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Rabies virus isolates of India – Simultaneous existence of two distinct evolutionary lineages



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ABSTRACT

Rabies is a fatal viral disease of serious public health implication. The disease is enzootic in India. In the present study, thirty six rabies virus isolates were obtained from terrestrial mammals of India during 2002–2012. Ecto-domain coding region of the glycoprotein gene from all the isolates were sequenced and the phylogenetic analysis was performed in relation to the global rabies and rabies related virus isolates. The Indian isolates grouped into two distinctly separate lineages with majority of the Indian isolates in Arctic like 1 lineage and the remaining isolates in sub-continental lineage. Isolates of the two distinct lineages were identified simultaneously from the same geographical region. Time scaled phylogenetic tree indicated that the sub-continental lineage of the virus is one of the earliest clade of rabies virus that diverged from bat rabies virus. On the contrary, the Arctic-like 1 lineage of India appeared to be a more recent divergence event. The amino acid sequence comparison revealed that all the major antigenic sites were almost conserved among the Indian isolates whereas few amino acid variations could be identified around site I Ia, minor site I and IV. The d_N/d_S study based on G ecto-domain is in support of the earlier reports of strong purifying selection. In conclusion, it is evident that the Indian rabies virus isolates are of two major distinct lineages with distant phylogenetic and evolutionary relationship.

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1. Introduction

Rabies, a viral disease, is widespread in all parts of India except in the island provinces, Andaman, Nicobar, and Lakshadweep (Sudarshan et al., 2007). The genome of rabies virus (RV), consist of a single stranded, non segmented, negative sense RNA. It belongs to the genotype-1 of the genus Lyssavirus and the family Rhabdoviridae (Tordo et al., 1986). RV can infect a wide range of wild and domestic mammals, and also humans. Though, the infection can be prevented by vaccination, there is no effective treatment after the manifestation of the disease. In the developing countries dogs are major vectors in spreading the virus and have been responsible for an estimated 55,000 human deaths annually (WHO, 2005). Non-immunized dogs are the main source of infection to other mammals (Tang et al., 2005).

The viral genome encodes five proteins in the order of 3'-N-P-M-G-L-5': Nucleoprotein (N), Phosphoprotein (P), matrix protein (M), Glycoprotein (G) and RNA dependent RNA polymerase (L) (Wunner et al., 1988). The rabies virus glycoprotein (RVG) is a type-I transmembrane protein with a trimeric structure, and is anchored over the viral envelope. It is composed of an endodomain (ENDO), a transmembrane region (TM) and an ectodomain (ECTO). The glycoprotein is involved in determining the viral tropism and pathogenicity (Lafon, 1994; Wiktor et al., 1973). It is the immuno-dominant antigen carrying both B- and T-cell antigenic sites in the ectodomain. The protein also plays important roles in receptor recognition and membrane fusion (Benmansour et al., 1991; Delagneau et al., 1981; Coulon et al., 1998; Dietzschold et al., 1983; Prehaud et al., 1988; Tuffereau et al., 1998). The rabies virus neutralizing antibodies are essentially directed against the RVG. The RVG gene encodes a 524 amino acid (AA) product with a 19-AA signal peptide that is cleaved inside endoplasmic reticulum to yield a mature G protein (RVG). The mature RVG contains

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an N-terminal ecto-domain, a 22-AA transmembrane-domain (TM) and a C-terminal endo-domain of 44 AA (Badrane et al., 2001).

Phylogenetic studies are important to address the various biological aspects of infections such as the relationship among the virus isolates, origin, spread and migration patterns of the virus. Phylogenic study of the rabies virus strains in India was initially based on just a few isolates (Jayakumar et al., 2004; Kuzmin et al., 2004) but later extended to a much larger number (Nadin-Davis et al., 2007; Nagarajan et al., 2006, 2009; Reddy et al., 2011). However, sequence information on RVG is available only for few Indian rabies virus isolates. RVG based phylogeny is indeed important considering its vital role in viral pathogenesis, neuro-virulence, host adaptation, etc. (Badrane and Tordo, 2001; Badrane et al., 2001; Real et al., 2005).

In the present study, sequences of RVG ecto-domain coding region of 36 isolates which were collected from a wide geographical area across India were determined. The phylogenic relationship and evolutionary lineage of these isolates were studied from a global context. Our study provided evidence for the simultaneous prevalence of very early and recent evolutionary lineage of rabies virus strains in India.

2. Materials and methods

2.1. Samples and sample processing

Postmortem samples of brain and/or salivary gland tissues, from animals/humans which died of rabies symptoms, were used in the study. The samples were collected during 2002–2012 from different parts of India *viz.*, Andhra Pradesh (IAP), Tamil Nadu (ITN), Kerala (IKE), Karnataka (IKA), Maharashtra (IMA) and Uttar Pradesh (IUP) (Fig. 1). These isolates were sampled from seven different species of terrestrial mammals. Eighteen isolates from dogs, four from humans, seven from cattle, two each from buffaloes, horses, and goats, and one isolate from an elephant were collected. Impression smears were prepared from the tissue samples and then a 20% homogenate of the respective tissue samples was prepared in phosphate-buffered saline containing 2% horse serum. The impression smears were acetone fixed and stored at +4 °C until further use while the tissue homogenates were stored at -80 °C.

2.2. Laboratory test to identify rabies antigen/genome

Impression smears were developed with rabies N-gene specific mAb-FITC conjugate (Light DiagnosticsTM Rabies DFA Reagent; Dean et al., 1996). N-gene (Nagarajan et al., 2009) and Ψ -gene specific RT-PCRs (Nagarajan et al., 2006) were performed to determine the presence of rabies viral genomes in the tissue homogenates. The virus in tissue homogenate was also amplified by intracerebral mouse inoculation to rule out the possible false negative results which might arise due to poor sample quality.

2.3. RNA extraction and RT-PCR

The samples with positive result in any of the above mentioned tests were further processed and were subjected to rabies G gene specific RT-PCR. Total RNA was extracted either from the post mortem tissue homogenates or mouse brain tissue homogenates using TRIzol[®] reagent (Invitrogen, USA), following the manufacturer's instructions. G gene specific primers were designed with Primer3-Plus software (http://primer3plus.com), based on the available G gene sequences of the Indian isolates (DQ255915 to DQ255943) and degenerate bases were included wherever necessary (Table 1). The coding sequence of RVG ecto-domain of all the isolates was amplified by RT-PCRs as two overlapping fragments.

One step RT-PCR (Qiagen, Germany) was performed using 500 ng of total RNA and the RT-PCR reaction was set up as per the protocol recommended by the manufacturer. The thermal profile employed for reverse transcription and PCR is as follows: One cycle of 50 °C for 30 min and polymerase activation at 94 °C for 10 min followed by 35 cycles of denaturation at 94 °C for 30 s, annealing at 55 °C for 45 s, and extension at 72 °C for 1 min. Finally a 10 min extension step at 72 °C was performed.

2.4. Sequencing and phylogenetic analysis

The amplicons were purified using QIAquick gel purification kit (QIAGEN, Germany) following the manufacturer's instruction. The purified products were sequenced with gene specific primers (which were used in RT-PCR amplification). Internal primers were used wherever necessary for getting complete sequence coverage from the PCR amplified fragments. Cycle sequencing was done with ABI Prism BigDye Terminator cycle sequencing ready reaction kit (v3.1; Applied Biosystems[®]) and the products were purified using EDTA-alcohol. Then the samples were resolved and analysed in a capillary gel using ABI XL 3130 in the Genetic analyzer (Applied Biosystems[®]).

Coding sequence of the RVG ecto-domain (1317 bp) was assembled from the sequence data using ClustalW v2 software for each of the isolate (Larkin et al., 2007). Apart from the 36 isolates of the present study, the sequences of 8 Indian rabies virus isolates from GenBank were used in the construction of the NJ tree. Additional 3 sequences of RV isolates from the Indian sub-continent (2 from Sri Lanka and 1 from Nepal) retrieved from the GenBank were included in this study. Representative sequences of RV isolates from South East Asian countries, South Korea, China, RV isolates of Artic-Artic like lineage, cosmopolitan lineage, RV isolates from bats, fixed strains of rabies virus (Flury-HEP, Pitman Moore) and rabies related viruses (RRV) were also included in the phylogenetic analysis. Details of the sequences were shown in the Table 2. The sequences were aligned using ClustalW and a NJ tree was plotted by MEGA version 6 (Tamura et al., 2013). The sequences were aligned using ClustalW and a NJ tree was plotted by MEGA version 6 (Tamura et al., 2013). Following multiple alignment, the Bayesian Information Criterion (BIC), maximum likelihood values and Akaike Information Criterion corrected (AICc) scores were also determined for the maximum likelihood fits based on the data specific model to generate the phylogenetic tree. The ML tree topology was evaluated using both neighbor-joining (NJ) and ML methods with 1000 and 500 bootstrap replicates respectively.

2.5. Evolutionary analysis

Molecular evolutionary rate and the divergence times were coestimated and the Bayesian maximum clade credibility phylogenetic tree was constructed using Bayesian Markov Chain Monte Carlo (MCMC) analysis implemented in BEAST software package, v1.8.0 (Drummond et al., 2012). The GTR + I + G nucleotide substitution model was determined as the best fit based on the Akaike Information Criterion (AIC) scores (Posada, 2008). An uncorrelated lognormal relaxed clock model along with a coalescent tree prior was chosen and the input file for BEAST analysis was obtained using BEAUti software v1.8.0, where the sequences were tip dated according to the year of collection. The MCMC chains were run for a chain length of 2×10^8 and sampled at every thousand generations. The nucleotide substitution rate (substitutions/site/year) and the time to Most Recent Common Ancestor (tMRCA) values were obtained from the Tracer, v1.5. The posterior tree distributions were summarized using Tree annotator with the exclusion of the initial ten percent of trees and visualised in FigTree v1.3.1.



Fig. 1. Map of India showing the geographical locations of the different lineages of RV isolates of Indian origin (Map source: Yuvaraj et al., 2013).

Table 1				
Sequences of the primers us	ed in the C	gene amplifi	ication by	RT-PCR.

_	•		.	
	S. No.	Primer ID	Sequence (5'-3')	Nucleotide position in full length rabies viral RNA ^a
	1	GP1 For	CGCTGCATTTTRTCARAGT	3221-3239
	2	GP1 Rev	GGAGGGCACCATTTGGTMTC	4116-4135
	3	GP2 For	GATGARAGAGGCCTRTATAAG	4005-4025
	4	GP2 Rev	RCCRCTYTTATATGACTCCCA	4854-4874

^a GenBank ID for the reference sequence - M13215.

2.6. Deduced amino acid sequence comparison

The deduced amino acid sequences were analysed to identify the variations in the major and minor immuno-dominant sites among the Indian isolates and other Asian isolates. Representative amino acid sequences containing at least a single amino acid difference were used for the analysis. Similarly the potential N-glycosylation sites were also examined (Wunner et al., 1985; Prehaud et al., 1988; Benmansour et al., 1991). WINA software was used to plot a d_N and d_S analysis graph, to estimate the proportions of the

Table 2

Information on rabies and rabies related virus isolates used in the present study for Phylogenetic analysis.

