



SINDUSFARMA



Coronavírus

Uma ameaça do passado, do presente e do futuro.

Histórico, conceituação e classificação.

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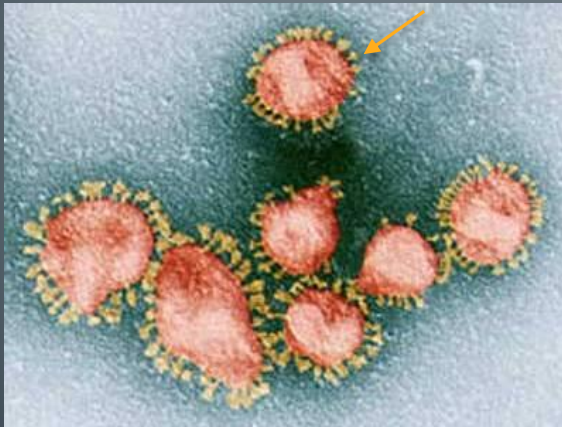
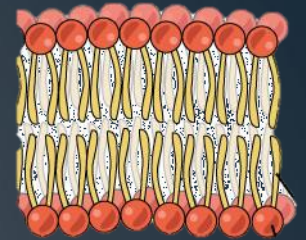
Coronavírus

- Origem da nomenclatura
- Aspectos da partícula viral
- Genoma viral
- Classificação
- Origem evolutiva
- Ciclo de Replicação
- Coronavíruses humanas e animais
- Coronavírus de morcegos

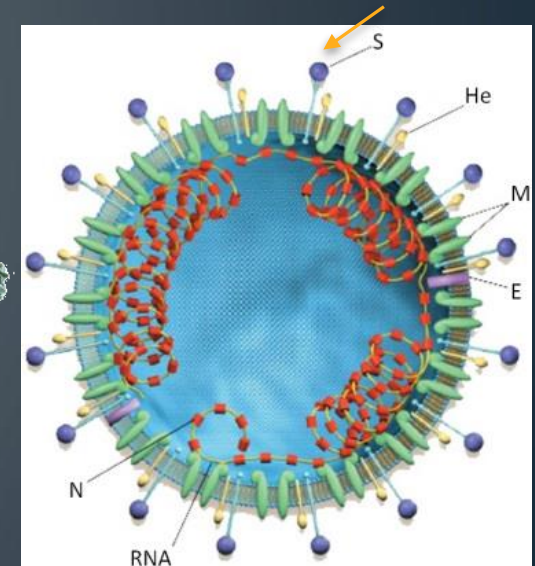
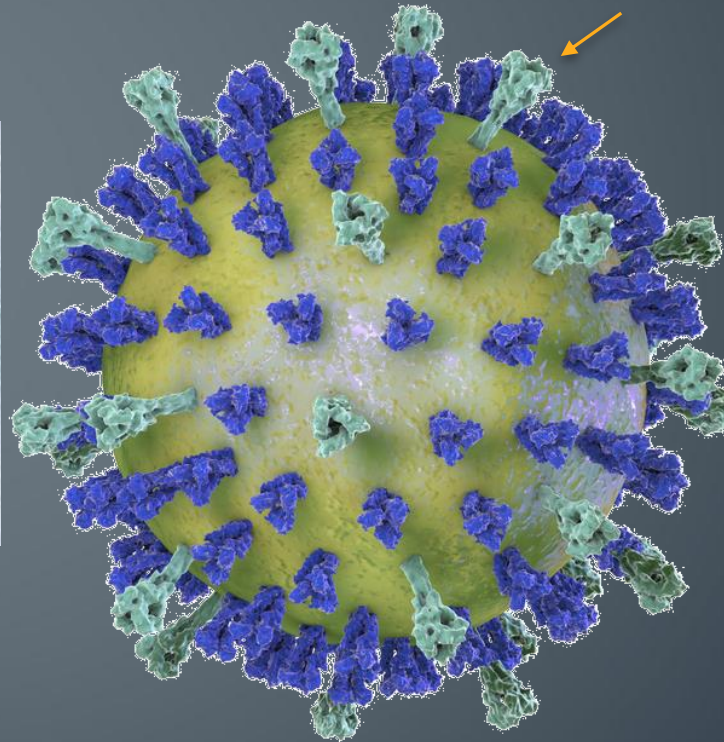
Coronavírus – Partícula viral (vírion)

➤ Vírus envelopados

➤ Apresentam aspecto de coroa ao microscópio eletrônico



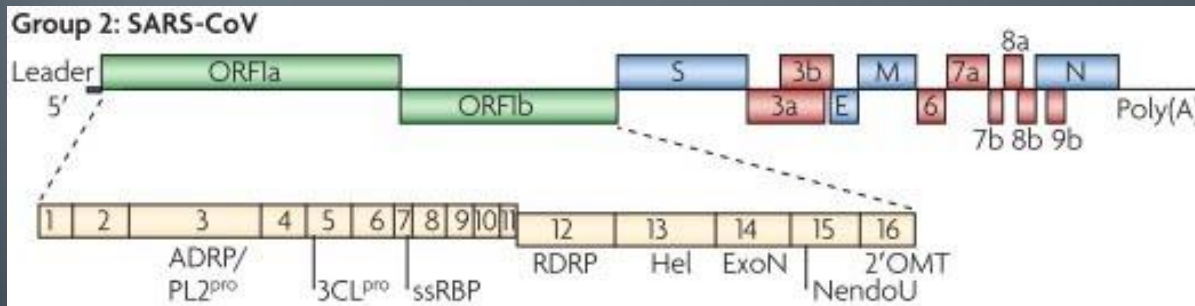
Content Providers(s): CDC/Dr. Fred Murphy - This media comes from the [Centers for Disease Control and Prevention's Public Health Image Library](#) (PHIL)



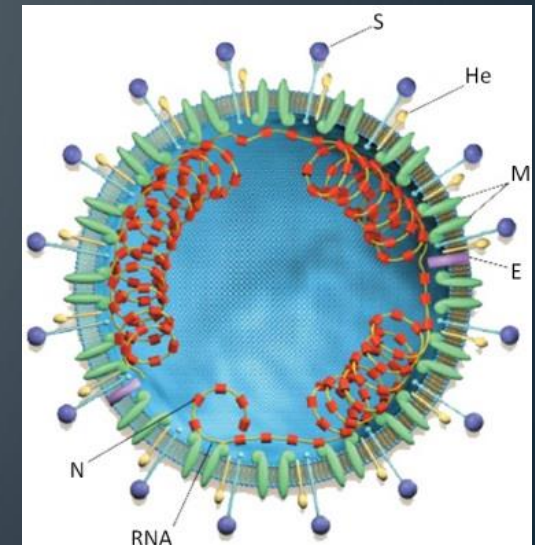
Holmes KV. N Engl J Med 2003; 348:1948-1951

Coronavírus – Características Genômicas

- RNA polaridade positiva (atua como RNAm)
- Linear não segmentado
- É o maior genoma entre os virus de RNA (~27 a 32 mil bases)
- **Proteína Não estruturais (ORF1ab) + Proteínas Estruturais + Proteínas acessórias**

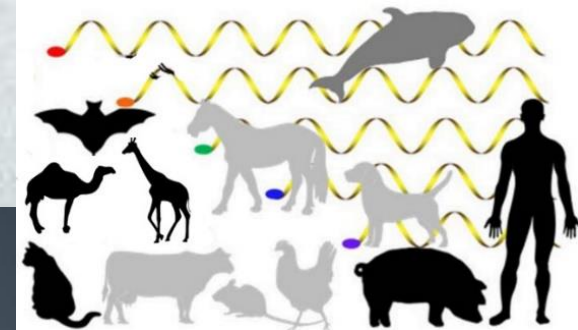


Perlman e Netland. Nature Reviews
Microbiology 7, 439-450 (June 2009).



