

In-silico molecular analysis of rabies virus across regions

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Abstract Rabies is a preventable viral disease of mammals most often transmitted through the bite of a rabid animal. Almost all human deaths caused by rabies occur in Asia and Africa. There are approximately 55000 human deaths annually from rabies worldwide. The disease affects domestic and wild animals and is spread to people through close contact with infected materials usually saliva via bites and scratches. The objective of this study was to determine the phylogenetic structure of rabies viruses across species and geographical locations. A total of 22 Rabies virus sequences from 5 species (Dog, Cat, Cow, Wolf and Fox) across 8 locations (Nigeria, India, Ghana, Pakistan, Niger, Brazil, Argentina and Texas) were obtained from the GenBank. A Neighbor-joining tree on the basis of genetic distances depicting phylogenetic relationship among Rabies viruses was constructed using the complete deletion and p-distance option using the MEGA VERSION 5 SOFTWARE. The phylogenetic analysis revealed a strong subdivision of rabies viruses by geographical location. The phylogenetic groups also formed clusters associated with species from which the virus is isolated.

Keywords Rabies virus; Phylogeny; In-silico; Across regions

Introduction

The rabies virus of the Rhabdoviridae family is the major Lyssavirus responsible for majority of human and animal rabies cases. Rabies is a preventable viral disease of mammals most often transmitted through the bite of a rabid animal (CDC). The rabies virus infects the central nervous system, ultimately causing disease and death. All species of mammals are susceptible to rabies infection but only a few species are important as reservoirs for the disease. Almost all human deaths caused by rabies occur in Asia and Africa. There are approximately 55000 human deaths annually from rabies worldwide. The disease affects domestic and wild animals and is spread to people through close contact with infected materials usually saliva via bites and scratches (WHO). Rabies is a neglected disease of poor and vulnerable populations whose deaths are rarely reported. Under-reporting of rabies also prevents mobilization of resources from the international community for the elimination of human-dog mediated rabies. The rabies viral genome

is a nonsegmented single-stranded negative-sense RNA of approximately 12 kb, which encodes a nucleoprotein (N), a phosphoprotein (P), a matrix protein (M), a glycoprotein (G), and a polymerase (L) (Wunner et al., 1988). Understanding the transmission dynamics and genetic diversity of rabies provides useful information for establishing a rabies control strategy (Denduangboripant et al., 2005). As a group, the lyssaviruses are characterized by their ecological association with specific mammalian species, which act as vectors for their transmission, such that a number of phylogenetic lineages co-circulate among a range of mammalian hosts (Davis et al., 2005). Lyssaviruses are zoonotic infections that invariably spill over into non-reservoir hosts (humans, bovines, small ruminants, cats etc). Onward transmission within these dead-end hosts is not sustained, so the successful transmission of RABV in new host species is likely to represent a major adaptive challenge (Kuiken et al., 2006). The objective of this study is to determine the phylogenetic structure of rabies viruses

across specie and geographical locations.

Materials and Methods

A total of 22 Rabies virus sequences from 5 species (Dog, Cat, Cow, Wolf and Fox) across 8 locations (Nigeria, India, Ghana, Pakistan, Niger, Brazil, Argentina and Texas) were obtained from the GenBank. The GenBank accession nos are FJ228677.1, FJ228678.1, FJ228681.1, FJ228683.1 (Fox): HM368163.1 (Cat), DQ105964.1 (Wolf), DQ105964.1 (Cow), EU038108.1 EU038106.1 EU038105.1 EU038103.1, HM368162.1 HM368160.1 FJ545679.1 FJ545678.1 FJ545674.1, FJ545678.1 FJ545674.1, DQ105963.1, AY654585.1 JN106463.1 AY233451.1, AY233450.1 (Dog). Sequence alignments were carried out using clusterW w (Larskin et al., 2007). A Neighbor-joining tree on the basis of genetic distances depicting phylogenetic relationship among Rabies viruses was constructed using the complete deletion and p-distance option using the MEGA VERSION 5 SOFTWARE (Tamura et al., 2011) (Figure 1).

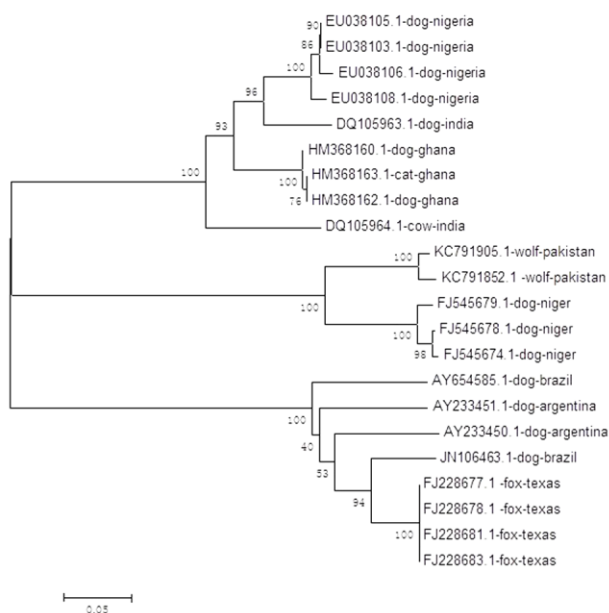


Figure 1 Phylogenetic tree derived from nucleotide sequences of rabies viruses using the Neighbor-Joining method