1Adv-B0CHBuffabAddm 2 Pachach200KTSP7163KE-477CTCovKaruia2004KTSP7164KE-477CTCovKaruia2004KTSP7165KK-877CTCovKaruia2004KTSP7176KK-887CTDagKaruia2004KTSP7177MAKBBCTDagKaruia2004KTSP7188KK-807CTDagKaruia2004KTSP7189KK-807CTDagKaruia2004KTSP71910KK-807CTDagKaruia2004KTSP71911KK-807CTDagKaruia2004KTSP71912KK-8101CTDagKaruia2004KTSP72413KK-8107CTDagKaruia2004KTSP72414KK-8107CTDagKaruia2004KTSP72415KK-8107CTDagKaruia2004KTSP72416KK-8107CTDagKaruia2004KTSP72417KK-8107CTDagKaruia2004KTSP72418KK-8107CTDagKaruia2004KTSP72419KK-8107CTDagKaruia2004KTSP72410KK-8107CTDagKaruia2004KTSP72411KK-8107CTDagKaruia2004KTSP	S. No.	Virus reference	Genotype	Host	Place of origin	Year	Accession No.
12 12<	1	IAP-R91	GT1	Buffalo	Andhra Pradesh	2002	KF150716
3 IRE-R7 CT1 Cov Kerala 2004 RF150712 5 IRE-B8 CT1 Dog Kerala 2004 RF150712 5 IRE-B8 CT1 Dog Kerala 2004 RF150713 6 IRE-B87 CT1 Dog Kerala 2004 RF150713 7 IRE-B87 CT1 Dog Kerala 2004 RF150713 8 IRF B07 CT1 Dog Kerala 2004 RF150713 10 IRF B101 CT1 Dog Kerala 2004 RF150713 11 IRF B101 CT1 Dog Kerala 2004 RF150723 12 IRF B101 CT1 Cort Kerala 2004 RF150723 13 IRF B101 CT1 Cort Kerala 2004 RF150723 14 IRF B101 CT1 Cort Kerala 2004 RF150723 15 IRF B111 CT1 <td< td=""><td>2</td><td>IKF-R73</td><td>GT1</td><td>Buffalo</td><td>Kerala</td><td>2004</td><td>KF150710</td></td<>	2	IKF-R73	GT1	Buffalo	Kerala	2004	KF150710
ide ide <td>3</td> <td>IKE-R77</td> <td>CT1</td> <td>Cow</td> <td>Kerala</td> <td>2004</td> <td>KF150711</td>	3	IKE-R77	CT1	Cow	Kerala	2004	KF150711
5 Dog Kenda 2004 KP150713 66 IR2-887 GT1 Dog Mahashra 2004 KP150714 7 IKA-883 GT1 Dog Mahashra 2004 KP150714 8 IKZ-804 GT1 Dog Mahashra 2004 KP150717 9 IKZ-804 GT1 Dog Kenda 2004 KP150721 10 IKZ-800 GT1 Dog Kenda 2004 KP150721 11 IKZ-8109 GT1 Dog Kenda 2004 KP150721 12 IKZ-8109 GT1 Dog Kenda 2004 KP150725 13 IKZ-8113 GT1 God Kenda 2004 KP150724 14 IKZ-8113 GT1 Dog Kenda 2004 KP150725 15 IKZ-8113 GT1 Dog Kenda 2004 KP150726 16 IKZ-8122 GT1 Dog Kenda 2	1	IKE-R78	CT1	Cow	Kerala	2004	KF150717
isc.es? OT Carr Korak 2004 RF30713 7 MAAsas GT Dog Kerala 2004 RF30713 8 KK-807 GT Dog Kerala 2004 RF30713 10 KK-807 GT Dog Kerala 2004 RF30713 11 KK-807 GT Dog Kerala 2004 RF30713 12 KK-8108 GT Dog Kerala 2004 RF150721 13 KK-8108 GT Dog Kerala 2004 RF150721 14 KK-8110 GT Cov Kerala 2004 RF150725 15 KK-8110 GT Cov Kerala 2004 RF150725 16 KK-8112 GT Cov Kerala 2004 RF150721 17 KK-8123 GT Dog Kranaka 2004 RF150733 21 KK-8124 GT Dog Kranaka	5	IKE-R86	CT1	Dog	Kerala	2004	KF150712
NA ABS CTI Dag Molasolitor 2004 CTISP15 8 IKC-R94 CTI Dag Kenala 2004 KTISP17 9 IKC-R97 CTI Dag Kenala 2004 KTISP17 10 IKC-R01 CTI Dag Kenala 2004 KTISP17 11 IKC-R01 CTI Dag Kenala 2004 KTISP17 11 IKC-R01 CTI Dag Kenala 2004 KTISP17 13 IKC-R01 CTI Catter Kenala 2004 KTISP17 14 IKC-R01 CTI Cov Kenala 2004 KTISP17 15 IKC-R01 CTI Dag Kenala 2004 KTISP17 16 IKC-R01 CTI Dag Kenala 2004 KTISP17 16 IKC-R01 CTI Dag Kenala 2004 KTISP179 17 Dag Kenala 2004 KTI	5	IVE D07	CT1	Calf	Korala	2004	KI 150715 VE150714
b INC.BA CIT Dog North Statut OPEN Cital Statut Cital Statut 9 IKS-R01 CIT Cattle Kenala 2004 KT150718 11 IKS-R01 CIT Cattle Kenala 2004 KT150721 12 IKS-R07 CIT Dog Kenala 2004 KT150721 12 IKS-R07 CIT Dog Kenala 2004 KT150721 13 IKS-R01 CIT Castle Kenala 2004 KT150723 14 IKS-R01 CIT Castle Kenala 2004 KT150725 15 IKS-R01 CIT Dog Kenala 2004 KT150726 16 IKS-R01 CIT Dog Karaala 2004 KT150729 17 IKS-R01 CIT Dog Karaala 2004 KT150729 18 IKS-R02 CIT Dog Karaala 2004 KT150729 19	0	INL-RO7	GT1	Dog	Maharashtra	2004	KF150714
9 NG-87 Crit Dag Notak 2014 Kristion 101 IKG-8101 Crit Dag Kenah 2004 Kristion 112 IKG-8105 Crit Dag Kenah 2004 Kristion 113 IKG-8109 Crit Dag Kenah 2004 Kristion 114 IKG-810 Crit Dag Kenah 2004 Kristion 115 IKG-8114 Crit Car Kenah 2004 Kristion 116 IKG-8114 Crit Cow Kenah 2004 Kristion 117 IKG-8114 Crit Dag Kenah 2004 Kristion 118 IKG-812 Crit Dag Kenah 2004 Kristion 118 IKG-812 Crit Dag Kenah 2004 Kristion 118 IKG-812 Crit Dag Karnataka 2004 Kristion 118 IKG-812 Cr	/		GT1	Dog	Widildi dSilti d	2004	KF150715 VE150717
10 RC-R10 Critic Partial Model Model <t< td=""><td>0</td><td>IKE-K94</td><td>GT1</td><td>Dog</td><td>Kerala</td><td>2004</td><td>KF150717</td></t<>	0	IKE-K94	GT1	Dog	Kerala	2004	KF150717
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In Ind Ind Dag Mathe Adda Mathematical 111 Inter-Name Control Dep Mathematical 2004 KF 157221 114 IKE-R110 GT1 Carde Kerala 2004 KF 15723 115 IKE-R114 GT1 Cov Kerala 2004 KF 15723 116 IKE-R114 GT1 Cov Kerala 2004 KF 15723 117 IKE-R113 GT1 Dep Kerala 2004 KF 15723 118 IKE-R123 GT1 Dep Karnataka 2004 KF 15723 118 IKE-R133 GT1 Dep Karnataka 2004 KF 15073 119 IKE-R135 GT1 Dep Karnataka 2004 KF 15073 123 IKE-R135 GT1 Dep Karnataka 2004 KF 15073 124 IKE-R135 GT1 Dep Karnataka 2005 KF 15073 125	10	IKE-RIUI	GII	Cattle	Kerala	2004	KF150719
12 RE-R10 G11 Dog Merala 2004 ME130/21 114 RE-R10 G11 Codte Kerala 2004 KE150723 15 RE-R11 G11 Codte Kerala 2004 KE150723 15 RE-R11 G11 Cow Kerala 2004 KE150723 17 RE-R121 G11 Dog Kerala 2004 KE150726 18 RE-R123 G11 Dog Karnataka 2004 KE150727 19 RA-R144 G11 Dog Karnataka 2004 KE150723 21 RA-R144 G11 Dog Karnataka 2005 KE150733 22 RA-R148 G11 Dog Maharatara 2005 KE15073 23 IRA-R18 G11 Dog Maharatara 2005 KE15073 24 ITN-R148 G11 Dog Andra Padesh 2005 KE15073 25 IRE-R151 <	11	IKE-R106	GII	Dog	Kerala	2004	KF150720
13 RE-8109 CT1 Dog Kerala 2004 KT30722 15 RE-8114 CT1 Cole Kerala 2004 KT30723 17 RE-8116 CT1 Cow Kerala 2004 KT30723 17 RE-8116 CT1 Dog Kerala 2004 KT50725 18 RE-8121 CT1 Dog Karataka 2004 KT50725 20 RA-8132 CT1 Dog Karataka 2004 KT50726 21 RE-8132 CT1 Dog Karataka 2004 KT50726 22 RE-8145 CT1 Dog Karataka 2005 KT50731 23 RE-8154 CT1 Dog Tamil Nada 2005 KT50731 24 RE-8154 CT1 Dog Ambra Mate 2008 KT50731 25 RE-8154 CT1 Dog Ambra Mate 2008 KT50737 26 RE-8155 CT1	12	IKE-R107	GI1	Dog	Kerala	2004	KF150721
14 RE-8110 CT1 Catle Kerala 2004 KF30723 15 RE-8116 CT1 Carr Kerala 2004 KF30723 17 RE-8116 CT1 Dog Kerala 2004 KF30723 18 RE-8123 CT1 Dog Kerala 2004 KF30723 20 RA-8123 CT1 Dog Karnataka 2004 KF30723 21 RA-8132 CT1 Dog Karnataka 2004 KF30733 22 RA-8142 CT1 Dog Karnataka 2004 KF30733 23 RA-8148 CT1 Dog Karnataka 2005 KF30733 24 MA-8189 CT1 Dog Karnataka 2005 KF30734 25 RE-8154 CT1 Dog Andhar Andesh 2008 KF30734 26 RE-8154 CT1 Dog Andhar Andesh 2018 KF30734 27 RA-8183 <td< td=""><td>13</td><td>IKE-R109</td><td>GT1</td><td>Dog</td><td>Kerala</td><td>2004</td><td>KF150722</td></td<>	13	IKE-R109	GT1	Dog	Kerala	2004	KF150722
15 RCF-R11 CT1 Coart Kerala 2004 K19724 16 RCF-R114 CT1 Coart Kerala 2004 K19725 17 RCK-R121 CT1 Coart Kerala 2004 K19727 19 RCK-R122 CT1 Dog Karnataka 2004 K19728 20 RCK-R122 CT1 Dog Karnataka 2004 K19728 21 RCK-R142 CT1 Dog Karnataka 2004 K19732 22 RCK-R144 CT1 Dog Karnataka 2004 K19732 23 RTN-R148 CT1 Dog Marnataka 2008 K19732 24 RCR-R189 CT1 Human Maharashtra 2008 K197373 25 MA-R189 CT1 Dog Andhra Fradesh 2001 K197373 26 MA-R190 CT1 Dog Andhra Fradesh 2011 K197373 27 MA-R193	14	IKE-R110	GI1	Cattle	Kerala	2004	KF150723
16 RE-R114 CT Cow Kerala 2004 K12725 17 RE-R113 CT Cog Kerala 2004 K12725 18 RE-R113 CT Cog Kerala 2004 K12725 19 MK-R112 CT Dog Karataka 2004 K15725 21 RK-R142 CT Dog Karataka 2004 K15723 22 RK-R144 CT Dog Karataka 2004 K15733 23 RK-R145 CT Dog Karataka 2005 K15733 24 ITK-R148 CT Dog Karataka 2005 K15733 25 IKE-R155 CT Dog Andhra Padesh 2009 K15733 25 MA-R190 CT Dog Andhra Padesh 2009 K15733 26 MA-R191 CT Dog Andhra Padesh 2011 K15733 27 MA-R193 CT	15	IKE-R111	GT1	Goat	Kerala	2004	KF150724
17 IKE-R121 CT1 Dog Kerala 2004 KP12727 18 IKE-R121 CT1 Dog Karnataka 2004 KP13772 19 IKA-R129 CT1 Dog Karnataka 2004 KP13773 10 IKA-R142 CT1 Dog Karnataka 2004 KP13731 21 IKA-R144 CT1 Dog Marrataka 2004 KP13732 223 IKA-R146 CT1 Dog Marrataka 2005 KP15733 234 IKK-R154 CT1 Bephant Kerlaka 2005 KP15734 245 IKK-R154 CT1 Human Maftra Pradesh 2009 KP15736 254 IKK-R154 CT1 Human Andtra Pradesh 2009 KP15737 264 IKK-R154 CT1 Human Andtra Pradesh 2011 KP15737 274 IAP-R193 CT1 Human Andtra Pradesh 2011 KP15774 <td< td=""><td>16</td><td>IKE-R114</td><td>GT1</td><td>Cow</td><td>Kerala</td><td>2004</td><td>KF150725</td></td<>	16	IKE-R114	GT1	Cow	Kerala	2004	KF150725
IRE-R121 CT Coat Kerala 2004 K150727 19 IKA-R129 CT Dog Karnataka 2004 K150728 20 IKA-R121 CT Dog Karnataka 2004 K150728 21 IKA-R122 CT Dog Karnataka 2004 K150731 22 IKK-R144 CT Dog Tamitaka 2004 K150731 23 IMA-R146 CT Dog Tamitaka 2005 K150731 24 IIKK-R155 CT Cow Kerala 2005 K150731 25 IKK-R155 CT Cow Kerala 2009 K150731 26 IKK-R155 CT Human Maharashtra 2009 K150731 27 IMA-R189 CT Human Andhra Pradesh 2011 K150731 28 IAP-R192 CT Human Andhra Pradesh 2011 K150742 24 IAP-R193 CT	17	IKE-R116	GT1	Dog	Kerala	2004	KF150726
19 RA-R129 CT1 Dog Karnataka 2004 K15722 21 RA-R132 CT1 Dog Karnataka 2004 K15722 21 RA-R142 CT1 Dog Karnataka 2004 K15722 21 RA-R144 CT1 Dog Karnataka 2004 K15723 22 RFN-R144 CT1 Dog Karnataka 2005 K15733 23 RFS-R154 CT1 Elephant Kerala 2005 K157373 24 RFA-R155 CT1 Human Mafarsitha 2009 K157373 25 RFA-R192 CT1 Dog Andtra Fradesh 2009 K157373 26 MAP-R192 CT1 Dog Andtra Fradesh 2011 K157374 30 IAP-R192 CT1 Human Andtra Fradesh 2011 K157374 31 IAP-R195 CT1 Human Andtra Fradesh 2011 K157074 32	18	IKE-R121	GT1	Goat	Kerala	2004	KF150727
210 KX-R132 GT1 Dog Karntaka 204 KF150730 221 KK-R142 GT1 Dog Karntaka 2044 KF150731 223 MK-R146 GT1 Dog Mainsaftra 2004 KF150732 23 MK-R146 GT1 Dog Mainsaftra 2004 KF150734 245 MK-R145 GT1 Dog Amarshira 2005 KF150736 255 MK-R189 GT1 Dog Andrap Pracesh 2009 KF150736 280 APR-R190 GT1 Dog Andrap Pracesh 2009 KF150738 291 APR-R191 GT1 Dog Andrap Pracesh 2011 KF150734 202 APR-R194 GT1 Human Andrap Pracesh 2011 KF15074 203 APR-R194 GT1 Human Andrap Pracesh 2011 KF15074 204 APR-R194 GT1 Human Andrap Pracesh 2012 KF15073 <t< td=""><td>19</td><td>IKA-R129</td><td>GT1</td><td>Dog</td><td>Karnataka</td><td>2004</td><td>KF150728</td></t<>	19	IKA-R129	GT1	Dog	Karnataka	2004	KF150728
11 Nor. Nor. Nor. Nor. Nor. Nor. 22 IKA-R144 GTI Dog. Maharashtra. 2004 KF150731 23 IMA-R146 GTI Dog. Tamil Nafu. 2005 KF150731 24 ITN-R148 GTI Dog. Tamil Nafu. 2005 KF150731 25 IKE-R153 GTI Dog. Andra Pracesin 2005 KF150737 26 IKE-R153 GTI Dog. Andran Pracesin 2009 KF150737 27 MA-R193 GTI Dog. Andran Pracesin 2009 KF150739 31 IAP-R192 GTI Human Andran Pracesin 2011 KF150741 32 IAP-R195 GTI Human Andran Pracesin 2012 KF150743 33 IAP-R195 GTI Human Andran Pracesin 2012 KF150743 35 IUP-R198 GTI Horse UITA Pradesin 2012 KF150743	20	IKA-R132	GT1	Dog	Karnataka	2004	KF150729
