

Antigenic and molecular characterization of rabies virus in Argentina

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Abstract

The nucleoprotein genes of 54 human, domestic and wild animals rabies isolates obtained in Argentina between 1995 and 2002 were characterized using monoclonal antibodies and partial gene sequence analysis. The antigenic and genetic diversities of rabies virus in samples from bat and bat-related cases were studied, leading to the identification of five distinct genetic variants. Rabies viruses isolated from vampire bat related cases were very similar to each other, showing 98.9% overall similarity. Specific antigenic variants (AgV) were detected associated with different insectivorous bats species, in samples from *Tadarida brasiliensis* and *Eumops patagonicus* bats. In contrast, isolates from *Myotis* sp. and *Histiotus* sp. bats could not be matched to any antigenic type. Additionally, bat rabies cases were also detected in southern provinces previously considered rabies-free. Finally, two independent antigenic and genetic variants co-circulating in northern Argentina were found in isolates obtained from dogs and dog-related cases, suggesting two independent cycles of virus transmission.

This is the first national coordinated study of antigenic as well as molecular epidemiology of rabies in Argentina. The information presented here will improve our knowledge about rabies epidemiology and therefore, will assist preventing fatal human cases.

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Keywords: Rabies; Antigenic variant; Molecular epidemiology

1. Introduction

Rabies is a fatal infection of the central nervous system generally acquired through virus-contaminated saliva transmitted by the bite of a rabid animal. The virus circulates through two different epidemiological cycles: urban rabies, where the domestic dog is the main reservoir and transmitter, and sylvatic rabies, where several wildlife species act as reservoirs and/or transmitters.

The prototype of rabies virus (RV), lyssavirus, contains a non-segmented 12 Kb negative-sense RNA genome that encodes for five genes: N, P, M, G and L (Tordo et al., 1986). The highly conserved and abundant nucleoprotein (N), a key structural component of the viral ribonucleoprotein core essential to viral propagation (Yang et al., 1998), constitutes the main target for rabies diagnosis (Dean, 1996).

Analysis of rabies isolates from human and animal cases using monoclonal antibodies (Mabs) directed to the nucleoprotein, provides useful information about the geographical and temporal distribution of viral variants associated with outbreaks of rabies. A previous study conducted in 17 several

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Table 1
Distribution of rabies isolates in Argentina

