/product="K1 protein"
/protein_id="ABV02886.1"
/db_xref="GI:157057797"
/translation="TPYRLTCLSNASLPISWYCNNTLSRLTERTLFPVTIACNFTCV
EQSGHRQSIWITWHAQPVLQTLCAQPSNTVTG"
ORIGIN
1 aacgccttac aggttgacct gtctgtctaa tgcattcttg ccaatatacct ggtattgcaa
61 caataactcgg ctttcccgac tgacggagag aacacttttt cctgtcacca ttgcctgcaa
121 ttttacttgt gtggaacaat ctgggcatcg acagagcatt tggattacat ggcattgcaca
181 acctgtctta caaaccttgt gtgcacagcc atcaaacaca gtcacttgtg g//

LOCUS EU116408 242 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK40 K1 protein (K1) gene,
partial cds.
ACCESSION EU116408
VERSION EU116408.1 GI:157057794
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 242)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 242)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..242
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="C"
/isolate="BRBtu/SK40"
/isolation_source="plaque stage Kaposi sarcoma lesion in a
44 year old HIV-negative male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>242
/gene="K1"
CDS <1..>242
/gene="K1"
/codon_start=1
/product="K1 protein"
/protein_id="ABV02885.1"
/db_xref="GI:157057795"
/translation="ISTPYTLTCPSNTSLPTSWYCNTRLVRLTQQTFTVVTLICNFS
CVGQSGHRHSLWITWYPQVQLQLCGQPSNTVTCGQ"
ORIGIN
1 atttcaacgc cttacacgtt gacctgtccg tctaatacat ccttgccaac atcctggtat
61 tgcaacgata ctggccttgt acgactgacg cagcaaacat tcaactgttgt cacccttata
121 tgcaatttta gttgtgtggg acaatctggg catcgacaca gcctttggat tacatggtat
181 ccacaacctg tcttacaac cttgtgtgga caaccatcaa acacagtcac ttgtgggtcag
241 ca//

LOCUS EU116407 232 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK37 K1 protein (K1) gene,
partial cds.
ACCESSION EU116407
VERSION EU116407.1 GI:157057792
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 232)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 232)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..232
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK37"
/isolation_source="plaque stage Kaposi sarcoma lesion in a
87 year old female patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>232
/gene="K1"
CDS <1..>232
/gene="K1"
/codon_start=3
/product="K1 protein"
/protein_id="ABV02884.1"
/db_xref="GI:157057793"
/translation="TPYRLTCLSNASLPISWYCNNTLSRLTERTLFPVTIACNFTCV
EQSGHRQSIWITWHAQPVLQTLCAQPSNTVTCG"
ORIGIN
1 caacgcctta caggttgacc tgtctgtcta atgcatacctt gccaatatcc tggatttgca
61 acaataactcg gctttcccga ctgacggaga gaacactttt tcctgtcacc attgcctgca
121 attttacttg tgtggaacaa tctgggcatac gacagagcat ttggattaca tggcatgcac
181 aacctgtctt acaaaccttg tgtgcacagc catcaaacac agtcacttgt gg//

LOCUS EU116406 234 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK36 K1 protein (K1) gene,
partial cds.
ACCESSION EU116406
VERSION EU116406.1 GI:157057790
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 234)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 234)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..234
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="C"
/isolate="BRBtu/SK36"
/isolation_source="tumoral stage Kaposi sarcoma lesion in
a 41 year old HIV-negative male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>234
/gene="K1"
CDS <1..>234
/gene="K1"
/codon_start=3
/product="K1 protein"
/protein_id="ABV02883.1"
/db_xref="GI:157057791"
/translation="YTLTCPSNTSLPTSWYCNDTQLLRLLTQQLTVDTLICNFSCVGQ
SGHRHSLWITWYPQVLQTLGQPSNTVTGCGQ"
ORIGIN
1 cttacacggtt gacctgtccg tctaatacat ccttgccaac atcctgggtat tgcaacgata
61 ctcagctttt gcgactgacg cagcaaacaat taactgttga cacccttatc tgcaatttta
121 gttgtgtggg acaatctggg catcgacaca gcctttggat tacatgggtat ccacaacctg
181 tcttacaac cttgtgtgga caaccatcaa acacagtcac ttgtgggtcag caag//

LOCUS EU116405 245 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK33 K1 protein (K1) gene,
partial cds.
ACCESSION EU116405
VERSION EU116405.1 GI:157057788
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 245)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 245)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..245
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="C"
/isolate="BRBtu/SK33"
/isolation_source="visceral stage Kaposi sarcoma lesion in
a 53 year old HIV-positive male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>245
/gene="K1"
CDS <1..>245
/gene="K1"
/codon_start=2
/product="K1 protein"
/protein_id="ABV02882.1"
/db_xref="GI:157057789"
/translation="ISTPYTLTSPNTSLPTSWYCNDRLLRLTQQTFTVVTLICNFS
CVGQSGHRHSLWITWYPQPVLTLCGQPSNTVTGCGQ"
ORIGIN
1 gatttcaacg ctttacacgt tgacctgtcc gtctaataca tccttgccaa catcctggta
61 ttgcaacgat actcggcttc tccgactgac gcagcaaaca ttcaactgtg tcacccttat
121 ctgcaatttt agttgtgtgg gacaatctgg gcatcgacac agcctttgga ttacatggta
181 tccacaacct gtcttataaa ccttgtgtgg acaaccatca aacacagtca cttgtgggtca
241 gcaag//

LOCUS EU116404 230 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK32 K1 protein (K1) gene,
partial cds.
ACCESSION EU116404
VERSION EU116404.1 GI:157057786
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 230)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 230)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..230
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK32"
/isolation_source="tumoral stage Kaposi sarcoma lesion in
a 41 year old male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>230
/gene="K1"
CDS <1..>230
/gene="K1"
/codon_start=3
/product="K1 protein"
/protein_id="ABV02881.1"
/db_xref="GI:157057787"
/translation="TPYKLTCLSNASLPISWYCNDRFLRTERLFPVTIPCNFTCV
EQSGHRQSIWITWHAQPVLQTLCAQPSNTVTC"
ORIGIN
1 caacgcctta caagttgacc tgtctgtcta atgcacacctt gccaatatcc tggatttgca
61 acgataactcg gcttttccga ctgacggaga gaacactttt tcctgtcacc attccctgca
121 attttacttg tgtggaacaa tctgggcatac gacagagcat ttggattaca tggcatgcac
181 aacctgtctt acaaaccttg tgtgcacagc catcaaacac agtcacttgt//

LOCUS EU116403 247 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK31 K1 protein (K1) gene,
partial cds.
ACCESSION EU116403
VERSION EU116403.1 GI:157057784
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 247)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 247)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..247
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK31"
/isolation_source="plaque stage Kaposi sarcoma lesion in a
40 year old HIV-positive male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>247
/gene="K1"
CDS <1..>247
/gene="K1"
/codon_start=3
/product="K1 protein"
/protein_id="ABV02880.1"
/db_xref="GI:157057785"
/translation="VISTPYRLTCLSNASLPISWYCNNTRLSRLTERTLFPVTIACNF
TCVEQSGHRQSIWITWHAQPVLQTLCAQPSNTVTCGQ"
ORIGIN
1 gagtgatttc aacgccttac aggttgacct gtctgtctaa tgcattccttg ccaatatacct
61 ggtattgcaa caatactcgg ctttcccgac tgacggagag aacacttttt cctgtcacca
121 ttgcctgcaa ttttacttgt gtggaacaat ctgggcatcg acagagcatt tggattacat
181 ggcattgcaca acctgtctta caaaccttgt gtgcacagcc atcaaacaca gtcacttgtg
241 gtcagca//