223 IKA-R144 GT1 Dog Kamatala 2004 KF150732 234 ITM-R148 GT1 Dog Tamil Natu 2005 KF150732 245 IKK-R154 GT1 Dog Tamil Natu 2005 KF150732 256 IKK-R154 GT1 Dog Andhra Pradesh 2009 KF150735 271 IMA-R189 GT1 Human Maharshtra 2009 KF150736 281 IAP-R193 GT1 Dog Andhra Pradesh 2009 KF150736 281 IAP-R193 GT1 Dog Andhra Pradesh 2011 KF150731 283 IAP-R193 GT1 Dog Andhra Pradesh 2011 KF150743 393 IAP-R193 GT1 Human Andhra Pradesh 2012 KF150742 394 IAP-R195 GT1 Horse Utra Pradesh 2012 KF150743 395 UP-R197 GT1 Horse Utra Pradesh 2012 KF150743	21	IKA-R142	GT1	Dog	Karnataka	2004	KF150730
23 IMA. R146 CT1 Dog Maharashtra 204 [KT50732] 24 ITN-R148 CT1 Dog Taill Nadu 2005 [KT50733] 25 IKK-R155 CT1 Elephant Kernla 2005 [KT50733] 26 IKK-R155 CT1 Human Maharashtra 2008 RT50736 27 IMA-R189 CT1 Dog Andran Pradesh 2009 RT50736 28 IA/R-R193 CT1 Dog Andran Pradesh 2009 RT50736 29 IA/R-R192 CT1 Dog Andran Pradesh 2011 KT510732 31 IA/R-R195 CT1 Human Andran Pradesh 2012 KT510742 33 IA/R-R196 CT1 Human Andran Pradesh 2012 KT510743 35 IUP-R198 CT1 Horse Utar Pradesh 2012 KT510742 36 IUP-R198 CT1 Horse Utar Pradesh 2012 KT510742	22	IKA-R144	GT1	Dog	Karnataka	2004	KF150731
24 IN-R 14.8 CT1 Dog Tamil Nach 2005 RF150733 25 IKE-R 15.5 CT1 Elphant Kerala 2005 KF150735 26 IKA-R 18.9 CT1 Dog Andha Fadesh 2009 KF150735 28 IAP-R 191 CT1 Dog Andha Fadesh 2009 KF150737 29 IAP-R 191 CT1 Dog Andha Fadesh 2009 KF150738 30 IAP-R 192 CT1 Human Andha Fadesh 2011 KF150734 31 IAP-R 193 CT1 Human Andha Fadesh 2011 KF150743 32 IAP-R 195 CT1 Human Andha Fadesh 2012 KF150743 33 IAP-R 195 CT1 Human Andha Fadesh 2012 KF150743 34 IAP-R 195 CT1 Vaccine strain 2012 KF150743 35 IIAP Adesh 2012 KF150744 2012 KF150744 36	23	IMA-R146	GT1	Dog	Maharashtra	2004	KF150732
25IKE-R154CT1CowKerala2005KF15073426IKE-R157IMA-R189CT1CowKerala2009KF15073527IMA-R189CT1DogAndhra Pradesh2009KF15073729IAP-R191CT1DogAndhra Pradesh2009KF15073831IAP-R192CT1DogAndhra Pradesh2011KF15074032IAP-R193CT1HumanAndhra Pradesh2011KF15074133IAP-R194CT1HumanAndhra Pradesh2012KF15074334IAP-R195CT1HumanAndhra Pradesh2012KF15074435IUP-R196CT1DogAndhra Pradesh2012KF15074436IUP-R198CT1HorseUtar Pradesh2012KF15074437PVCT1PradesUtar Pradesh2012KF15074438IUP-R198CT1HorseUtar Pradesh2012KF15074439IUP-R198CT1Pradesh2012KF15074431IUP-R198CT1Pradesh2012KF15074434IUP-R198CT1HorseUtar Pradesh2012KF15074434IUP-R198CT1Pradesh2012KF15074435Iup-R198CT1DogIndia2006KF14572134Iup-R198CT1HumanIndia2005KF15073134Iup-R198CT1Dog<	24	ITN-R148	GT1	Dog	Tamil Nadu	2005	KF150733
26KK-R185CT1CowKerala2005KF15073527IMA-R189CT1HumanMaharashtra2009KF15073728IAP-R191CT1DogAndhra Pradesh2009KF15073730IAP-R192CT1DogAndhra Pradesh2009KF15073931IAP-R193CT1HumanAndhra Pradesh2011KF15074032IAP-R193CT1HumanAndhra Pradesh2011KF15074133IAP-R195CT1HumanAndhra Pradesh2012KF15074234IAP-R195CT1HumanAndhra Pradesh2012KF15074335IUP-R197CT1HorseUtar Pradesh2012KF15074336IUP-R198CT1Vaccine strainVEVEVE37PVCT1Vaccine strainVEVEVE38India, CT1, J98CT1DogIndia1988R4237121409902NPL'1984CT1DogIndia2006R4856292941H-B-81322, SRLCT1DogIndia2006R4956132429427, SRLCT1DogIndia2010CO99681243NNV-RA#-HudiaCT1HumanIndia2006R495715123144Germany, Tp-IndiaCT1DogIndia2006R495715123145UK, Forn-IndiaCT1DogIndia2001R49547146India, LP	25	IKE-R154	GT1	Elephant	Kerala	2005	KF150734
27MA-R189CT1HumanMahrashtra2009KF1507328MA-R190CT1DogAndhra Pradesh2009KF15073729MA-R191CT1DogAndhra Pradesh2009KF15073931MA-R192CT1DogAndhra Pradesh2011KF15074032MA-R193CT1HumanAndhra Pradesh2011KF15074133MA-R195CT1HumanAndhra Pradesh2012KF15074134MA-R1956CT1BogAndhra Pradesh2012KF15074335UD-R195CT1HorseUtta Pradesh2012KF15074336UD-R195CT1HorseUtta Pradesh2012KF15074437PVCT1Vaccite strainUtta Pradesh2012KF15074438CV5CT1DogIndia1998RU88154409902/NF11985CT1GoatNepal1998RU8815441HorsST1ANAST1ANA2005KF15074444HorsST1ANA1998RU881544108915645India CT1HumanIndia1998RU8815446Hada UP_EF151221CT1HumanIndia2005K715074747O4029AFGCT1DogIndia1999KU8615448CHAND02.IndiaCT1DogIndia2005K00747847O4029AFGCT1DogIndia2016<	26	IKE-R155	GT1	Cow	Kerala	2005	KF150735
28IAP-R190CT1DogAndhra Pradesh2009KF15073739IAP-R191CT1DogAndhra Pradesh2009KF15073831IAP-R192CT1DogAndhra Pradesh2011KF15074032IAP-R194CT1HumanAndhra Pradesh2011KF15074133IAP-R195CT1HumanAndhra Pradesh2011KF15074234IAP-R195CT1DogAndhra Pradesh2012KF15074335IUP-R197CT1DogAndhra Pradesh2012KF15074336UP-R197CT1HorseUtra Pradesh2012KF15074337PVCT1Vaccine strainKF15074338CVSCT1Qaccine strain39India (L1198)CT1GoatNralaka1998EU08615441H-08-1320,SRLCT1DogSri Lanka1998EU0861544294237,SRLGT1DogIndia1998EU08613643NNV-RAB-H_IndiaCT1HumanIndia2005K795631944Grmany.Trp-IndiaGT1DogIndia1999EF15123145UK.from-IndiaGT1DogIndia1999EF15123146India_Q23540GT1DogIndia2001QQ2478347O4029A7CGT1DogIndia2001QQ23504048CHAND02_IndiaGT1<	27	IMA-R189	GT1	Human	Maharashtra	2009	KF150736
Pert Part Part Part Part Part Part 	28	IAP-R190	GT1	Dog	Andhra Pradesh	2009	KF150737
30IAP-R192CT1DogAndhra Pradesh2009KF15073931IAP-R193CT1HumanAndhra Pradesh2011KF15074132IAP-R194CT1HumanAndhra Pradesh2011KF15074233IAP-R195CT1DogAndhra Pradesh2012KF15074334IAP-R196CT1DogAndhra Pradesh2012KF15074335ILP-R197CT1HorseUttar Pradesh2012KF15074336ILP-R198CT1Vaccies strainVKF15074537PVCT1Vaccies strain1998KF15074538O'SCT1GoatNegal1998KF15074540900XPE 1988CT1OrgIndia1998KF05815441H-68-130.SRLCT1DogSr Lanka2006FF37215429257.SRLCT1DogSr Lanka2005FF3721543NNV-RAB-HuñaCT1HumanIndia2005FF3721544Grmany.Trp-IndiaCT1DogIndia1999FF15123145UK,forn-IndiaCT1DogIndia1999FF15123146India.UP.GF151231CT1DogIndia1999FF15123147G4293FGGT1DogIndia1999EU08613051900KCKGT1DogIndia1999EU08613052911GKGGT1DogIndia1	29	IAP-R191	GT1	Dog	Andhra Pradesh	2009	KF150738
11IAP-R193CT1HumanAndn'ra Pradesh2011KF 15074132IAP-R195CT1HumanAndn'ra Pradesh2011KF 15074233IAP-R195CT1HorsAndn'ra Pradesh2012KF 15074335IUP-R197CT1HorseUttar Pradesh2012KF 15074336IUP-R197CT1HorseUttar Pradesh2012KF 15074537PVCT1Vaccine strainVVV38CVSCT1OgIndia1998AV237121409902NE7_1998CT1OgIndia1998AV23712141HoB-1320_SRLCT1HumanSi Lanka2008AS5632914294257_SRLCT1HumanIndia2006F43721543NN-KAB-H_IndiaCT1HumanIndia2006F43721544Cerman_T-ph-diaCT1HumanIndia2010CU98681645UK,from-IndiaCT1DogIndia2004E108615646India_L0074978CT1DogIndia2004E10861524704029AFCCT1DogIndia2004E108615248CHANDO3.IndiaCT1DogIndia2004E10861535199130.IndiaCT1DogIndia2004E10861525299131.RCT1DogIndia2004E10861515399130.NCT1Dog	30	IAP-R192	GT1	Dog	Andhra Pradesh	2009	KF150739
12AP-R194CT1HumanAndn'ra Pradesh2011KF15074133IAP-R196CT1DogAndn'ra Pradesh2012KF15074334IUP-R196CT1DogNutar Pradesh2012KF15074335IUP-R198CT1HorseUtar Pradesh2012KF15074536IUP-R198CT1Vaccine strainKF150745KF15074537PVCT1Vaccine strainNutar Pradesh2012KF15074538CVSCT1OgIndia1998AV237121409902NFP_1998CT1CoatNepal1998EU08615441H-08-1320_SRLCT1DogSi Lanka1986EU08615643NNV-KAP-H_IndiaCT1HumanIndia2005AV25719144Cermany_Trp-IndiaCT1HumanIndia2006EF15123145UK_form-IndiaCT1DogIndia1999EU08615846India_UP_EF151231CT1DogIndia1999EU0861784704022AFCCT1DogIndia2001C023304051998CRCCT1DogIndia2001EU08613051998CRCCT1DogIndia2001EU08613051998CRCCT1DogIndia2001EU08613051998CRCCT1DogIndia2001EU08613051998CRCCT1DogIndia	31	IAP-R193	GT1	Human	Andhra Pradesh	2011	KF150740
34MA-R195CT1HumanAndhra Pradesh2011KF15074234MA-R1956CT1DogAndhra Pradesh2012KF15074335IUP-R197CT1HorseUttar Pradesh2012KF15074436IUP-R198CT1HorseUttar Pradesh2012KF15074437PVCT1Vaccine strain2012KF15074538CVSCT1DogIndia1998AV237121409902NEJ 1988CT1DogNepal1998AV23712141H-08-1320_SRLCT1HumanSi Lanka2008AB5692994294257_SRLCT1DogSi Lanka1998EU08615643NNV-RAB-H_IndiaCT1HumanIndia2005LF437215144Germany_Trp-IndiaCT1HumanIndia2001CU38881145UK_Forn-IndiaCT1DogIndia1999EF13123146India_UP_EF151231CT1DogIndia2005DQ074784704029AFCCT1DogCambodia1999EU08613051India_CQ233040CT1DogCambodia1999EU0861315310161VNMCT1DogCambodia1999EU086152549910AOCT1DogCambodia1999EU086152559913BRCT1DogSouth Korea2003EU086151549910AOCT1Dog </td <td>32</td> <td>IAP-R194</td> <td>GT1</td> <td>Human</td> <td>Andhra Pradesh</td> <td>2011</td> <td>KF150741</td>	32	IAP-R194	GT1	Human	Andhra Pradesh	2011	KF150741
14M-R-196CT1DogMuhra Pradesh2012KF15074335IUP-R198CT1HorseUttar Pradesh2012KF15074537PVCT1Vaccine strain2012KF15074538CVSGT1DogIndia1998AY237121409902NFP_1998CT1GoatNepal1998AY23712141H-06-1320_SRLGT1HumanSri Lanka2006E4365564294257_SRLCT1DogSri Lanka2006E43721543NNV-RAB-H_IndiaGT1HumanIndia2005AY956319144Germany_Tp-IndiaGT1HumanIndia2005AY956319145UK_from-IndiaGT1DogIndia2001GU3088146India_DQ074978GT1DogIndia2001GU30861344704029AFCGT1DogIndia2001GU308613448CHAND03_IndiaGT1DogIndia1999E108613951900RCGGT1DogIndia1998E1086139529011CACGT1DogAmbodia1999E10861395301016VNMGT1DogAmbodia1999E1086139549010LACGT1DogAmbodia1999E108613955913IRGT1DogMyanar1999E1086139549010LACGT1DogSouth Korea2003	33	IAP-R195	GT1	Human	Andhra Pradesh	2011	KF150742
35IUP-R197CT1HorseUttar Pradesh2012KF15074436IUP-R198CT1Vaccine strain2012KF15074537PVCT1Vaccine strain2012KF15074538CVSCT1Orac ine strain1998AV23712139India_CH_1998CT1DogIndia1998AV237121409002NPC_1998CT1CoatNepal1998EU08615441Hob-1320_SRLCT1HumanSit Lanka2006EF4372154294257_SRLCT1HumanIndia2006EF43721543NNV-RA8-H_IndiaCT1HumanIndia2006EF43721544Germany_Trp-IndiaCT1HumanIndia2004EU08612845UK_from-IndiaCT1DogIndia1999EP13123146India_UP_EF151231CT1DogIndia1999A987474704029AFCCT1DogIndia2001C23304051India_CQ233040CT1DogCambodia1999EU08613052911CBCCT1DogCambodia1999EU0861525301015VNMCT1DogSouth Korea2003EU08615254910LAOCT1DogSouth Korea2003EU086152559313BRCT1DogSouth Korea2003EU0861525604030PHICT1DogSouth Korea <td< td=""><td>34</td><td>IAP-R196</td><td>GT1</td><td>Dog</td><td>Andhra Pradesh</td><td>2012</td><td>KF150743</td></td<>	34	IAP-R196	GT1	Dog	Andhra Pradesh	2012	KF150743
36UP-R198CT1HorseUttar Pradesh212KF15074537PVCT1Vaccine strain	35	IUP-R197	GT1	Horse	Uttar Pradesh	2012	KF150744
37 PV CT1 Vaccine strain 38 CVS CT1 Dog India 1998 AV237121 40 9002NEP, 1998 CT1 Coat Nepal 1998 EU086154 41 H-80-1320,SRL CT1 Dog Sri Lanka 2008 A8569299 42 94257,SRL CT1 Dog Sri Lanka 2006 EF437215 44 Germany,Trp-India CT1 Human India 2005 EF437215 45 UK,forn-India CT1 Human India 2010 CU35881 46 India,UP,EF151231 CT1 Dog Affanistan 2004 EU086128 47 04029AFG CT1 Dog Affanistan 2001 CQ233040 50 India,CQ233040 CT1 Dog Cambodia 1999 EU086130 51 9906CBC CT1 Dog Cambodia 1998 EU086130 52 9911BK CT1 Dog Cambodia 1999 EU086130 52 9911CA CT1<	36	IUP-R198	GT1	Horse	Uttar Pradesh	2012	KF150745
38 CVS CT1 Vaccine strain 39 India, CH,1988 CT1 Dog India, Maga P198 EU086154 41 H-08-1320_SRL CT1 Human Sri Lanka 1986 EU086154 42 94257_SRL CT1 Human Sri Lanka 1986 EU086156 43 NNV-RAB-H_India CT1 Human India 2006 EF437215 44 Germany, Trp-India CT1 Human India 2010 CU93681 45 UK,from-India CT1 Dog India 1999 EF151231 47 04029AFC CT1 Dog India 2004 EU086128 48 CHAND03,India CT1 Dog India 2001 CQ23040 51 9908CBC CT1 Dog India 1999 EU086131 52 9911CBC CT1 Dog Cambodia 1999 EU086132 53 01016VNM CT1 Dog	37	PV	GT1	Vaccine strain			