| Isolates | Species | Location | Date | Antigenic variant | Genetic variant |
|------------|----------------------------------|----------------------------------|------|-------------------|-----------------|
| Bamsbt121 | <i>Myotis</i> sp bat | 3 de febrero, Buenos Aires | 2001 | ND | A5 |
| Batbbt122 | <i>Tadarida brasiliensis</i> bat | La Matanza, Buenos Aires | 2001 | 4 | A2 |
| Batbbt123 | <i>Tadarida brasiliensis</i> bat | 3 de febrero, Buenos Aires | 2001 | 4 | A2 |
| Batbbt125 | <i>Tadarida brasiliensis</i> bat | 3 de febrero, Buenos Aires | 2001 | 4 | A4 |
| Chabv129 | Cattle | Gral San Martín, Chaco | 2002 | 3 | A1 |
| Chabv66 | Cattle | San Martín, Chaco | 2000 | 3 | A1 |
| Chabv72 | Cattle | Puerto Veloz, Chaco | 2000 | 3 | A1 |
| Chabv74 | Cattle | Colonia Mixta, Chaco | 2000 | 3 | A1 |
| Chabv76 | Cattle | La Leonesa, Chaco | 2000 | 3 | A1 |
| Chabv78 | Cattle | Colonia Mixta, Chaco | 2000 | 3 | A1 |
| Chabv86 | Cattle | La Leonesa, Chaco | 2001 | 3 | A1 |
| Chabv94 | Cattle | Las Palmas, Chaco | 2001 | 3 | A1 |
| Chadg120 | Dog | Pampa Almiron, Chaco | 2001 | 2 | Bb1 |
| Chafx08 | Fox | Laguna Limpia, Chaco | 1999 | NA | A1 |
| Chafx119 | Fox | Pampa Almiron, Chaco | 2001 | 2 | Bb1 |
| Chahr90 | Horse | Colonia Mixta, Chaco | 2001 | 3 | A1 |
| Chutbbt124 | <i>Tadarida brasiliensis</i> bat | Puerto Madryn, Chubut | 2001 | 4 | A2 |
| Ctebv01 | Cattle | Beron de Estrada, Corrientes | 1999 | 3 | A1 |
| Ctebv55 | Cattle | Colonia Romero, Corrientes | 2000 | 3 | A1 |
| Ctebv77 | Cattle | Concepción Corrientes | 2000 | 3 | A1 |
| Ctebv79 | Cattle | San Miguel, Corrientes | 2000 | 3 | A1 |
| Ctehm82 | Human | San Luis del Palmar, Corrientes | 2001 | 3 | A1 |
| Forbv07 | Cattle | Laishi, Formosa | 1999 | 3 | A1 |
| Forbv107 | Cattle | Potrero de los caballos, Formosa | 2001 | 3 | A1 |
| Fordg53 | Dog | Pozo del Tigre, Formosa | 2000 | 2 | B1b |
| Fordg71 | Dog | Pirane, Formosa | 2000 | 2 | B1b |
| Forhr96 | Horse | Presidente Irigoyen, Formosa | 2001 | 3 | A1 |
| Jujdg40 | Dog | La Quiaca, Jujuy | 1997 | 2 | B1a |
| Salct41 | Cat | Oran, Salta | 1998 | 1 | B2 |
| Salct47 | Cat | Oran, Salta | 1999 | 1 | B2 |
| Salct49 | Cat | Oran, Salta | 1999 | 1 | B2 |
| Salct50 | Cat | Oran, Salta | 1999 | 1 | B2 |
| Saldg126 | Dog | Oran, Salta | 2002 | 1 | B2 |
| Saldg146 | Dog | Oran, Salta | 2002 | 1 | B2 |
| Saldg15 | Dog | Hipolito Irigoyen, Salta | 1999 | 1 | B2 |
| Saldg17 | Dog | Oran, Salta | 1999 | 1 | B2 |
| Saldg19 | Dog | Ingeniero Tabacal, Salta | 1999 | 1 | B2 |
| Saldg20 | Dog | Hipolito Irigoyen, Salta | 1999 | 1 | B2 |
| Saldg21 | Dog | Hipolito Irigoyen, Salta | 2000 | 1 | B2 |
| Saldg42 | Dog | Oran, Salta | 1999 | 1 | B2 |
| Saldg43 | Dog | Oran, Salta | 1999 | 1 | B2 |
| Saldg44 | Dog | Oran, Salta | 1999 | 1 | B2 |
| Saldg45 | Dog | Oran, Salta | 1999 | 1 | B2 |
| Saldg46 | Dog | Rio Blanco, Salta | 1999 | 1 | B2 |
| Saldg48 | Dog | Hipolito Irigoyen, Salta | 1999 | 1 | B2 |
| Saldg51 | Dog | Hipolito Irigoyen, Salta | 1999 | 1 | B2 |
| Sfeepbt118 | <i>Eumops patagonicus</i> bat | Rosario, Santa Fe | 2001 | 4 | A2 |
| Sfemmbt116 | <i>Myotis nigricans</i> bat | Rosario, Santa Fe | 2001 | ND | A5 |
| Stchmbt80 | <i>Histiotus montanus</i> bat | Rio Turbio, Santa Cruz | 2000 | ND | A3 |
| Tucdg35 | Dog | Concepcion, Tucuman | 1995 | 2 | B1a |
| Tucdg36 | Dog | Aguilares, Tucuman | 1995 | 2 | B1a |
| Tucdg37 | Dog | Rio Seco, Tucuman | 1995 | 2 | B1a |
| Tucdg38 | Dog | Aguilares, Tucuman | 1996 | 2 | B1a |
| Tucdg39 | Dog | Chigliasta, Tucuman | 1996 | 2 | B1a |

NA: Not available; ND: not determined.

Latin American and Caribbean countries, identified eight distinct antigenic variants (AgV) of rabies virus, concluding that different animal reservoirs might have been responsible for maintenance and transmission of these variants (Diaz et al., 1994). In addition, molecular characterization of rabies

virus isolates enables the identification of epidemiologic links that cannot be otherwise established by antigenic typing (de Mattos et al., 1996, 1999, 2000).

Dog vaccination programs successfully reduced the number of cases of rabies in the northern and center provinces of

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