LOCUS EU116402 235 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK30 K1 protein (K1) gene,
partial cds.
ACCESSION EU116402
VERSION EU116402.1 GI:157057782
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 235)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 235)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..235
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK30"
/isolation_source="tumoral stage Kaposi sarcoma lesion in
a 71 year old male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>235
/gene="K1"
CDS <1..>235
/gene="K1"
/codon_start=3
/product="K1 protein"
/protein_id="ABV02879.1"
/db_xref="GI:157057783"
/translation="PYRLTCLSNASLPISWYCNNTLSRLTERTLFPVTIACNFTCVE
QSGHRQSIWITWHAQPVLQTLCAQPSNTVTCGQ"
ORIGIN
1 cgccttacag gttgacctgt ctgtctaatt catccttgcc aatatacctgg tattgcaaca
61 atactcggct ttcccgactg acggagagaa cactttttcc tgtcaccatt gcctgcaatt
121 ttacttgtgt ggaacaatct gggcatcgac agagcatttg gattacatgg catgcacaac
181 ctgtcttaca aaccttgtgt gcacagccat caaacacagt cacttgtggt cagca//

LOCUS EU116401 221 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK29 K1 protein (K1) gene,
partial cds.
ACCESSION EU116401
VERSION EU116401.1 GI:157057780
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 221)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 221)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..221
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK29"
/isolation_source="tumoral stage Kaposi sarcoma lesion in
a 59 year old HIV-positive male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>221
/gene="K1"
CDS <1..>221
/gene="K1"
/codon_start=1
/product="K1 protein"
/protein_id="ABV02878.1"
/db_xref="GI:157057781"
/translation="PYTLTCLSDASLPISWYCNDTRLRLRPTVTVATITCNFTCVE
QSGHRQSIWITWHTQPVLQTLCAQPSNTVT"
ORIGIN
1 ccttacacgt tgacctgtct gtctgatgca tccttgccaa tctcctggta ttgcaacgat
61 actcggcttt tgcgactgac gaggccaaca gtcactgttg ccaccattac ctgcaatttt
121 acttgtgtgg aacaatctgg gcatcgacag agcatttgga ttacatggca tacacaacct
181 gtcttacaaa ctttgtgtgc acagccatca aacacagtca c//

LOCUS EU116400 240 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK28 K1 protein (K1) gene,
partial cds.
ACCESSION EU116400
VERSION EU116400.1 GI:157057778
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 240)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 240)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..240
/organism="Human herpesvirus 8"
/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK28"
/isolation_source="tumoral stage Kaposi sarcoma lesion in
a 83 year old HIV-negative male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
tgctgaccacaagtgactgt"
gene <1..>240
/gene="K1"
CDS <1..>240
/gene="K1"
/codon_start=2
/product="K1 protein"
/protein_id="ABV02877.1"
/db_xref="GI:157057779"
/translation="STPYRLTCLSNASLPISWYCNNTLSRLTERTLFPVTIACNFTC
VEQSGHRQSIWITWHAQPVLQTLCAQPSNTVTCGQ"
ORIGIN
1 ttcaacgcct tacaggttga cctgtctgtc taatgcatcc ttgccaatat cctggatttg
61 caacaatact cggctttccc gactgacgga gagaacactt tttcctgtca ccattgcctg
121 caattttact tgtgtggaac aatctgggca tcgacagagc atttggtatta catggcatgc
181 acaacctgtc ttacaaacct tgtgtgcaca gccatcaaac acagtcactt gtggtcagca
//

LOCUS EU116399 243 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK27 K1 protein (K1) gene,
partial cds.
ACCESSION EU116399
VERSION EU116399.1 GI:157057776
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 243)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 243)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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/mol_type="genomic DNA"
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/isolate="BRBtu/SK27"
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a 28 year old HIV-positive male patient"
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CDS <1..>243
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TCVEQSGHRQSIWITWHAQPVLQTLCAQPSNTVTCG"
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61 ggtattgcaa cgatactcgg cttttccgac tgacggagag aacacttttt cctgtcacca
121 ttccctgcaa ttttacttgt gtggaacaat ctgggcatcg acagagcatt tggattacat
181 ggcattgcaca acctgtctta caaaccttgt gtgcacagcc atcaaacaca gtcacttggtg
241 gtc//

LOCUS EU116398 247 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK26 K1 protein (K1) gene,
partial cds.
ACCESSION EU116398
VERSION EU116398.1 GI:157057774
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 247)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 247)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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/mol_type="genomic DNA"
/serotype="C"
/isolate="BRBtu/SK26"
/isolation_source="plaque stage Kaposi sarcoma lesion in a
69 year old HIV-negative male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
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CDS <1..>247
/gene="K1"
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/product="K1 protein"
/protein_id="ABV02875.1"
/db_xref="GI:157057775"
/translation="VISTPYTLTGPSNTSLPTSWYCNDTSLRLTHQTFTAVNLTCNF
SCVGQSGHRHSLWITWYTQPVLQTFGQPSNTVTCGQ"
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61 ggtattgcaa cgatacttcg cttctccgac tgacgcatca aacattcact gctgtcaacc
121 ttacctgcaa ttttagttgt gtgggacaat ctgggcatcg acacagcctt tggattacat
181 ggtatacaca acctgtctta caaaccttct gtggacaacc atcaaacaca gtcacttggtg
241 gtcagca//

LOCUS EU116397 239 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK25 K1 protein (K1) gene,
partial cds.
ACCESSION EU116397
VERSION EU116397.1 GI:157057772
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 239)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 239)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..239
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/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK25"
/isolation_source="tumoral stage Kaposi sarcoma lesion in
a 77 year old male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
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CDS <1..>239
/gene="K1"
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CVEQSGHRQSIWITWHVQPVLQTLCAQPSNTVTCTG"
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61 ttgcaacgat actcggcttt ggcgactgac gactcaaaca ttgactgcta gcaccattac
121 ctgcaatttt acttgtgtgg aacaatctgg gcatcgacag agcatttgga ttacatggca
181 tgtacaacct gtcttacaaa ccttgtgtgc acagccatca aacacagtca cttgtggtc
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LOCUS EU116396 235 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK24 K1 protein (K1) gene,
partial cds.
ACCESSION EU116396
VERSION EU116396.1 GI:157057770
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 235)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 235)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK24"
/isolation_source="plaque stage Kaposi sarcoma lesion in a
39 year old HIV-positive male patient"
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/db_xref="taxon:37296"
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CDS <1..>235
/gene="K1"
/codon_start=3
/product="K1 protein"
/protein_id="ABV02873.1"
/db_xref="GI:157057771"
/translation="PYKLTCLSNASLPISWYCNDTRLFRLTERTLFPVTIPCNFTCVE
QSGHRQSVWITWHAQPVLQTLCAQPSNTVTCGQ"
ORIGIN
1 cgccttacaa gttgacctgt ctgtctaatt catccttgcc aatatacctgg tattgcaacg
61 atactcggct tttccgactg acggagagaa cactttttcc tgtcaccatt ccctgcaatt
121 ttacttgtgt ggaacaatct gggcatcgac agagcgtttg gattacatgg catgcacaac
181 ctgtcttaca aaccttgtgt gcacagccat caaacacagt cacttgtggt cagca//

LOCUS EU116395 232 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK22 K1 protein (K1) gene,
partial cds.
ACCESSION EU116395
VERSION EU116395.1 GI:157057768
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 232)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 232)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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/isolate="BRBtu/SK22"
/isolation_source="patch stage Kaposi sarcoma lesion in a
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/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
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/gene="K1"
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CVEQSGHRQSIWITWHAQPVLQTLCAQPSNTVT"
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121 tgcaatttta cttgtgtgga acaatctggg catcgacaga gcatttggat tacatggcat
181 gcacaacctg tcttacaac cttgtgtgca cagccatcaa acacagtcac tt//

LOCUS EU116394 239 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK20 K1 protein (K1) gene,
partial cds.
ACCESSION EU116394
VERSION EU116394.1 GI:157057766
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 239)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 239)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
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/gene="K1"
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/product="K1 protein"
/protein_id="ABV02871.1"
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CVEQSGHRQSVWITWHAQPVLQTLCAQPSNTVTCG"
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61 tgcaacgata ctgggctttt ccgactgacg gagagaacac tttttcctgt taccattccc
121 tgcaatttta cttgtgtgga acaatctggg catcgacaga gcgtttggat tacatggcat
181 gcacaacctg tcttacaac cttgtgtgca cagccatcaa acacagtcac ttgtgggtca//