39India, CH, 1998CTiDogIndia1998AV237121409902NEP, 1998CTiGoatNepal1998EU08615441H-08-1320_SRLCTiHumanSri Lanka2008AB5692994294257_SRLGTiDogSri Lanka1986EU08615643NNV-KAB-H_IndiaGTiHumanIndia2005AY95631944Germany, Trp-IndiaGTiHumanIndia2005AY95631945UK, from-IndiaGTiDogIndia2005AY95631946India_UP_EFI51231GTiDogIndia2004EU0861284704029AFGGTiDogIndia2001C023304050India, C0233040GTiDogIndia2001C023040519908CBGGTiDogCambodia1998EU086131529911CBGGTiDogCambodia1998EU0861315301016VMMGTiDogNyannar1999EU086132559913BRGTiDogNyannar1999EU086153570303INDOGTiDogSouth Korea2003EU08615158KRVC0802GTiDogSouth Korea2008CU93702960KRVD60901GTiDogSouth Korea2008CU93703961SKRDC204HCGTiDogSouth Korea2008CU93703963HUN-1-HMGTi	38	CVS	GT1	Vaccine strain			
409902NEP_1998CT1GoatNepal1998EU08615441H-06-1320_SRLCT1HumanItalnka2006EF4372154294257_SRCT1HumanIndia2006EF43721543NNV-RAB-H_IndiaCT1HumanIndia2006EF43721544Cermany, Trp-IndiaCT1HumanIndia2010C093681145UK_from-IndiaCT1DogIndia1999PF5123146India_UP_EF151231CT1DogAfghanistan2004EU0861284704029AFCCT1DogIndia2005D097497848CHANDO3 IndiaCT1DogIndia2005D007497850India_C0233040CT1DogCambodia1998EU086130519905CBGCT1DogCambodia1998EU0861315301016VMCT1DogCambodia1999EU086152559913BRCT1DogLaos1999EU086155570303IND0CT1DogSouth Korea2004EU08615158KRVC0801CT1DogSouth Korea2008C0937025599913BRCT1DogSouth Korea2008C09370255690303IND0CT1DogSouth Korea2008C09370255703031ND0CT1DogSouth Korea2008C093702559KRVC0802CT1	39	India_CH_1998	GT1	Dog	India	1998	AY237121
41H-08-1320_SRLCT1HumanSri Lanka2008ABS692994294257_SRLCT1DogSri Lanka1986EU08615643NNV-RAB-H_IndiaCT1HumanIndia2006EF43721544Cermany_Trp-IndiaGT1HumanIndia2001CU936831145UK_from-IndiaGT1HumanIndia1999EF15123146India_UP_EF151231GT1DogIndia1999AP98747470402347GGT1DogIndia2001CQ23304050India_Q074978CT1DogIndia2001CQ233040519908CBGGT1DogCambodia1999EU086130529911CBGGT1DogCambodia1999EU0861305301016VNMGT1DogMyanmar1999EU086152549913BRGT1DogMyanmar1999EU086155559913BRGT1DogMyanmar1999EU0861555604030PHGT1DogSouth Korea2008CG93702559SKRVC6021GT1DogSouth Korea2008CG93702559KRVC6021GT1DogSouth Korea1999DQ07610961KRVR0901GT1DogSouth Korea1990Q007610962SKRVC6020HCGT1DogSouth Korea1990Q007610963HUN1-HMGT1Human	40	9902NEP_1998	GT1	Goat	Nepal	1998	EU086154
4294257_SRLCT1DogSri Lanka1986EU08615643NNV-RAB-H_IndiaCT1HumanIndia2006EF43721544Germany_Trp-IndiaCT1HumanIndia2010CU93688145UK_from-IndiaCT1DogIndia1999EF1512314704029AFCCT1DogIndia1999AY9874748CHAND03_IndiaCT1DogIndia2005DQ07497849India_CQ233040CT1DogIndia2001CQ233040519908CBCCT1DogCambodia1999EU086130529911CBCCT1DogCambodia1999EU0861305301016VNMCT1DogLaos1999EU086152549910LAOCT1DogLaos1999EU086152559913BIRCT1DogMyamar1999EU086152559913BIRCT1DogMyamar1999EU086152570303INDOCT1DogNut Korea2008CU93702960KRVR0907CT1DogSouth Korea2008CU93702960KRVR0907CT1DogSouth Korea2008CU93702961SKRDC0204HCCT1DogSouth Korea2008CU93703061SKRDC0204HCCT1DogSouth Korea2008CU937030629RARM033_LCanadaCT1PogSouth	41	H-08-1320_SRL	GT1	Human	Sri Lanka	2008	AB569299
43NNV-RAB-H_IndiaCT1HumanIndia2005FF43721544Germany_Trp-IndiaGT1HumanIndia2010GU93681145UK_from-IndiaGT1DogIndia1999EF15123146India_UP_EF151231GT1DogIndia1999EF1512314704029AFGGT1DogIndia1999AY9874748CHAND03_IndiaGT1DogIndia2001GQ23040519908CBGGT1DogIndia2001GQ23040519908CBGGT1DogCambodia1998EU086130529911CBGGT1DogCambodia1998EU0861515301016VNMGT1DogLaos1999EU086152549913BIRGT1DogMamar1999EU086152559013BIRGT1DogMyamar1999EU08615158KRVR0901GT1DogMyamar1999EU08615158KRVR0907GT1DogSouth Korea2008CU93702559KRVC0802GT1DogSouth Korea2008CU93703061SKRDC9001CYGT1DogSouth Korea2008CU93703062SKRDC0204HCGT1DogSouth Korea2008CU93703063HUN1-HMGT1DogSouth Korea2008CU93703064851339_USAGT1FACanada <td< td=""><td>42</td><td>94257_SRL</td><td>GT1</td><td>Dog</td><td>Sri Lanka</td><td>1986</td><td>EU086156</td></td<>	42	94257_SRL	GT1	Dog	Sri Lanka	1986	EU086156
44Germany_Trp-IndiaGT1HumanIndia2005AY95631945UK_from-IndiaGT1HumanIndia2010GU9368146India, UP_EF151231GT1DogIndia1999EF1512314704029AFGGT1DogIndia1999AY9874748CHAND03_IndiaGT1DogIndia2001GQ23304050India, CQ233040GT1DogCambodia1998EU086130519908CBGGT1DogCambodia1998EU0861315301016VNMGT1DogCambodia1999EU086152549910LAOGT1DogLaos1999EU086152559913BIRGT1DogHindippines2003EU0861525604030PH1GT1DogIndonesia2003EU086155570303INDOGT1DogNotrera2003EU08615158KRVG0901GT1DogSouth Korea2008CU93702960KRVG0907GT1DogSouth Korea2008CU93702961SKRDG2901GYGT1DogSouth Korea2009CU93703962SKRDC6204H1CGT1DogSouth Korea1990QU7610063HUN1-HMGT1Raccon dogSouth Korea1990QU761036486-1393_USAGT1Raccon dogSouth Korea1990RVU1173767NY71_Canada<	43	NNV-RAB-H_India	GT1	Human	India	2006	EF437215
45UK_from-IndiaCT1HumanIndiaIndiaQ10CU9368146India_UP_EF151231GT1DogIndia1999EF1512314704029AFCGT1DogIndia2004EU08612848CHAND03_IndiaGT1DogIndia2005DQ7497850India_GQ233040GT1DogIndia2005QQ74978519908CBCGT1DogCambodia1999EU086131529911CBGGT1DogCambodia1998EU0861395301016VNMGT1DogCambodia1999EU086159549910LAOGT1DogMammar1999EU08615955913BIRGT1DogMyanmar1999EU0861595604030PH1GT1DogMyanmar1999EU086155570303INDOGT1DogIndonesia2003EU08615158KRVC8001GT1Raccoon dogSouth Korea2008GU3702560KRVD8007GT1DogSouth Korea2009GU3702961SKRDC901GYGT1DogSouth Korea2009GU3703061SKRDC901GYGT1DogSouth Korea2002Q07609363HUN1-HMGT1HumanHungan1999RVU17526486-1393_USAGT1RaccoonCanada1990RVU17526590RABN931_CanadaGT1Ra	44	Germany_Trp-India	GT1	Human	India	2005	AY956319
46India_UP_EF151231GT1DogIndia1999EF1512314704029AFGGT1DogAfghanistan2004EU08612848CHAND3_IndiaGT1DogIndia2005DQ07497849India_C0233040GT1DogIndia2005DQ07497850India_C0233040GT1DogIndia2006CQ233040519908CBGGT1DogCambodia1999EU086130529911CBGGT1DogVietnam2001EU08613153010F6VMMGT1DogVietnam2004EU08615255913BIRGT1DogMyamar1999EU0861525604030PH1GT1DogIndonesia2003EU0861515703003INDOGT1DogSouth Korea2008GU39702559KRVC0802GT1DogSouth Korea2008GU39702960KRVC0801GT1DogSouth Korea2002Q007610061SKRDC204HCGT1DogSouth Korea2002D007610363HUN1-HMGT1HumanHungary2001A73254626486-1393.USAGT1SkunkCanada1990RVU1173767NY77_CanadaGT1DogCanada1990RVU117376892R61741_CanadaGT1SkunkCanada1991A732546269MEXN0136_CanadaGT1Dog<	45	UK_from-India	GT1	Human	India	2010	GU936881
4704029AFGCT1DogAfghanistan2004EU08612848CHAND03_IndiaCT1DogIndia1999AY9874749India_CQ233040CT1DogIndia2005DQ07497850India_CQ233040CT1DogIndia2001G2233040519908CBGCT1DogCambodia1999EU086130529911CBCCT1DogCambodia1998EU0861315301016VNMCT1DogLaos1999EU086152549910LAOCT1DogMyanmar1999EU086152559913BIRCT1DogIndonesia2003EU0861555703003INDOCT1DogIndonesia2008GU93702558KRV6901CT1DogSouth Korea2008GU93702560KRV6802CT1DogSouth Korea2008GU93702561SKRDG2004HCCT1DogSouth Korea1999DQ07610062SKRDG2004HCCT1DogSouth Korea1990DQ07610063HUN1-HMCT1HumanHungary2001A73254626486-1393_USACT1SkunkCanada1990RVU117326693RABN0113_CanadaCT1RacconCanada1993RVU1173267NY771_CanadaCT1RacconCanada1993RVU117326892RBC1741_CanadaCT1	46	India_UP_EF151231	GT1	Dog	India	1999	EF151231
48CHAND03_IndiaCT1DogIndia1999AY9874749India_DQ074978CT1DogIndia2005DQ07497850India_CQ233040CT1DogIndia2001CQ233040519908CBCCT1DogCambodia1999EU086130529911CBCCT1DogCambodia1998EU0861595301016VMMCT1DogVietnam2001EU086159549910LAOCT1DogMyanmar1999EU086152559913BIRCT1DogMyanmar1999EU0861555604030PH1CT1DogMyanmar2003EU0861555703003INDOCT1DogSouth Korea2008CU93702559KRVC802CT1DogSouth Korea2008CU93702960KRVE0807CT1DogSouth Korea2008CU93703061SKRDC9204HCCT1DogSouth Korea2002DQ07609362SKRDC9204HCCT1DogSouth Korea1999DQ07610363HUN1-HMCT1KorkCanada1993RVU17376486-1393_USACT1SkunkCanada1993RVU17376590RABN9341_CanadaCT1RecfonCanada1993RVU17376693RABN0113_CanadaCT1RecfonCanada1993RVU173767NY771_CanadaCT1Dog </td <td>47</td> <td>04029AFG</td> <td>GT1</td> <td>Dog</td> <td>Afghanistan</td> <td>2004</td> <td>EU086128</td>	47	04029AFG	GT1	Dog	Afghanistan	2004	EU086128
49India_DQ074978CT1DogIndia2005DQ07497850India_CQ233040GT1DogCambodia2001CQ233040519908CBGGT1DogCambodia1999EU086131529911CBGGT1DogCambodia1998EU0861315301016VNMGT1DogLaos1999EU086152549910LAOGT1DogMyanmar1999EU086152559913BIRGT1DogMyanmar1999EU0861535604030PHIGT1DogIndonesia2003EU0861515703003INDOGT1DogSouth Korea2008CU93702559KRVR0901GT1Raccon dagSouth Korea2008CU93702560KRVB0907GT1DogSouth Korea2009CU93703061SKRDC9901KYGT1DogSouth Korea1999DQ07610062SKRDC9024HCGT1DogSouth Korea1999DQ07610663HUN1-HMGT1HumanHungary2001AF3254626486-1393_USAGT1FaxKankCanada1993RVU117326693RABN0341_CanadaGT1Red foxCanada1993RVU1173267NY771_CanadaGT1RacconCanada1993LU2354776892RE01741_CanadaGT1RacconCanada1993LU271569MEX1-DG </td <td>48</td> <td>CHAND03_India</td> <td>GT1</td> <td>Dog</td> <td>India</td> <td>1999</td> <td>AY98747</td>	48	CHAND03_India	GT1	Dog	India	1999	AY98747
50India_GQ233040GT1DogIndia2001GQ233040519908CBGGT1DogCambodia1998EU086130529911CBGGT1DogCambodia1998EU0861315301016VNMGT1DogLaos1999EU086152549910LAOGT1DogLaos1999EU086152559913BRGT1DogMyanmar1999EU0861525604030PH1GT1DogIndonesia2004EU0861555703003INDOGT1DogIndonesia2008CU93702558KRVR0901GT1Raccoon dogSouth Korea2008CU93702959KRVC0802GT1DogSouth Korea2009CU93703060KRVB0907GT1DogSouth Korea1999D007610061SKRDG204HCGT1DogSouth Korea1999D00760363HUN1-HMGT1HumanHungary2001AF3254626486-1393_USAGT1SkunkCanada1993RVU117376693RABN013_CanadaGT1RdcoonCanada1993RVU1173767NY71_CanadaGT1DogMexico1991AF3254776892RBG1741_CanadaGT1DogMexico1991AF32547769MEX1-DCGT1DogMexico1991AF325477710205CH1GT1DogChina<	49	India_DQ074978	GT1	Dog	India	2005	DQ074978
519908CBGGT1DogCambodia1999EU086130529911CBGGT1DogCambodia1998EU0861315301016VNMGT1DogVietnam2001EU086159549910LAOGT1DogLaos1999EU086152559913BRGT1DogMyanmar1999EU0861515604030PH1GT1DogMyanmar2004EU0861555703003INDOGT1DogIndonesia2003EU08615158KRVR0901GT1DogSouth Korea2008GU93702559KRVC0802GT1DogSouth Korea2009GU93703061SKRDG901GYGT1DogSouth Korea2002DQ07610062SKRDG9204HCGT1DogSouth Korea2002DQ07610063HUN1-HMGT1HumanHungary2001AF3254626486-1393_USAGT1FoxUSA1986CU9368806590RABN9341_CanadaGT1RaccoonCanada1993RVU117376693RABN0113_CanadaGT1RaccoonCanada1992AF34430569MEX1-DGGT1DogMexico1993RVU117376892RBG1741_CanadaGT1DogChina1992AF34430569MEX1-DGGT1DogChina1992EU0861357102050CHIGT1DogChina <td>50</td> <td>India_GQ233040</td> <td>GT1</td> <td>Dog</td> <td>India</td> <td>2001</td> <td>GQ233040</td>	50	India_GQ233040	GT1	Dog	India	2001	GQ233040