Holmes KV. N Engl J Med
2003; 348:1948-1951

Coronavírus – Hospedeiros e doenças relacionadas



➤ **Hospedeiros: Grande diversidade de aves e mamíferos**

➤ **Associados com doenças respiratórias*, entéricas*, hepáticas e neurológicas**

Virus	Host species	Sites of infection	Clinical disease
Alphacoronaviruses			
CCoV	Canine	GI tract	Gastroenteritis
FeCoV	Felidae	GI tract, respiratory	Gastroenteritis
EIPV	Felidae	Systemic disease	Peritonitis, wasting disease
HCoV-229E	Human	Respiratory	Upper respiratory tract infection
HCoV-NL63	Human	Respiratory	Upper respiratory tract infection, croup
PEDV	Pig	GI tract	Gastroenteritis
TGEV	Pig	GI tract, respiratory	Gastroenteritis
BatCoV	Bat	GI tract, respiratory	Unknown
Rabbit CoV	Rabbit	Heart, GI tract, respiratory	Enteritis, myocarditis
Betacoronaviruses			
BCoV	Bovine, ruminants	GI tract, respiratory	Enteritis, upper and lower respiratory tract infection
HCoV-OC43	Human	Respiratory	Upper respiratory tract infection
HCoV-HKU1	Human	Respiratory	Upper and lower respiratory tract infection
MHV	Mouse, rat	GI tract, liver, brain, lungs	Gastroenteritis, hepatitis, encephalitis, chronic demyelination
PHEV	Pig	Respiratory, brain	Vomiting, wasting, encephalomyelitis
RCoV	Rat	Respiratory, salivary and lachrymal glands, urogenital tract	Respiratory tract infection, metritis, sialodacryoadenitis
SARS-CoV	Human	Respiratory, GI tract	Pneumonia (SARS)
BatCoV	Bat	GI tract, respiratory	Unknown
Gammacoronaviruses			
IBV	Chicken	Respiratory, kidney	Bronchitis, nephritis
TuCoV	Turkey	GI tract	Gastroenteritis

➤ **Grupo com grande potencial de transmissão entre espécies diferentes e rápida adaptação (spillover)**

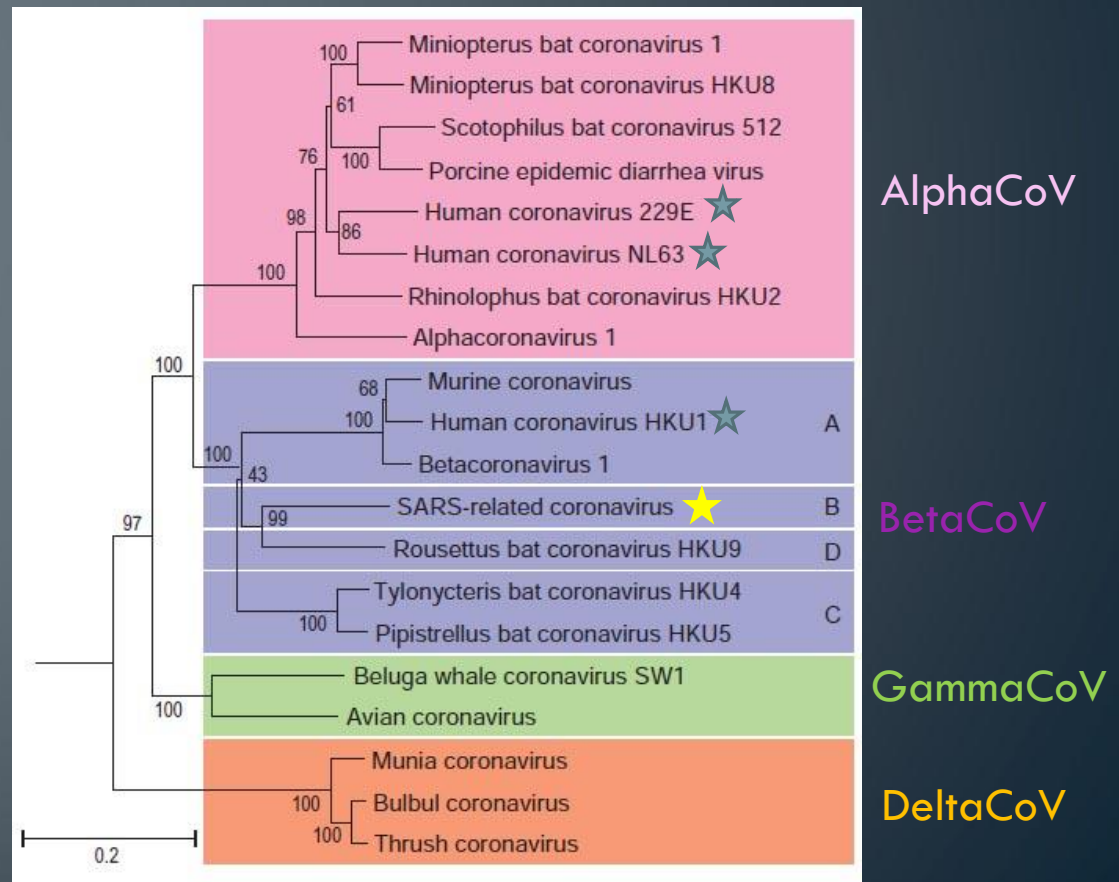
- ✓ **Alta taxa de mutação**
- ✓ **Elevada taxa de recombinação**
- ✓ **Tamanho do genoma**