LOCUS EU116393 243 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK15 K1 protein (K1) gene,
partial cds.
ACCESSION EU116393
VERSION EU116393.1 GI:157057764
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 243)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 243)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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/db_xref="taxon:37296"
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CVGQSGHRHSLWITWYPQPVLTLCGQPSNTVTGCGQ"
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61 ttgcaacgat actcggcttc tccgactgac gcagcaaaca ttcaactgtg tcacccttat
121 ctgcaatttt agttgtgtgg gacaatctgg gcatcgacac agcctttgga ttacatggta
181 tccacaacct gtcttataaa ccttgtgtgg acaaccatca aacacagtca cttgtggtca
241 gca//

LOCUS EU116392 226 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK14 K1 protein (K1) gene,
partial cds.
ACCESSION EU116392
VERSION EU116392.1 GI:157057762
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 226)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 226)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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/serotype="A"
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/isolation_source="plaque stage Kaposi sarcoma lesion in a
29 year old HIV-positive female patient"
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/db_xref="taxon:37296"
/country="Brazil"
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ORIGIN
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61 atactcggct ttggcgactg acgaacacaa cagtctctgc tgtcaccttc gtctgcaatt
121 ttactttgtgt ggaacaatct gggcatcgac agagcatttg gattacatgg catgcacaac
181 ctgtcttaca aaccttgtgt gcacagccat caaacacagt cacttg//

LOCUS EU116391 246 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK13 K1 protein (K1) gene,
partial cds.
ACCESSION EU116391
VERSION EU116391.1 GI:157057760
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 246)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 246)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..246
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a 65 year old HIV-negative male patient"
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CVGQSGHRHSLWITWYPQVQLTLCGQPSNTVTGQQG"
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1 gatttcaacg ctttacacgt tgacctgtcc gtctaataca tccttgccaa catcctggta
61 ttgcaacgat actcagcttt tgcgactgac gcagcaaaca ttaactgttg acaccattat
121 ctgcaatttt agttgtgtgg gacaatctgg gcatcgacac agcctttgga ttacatggta
181 tccacaacct gtcttacaaa ccttgtgtgg acaaccatca aacacagtca cttgtgggtca
241 gcaagg//

LOCUS EU116390 237 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK10 K1 protein (K1) gene,
partial cds.
ACCESSION EU116390
VERSION EU116390.1 GI:157057758
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 237)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 237)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..237
/organism="Human herpesvirus 8"
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/isolate="BRBtu/SK10"
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a 49 year old HIV-negative male patient"
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GRSGHRHSLWMAWYAPPVLQTLCRQPANTVTCGQ"
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1 aacgccttac acgttgacct gtccgtctaa tacatccttg ccaacatcct ggtattgcaa
61 cgatactcgg cttttccgac tgacggggga cacattcact gttgtcaacc ttatgtgcaa
121 tttttcttgt gtgggacgat ctgggcatcg acacagcctt tggatggcat ggtatgcacc
181 acctgtctta caaaccttgt gtagacaacc agcaaacaca gtcacttggt gtcagca//

LOCUS EU116389 231 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK09 K1 protein (K1) gene,
partial cds.
ACCESSION EU116389
VERSION EU116389.1 GI:157057756
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 231)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 231)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..231
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/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK09"
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21 year old HIV-negative female patient"
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/db_xref="taxon:37296"
/country="Brazil"
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CDS <1..>231
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QSGHRQSIWITWHAQPVLQTLCAQPSNTVTCG"
ORIGIN
1 cgccttacaa gttgacctgt ctgtctaattg catccttgcc aatatcctgg tattgcaacg
61 atactcggct tttccgactg acggagagaa cactttttcc tgtcaccatt ccctgcaatt
121 ttacttgtgt ggaacaatct gggcatcgac agagcatttg gattacatgg catgcacaac
181 ctgtcttaca aaccttgtgt gcacagccat caaacacagt cacttgtggt c//

LOCUS EU116388 230 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK08 K1 protein (K1) gene,
partial cds.
ACCESSION EU116388
VERSION EU116388.1 GI:157057754
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 230)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 230)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..230
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/isolate="BRBtu/SK08"
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/country="Brazil"
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CDS <1..>230
/gene="K1"
/codon_start=1
/product="K1 protein"
/protein_id="ABV02865.1"
/db_xref="GI:157057755"
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EQSGHRQSIWITWHAQPVLQTLCAQPSNTVTCG"
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61 gatactcggc ttttccgact gacggagaga acactttttc ctgtcaccat tccctgcaat
121 tttacttgtg tggaacaatc tgggcatcga cagagcattt ggattacatg gcatgcacaa
181 cctgtcttac aaaccttgtg tgcacagcca tcaaacacag tcacttgtgg//

LOCUS EU116387 239 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK05 K1 protein (K1) gene,
partial cds.
ACCESSION EU116387
VERSION EU116387.1 GI:157057752
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 239)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 239)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..239
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/mol_type="genomic DNA"
/serotype="A"
/isolate="BRBtu/SK05"
/isolation_source="patch stage Kaposi sarcoma lesion in a
24 year old HIV-positive male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
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/gene="K1"
CDS <1..>239
/gene="K1"
/codon_start=1
/product="K1 protein"
/protein_id="ABV02864.1"
/db_xref="GI:157057753"
/translation="STPYKLTCLSNASLLISWYCNDRFLRLTERTLFPVTIPCNFTC
VEQSGHRQSIWITWHAQPVLQTLCAQPSNTVTCGQ"
ORIGIN
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61 aacgatactc ggctttttccg actgacggag agaacacttt ttcctgtcac cattccctgc
121 aattttactt gtgtggaaca atctgggcat cgacagagca tttggattac atggcatgca
181 caacctgtct tacaaacctt gtgtgcacag ccatcaaaca cagtcacttg tggtcagca//

LOCUS EU116386 247 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK04 K1 protein (K1) gene,
partial cds.
ACCESSION EU116386
VERSION EU116386.1 GI:157057750
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 247)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 247)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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/mol_type="genomic DNA"
/serotype="C"
/isolate="BRBtu/SK04"
/isolation_source="plaque stage Kaposi sarcoma lesion in a
33 year old HIV-positive male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
/PCR_primers="fwd_seq: gagtgatttcaacgccttac, rev_seq:
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gene <1..>247
/gene="K1"
CDS <1..>247
/gene="K1"
/codon_start=3
/product="K1 protein"
/protein_id="ABV02863.1"
/db_xref="GI:157057751"
/translation="VISTPYTLTGPSNTSLPTSWYCNDRLLRLTQQTFTVNLICNF
SCVGQSGHRHSLWITWYPQVPLQTLGQPSNTVTCGQ"
ORIGIN
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61 ggtattgcaa cgatactcgg cttctccgac tgacgcagca aacattcact gttgtcaacc
121 ttatctgcaa ttttagttgt gtgggacaat ctgggcatcg acacagcctt tggattacat
181 ggtatccaca acctgtctta caaaccttgt gtggacaacc atcaaacaca gtcacttggtg
241 gtcagca//

LOCUS EU116385 235 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK03 K1 protein (K1) gene,
partial cds.
ACCESSION EU116385
VERSION EU116385.1 GI:157057748
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 235)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 235)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
source 1..235
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/serotype="C"
/isolate="BRBtu/SK03"
/isolation_source="tumoral stage Kaposi sarcoma lesion in
a 75 year old HIV-negative male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
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CDS <1..>235
/gene="K1"
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/product="K1 protein"
/protein_id="ABV02862.1"
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/translation="PYTLTCPSDTSLPTSWYCNDRLLRLTQDTLIVVDLICNFSCVG
QSGHRHSLWMTWSAQPVLTLC EQPANTVTCGQQ"
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61 actcggcttc tccgactgac gcaggacaca ttaattgttg tgcaccttat ctgcaatttt
121 tcttgtgtgg gacaatctgg gcatcgacac agcctttgga tgacatggtc tgcacaacct
181 gtcttacaaa ctttgtgtga acaaccagca aacacagtca ctttgtgtga gcaag//