529911CBCGT1DogCambodia1998EU0861315301016VNMGT1DogVietnam2001EU086159549910LAOGT1DogLaos999EU086152559913BIRGT1DogMyanmar1999EU0861595604030PHIGT1DogPhilippines2004EU0861515703003INDOGT1DogIndonesia2008CU93702558KRVC0802GT1DogSouth Korea2008GU93702960KRVB0907GT1DogSouth Korea2009GU93703061SKRDC9001CYGT1DogSouth Korea2002DQ07609362SKRDC904HCGT1DogSouth Korea2002DQ07609363HUN1-HMGT1HumanHungary2001AF3254626486-1393_USAGT1RacconGanada1990RVU117376693RABN013_CanadaGT1RacconCanada1993RVU1173767NY71_CanadaGT1DogCanada1991AF3254776892RBG1741_CanadaGT1DogMexico1991AF32547769MEX1-DGGT1DogChina1992EU0861357102050CHIGT1DogChina1992EU0861457205006CHIGT1DogChina1992EU0861457305009CHIGT1DogChina <t< td=""><td>51</td><td>9908CBG</td><td>GT1</td><td>Dog</td><td>Cambodia</td><td>1999</td><td>EU086130</td></t<>	51	9908CBG	GT1	Dog	Cambodia	1999	EU086130
5301016VNMGT1DogVietnam2001EU086159549910LAOGT1DogLaos1999EU086152559913BIRGT1DogMyanmar1999EU0861295604030PHIGT1DogPhilippines2004EU0861555703003INDOGT1DogIndonesia2003EU08615158KRVR0901GT1Raccoon dogSouth Korea2008GU93702559KRVC0802GT1DogSouth Korea2009GU93703060KRVB0907GT1CattleSouth Korea1999DQ07610061SKRDC9901GYGT1DogSouth Korea1999DQ07610062SKRDG0204HCGT1DogSouth Korea1999DQ07610063HUN1-HMGT1HumanHungary2001AF3254626486-1393_USAGT1FoxUSA1986GU9368806590RABN9341_CanadaGT1Red foxCanada1993RVU1173767NY771_CanadaGT1DogMexico1991AF3254776892RBC1741_CanadaGT1DogMexico1991AF325477709811CH1GT1DogChina1992EU0861357102050CH1GT1DogChina1992EU086145720506CH1GT1DogChina1992EU086145730509CH1GT1Dog	52	9911CBG	GT1	Dog	Cambodia	1998	EU086131
54 9910LAO GT1 Dog Laos 1999 EU086152 55 9913BIR GT1 Dog Myanmar 1999 EU086129 56 04030PHI GT1 Dog Philippines 2004 EU086151 57 03003INDO GT1 Dog Indonesia 2003 EU086151 58 KRVR0901 GT1 Dog South Korea 2008 GU937025 59 KRVC0802 GT1 Dog South Korea 2009 GU937029 60 KRVB0907 GT1 Dog South Korea 2002 DQ076100 61 SKRDC9001GY GT1 Dog South Korea 2002 DQ076100 62 SKRDC0204HC GT1 Dog South Korea 2002 DQ076100 63 HUN1-HM GT1 Human Hungary 2001 AF325462 64 86-1393_USA GT1 Skunk Canada 1999 DQ07100 65	53	01016VNM	GT1	Dog	Vietnam	2001	EU086159
55 9913BIR CT1 Dog Myanmar 1999 EU086129 56 04030PHI CT1 Dog Philippines 2004 EU086155 57 03003INDO CT1 Dog Indonesia 2003 EU086151 58 KRVR0901 CT1 Raccoon dog South Korea 2008 GU937025 59 KRVC0802 CT1 Dog South Korea 2009 GU937029 60 KRVB0907 CT1 Cattle South Korea 2009 GU937030 61 SKRDC9204HC CT1 Dog South Korea 2002 DQ076100 62 SKRDG0204HC CT1 Dog South Korea 2002 DQ076093 63 HUN1-HM GT1 Human Hungary 2001 AF325462 64 86-1393_USA GT1 Red fox Canada 1990 RVU11737 67 NY771_Canada GT1 Red fox Canada 1992 AF344305 <tr< td=""><td>54</td><td>9910LAO</td><td>GT1</td><td>Dog</td><td>Laos</td><td>1999</td><td>EU086152</td></tr<>	54	9910LAO	GT1	Dog	Laos	1999	EU086152
5604030PHICT1DogPhilippines2004EU0861555703003INDOGT1DogIndonesia2003EU08615158KRVK0901GT1Raccoon dogSouth Korea2008CU93702559KRVC0802GT1DogSouth Korea2008CU93702960KRVB0907GT1CattleSouth Korea2009CU93703061SKRDC9901GYGT1DogSouth Korea2002DQ07610062SKRDC0204HCGT1DogSouth Korea2002DQ07609363HUN1-HMGT1HumanHungary2001AF3254626486-1393_USAGT1FoxUSA1986CU93868006590RABN9341_CanadaGT1Red foxCanada1990RVU117526693RABN0113_CanadaGT1RaccoonCanada1993RVU1173767NY771_CanadaGT1DogMexico1991AF325477709811CHIGT1DogMexico1991AF325477709811CHIGT1DogChina1992EU0861357102050CHIGT1DogChina1992EU0861477205006CHIGT1DogChina2004EU0861477305009CHIGT1DogChina2004EU08615074FRA1-FXGT1FoxFrance1991AF325461	55	9913BIR	GT1	Dog	Myanmar	1999	EU086129
57 03003INDO CT1 Dog Indresia 2003 EU086151 58 KRVR0901 GT1 Raccoon dog South Korea 2008 GU937025 59 KRVC0802 GT1 Dog South Korea 2008 GU937029 60 KRVB0907 GT1 Cattle South Korea 2009 GU937030 61 SKRDG901GY GT1 Dog South Korea 2002 DQ076100 62 SKRDG0204HC GT1 Dog South Korea 2002 DQ076093 63 HUN1-HM GT1 Human Hungary 2001 AF325462 64 86-1393_USA GT1 Fox USA 1986 GU936880 65 90RABN9341_Canada GT1 Red fox Canada 1993 RVU11737 66 93RABN0113_Canada GT1 Raccoon Canada 1992 AF344305 69 MEX1-DG GT1 Dog Mexico 1991 AF325477	56	04030PHI	GT1	Dog	Philippines	2004	EU086155
58KRVR0901GT1Raccoon dogSouth Korea2008GU93702559KRVC0802GT1DogSouth Korea2009GU93703060KRVB0907GT1CattleSouth Korea2009GU93703061SKRDC0204HCGT1DogSouth Korea1999DQ07610062SKRDC0204HCGT1DogSouth Korea2002DQ07609363HUN1-HMGT1HumanHungary2001AF3254626486-1393_USAGT1FoxUSA1986GU9368806590RABN9341_CanadaGT1RkunkCanada1990RVU117526693RABN0113_CanadaGT1RaccoonCanada1993RVU1173767NY771_CanadaGT1NkunkCanada1992AF3443056892RBG1741_CanadaGT1SkunkCanada1992AF34430569MEX1-DGGT1DogMexico1991AF325477709811CHIGT1DogChina1992EU0861357102050CHIGT1DogChina1992EU0861477205006CHIGT1DogChina2004EU0861477305009CHIGT1DogChina2004EU08615074FRA1-FXGT1FoxFrance1991AF325461	57	03003INDO	GT1	Dog	Indonesia	2003	EU086151
59KRVC0802GT1DogSouth Korea2008GU93702960KRVB0907GT1CattleSouth Korea2009GU93703061SKRDG9901GYGT1DogSouth Korea1999DQ07610062SKRDG0204HCGT1DogSouth Korea2002DQ07609363HUN1-HMGT1HumanHungary2001AF3254626486-1393_USAGT1FoxUSA1986GU9368806590RABN9341_CanadaGT1SkunkCanada1990RVU117526693RABN0113_CanadaGT1Red foxCanada1993RVU1173767NY771_CanadaGT1RacconnCanada1992AF3443056892RBG1741_CanadaGT1DogMexico1991AF325477709811CHIGT1DogChina1992EU0861357102050CHIGT1DogChina1992EU0861457205006CHIGT1DogChina2004EU0861477305009CHIGT1DogChina2004EU08614774FRA1-FXGT1FoxFrance1991AF325461	58	KRVR0901	GT1	Raccoon dog	South Korea	2008	GU937025
60KRVB0907GT1CatleSouth Korea2009GU93703061SKRDG9901GYGT1DogSouth Korea1999DQ07610062SKRDG0204HCGT1DogSouth Korea2002DQ07609363HUN1-HMGT1HumanHungary2001AF3254626486-1393_USAGT1FoxUSA1986G0368806590RABN9341_CanadaGT1SkunkCanada1990RVU117526693RABN0113_CanadaGT1Red foxCanada1993RVU1173767NY771_CanadaGT1RaccoonCanada1992AF3443056892RBG1741_CanadaGT1DogMexico1991AF325477709811CHIGT1DogChina1992EU0861357102050CHIGT1DogChina1992EU0861457205006CHIGT1DogChina2004EU0861477305009CHIGT1DogChina2005EU08615074FRA1-FXGT1FoxFrance1991AF325461	59	KRVC0802	GT1	Dog	South Korea	2008	GU937029
61SKRDG9901GYGT1DogSouth Korea1999DQ07610062SKRDG0204HCGT1DogSouth Korea2002DQ07609363HUN1-HMGT1HumanHungary2001AF3254626486-1393_USAGT1FoxUSA1986GU9368806590RABN9341_CanadaGT1SkunkCanada1993RVU117376693RABN0113_CanadaGT1Red foxCanada1993RVU1173767NY771_CanadaGT1RaccoonCanada1992AF3443056892RBG1741_CanadaGT1SkunkCanada1992AF34430569MEX1-DGGT1DogMexico1991AF325477709811CHIGT1DogChina1992EU0861357102050CHIGT1DogChina1992EU0861457205006CHIGT1DogChina2004EU0861477305009CHIGT1DogChina2005EU08615074FRA1-FXGT1FoxFrance1991AF325461	60	KRVB0907	GT1	Cattle	South Korea	2009	GU937030
62SKRDG0204HCGT1DogSouth Korea2002DQ07609363HUN1-HMGT1HumanHungary2001AF3254626486-1393_USAGT1FoxUSA1986GU9368806590RABN9341_CanadaGT1SkunkCanada1990RVU117526693RABN0113_CanadaGT1Red foxCanada1993RVU1173767NY771_CanadaGT1RaccoonCanada1995U272156892RBG1741_CanadaGT1SkunkCanada1992AF34430569MEX1-DGGT1DogMexico1991AF325477709811CHIGT1DogChina1998EU0861357102050CHIGT1DogChina1992EU0861477205006CHIGT1DogChina2004EU0861477305009CHIGT1DogChina2005EU08615074FRA1-FXGT1FoxFrance1991AF325461	61	SKRDG9901GY	GT1	Dog	South Korea	1999	DO076100
63HUN1-HMGT1HumanHungary2001AF3254626486-1393_USAGT1FoxUSA1986GU9368806590RABN9341_CanadaGT1SkunkCanada1990RVU117526693RABN0113_CanadaGT1Red foxCanada1993RVU1173767NY771_CanadaGT1RaccoonCanada1995U272156892RBC1741_CanadaGT1SkunkCanada1992AF34430569MEX1-DGGT1DogMexico1991AF325477709811CHIGT1DogChina1992EU0861357102050CHIGT1HumanChina1992EU0861457205006CHIGT1DogChina2004EU0861477305009CHIGT1DogChina2005EU08615074FRA1-FXGT1FoxFrance1991AF325461	62	SKRDG0204HC	GT1	Dog	South Korea	2002	DO076093
64 86-1393_USA GT1 Fox USA 1986 GU936880 65 90RABN9341_Canada GT1 Skunk Canada 1990 RVU11752 66 93RABN0113_Canada GT1 Red fox Canada 1993 RVU11737 67 NY771_Canada GT1 Raccoon Canada 1995 U27215 68 92RBC1741_Canada GT1 Skunk Canada 1992 AF344305 69 MEX1-DG GT1 Dog Mexico 1991 AF325477 70 9811CHI GT1 Dog Mexico 1998 EU086135 71 02050CHI GT1 Human China 1992 EU086145 72 05006CHI GT1 Dog China 2004 EU086147 73 05009CHI GT1 Dog China 2005 EU086150 74 FRA1-FX GT1 Fox France 1991 AF325461	63	HUN1-HM	GT1	Human	Hungary	2001	AF325462
6590RABN9341_CanadaGT1SkunkCanada1990RVU17526693RABN0113_CanadaGT1Red foxCanada1993RVU173767NY771_CanadaGT1RaccoonCanada1995U272156892RBG1741_CanadaGT1SkunkCanada1992AF34430569MEX1-DGGT1DogMexico1991AF325477709811CHIGT1DogChina1992EU0861357102050CHIGT1DogChina1992EU0861457205006CHIGT1DogChina2004EU0861477305009CHIGT1DogChina2005EU08615074FRA1-FXGT1FoxFrance1991AF325461	64	86-1393_USA	GT1	Fox	USA	1986	GU936880
6693RABN0113_CanadaGT1Red foxCanada1993RVU1173767NY771_CanadaGT1RacconCanada1995U272156892RBG1741_CanadaGT1SkunkCanada1992AF34430569MEX1-DGGT1DogMexico1991AF325477709811CHIGT1DogChina1992EU0861357102050CHIGT1HumanChina1992EU0861457205006CHIGT1DogChina2004EU0861477305009CHIGT1DogChina2005EU08615074FRA1-FXGT1FoxFrance1991AF325461	65	90RABN9341 Canada	GT1	Skunk	Canada	1990	RVU11752
67 NY771_Canada GT1 Raccon Canada 1995 U27215 68 92RBG1741_Canada GT1 Skunk Canada 1992 AF344305 69 MEX1-DG GT1 Dog Mexico 1991 AF325477 70 9811CHI GT1 Dog China 1992 EU086135 71 02050CHI GT1 Dog China 1992 EU086145 72 05006CHI GT1 Dog China 2004 EU086147 73 05009CHI GT1 Dog China 2005 EU086150 74 FRA1-FX GT1 Fox France 1991 AF325461	66	93RABN0113_Canada	GT1	Red fox	Canada	1993	RVU11737
68 92RBG1741_Canada GT1 Skunk Canada 1992 AF34305 69 MEX1-DG GT1 Dog Mexico 1991 AF325477 70 9811CHI GT1 Dog Mexico 1992 EU086135 71 02050CHI GT1 Human China 1992 EU086145 72 05006CHI GT1 Dog China 2004 EU086147 73 05009CHI GT1 Dog China 2005 EU086150 74 FRA1-FX GT1 Fox France 1991 AF325461	67	NY771_Canada	GT1	Raccoon	Canada	1995	U27215
69 MEX1-DG GT1 Dog Mexico 1991 AF325477 70 9811CHI GT1 Dog China 1998 EU086135 71 02050CHI GT1 Human China 1992 EU086145 72 05006CHI GT1 Dog China 2004 EU086147 73 05009CHI GT1 Dog China 2005 EU086150 74 FRA1-FX GT1 Fox France 1991 AF325461	68	92RBG1741 Canada	GT1	Skunk	Canada	1992	AF344305
70 9811CHI GT1 Dog China 1998 EU086135 71 02050CHI GT1 Human China 1992 EU086145 72 05006CHI GT1 Dog China 2004 EU086147 73 05009CHI GT1 Dog China 2005 EU086150 74 FRA1-FX GT1 Fox France 1991 AF325461	69	MEX1-DG	GT1	Dog	Mexico	1991	AF325477
71 02050CHI GT1 Human China 1992 EU086145 72 05006CHI GT1 Dog China 2004 EU086147 73 05009CHI GT1 Dog China 2005 EU086150 74 FRA1-FX GT1 Fox France 1991 AF325461	70	9811CHI	GT1	Dog	China	1998	EU086135
72 05006CHI GT1 Dog China 2004 EU086147 73 05009CHI GT1 Dog China 2005 EU086150 74 FRA1-FX GT1 Fox France 1991 AF325461	71	02050CHI	GT1	Human	China	1992	EU086145
73 05009CHI GT1 Dog China 2005 EU086150 74 FRA1-FX GT1 Fox France 1991 AF325461	72	05006CHI	GT1	Dog	China	2004	EU086147
74 FRA1-FX GT1 Fox France 1991 AF325461	73	05009CHI	GT1	Dog	China	2005	EU086150
	74	FRA1-FX	GT1	Fox	France	1991	AF325461