Coronavírus – Classificação

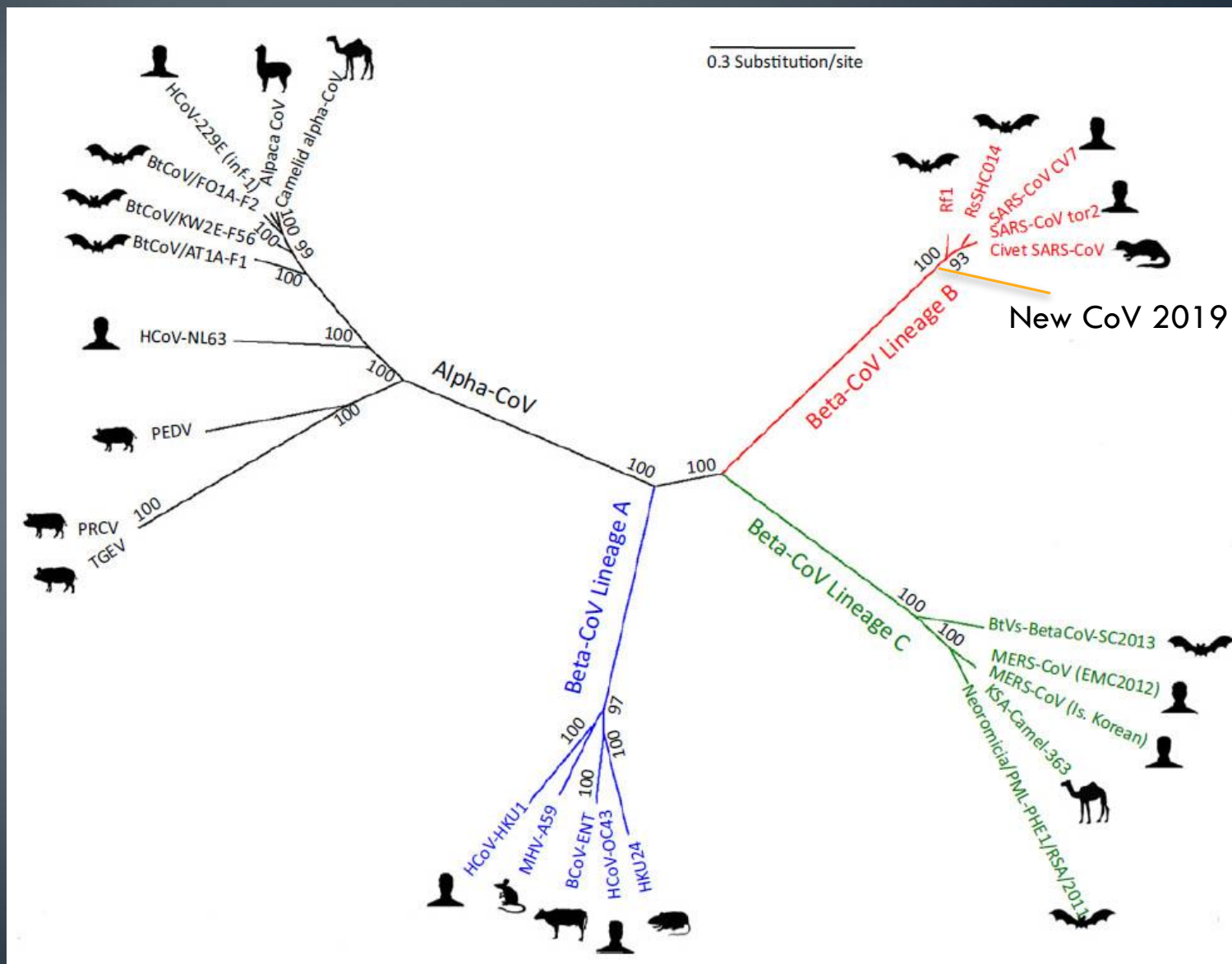
- ❖ **Ordem: Nidovirales**
- ❖ **Familia: Coronaviridae**
- ❖ **Genero: - *Alphacoronavirus*, *Betacoronavirus*: predominantemente em mamíferos**
- *Gammacoronavirus*, *Deltacoronavirus*: predominantemente em aves

Virus	Host species
Alphacoronaviruses	
CCoV	Canine
FeCoV	Felidae
FIPV	Felidae
HCoV-229E	Human
HCoV-NL63	Human
PEDV	Pig
TGEV	Pig
BatCoV	Bat
Rabbit CoV	Rabbit

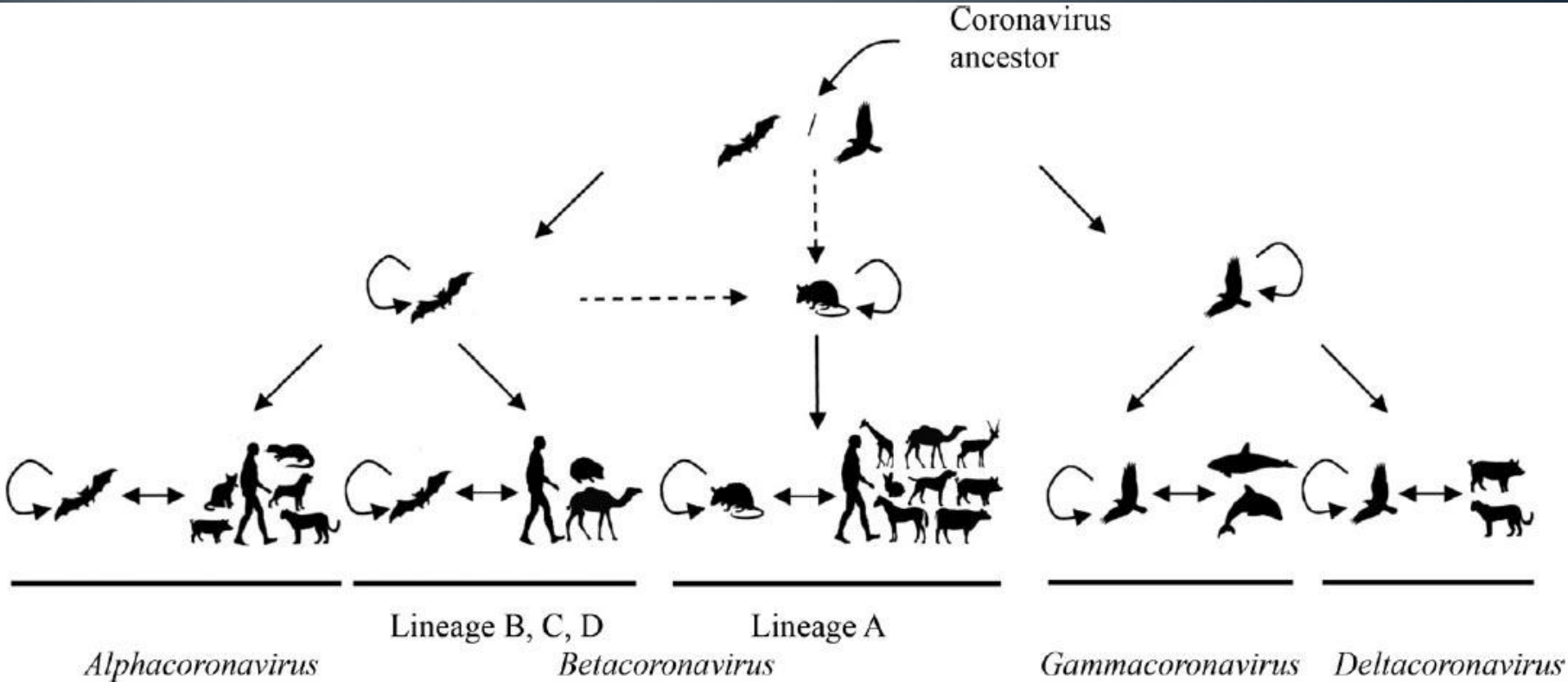
Betacoronaviruses	
BCoV	Bovine, ruminants
HCoV-OC43	Human
HCoV-HKU1	Human
MHV	Mouse, rat
SARS-CoV	Human, Bats
BatCoV	Bat
MERS-CoV	Camels, Human, Bats