LOCUS EU116384 236 bp DNA linear VRL 12-SEP-2007
DEFINITION Human herpesvirus 8 isolate BRBtu/SK81 K1 protein (K1) gene,
partial cds.
ACCESSION EU116384
VERSION EU116384.1 GI:157057746
KEYWORDS .
SOURCE Human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
ORGANISM Human herpesvirus 8
Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
Gammaherpesvirinae; Rhadinovirus.
REFERENCE 1 (bases 1 to 236)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Kaposi sarcoma herpesvirus/Human herpesvirus 8 strains in Kaposi
sarcoma lesions from Brazilian patients
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 236)
AUTHORS Elgui de Oliveira,D., Ramos da Silva,S. and Ferraz da Silva,A.P.
TITLE Direct Submission
JOURNAL Submitted (22-AUG-2007) Pathology, Botucatu School of Medicine, Sao
Paulo State University, UNESP, Faculdade de Medicina de Botucatu,
Patologia, Rubiao Junior s/n, Botucatu, Sao Paulo 18618-000, Brazil
FEATURES Location/Qualifiers
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/serotype="C"
/isolate="BRBtu/SK81"
/isolation_source="plaque stage Kaposi sarcoma lesion in a
62 year old HIV-negative male patient"
/specific_host="Homo sapiens"
/db_xref="taxon:37296"
/country="Brazil"
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gene <1..>236
/gene="K1"
CDS <1..>236
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/product="K1 protein"
/protein_id="ABV02861.1"
/db_xref="GI:157057747"
/translation="TPYTLTCPSNTSLPTSWYCNDRLLRLTQQTFTVVTLICNFSCV
GQSGHRHSLWITWYPQVVLQTLGQPSNTVTCGQ"
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61 gatactcggc ttctccgact gacgcagcaa acattcactg ttgtcaccct tatctgcaat
121 tttagtgttg tgggacaatc tgggcatcga cacagccttt ggattacatg gtatccacaa
181 cctgtcttac aaaccttgtg tggacaacca tcaaacacag tcacttgtgg tcagca//

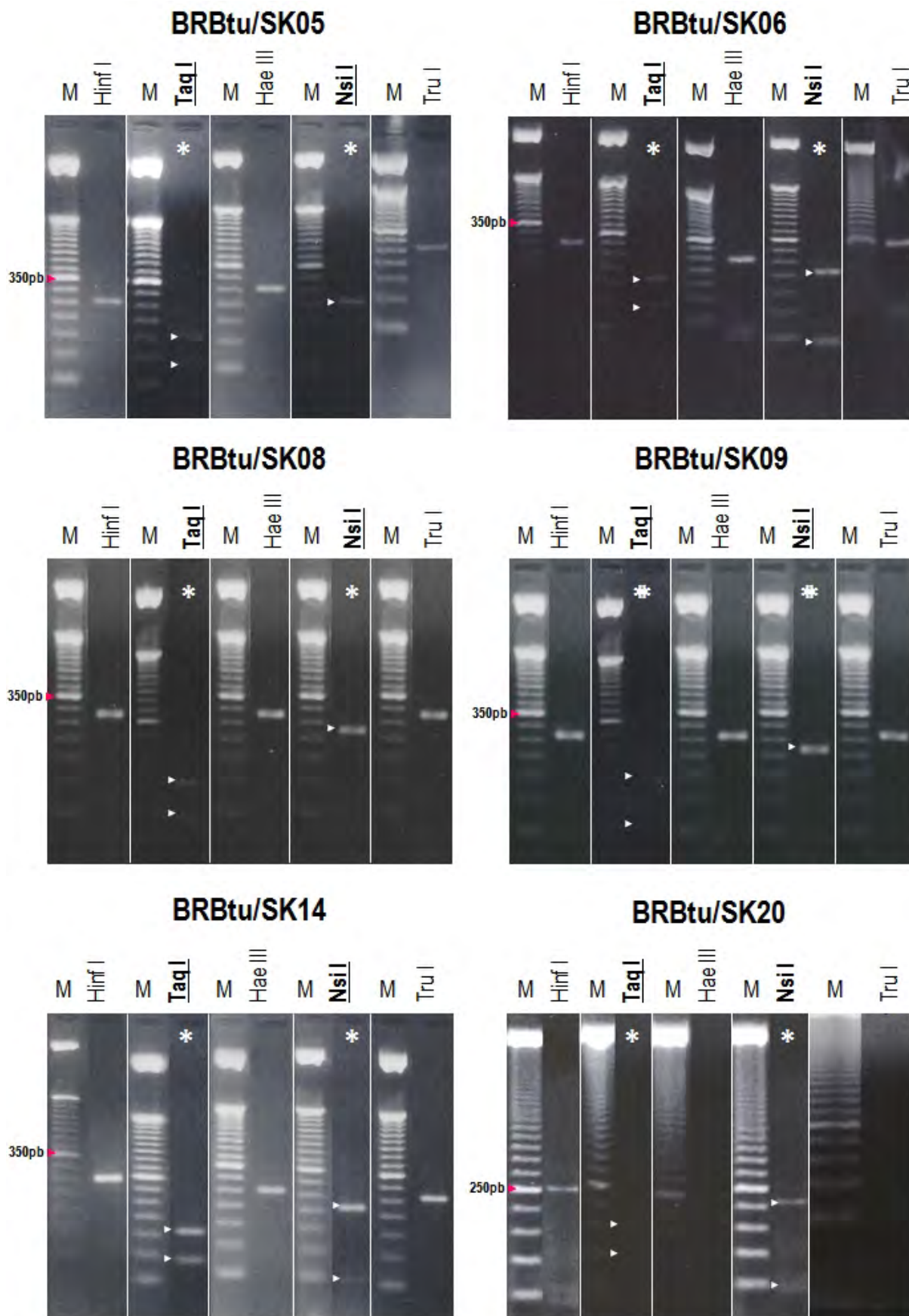


FIGURA 1 - Amostras de sarcoma de Kaposi com **genótipo A** do KSHV/HHV-8 após análise de segmentos de 247pb da ORF-K1 viral por PCR-RFLP. Nas reações destacadas (*), são apresentados os fragmentos obtidos (cabeça de seta) após a digestão com a enzima utilizada.