Table 2 (continued)

S. No.	Virus reference	Genotype	Host	Place of origin	Year	Accession No.
75	USA8-BT	GT1	Bat	USA	1981	AF325494
76	USA7-BT	GT1	Bat	USA	1979	AF298141
77	ARG1-BT	GT1	Bat	Argentina	1991	AF325493
78	YUG1-BV	GT1	Bovine	Yugoslavia	1984	AF325463
79	POL1-RD	GT1	Raccoon dog	Poland	1985	AF325464
80	POL2-HM	GT1	Human	Poland	1985	AF325465
81	IRN1-HM	GT1	Human	Iran	1988	AF325472
82	9704ARG_Bat	GT1	Bat	Argentina	1997	EU293116
83	ABL-AUS_Bat	GT7	Bat	Australia	1997	AF006497
84	EBL1-POL_Bat	GT5	Bat	Poland	1985	AF298142
85	EBL2-HOL_Bat	GT6	Bat	Holland	1986	AF298145
86	Duv2-SAF_Bat	GT4	Bat	South Africa	1981	AF298147
87	Lag-NGA_Bat	GT2	Bat	Nigeria	1956	AF298148
88	Mok-ETH_Cat	GT3	Cat	Ethiopia	1990	U17064
89	8805CAM		Unknown	Cameroon	1988	AF325481
90	Flury-HEP		Vaccine strain			GU565704
91	Pitman_Moore		Vaccine strain			AJ871962