Coronavírus Humanos- relação evolutiva



Coronavírus – Histórico Evolutivo



Coronavírus - Replicação Viral

Fases da replicação viral:

1. Adsorção (Spike/receptor)
2. Liberação genoma viral p/ interior celular
3. Tradução enzimas do complexo Replicação/Transcrição (pol1ab)
4. Transcrição RNAm em segmentos de polaridade neg.
5. Transcrição RNAm em segmentos de polaridade +
6. Tradução Proteínas
7. Replicação RNA gênomico
8. Composição do novo vírion
9. Liberação partícula viral

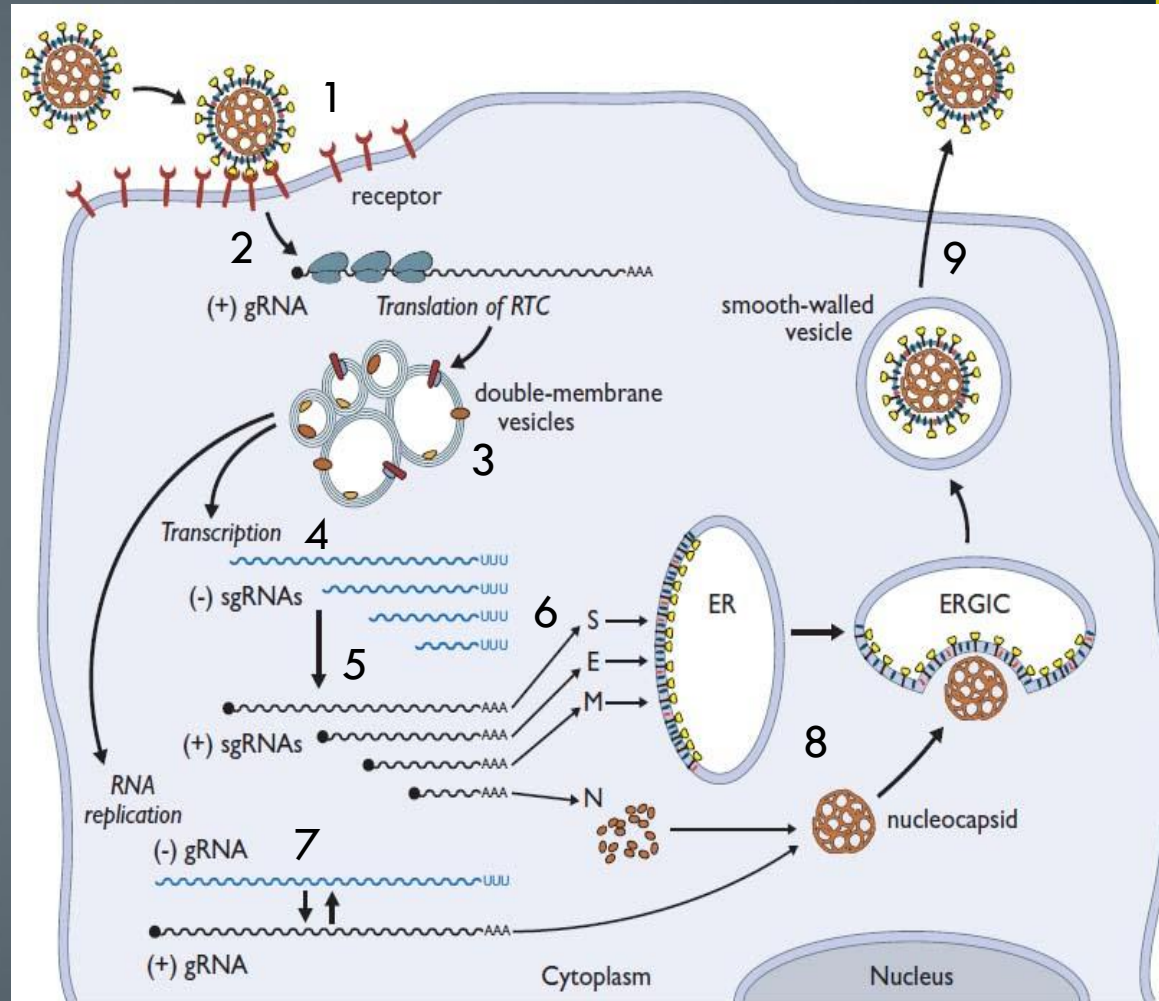
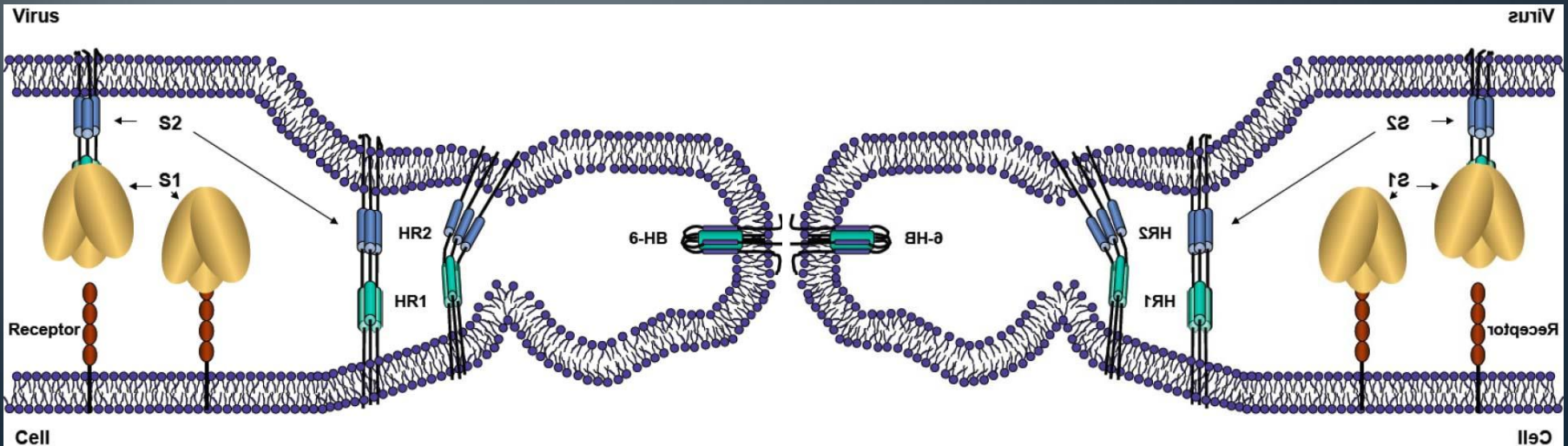
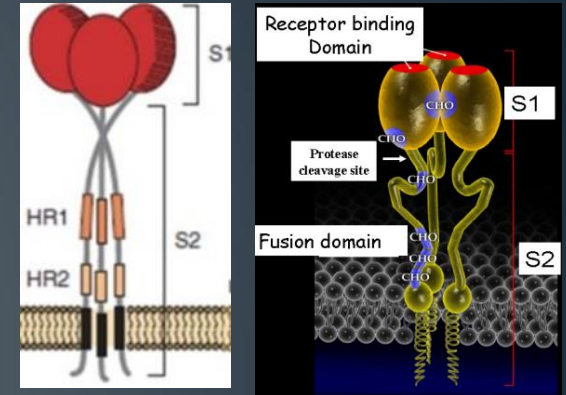
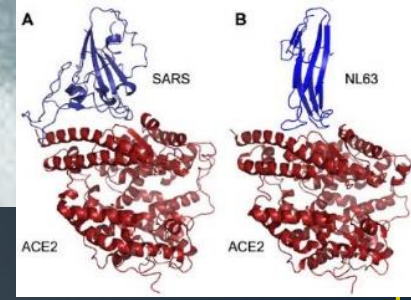