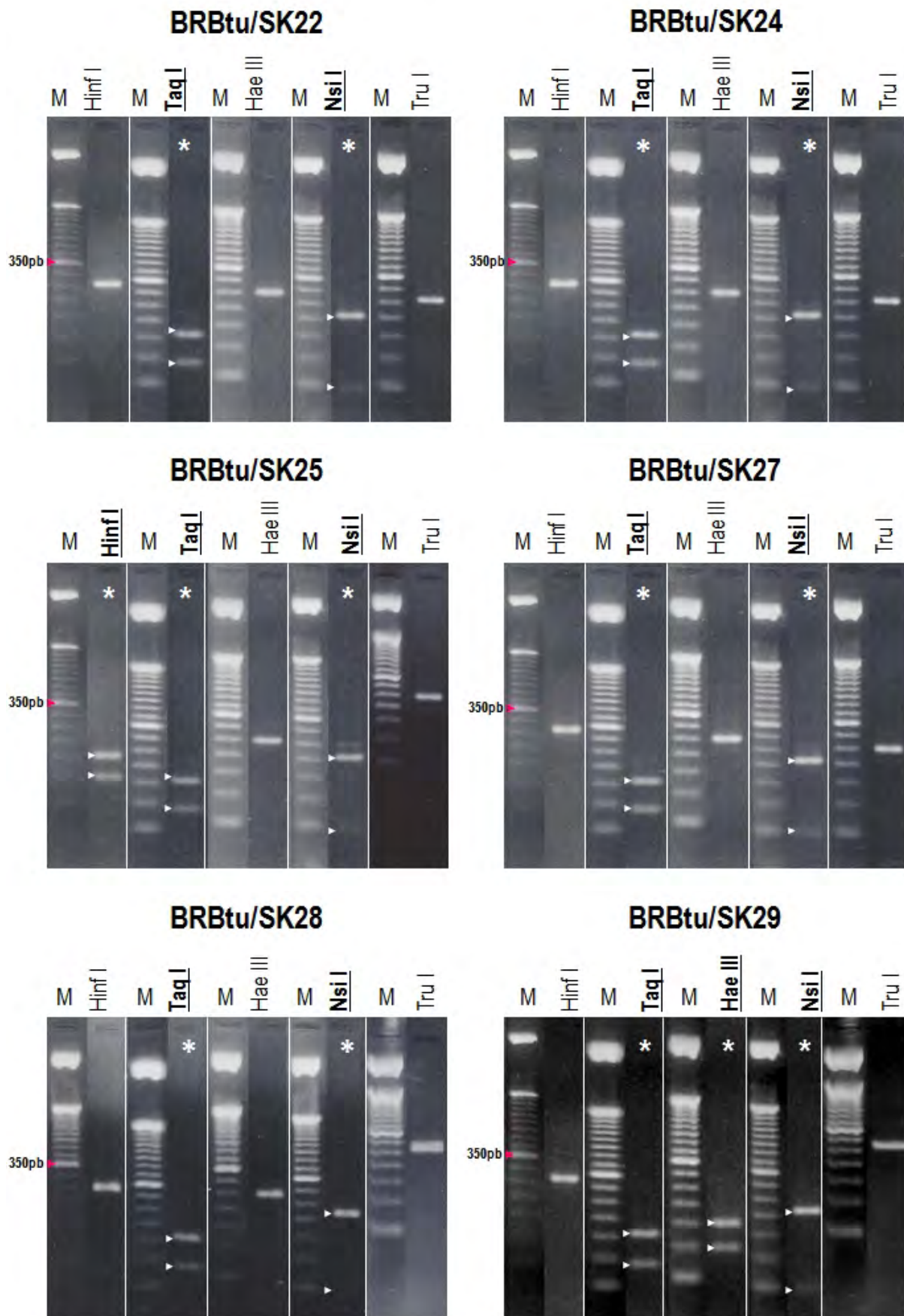


FIGURA 1 - Continuação

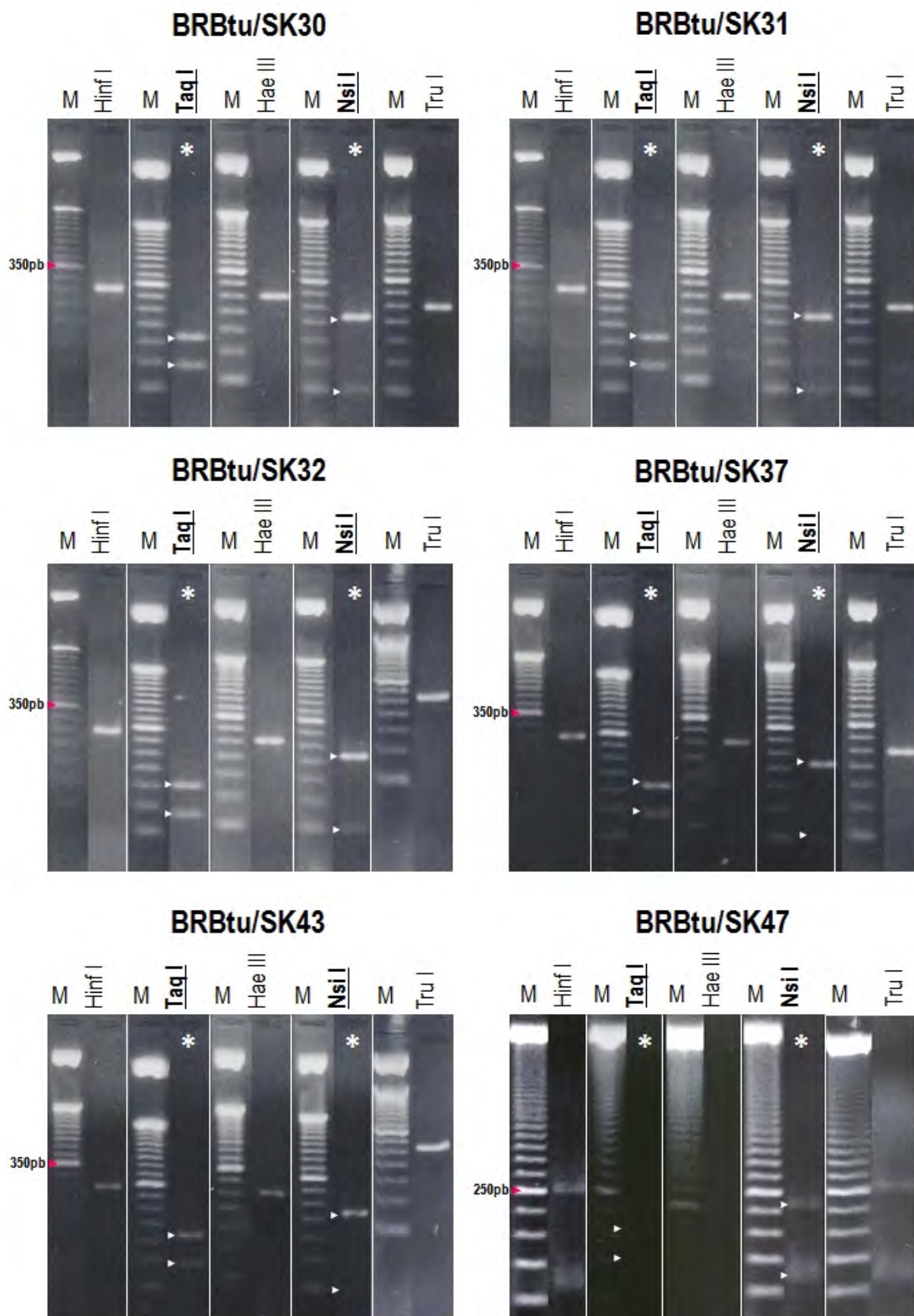


FIGURA 1 - Continuação

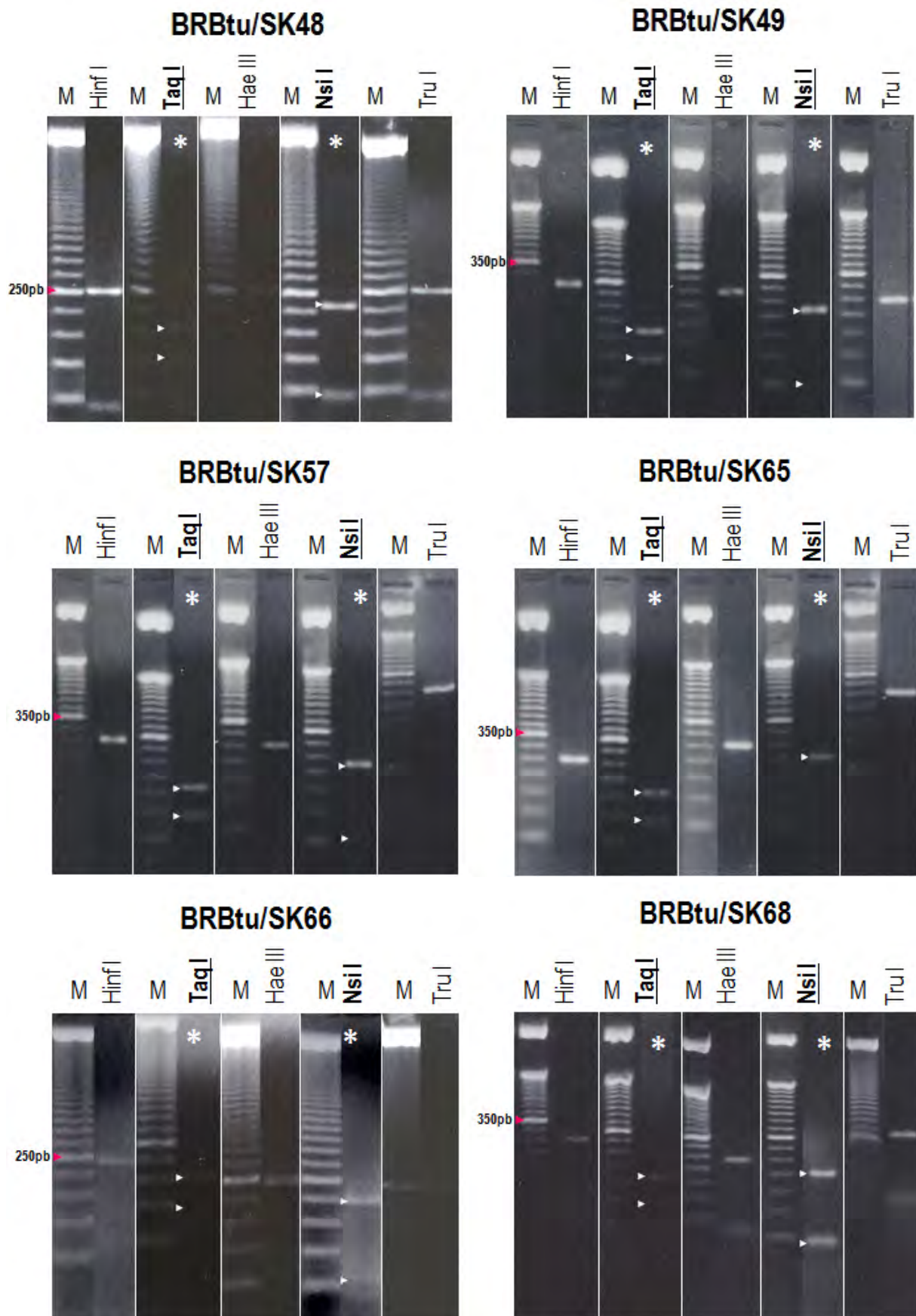


FIGURA 1 - Continuação

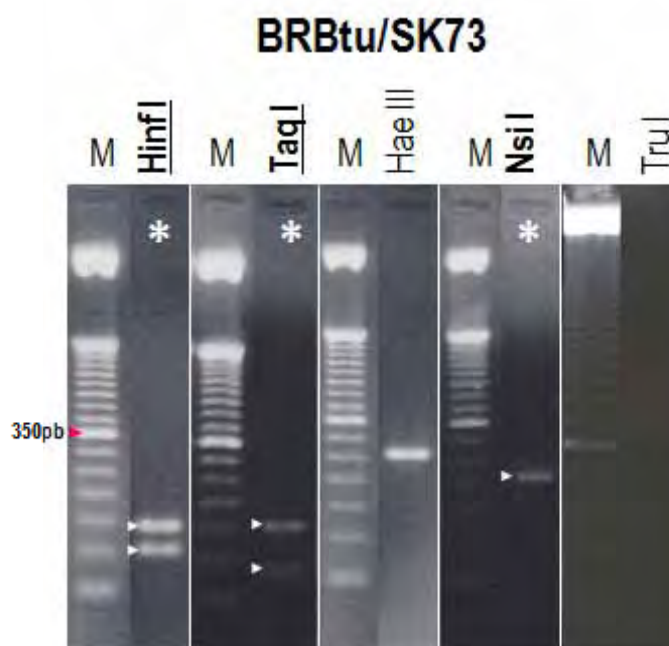


FIGURA 1 - Continuação

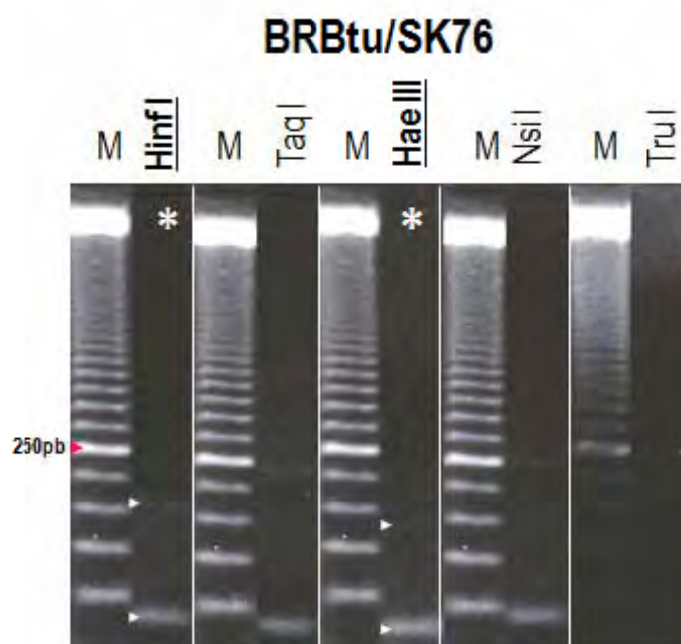


FIGURA 2 - Amostra de sarcoma de Kaposi com **genótipo B** do KSHV/HHV-8 após análise de segmentos de 247pb da ORF-K1 viral por