synonymous substitutions (d_s) and non-synonymous substitutions (d_N) for the entire RVG ecto-domain sequence of Indian isolates (Nei and Gojobori, 1986; Endo et al., 1996).

3. Results

Postmortem tissue samples were processed for rabies virus identification and isolation. Virus was detected by direct fluorescent antibody (DFA) test (Dean et al., 1996), RT-PCR and mouse inoculation test (Koprowski, 1996). Positive samples were used for nucleotide sequencing. Sequence data of RVG ecto-domain coding region was generated for 36 Indian rabies virus isolates in the present study. Two of the fixed strains of rabies virus (challenge virus standard – CVS and Pasteur virus strain – PV) from our repository were also sequenced (Table 2).

3.1. NJ tree analysis for G ecto-domain coding sequence

NJ tree indicated that the Indian isolates were of two different lineages with one of the Indian lineages (Indian lineage 1) was within the Arctic-like lineage (Fig. 2). While the Indian isolates were within the Arctic-like 1 lineage the South Korean isolates of rabies virus were in the Arctic-like 2 lineage. Another lineage is a distinctly separate sub-continental lineage (Indian lineage 2) and the sub-continental lineage contained Sri Lankan and Nepal isolates of RV apart from the Indian RV isolates. The Arctic-like 1 lineage is the predominant lineage among the Indian isolates for which sequence information is available. Thirty six of the 44 Indian isolates belonged to this lineage and an Afghan isolate (04029AFG) was also found clustered among the Indian isolates in this group. The sub-continental lineage comprised 6 Indian isolates, one representative Nepal isolate (many Nepal isolates of this lineage were reported by Pant et al., 2013) and two Sri Lankan isolates. Two Indian isolates were in cosmopolitan lineage and were closer to the fixed strains of RV.