FIGURE 28.6. Overview of coronavirus replication (see text for details).

Penetração viral (Spike x Receptor)

- Spike - responsável pelo reconhecimento do receptor celular (Receptor Binding Domain)
- Cada coronavirus apresenta um receptor celular específico
 - responsável pelo tropismo tecidual e determinação do hospedeiro
- Mutações, deleções e recombinações no gene Spike permitem a adaptação para novos tecidos e Hospedeiros



Histórico da identificação de Coronavírus

- **1936:** Vírus da Bronquite Infecciosa (IBV) (Aves)
- **1946:** Vírus da Gastroenterite Transmissível (TGEV) (Porcos)
- **1949:** Vírus da Hepatite de Murinos (MHV)
- **1966:** Coronavírus Humano 229E e OC43
- **1975:** Classificação oficial do novo gênero Coronavírus pelo ICTV
- **2003:** Coronavírus SARS
- **2004:** Coronavírus Humano NL63
- **2005:** Coronavírus Humano HKU1
- **2012:** Coronavírus MERS
- **2013:** Porcine Deltacoronavírus (suínos)
- **2017:** SADS – Coronavírus da Síndrome Aguda da Diarréia Severa (suínos)
- **2019:** New CoV 2019 (nomeclatura temporária)

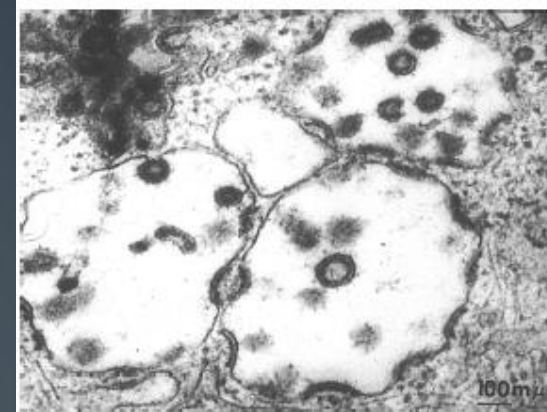


FIGURE 2. Strain 229E in WI-38 cells. Reprinted with permission from *J Virol.* 1967;1:1019–1027.

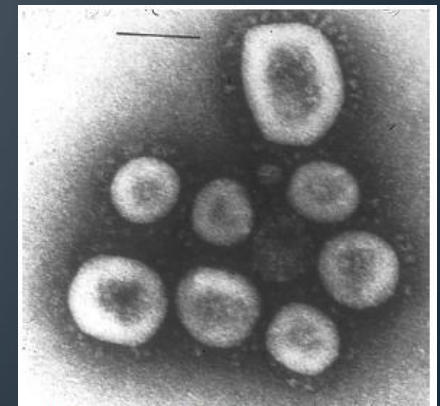
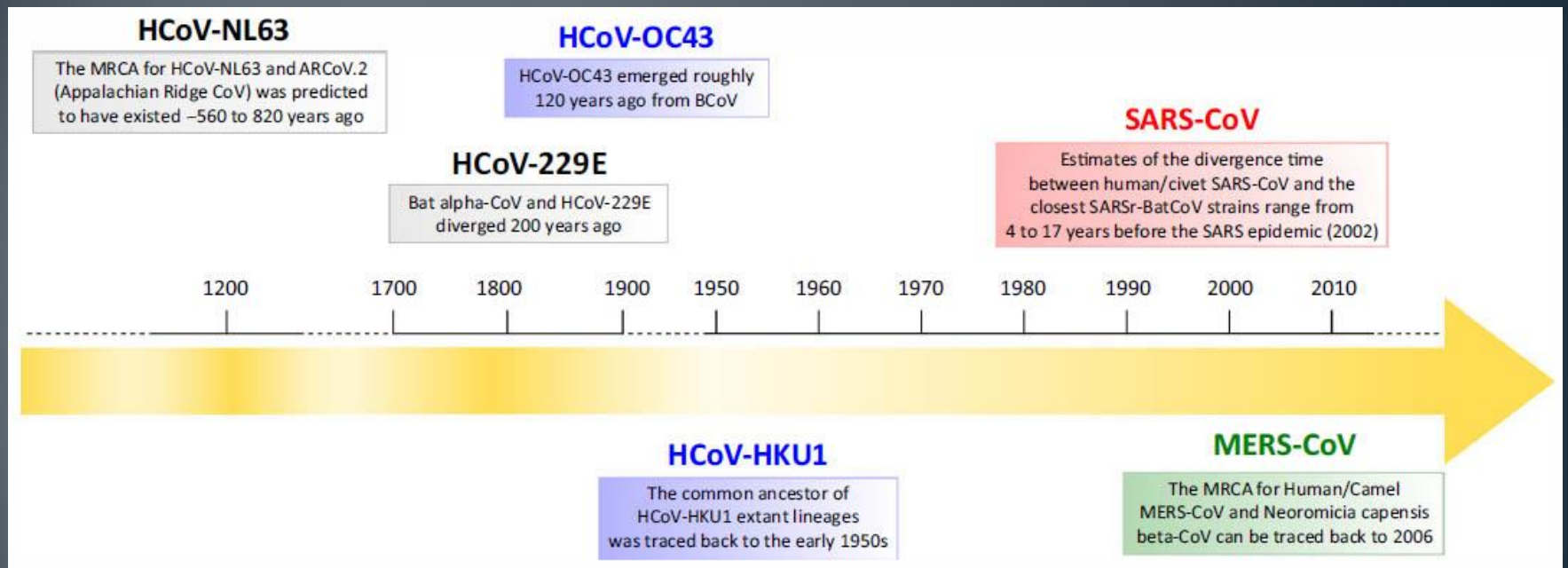


FIGURE 1. Coronavirus OC16. Reprinted with permission from *Proc Natl Acad Sci USA.* 1967;57:933–940.