PCR-RFLP. Nas reações destacadas (*), são apresentados os fragmentos obtidos (cabeça de seta) após a digestão com a enzima indicada.

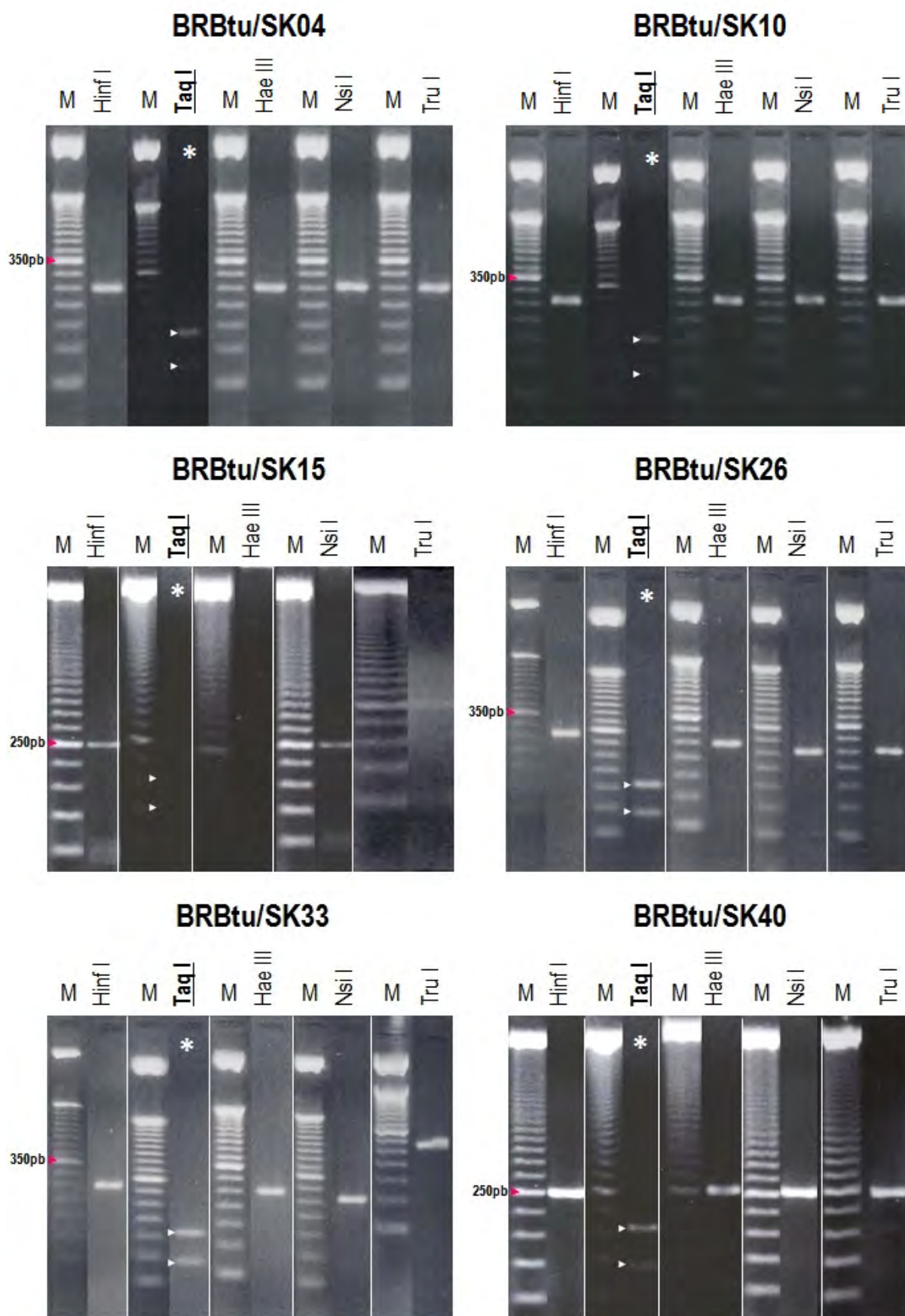


FIGURA 3 - Amostras de sarcoma de Kaposi com **genótipo C** do KSHV/HHV-8 após análise de segmentos de 247pb da ORF-K1 viral por PCR-RFLP. Nas reações destacadas (*), são apresentados os fragmentos obtidos (cabeça de seta) após a digestão com a enzima indicada.

