

# Bats and humans during the SARS-CoV-2 outbreak: The case of bat-coronaviruses from Mexico

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## Funding information

U.S. National Science Foundation, Grant/Award Number: DEB-1754393 and DEB-1441634; Consejo Nacional de Ciencia y Tecnología, Grant/Award Number: 463798 and 549963

## Abstract

The novel SARS-CoV-2 coronavirus has attracted attention due to the high number of human cases around the world. It has been proposed that this virus originated in bats, possibly transmitted to humans by an intermediate host, making bats a group of great interest during this outbreak. Almost 10% of the world's bat species inhabit Mexico, and 14 previous novel CoVs have been recorded in Mexican bats. However, the phylogenetic relationships between these viruses and the novel coronavirus are unknown. The aim of this communication was therefore to describe the phylogenetic relationships between Mexican bat-CoVs and SARS-CoV-2. We showed that Mexican bat-CoVs sequences are grouped into two genera, *Alphacoronavirus* and *Betacoronavirus*, and the new coronavirus is an independent clade within *Betacoronavirus*. Due to the diversity of CoVs in Mexican bats, the propensity of CoVs to shift hosts, the invasion mechanisms described for this new virus, and previous reports of animals infected by SARS-CoV-2, the risk of possible infection from humans to Mexican bats should not be discarded and warrants further analyses. To avoid future zoonotic infectious diseases and to limit persecution of bats, we urge researchers and the general population to take extreme precautions and avoid manipulation of bats during the current and future similar outbreaks.

## KEYWORDS

conservation, CoV, COVID-19, emerging infectious diseases, One Health

## 1 | INTRODUCTION

Since the first reports of a novel coronavirus associated with serious pneumonia disease from Wuhan in late December 2019 (Wu, Zhao, et al., 2020), several studies have attempted to identify the most likely origin of this new viral species, formally named SARS-CoV-2 (Jiang et al., 2020). Only seven species in two genera (*Alphacoronavirus* and *Betacoronavirus*) of the *Coronaviridae* family (Siddell et al., 2018) are recognized to infect humans and cause disease. Four of these—*HKU1*, *NL63*, *OC43* and *229E* (Corman, Muth, Niemeyer, & Drosten, 2018)—cause mild symptoms, while *SARS-CoV*, *MERS-CoV* and *SARS-CoV-2*

can cause severe diseases (Mohd, Al-Tawfiq, & Memish, 2016; Wu, Zhao, et al., 2020; Zaki, Van Boheemen, Bestebroer, Osterhaus, & Fouchier, 2012).

Worldwide, coronaviruses (CoVs) have a wide range of hosts, affecting terrestrial and marine vertebrates (Kasmi, Khataby, Souiri, & Ennaji, 2020; Wang et al., 2005). However, since the well-known human outbreaks of SARS and MERS in 2002 and 2012, respectively, (WHO, 2020a, 2020b), the number of studies on bats has increased due to indirect evidence suggesting a bat origin of several CoVs species (De Benedictis et al., 2014; Hu, Ge, Wang, & Shi, 2015; Mohd et al., 2016; Wacharapluesadee et al., 2013).

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Other bat-coronaviruses (bat-CoVs) clades have been related to SARS-CoV and MERS-CoV around the world (Annan et al., 2013; De Benedictis et al., 2014; Ge et al., 2013; Ithete et al., 2013; Lau et al., 2005; Li et al., 2005; Memish et al., 2013; Menachery et al., 2015), but on the American continent, few studies have been done in order to elucidate the phylogenetic relationships between native bat-CoVs and those causing human diseases (Carrington et al., 2008; Dominguez, O'Shea, Oko, & Holmes, 2007).

Within the Americas, Mexico is one of the countries with the world's highest levels of mammal diversity (Ceballos, 2013), inhabited by at least 139 of the 1,420 described bat species (Simmons & Cirranello, 2020). In other words, Mexico accounts for about 1.6% of the total continental surface area (Ceballos, 2013), but it supports almost 10% of all known bat species (Ramírez-Pulido, González-Ruiz, Gardner, & Arroyo-Cabrales, 2014; Simmons & Cirranello, 2020). In this country, at least 42 viral species with zoonotic potential have been recorded from 1900 to 2018; 14 of those are CoVs species (presumably new species), all which were found in bats (Anthony et al., 2013; Bentim-Góes et al., 2013; Colunga-Salas et al., 2020).