Histórico evolutivo de Coronavírus humanos



HCoV NL63: ancestral comum com CoV morcego datado de 560-830 anos (Morcegos)

HCoV-229E: 200 anos (Morcegos)

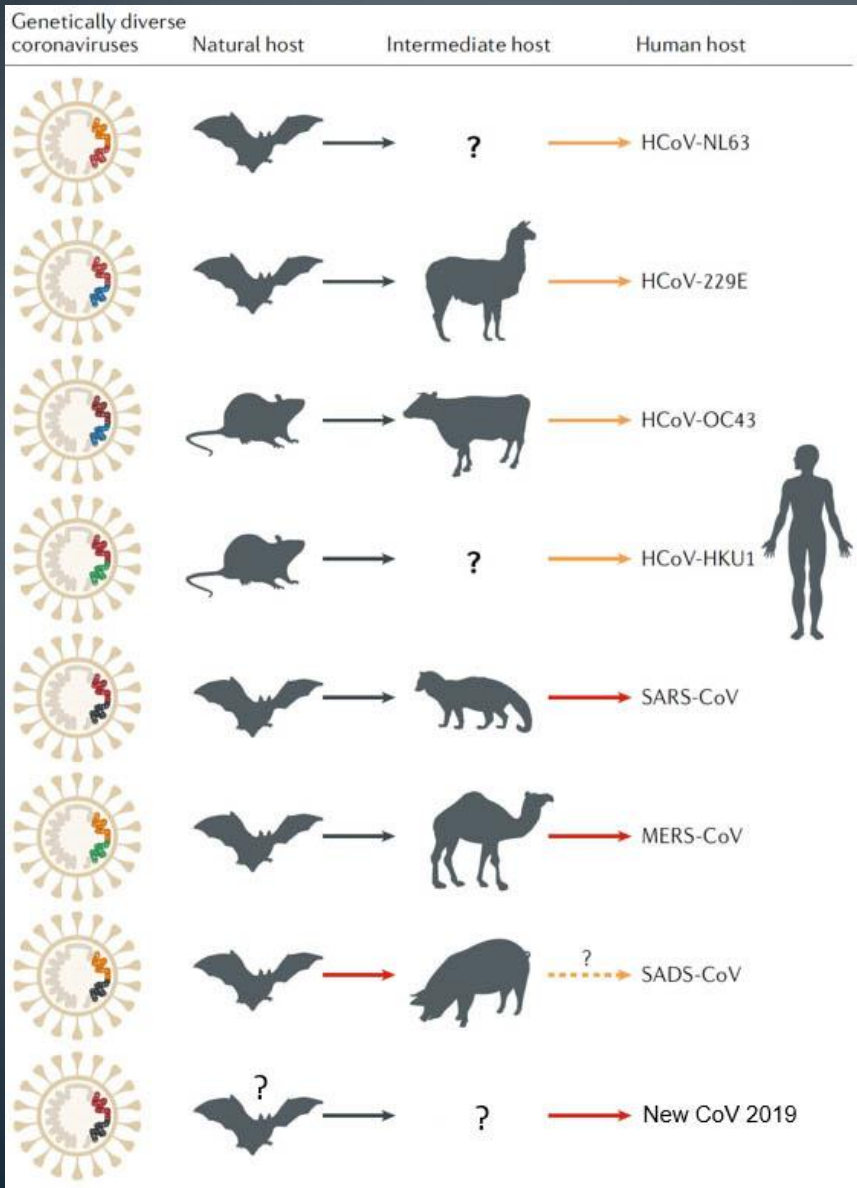
HCoV-OC43: 120 anos (Bovinos)

HCoV-HKU-1: 50 anos (Roedores)

SARS-CoV: 4 a 17 anos antes da Epidemia (Morcegos)

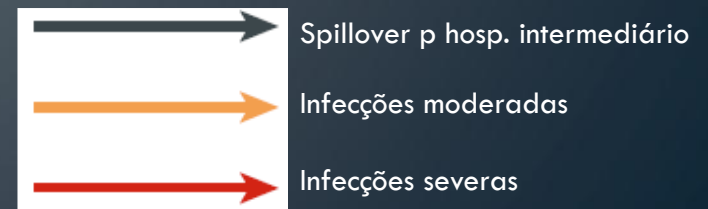
MERS-CoV: 2006 (Morcegos africanos)

Coronavírus humanos e emergentes



- . Coronavírus Humanos não emergentes, não zoonóticos.
- . Circulação anual e mundial.
- . Responsáveis por episódios de resfriado comum (0-20% casos de IRA)

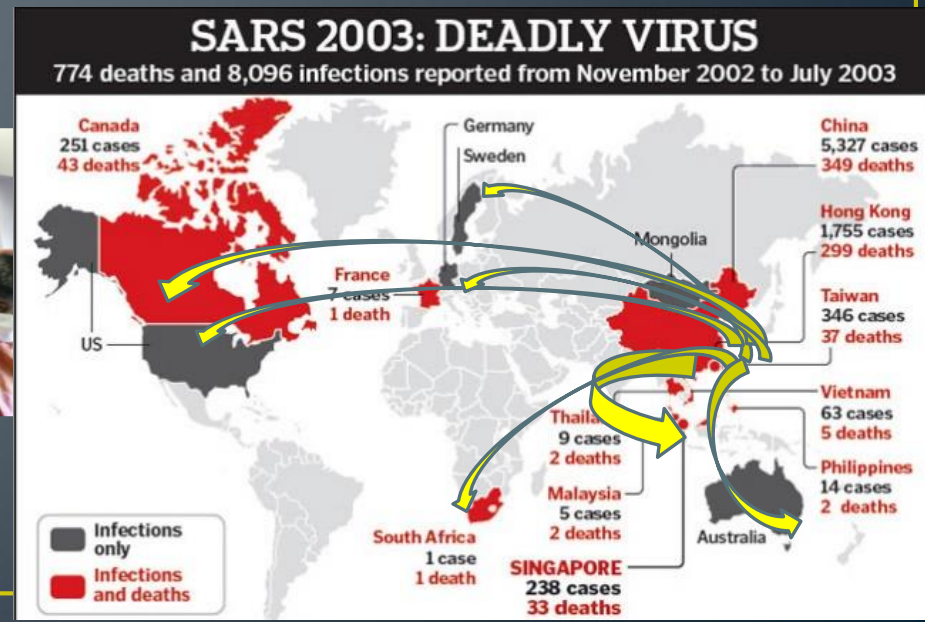
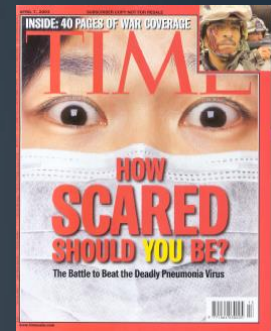
Coronavírus emergentes e zoonóticos