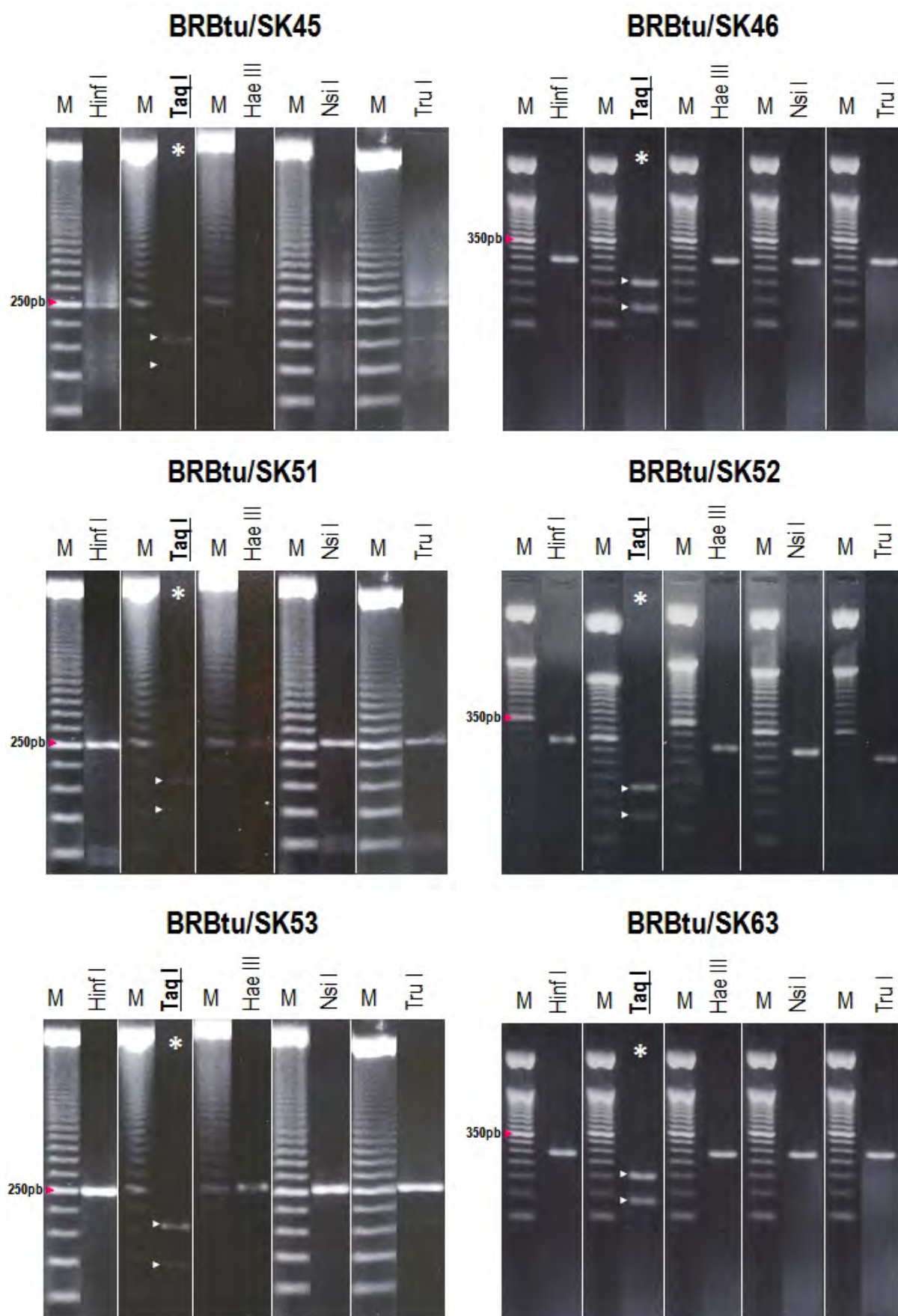


FIGURA 3 - Continuação

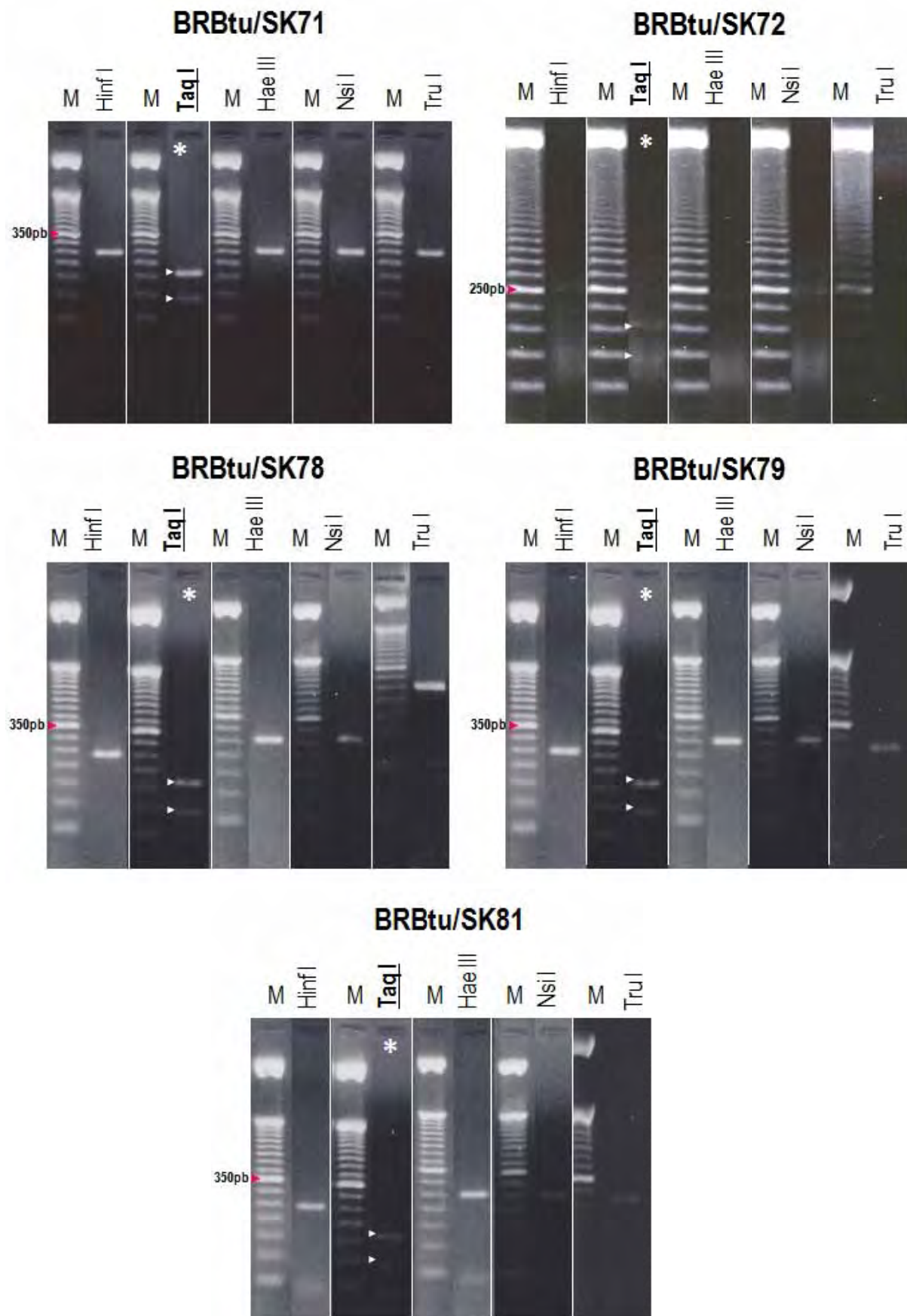


FIGURA 3 - Continuação

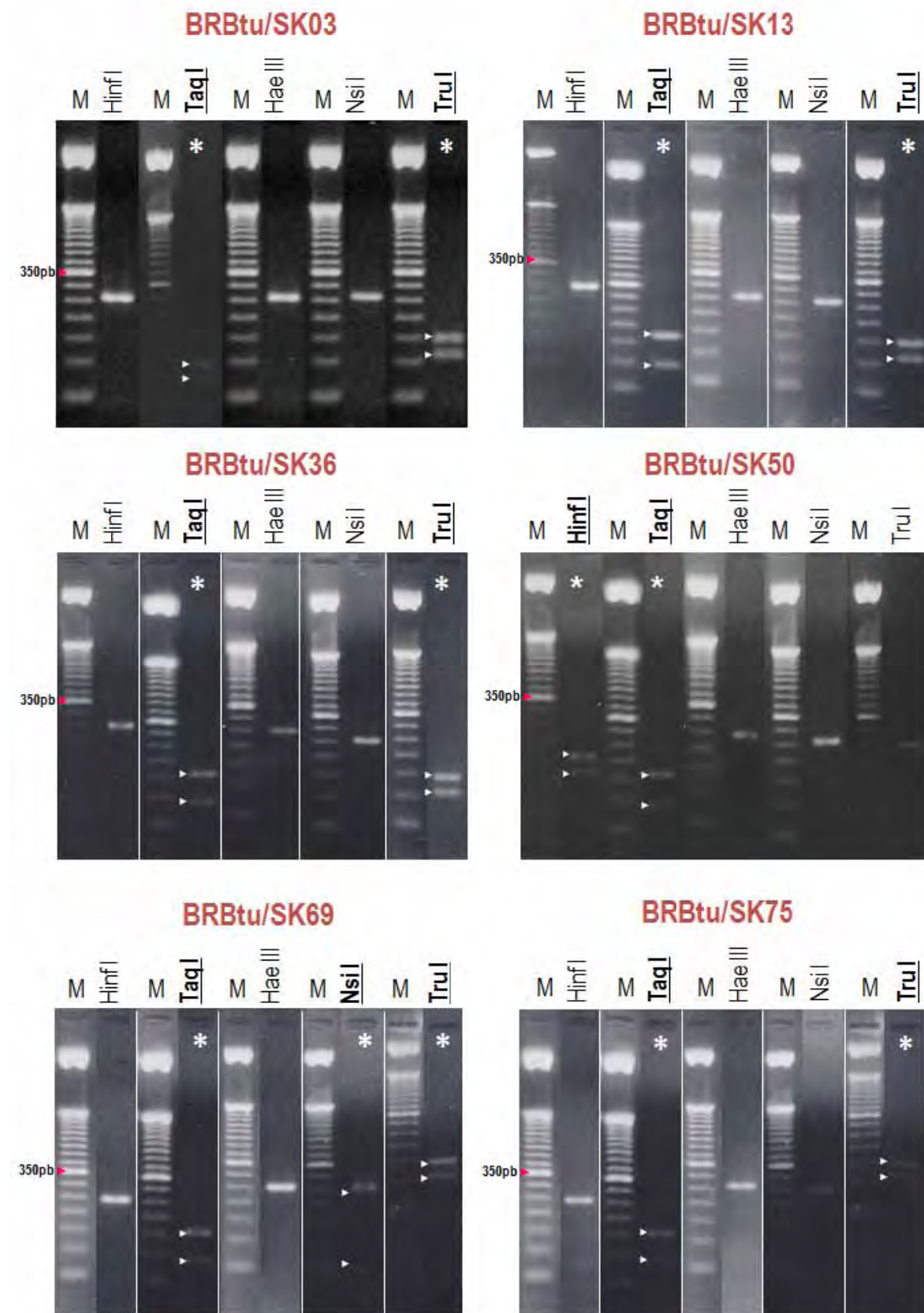


FIGURA 4 - Amostras de sarcoma de Kaposi com padrões não-descritos de PCR-RFLP após análise de segmentos de 247pb da ORF-K1 do KSHV/HHV-8. Nas reações destacadas (*), são apresentados os fragmentos obtidos (cabeça de seta) após a digestão com a enzima indicada. Após análise filogenética todas as amostras com padrões não-descritos agruparam-se com as de genótipo C.

TABELA 1: Seqüências de DNA da ORF-K1 do KSHV/HHV-8 obtidas da literatura e do presente estudo utilizadas nas análises filogenéticas.

Estudo, número (n) e procedência das amostras	Amostras*
Zong et al, 1999. (n=7) Linhagens celulares e amostras de pacientes dos Estados Unidos, África e Oceania (isolados-protótipo).	BCBL-R (AF133038); BCBL-B (AF133039); 431KAP (AF133040); ASM72 (AF133041); BC2 (AF133042); TSK10 (AF133043); ZSK3 (AF133044).
Caterino de Araújo et al. 2000. (não publicado). (n=33) Brasil.	BR2b (AF282184); BR2mn (AF282185); BR3s (AF282186); BR6mn (AF282187); BR7b (AF282188); BR8b (AF282189); BR9b (AF282190); BR10b (AF282191); BR12b (AF282192); BR14b (AF282193); BR14mn (AF282194); BR14s (AF282195); BR15b (AF282196); BR16c (AF282197); BR17b (AF282198); BR20s (AF282199); BR24b (AF282200); BR28b (AF282201); BR29b (AF282202); BR30 (AF282203); BR31b (AF282204); BR32b (AF282205); BR34b (AF282206); BR38b (AF282207); BR38mn (AF282208); BR41b (AF282209); BR42b (AF282210); BR42mn (AF282211); BR48b (AF282212); BR49b (AF282213); BR50b (AF282214); BR52b (AF282215); BR52mn (AF282216).