Bats are indisputably essential ecosystem components; they perform several invaluable ecosystem services such as pest controls, pollination and seed dispersal, among others (Kasso & Balakrishnan, 2013; Valitutto et al., 2020). However, it is estimated that almost 15% per cent of bat species are considered globally threatened with extinction by the IUCN, and 18% are Data Deficient (Voigt & Kingston, 2016). The major threats to bats are land-use change, urbanization, hunting, persecution, quarrying and general human intrusions into sylvatic areas (Voigt & Kingston, 2016). Unfortunately, emerging zoonotic viruses often lead to bat persecution and decrease the number of bat populations (Schneeberger & Voigt, 2016). Some of these negative pressures on bats could increase during this SARS-CoV-2 outbreak, as was recently reported by the media [<https://phys.org/news/2020-03-peru-blamed-coronavirus.html>], where in Peru, another biodiverse Latin American country, hundreds of bats were burned (SERFOR, 2020).

Host shifts have occurred recently in the evolutionary history of CoVs (Cui et al., 2007), and because of the current public health importance of the novel SARS-CoV-2 and previous reports that Mexican bats host some lineages of CoVs, the aim of this communication was to elucidate the phylogenetic relationship between the Mexican bat-CoVs and the novel SARS-CoV-2. Using that information, we also assess whether concerns that Mexican bats could host SARS-CoV-2 are justified.

## 2 | MATERIALS AND METHODS

All previously published sequences for the ORF1ab polyprotein of CoVs detected in 11 bat species distributed in Mexico were obtained from GenBank (Accession numbers: KC117184–KC117213). Additionally, representative novel SARS-CoV-2 sequences from all continents were also obtained from GenBank (Africa: MT066156, America: MT322424, Asia: NC\_045512, Australia: MT007544, and

Europe: MT077125). A multiple alignment was performed using the MUSCLE algorithm (Edgar, 2004) in AliView (Larsson, 2014).

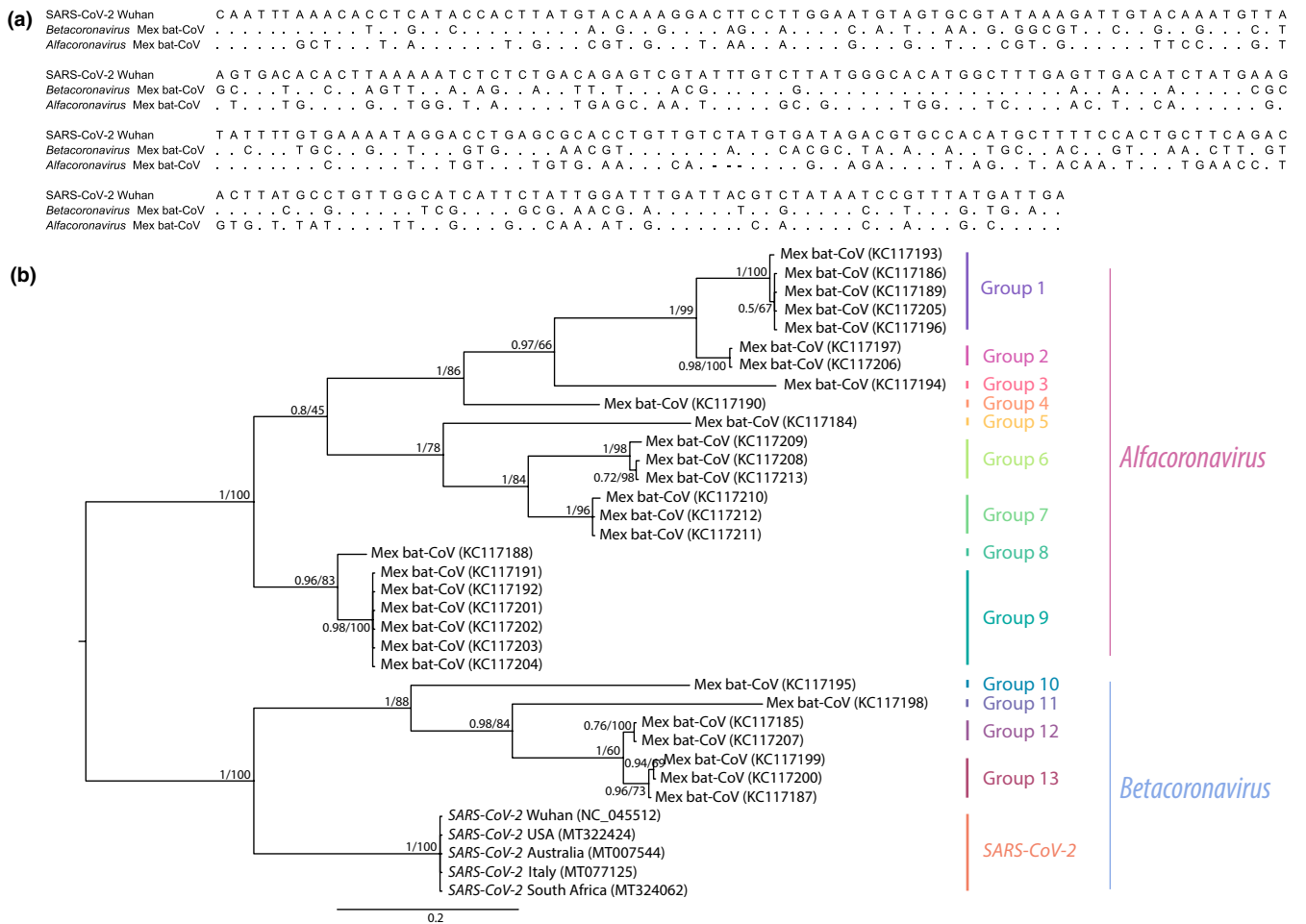
Phylogenetic relationships were inferred using two different analyses. For the first approach, in IQ-TREE (Nguyen, Schmidt, Von Haeseler, & Minh, 2015) the best-fit substitution model with the ModelFinder algorithm (Kalyaanamoorthy, Minh, Wong, Von Haeseler, & Jermin, 2017) was selected, through a full tree search for each model and according to the Bayesian information criterion. Then, the maximum likelihood (ML) phylogeny was estimated using the previously calculated substitution model, and we assessed branch support using 1,000 replicates of a non-parametric bootstrap.