SARS-CoV: 2002-2003



- Agente etiológico da Síndrome Respiratória Aguda Grave (SARS)
- Epidemia iniciada em Nov de 2002 na província de Guangdong, China
- Transmissão por secreções respiratórias (droplets)
- Atingiu 29 diferentes países em 6 meses
- N^o casos: 8096 / N^o de mortes: 774
- Taxa de mortalidade de 10%
- Originado de transmissão viral entre diferentes espécies



SARS-CoV e evidências de sua origem zoonótica

- ❖ Casos humanos ligados a mercados molhados (wet markets)
- ❖ Ausência de anticorpos contra SARS em sorotecas antes da epidemia
- ❖ Alta prevalência sorológica de Ac – SARS em comerciantes de animais
- ❖ Evidência sorológica e genética de vírus em animais comercializados nos wet markets
 - ❖ *Paguma larvata* – (Himalayan palm civet)
 - ❖ *Nyctereutes procyonoides* - Raccoon dogs

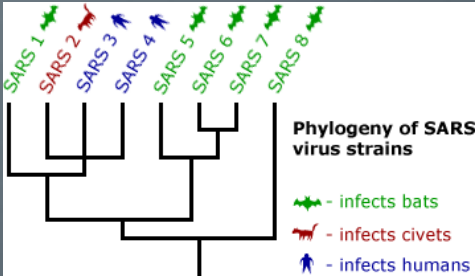


SARS-CoV e sua relação com morcegos

- ❖ Após a descoberta de SARS foi verificado uma alta prevalência de detecção de RNA de CoV similares ao CoV SARS (SARS-like CoV) em morcegos *Rhinolophus* da China (horseshoe bats) e outros coronavírus.
- ❖ Pesquisas posteriores indicaram a presença de CoV Sars like altamente similares ao SARS e com capacidade de utilizar o mesmo receptor celular da SARS (ACE2)

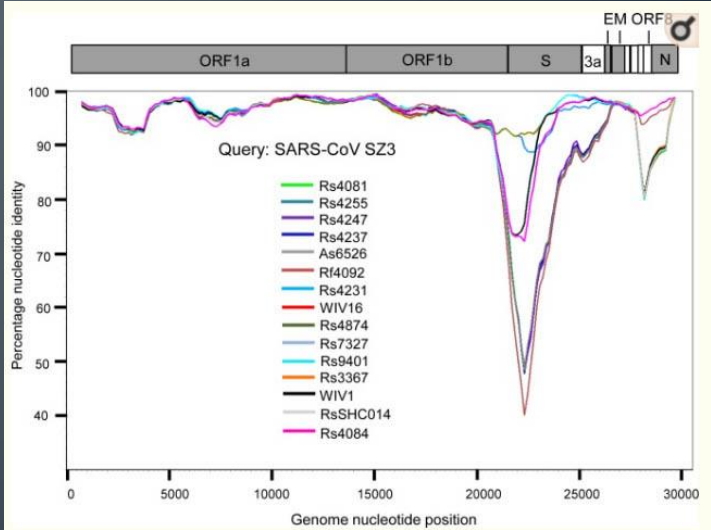


SARS host



PLoS Pathog. 2017 Nov; 13(11): e1006698. PMID: PMC5708621
Published online 2017 Nov 30. doi: [10.1371/journal.ppat.1006698](https://doi.org/10.1371/journal.ppat.1006698) PMID: [29190287](https://pubmed.ncbi.nlm.nih.gov/29190287/)

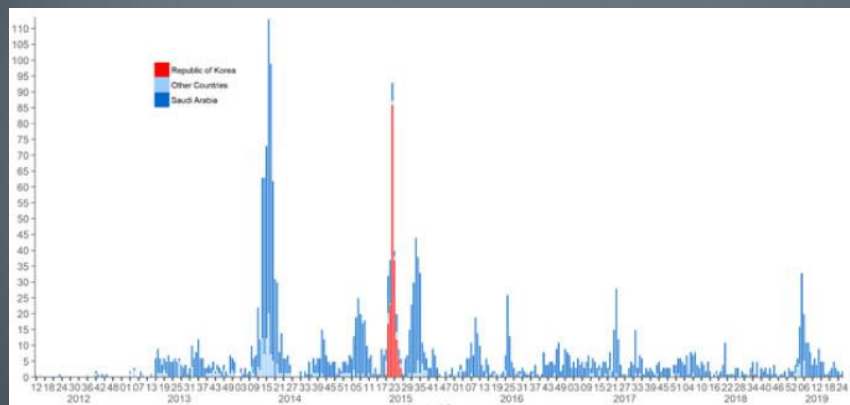
Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus



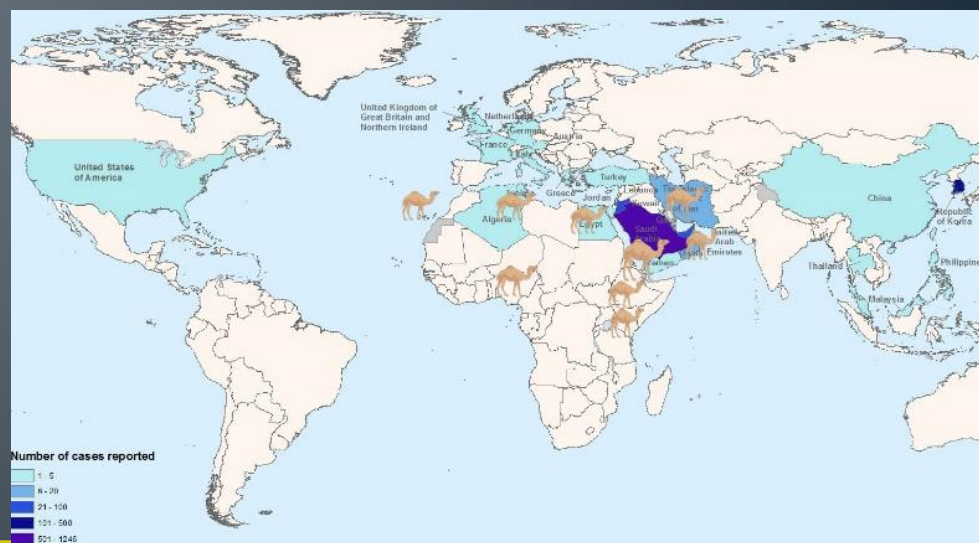
MERS-Coronavírus



- ❖ Agente etiológico da Síndrome Respiratória do Oriente Médio (MERS)
- ❖ Primeiro caso ocorreu no Reino da Arábia Saudita
- ❖ Situação epidemiológica atual: 2494 casos / 858 Mortes (Taxa mortalidade 34%)
- ❖ Encontrado em 27 países