Biggar et al, 2000 (n=2). População indígena do Brasil.	Tupi-1 (AF220292); Tupi-2 (AF220293).
Nascimento et al, 2005 (n=17). São Paulo, Brasil..	Bra/SP1 (AY378009); Bra/SP9 (AY378004); Bra/SP11 (AY377992); Bra/SP33 (AY377994); Bra/SP36 (AY377998); Bra/SP37 (AY377999); Bra/SP39 (AY378006); Bra/SP40 (AY378000); Bra/SP51 (AY378002); Bra/SP63 (AY378008); Bra/SP65 (AY377995); Bra/SP66 (AY377996); Bra/SP67 (AY378003); Bra/SP72 (AY378007); Bra/SP81 (AY377997); Bra/SP84 (AY377993); Bra/SP93 (AY378005).
Presente estudo, 2007 (n=44). Isolados obtidos de sarcoma de Kaposi (tecido fixado e incluído em parafina).	BRBtu/SK03 (EU116385); BRBtu/SK04 (EU116386); BRBtu/SK05 (EU116387); BRBtu/SK08 (EU116388); BRBtu/SK09 (EU116389); BRBtu/SK10 (EU116390); BRBtu/SK13 (EU116391); BRBtu/SK14 (EU116392); BRBtu/SK15 (EU116393); BRBtu/SK20 (EU116394); BRBtu/SK22 (EU116395); BRBtu/SK24 (EU116396); BRBtu/SK25 (EU116397); BRBtu/SK26 (EU116398); BRBtu/SK27 (EU116399); BRBtu/SK28 (EU116400); BRBtu/SK29 (EU116401); BRBtu/SK30 (EU116402); BRBtu/SK31 (EU116403); BRBtu/SK32 (EU116404); BRBtu/SK33 (EU116405); BRBtu/SK36 (EU116406); BRBtu/SK37 (EU116407); BRBtu/SK40 (EU116408); BRBtu/SK43 (EU116409); BRBtu/SK46 (EU116410); BRBtu/SK48 (EU116411); BRBtu/SK49 (EU116412); BRBtu/SK50 (EU116413); BRBtu/SK51 (EU126025); BRBtu/SK52 (EU116414); BRBtu/SK53 (EU116415); BRBtu/SK57 (EU116416); BRBtu/SK63 (EU116417); BRBtu/SK65 (EU116418); BRBtu/SK66 (EU116419); BRBtu/SK68 (EU116420); BRBtu/SK69 (EU116421); BRBtu/SK71 (EU116422); BRBtu/SK73 (EU116423); BRBtu/SK75 (EU116424); BRBtu/SK76 (EU116425); BRBtu/SK78 (EU116426); BRBtu/SK79 (EU116427); BRBtu/SK81 (EU116384);

* Nome do isolado (número de acesso na base de dados GenBank)