The second phylogenetic approach was performed using Bayesian inference (BI) in MrBayes 3.2 (Ronquist et al., 2012). However, because this software does not include all substitution models considered previously, PartitionFinder 2 (Guindon et al., 2010; Lanfear, Frandsen, Wright, Senfeld, & Calcott, 2017) was used to determine the best substitution model using the Bayesian information criterion. With this model, three hot chains and one cold chain were used in two independent runs of 10 million generations, sampling data every 1,000 iterations. The adequate convergence of our results and effective sample size (ESS > 200) were checked in Tracer 1.7 (Rambaut, Drummond, Xie, Baele, & Suchard, 2018). The final topology was obtained using a majority rule consensus tree and considering a burn-in of 25%.

## 3 | RESULTS AND DISCUSSION

This communication reveals the phylogenetic position of the novel SARS-CoV-2 virus with respect to all known Mexican bat-CoVs based on sequences of the ORF1ab polyprotein. In the 296 base pairs analysed, we detected 90 invariant sites (30.40%), 190 parsimony informative sites (64.18%) and 212 distinct sites (71.62%) (Figure 1a). The best substitution model was TPM2u + F+I + G4 (BIC = 6,236.09) for the ML analysis, and HKY + I+G (BIC = 6,329.57) for BI. We recovered similar topologies from both the ML and BI analyses, but branch support was stronger from Bayesian results (Figure 1b). In general, our results were similar to those previously reported by Anthony et al., (2013); we detected nine highly distinctive monophyletic groups in the genus *Alphacoronavirus*, and five well-supported monophyletic groups in the *Betacoronavirus* genus (Figure 1b, Table 1). The novel SARS-CoV-2 was a member of the *Betacoronavirus* genus (Figure 1b). Both ML and BI analyses coincided with the previous report that SARS-CoV-2 is a member of the *Betacoronavirus* genus (Gorbalenya et al., 2020).