Results and Discussion

The phylogenetic analysis reveals a strong subdivision of rabies viruses by geographical location (Table 1). The phylogenetic groups also form clusters associated with species from which the virus is isolated. It has been reported that the lyssaviruses are characterized by their ecological association with specific mammalian species, which act as vectors for their transmission, such that that a number of phylogenetic lineages co-circulate among a range of mammalian hosts (Davies et al., 2005). The phylogenetic structure may be explain by the importance of geographical barriers to gene flow as previously demonstrated for rabies virus in Europe (Bourhy et al., 1999). The closest relationship is seen between virus isolates from a dog and a Cat both from Ghana, followed by isolates from a Dog and Cow from India (Table 2).

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Table 1 Sequences used for phylogenetic analysis identified by region and specie

| S/N | Accession number | Location | Host | Base pairs |
|-----|------------------|----------|-----------|------------|
| 1 | FJ228677.1 | Texas | Fox | 264 |
| 2 | FJ228678.1 | -Texas | Fox | 264 |
| 3 | FJ228681.1 | Texas | Fox | 264 |
| 4 | FJ228683.1 | Texas | Fox | 264 |
| 5 | EU038108.1 | Nigeria | Dog | 1350 |
| 6 | EU038106.1 | Nigeria | Dog | 1350 |
| 7 | EU038105.1 | Nigeria | Dog | 1350 |
| 8 | EU038103.1 | Nigeria | Dog | 1350 |
| 9 | HM368163.1 | Ghana | Cat | 405 |
| 10 | HM368162.1 | Ghana | Dog | 405 |
| 11 | HM368160.1 | Ghana | Dog | 405 |
| | FJ545679.1 | | | |
| 12 | FJ545678.1 | Niger | Dog | 1575 |
| 13 | FJ545674.1 | Niger | Dog | 1575 |
| 14 | | Niger | Dog | 1575 |
| 15 | KC791905.1 | Wolf | Pakistan | 1572 |
| 16 | KC791852.1 | Wolf | Pakistan | 1572 |
| 17 | DQ105964.1 | Cow | India | 446 |
| 18 | DQ105963.1 | Dog | India | 446 |
| 19 | AY654585.1 | Dog | Brazil | 320 |
| 20 | JN106463.1 | Dog | Brazil | 320 |
| 21 | AY233451.1 | Dog | Argentina | 320 |
| 22 | AY233450.1 | Dog | ARgentina | 320 |

Table 2 Estimates of Evolutionary Divergence between Sequences

| | Fox Texas | Dog Nigeria | Cat Ghana | Dog Ghana | Dog Niger | Wolf Pakistan | Cow India | Dog India | Dog Brazil | Dog Argentina |
|-----------|------------|----------------|------------|--------------|------------|------------------|------------|------------|---------------|------------------|
| Fox Texas | - | | | | | | | | | |
| Dog | .605 | - | | | | | | | | |
| Nigeria | (.030) | | | | | | | | | |
| Cat | .590(.029) | .130(.020) | - | | | | | | | |
| Ghana | | | | | | | | | | |
| Dog | .590(.029) | .130(.020) | .000 | - | | | | | | |
| Ghana | | | | | | | | | | |
| Dog | .670(.029) | .613(.029) | .613(.029) | .613(.029) | - | | | | | |
| Niger | | | | | | | | | | |
| Wolf | .682(.029) | .613(.020) | .605(.029) | .605(.029) | .146(.023) | - | | | | |
| Pakistan | | | | | | | | | | |
| Cow | .594(.030) | .165(.022) | .149(.022) | .149(.022) | .617(.029) | .609(.031) | - | | | |
| India | | | | | | | | | | |
| Dog India | .613(.030) | .069(.015) | .107(.019) | .107(.019) | .628(.029) | .625(.030) | .146(.021) | - | | |
| Dog | .192(.025) | .594(.029) | .586(.029) | .586(.029) | .621(.030) | .617(.030) | .605(.030) | .617(.030) | - | |
| Brazil | | | | | | | | | | |
| Dog | .146(.022) | .613(.029) | .594(.029) | .594(.029) | .678(.029) | .655(.030) | .598(.020) | .625(.029) | .150(.024) | - |
| Argentina | | | | | | | | | | |

Note: The number of base differences per site from between sequences are shown with Standard error estimate(s). The analysis involved 10 nucleotide sequences. Codon positions included were 1st+2nd+3rd+Noncoding. All positions containing gaps and missing data were eliminated. There were a total of 261 positions in the final dataset. Evolutionary analyses were conducted in MEGA5 (Tamura et al., 2011)