There was no distinct pattern for the host species of isolation but isolates from the same geographical region clustered together. However, isolates of the two Indian lineages (Indian lineage 1 and 2) were found to exist almost simultaneously in the same area. All the isolates were genotype 1 rabies virus and rabies related virus has not been identified so for from the terrestrial mammals of India. The Indian RV isolates from the terrestrial mammals were phylogenetically distant from the bat isolates of RV which was reported in the Americas and other parts of the world. The isolates from other Asian countries such as China and south-east Asian countries formed a separate Asian lineage which is closer to the sub-continental lineage. The Indian lineage 1 is closer to the other Arctic and Arctic-like isolates from other parts of the world.

3.2. Time-scaled evolutionary tree

The maximum clade credibility tree using the ecto-domain sequences of G gene showed that the sub-continental lineage was the first to diverge from the bat rabies viruses (Fig. 3). On the contrary, the Arctic-like 1 lineage of India seemed to be a recent divergent event. Our inferred substitution rate for the ecto-domain of the G gene (7.5 \times 10⁻⁴; 95% HPD; 4.2 \times 10⁻⁴ to 1.2×10^{-3}) was higher than that of the previous estimate of 3.9×10^{-4} (95% HPD $1.2-6.5 \times 10^{-4}$) for the complete G gene (Bourhy et al., 2008). Hence, mean substitution rate for each codon position was estimated as previously suggested (Sullivan and Joyce, 2005) and a higher rate was observed in the third codon position (2.45) compared to first (0.31) and second (0.13), indicating a strong purifying selection of RVG ecto-domain. As per the present tree, the mean age of the most recent common ancestor for rabies viruses of non-flying mammals was around 288 years, in the past which is much lesser than the previous estimates (Bourhy et al., 2008). This also could be the result of the RVG ecto-domain's strong purifying selection which can obscure the age of the viral lineages and result in a much younger estimate for the ancestor (Wertheim and Kosakovsky, 2011; Suchard and Rambaut, 2009).

3.3. Comparison of translated amino acid sequences

Previously reported antigenic sites of the ecto-domain of rabies virus G protein (Benmansour et al., 1991) were analysed and the antigenic sites were found conserved across the Indian isolates. The major antigenic site-II was 100% conserved in Indian isolates (both at site IIa and IIb). The other major antigenic site (site-III) was mostly conserved among the Indian isolates except for one amino acid variation in ITN-R148 at the residue 337 (E337D). The other minor antigenic sites such as site I, site a and site b, c (former site IV), were mostly conserved except for one prominent change at site I. All the lineage 1 Indian isolates had L at 231 within the site I, whereas most of the lineage 2 isolates had P. The amino acid variations were predominant in the region between site IIa and site IIb. The variations were also found around site I/site IV and towards the C-terminal region of the G ecto-domain.

The amino acid sequence variations identified between the lineage 1 and lineage 2 isolates are shown in Table 3. The 426 (Q426L) variation was unique for all the lineage 2 isolates. This unique



Fig. 2. Neighbor-joining tree generated by 1317 bp of glycoprotein ecto-domain showing the genetic relationship of the rabies isolates. The percentage of bootstrap values given to the left of main branch. *Isolates of the present study.



Fig. 3. BEAST tree generated based on the rabies virus glycoprotein ecto-domain gene. The time scale is shown at the bottom.

variation and the other variations in combination can be used to differentiate the two lineages of Indian isolates. The variations at 164 and 243 were common for all sub-continental isolates and other Asian isolates.

The N-glycosylation sites at amino acid positions 37 and 319 were present in all the Indian isolates. Few of the Indian isolates had one more N-glycosylation site at amino acid positions 158 or 247 and therefore, the total N-glycosylation sites of Indian isolates ranged from 2 to 3. Arginine at 333, which is considered as an essential residue for neuro-virulence of the virus was found conserved in all the isolates of the present study (Fig. 4).

3.4. d_N and d_S analysis

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A d_N vs d_S analysis was performed using WINA software. The d_N/d_S ratio was plotted in a graph for the entire RVG ecto-domain sequence (Fig. 5). The d_N vs d_S analysis indicated that there was a strong purifying selection applied over the entire RVG ecto-domain region. However, many residues in the region between site IIa and IIb, and around site IV had $d_N > d_S$ and for one residue in the same region, it is $d_N > 2d_S$. Thus, the nucleotides downstream the coding region of major antigenic site IIa can tolerate non-synonymous substitutions without any deleterious effect on the virus.

Table 3

Amino acid variations between two different lineages of Indian rabies virus isolates across RVG ecto domain.

S. No.	Amino acid position in RVG	Substitutions
1	83	$K \rightarrow R$
2	102	$M \rightarrow L$
3	156	$S\toG$
4	164	$I \rightarrow V$
5	193	$T \rightarrow V$
6	231 ^a	$L \rightarrow P$
7	243	$M \rightarrow I$
8	426	$Q\toL$

^a Found within the antigenic site I of glycoprotein ecto domain.

4. Discussion

Rabies is one of the major public health threats in India and dogs are the primary source of virus spread. The studies on the viral dynamics using a substantially large number of G gene sequences of rabies virus isolates from India are sparse. RVG is the major determinant for the viral infection, antigenicity and pathogenicity and the host cell receptor recognition is mediated by RVG (Zhang et al., 2013; Benmansour et al., 1991; Thoulouze et al., 1998). Therefore, RVG based phylogeny was used for

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IMA-R189	<pre>(FPIYTIPDKLGFWSPIDIHHLSCFNNLV)</pre>	/EDEGC	INLSGF:	SYMELKVGY	ISAIKVNGFTCT	GVVTEAETYINFVGY	VTTTFKRKHF	RPTPDAC	FAAY	100
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IKE-R109		<mark></mark>		<mark>.</mark>					· · · · /	100
Trp-India		<mark></mark>		<mark>.</mark>	· <u>-</u>					100
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Fig. 4. Multiple alignment of partial deduced amino acid sequences of rabies virus glycoprotein. Colored boxes indicate antigenic sites; black solid boxes indicate potential N-glycosylation sites; Red box indicates Arginine 333 which is responsible for neuro-virulence. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

studying viral evolution and host adaptation (Badrane and Tordo, 2001; Meng et al., 2007). Apart from the phylogeny, translated amino acid sequence comparison and d_N vs d_S analysis was also performed in this study to rule out any antigenic variants.

In the present study, RVG ecto-domain coding region was sequenced for the 36 Indian rabies virus field isolates and their phylogenetic and evolutionary relationship were analyzed from the global context. Phylogenetically, rabies virus isolates got separated as per the established rabies virus clades such as Arctic, Arctic-like, Cosmopolitan, African, Asian, sub-continental, etc (Bourhy et al., 2008). The phylogenetic analysis identified two distinctly separate Indian lineages and the presence of two lineages among the rabies virus isolates of India was seen earlier using N gene phylogeny (Nagarajan et al., 2009; Nadin-Davis et al., 2007). The presence of virus from the Arctic like lineage (Arctic-like 1) in India was established by the earlier studies using N gene phylogeny and only two Indian isolates were identified with the sub-continental lineage (Nadin-Davis et al., 2007; Kuzmin et al., 2008) so far.

Majority of the Indian isolates of the present study were in Arctic-like 1 lineage and it is distributed all over India. Virus of this lineage is predominant in India and all the five north Indian isolates of the present study belonged to the Arctic-like 1 lineage. Five of the south Indian isolates and one north Indian isolate (obtained from GenBank) were part of the sub-continental lineage. However, sub-continental lineage was identified in a wide geographical region which spreads across Sri Lanka, India and Nepal (Pant et al., 2013). Thus, more isolates of sub-continental lineage can be identified if many north Indian samples are screened. The Arctic-like 1 lineage was reported from other sub-continental neighbors of India like Nepal, Bangladesh and Bhutan (Pant et al., 2013; Jamil et al., 2012; Reddy et al., 2011). The Arctic-like 1 lineage is the predominant lineage in the sub-continent region with the exception of Sri Lanka. All the reported isolates of Sri Lanka belonged to sub-continental lineage. A detailed analysis of the circulating virus isolates of Nepal revealed the simultaneous existence of both the lineages (Arctic-like and sub-continental) of rabies virus in the country which is similar to the Indian scenario (Pant et al., 2013). Therefore, the existence of sub-continental lineage in Bangladesh and Bhutan, and similarly the presence of Arctic-like lineage in Sri Lanka cannot be ruled out unless a large number of isolates are studied. In contrast, the Himalayan range has been acting as a barrier in preventing the spread of these lineages to China where Asian and cosmopolitan lineages were reported (Meng et al., 2007). Two of the Indian isolates grouped in cosmopolitan lineage and these isolates had very close sequence identity with the vaccine strains. In the NJ tree, these isolates grouped along with vaccine strains and therefore, these may be a result of laboratory cross contamination of vaccine viruses.

Many RV isolates belonging to the sub-continental lineage were identified in this study and these isolates were at the basal position among the rabies viruses of terrestrial mammals in the time scaled phylogenetic tree. These results indicate the probable origin of rabies virus of terrestrial mammals from this region. This observation is similar to that of Bourhy et al. (2008) who derived similar conclusion using the N gene phylogeny. However, their time scaled phylogenetic tree using a complete G gene data set indicated that the Asian lineage evolved first from the bat viruses, while the rest of the rabies lineages of the non-flying mammals evolved from the sub-continental lineage, albeit with a single isolate of sub-continental lineage in their analysis (Bourhy et al., 2008). Despite these observations, either bat rabies virus isolates or rabies virus isolates of terrestrial mammals which had close phylogenetic relationship with the bat rabies virus isolates were not reported yet from this region. A specific sample survey to identify rabies virus from bats of this region might provide better understanding on its prevalence.

As per the time scaled phylogenetic tree, it appears that the Arctic-like 1 clade of India is a more recent divergence event from the Arctic clade. The result supports the theory that the viruses of Arctic clade had descended towards south from fox to dogs instead of the northerly spread by species jump from dogs to fox (Nadin-Davis et al., 2007). This is in contrast to the N gene based time scale tree which suggested that the Arctic variants had probably evolved via a northerly spread (Kuzmin et al., 2008). However, these authors had used very few isolates (three in total) of Arctic-like 1 lineage viruses in their time scaled tree.

Thus, this region simultaneously has viruses from one of the early divergent events of the rabies virus towards terrestrial mammals and also the viruses with very recent divergent event. Additionally, rabies virus isolates of these two distinct lineages were identified in almost similar period from the same geographical



Fig. 5. Ratios of *d_N* to *d_S* along the G gene ecto-domain region. Threshold lines of the significance of the ratios are shown at values 1 and 2. A schematic representation of the G gene shows the different domains, SP, TM, ENDO, and ECTO, where antigenic sites are indicated with vertical black boxes.

region (one of the south Indian province of Kerala). Future studies might provide the status of possible recombination events between the lineages. However, the possibility of simultaneous infection with two different rabies virus isolates is very rare as the infection is 100% fatal. Additionally, the rabies viral RNA is closely associated with N protein which could prevent recombination events.

The overall d_N/d_S was very low as reported earlier for the rabies virus (Bourhy et al., 2008) and a strong purifying selection seems to be prevailing at majority of the G ecto-domain region. However, the region around the site IIa had many residues with $d_N > d_S$ and a similar observation was reported by Badrane et al. (2001) for rabies virus of carnivores. In the translated amino acid sequence comparison, all major antigenic sites were mostly conserved but variations were seen around site IIa, and minor sites I and IV. Experimental verification is necessary to find out whether these variations can affect the binding of the neutralizing antibodies with the major antigenic sites of rabies virus.

In conclusion, it is evident that the Indian rabies virus isolates are of two major distinct lineages with distant phylogenetic and evolutionary linkages. RV isolates in India are mostly canine variants and mass vaccination of dogs and intensifying public awareness about the disease are some of the ways of controlling the disease.

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