It is important to note that all analysed sequences of SARS-CoV-2 formed a monophyletic group that was separated from all of the Mexican CoVs and that this position was supported by the highest posterior probability and bootstrap values. This result confirms that the SARS-CoV-2 clade is not grouped with any of the CoVs hosted by Mexican bats. Therefore, Mexican bats do not currently represent a danger to the human population as reservoirs or transmitters of the



**FIGURE 1** Phylogenetic relationships among Mexican bat-CoVs and SARS-CoV-2. (a) ORF1ab segments of SARS-CoV-2 aligned against sequences of the *Alphacoronavirus* and *Betacoronavirus* genera from Mexican bat-CoVs, showing the differences throughout the segment. (b) Bayesian inference for coronaviruses previously reported from Mexican bats; branch labels show posterior probabilities/bootstraps support at each node; the scale bar indicates nucleotide substitutions per site

SAR-CoV-2 virus. However, given the diversity of CoVs in Mexican bats and the propensity for host shifts among CoVs (Cui et al., 2007), the risk of a possible infection from humans to Mexican bats should not be dismissed. Since bats and human populations are in close contact, future studies should focus on analysing whether human-to-bat transmission of SARS-CoV-2 is possible, and if so, the potential effects on bat populations.

Despite the lack of scientific reports of natural human-to-animal transmission of SARS-CoV-2, the United States Department of Agriculture (USDA) has reported the infection of a tiger, a lion, and two cats in New York (USDA, 2020). Although these animals have not developed severe acute respiratory syndrome, these reports support previous findings by Shi et al., (2020), who showed that experimental inoculation with human isolates of SARS-CoV-2 can replicate successfully in cats and ferrets, raising the possibility that human-animal infections may occur in nature.

Infection in animals by SARS-CoV-2 could be explained by the spike glycoprotein (S), which determines host specificity, and a glycan residue in the junction of the subunits 1 and 2 of this protein,

which seem to have a determinant role in viral infectivity due to its affinity with the angiotensin-converting enzyme 2 (ACE2) (Walls et al., 2020; Wan, Shang, Graham, Baric, & Li, 2020). Additionally, the receptor-binding domain (RBD) presents in the same glycoprotein causes this region of the genome to be the most variable part of CoVs, which is responsible for the host specificity of each species (Bolles, Donaldson, & Baric, 2011; Lu, Wang, & Gao, 2015; Wan et al., 2020; Wu, Wu, Liu, & Yang, 2020; Zhou et al., 2020). Specifically, the RBD present in SARS-CoV-2 seems to bind with high affinity to the ACE2 receptor of non-human mammals, including bats (Wan et al., 2020). Similar results have been described in another related bat-SARS-CoV, which supports the hypothesis of bat-human infections (Andersen, Rambaut, Lipkin, Holmes, & Garry, 2020; Bolles et al., 2011; Ge et al., 2013; Lu et al., 2015; Walls et al., 2020; Wan et al., 2020; Wang et al., 2014).

With all of this information in mind, this contribution supports and endorses the calls by the Mexican Mammalogy Society (Asociación Mexicana de Mastozoología, A.C., AMMAC), the USDA, the Center for Disease Control and Prevention (CDC) and

**TABLE 1** Bat species and the phylogenetic group of bat-CoVs that have been detected in them in Mexico. Bat habitats were obtained according to Ceballos (2013)

Bat family	Bat species	Genetic group	Bat habitat
Molossidae	<i>Nyctinomops laticaudatus</i>	MEX_bat-CoV-10(B)	Caves or cliffs cracks, constructions, foliage
	<i>Tadarida brasiliensis</i>	MEX_bat-CoV-7(A)	Caves, hollow trees, cellars, buildings
Mormoopidae	<i>Pteronotus parnelli</i>	MEX_bat-CoV-11(B)	Caves
Phyllostomidae	<i>Artibeus jamaicensis</i>	MEX_bat-CoV-3(A), MEX_bat-CoV-8(B), MEX_bat-CoV-9(B)	Caves, hollow trees, foliage, abandoned buildings, tunnels
	<i>Artibeus lituratus</i>	MEX_bat-CoV-9(B), MEX_bat-CoV-12(B), MEX_bat-CoV-13(B)	Caves, tunnels, trunks, abandoned buildings, bridges, leaves of some palms
	<i>Artibeus phaeotis</i>	MEX_bat-CoV-12(B), MEX_bat-CoV-13(B)	Caves, underside of large leaves
	<i>Carollia perspicillata</i>	MEX_bat-CoV-1(A)	Caves, trunks, tunnels, rock crevices, under leaves, constructions
	<i>Carollia sowelli</i>	MEX_bat-CoV-1(A), MEX_bat-CoV-2(A), MEX_bat-CoV-9(B)	Caves, crevices of rocks, houses, beneath bananas leaves
Vespertilionidae	<i>Lonchorina aurita</i>	MEX_bat-CoV-4(A)	Caves, tunnels, culverts
	<i>Eptesicus</i> sp.	MEX_bat-CoV-5(A)	–
	<i>Myotis velifer</i>	MEX_bat-CoV-6(A)	Mines, caves, cracks, buildings

Note: A = species from the *Alphacoronavirus* genus; B = species from the *Betacoronavirus* genus.

the IUCN Species Survival Commission—Bat Specialist Group (BSG) to avoid handling wild mammals—especially bats—during this SARS-CoV-2 outbreak and future similar epidemics in order to avoid generating cycles of infection between humans and wildlife. The objective is to prevent this new coronavirus and similar future outbreaks from entering native populations of bats or other mammals, at the same time avoiding negative actions that could endanger wildlife populations, such as hunting, persecution, quarrying and general human intrusions into sylvatic areas. However, if the handling of wildlife cannot be avoided, we endorse to following the good field hygiene guidance proposed by the BSG group ([https://www.iucnbsg.org/uploads/6/5/0/9/6509077/map\\_recomendations\\_for\\_researchers\\_v\\_1.0\\_final.pdf](https://www.iucnbsg.org/uploads/6/5/0/9/6509077/map_recomendations_for_researchers_v_1.0_final.pdf)). These recommendations follow the “One Health” approach, which addresses both wildlife and human health in order to achieve ecosystem health (Conti & Rabinowitz, 2011; Kahn, 2006; Zinsstag, Schelling, Waltner-Toews, & Tanner, 2011).

It is also important to highlight that, unfortunately, emerging zoonotic viruses often lead to bat persecution, decreasing the sizes of wild populations (Schneeberger & Voigt, 2016). In addition to the invaluable ecosystem services bats perform, preserving them also has important positive economic repercussions, they control agricultural pests, are pollinators and seed dispersers of many commercial plants, their guano is used as fertilizer in agriculture, they are used in research (e.g., echolocation, anti-coagulant compounds), and bat watching tourism is growing as a recreational activity that earns millions of dollars per year (Kasso & Balakrishnan, 2013; Voigt & Kingston, 2016). Therefore, putting bat communities at risk, either by exposing them to SARS-CoV-2 through human contact or through persecution, will have

consequences not only in natural ecosystems, but also on human economies.

In conclusion, the current risk to human health from Mexican bats serving as reservoirs or transmitting SARS-CoV-2 is null, since the SARS-CoV-2 clade is not closely related to any of the CoVs found in these bats. However, their potential infection by humans due to multiple indirect factors should be considered; otherwise, bat conservation could be threatened, and with it, all economic and ecosystem services they offer. Finally, it is important to remember and emphasize that responsible handling and use of wildlife is one of the most important measures to prevent current and future spillovers of infectious diseases between human and wildlife populations.

#### ACKNOWLEDGEMENTS

We thank Estefania Grostieta and Lucia Álvarez-Castillo for their comments in the earlier version of the manuscript. Pablo Colunga-Salas is a doctoral student from the Programa de Doctorado en Ciencias Biomédicas, Universidad Nacional Autónoma de México and has received a fellowship from the Mexican National Council for Science and Technology (CONACyT, 463798). Giovanni Hernández-Canchola was funding by the U.S. National Science Foundation (NSF DEB-1754393 and DEB-1441634), and CONACyT (549963).

#### ETHICAL APPROVAL

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required in this rapid communication since no animal samples were used.

## CONFLICT OF INTEREST

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest, non-financial interest in the subject matter or materials discussed in this manuscript.

## DATA AVAILABILITY STATEMENT

The data that support the results of this study are available in GenBank, under accession numbers: KC117184–KC117213 for Mexican bat-CoVs; and MT066156, MT322424, NC\_045512, MT007544, and MT077125 for the SARS-CoV-2 sequences.

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**How to cite this article:** Colunga-Salas P, Hernández-Canchola G. Bats and humans during the SARS-CoV-2 outbreak: The case of bat-coronaviruses from Mexico. *Transbound Emerg Dis*. 2020;00:1–6. <https://doi.org/10.1111/tbed.13751>