Mackay et al., 2015

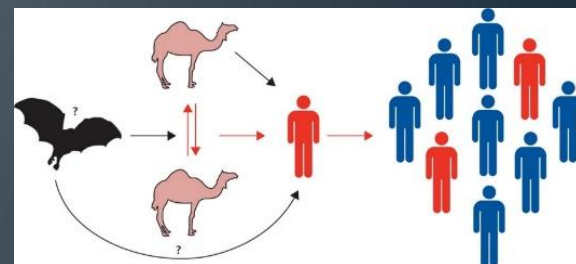
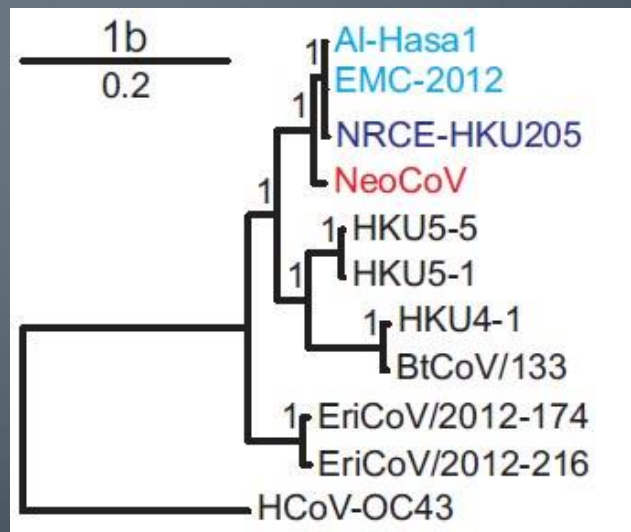
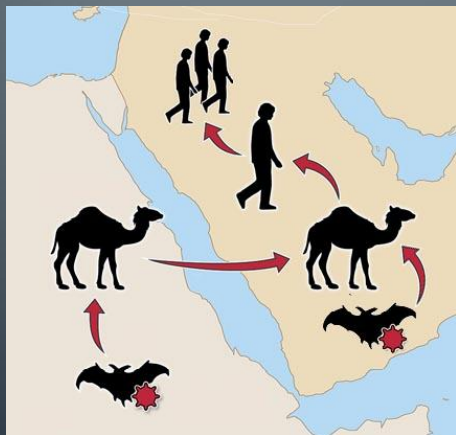


MERS-Coronavírus



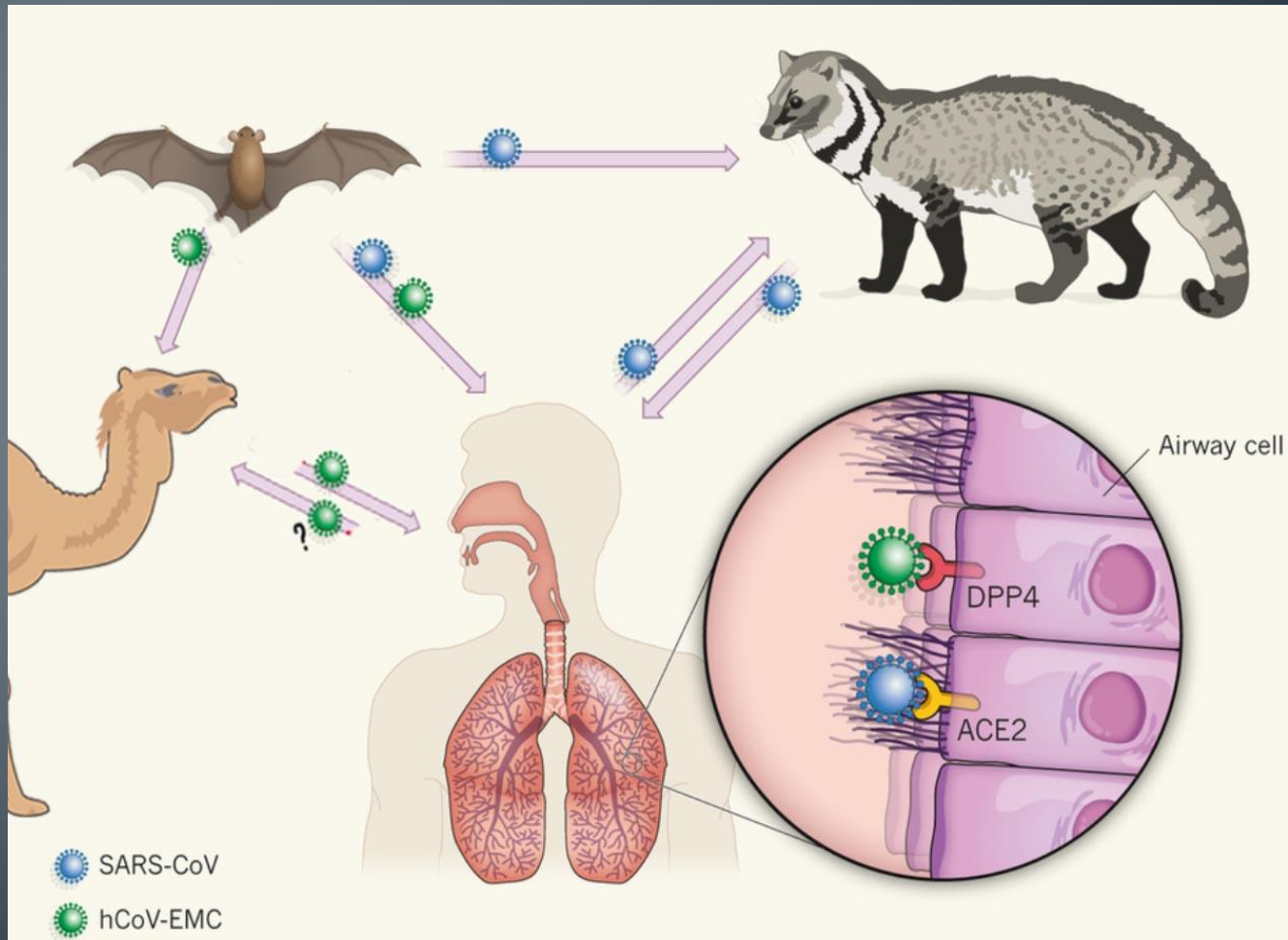
❖ Evidências da origem zoonótica

1. Alta relação filogenética com CoV de morcegos (HKU-4; HKU-5)
2. Detecção de RNA viral e obtenção de vírus infectantes de camelos
3. Observação da presença de Anticorpos contra CoV-MERS em amostras de sangue de camelo obtidas em diferentes países e datadas de até 20 anos anterior a descoberta viral
4. Detecção de vírus de alta similaridade em morcegos
 - ✓ *Taphozous perforates* do Reino da Arábia Saudita
 - ✓ *Neoromicia capensis* da África do Sul (85,6% de identidade nt).



Coronavirus CoV-SARS e CoV-MERS em morcegos

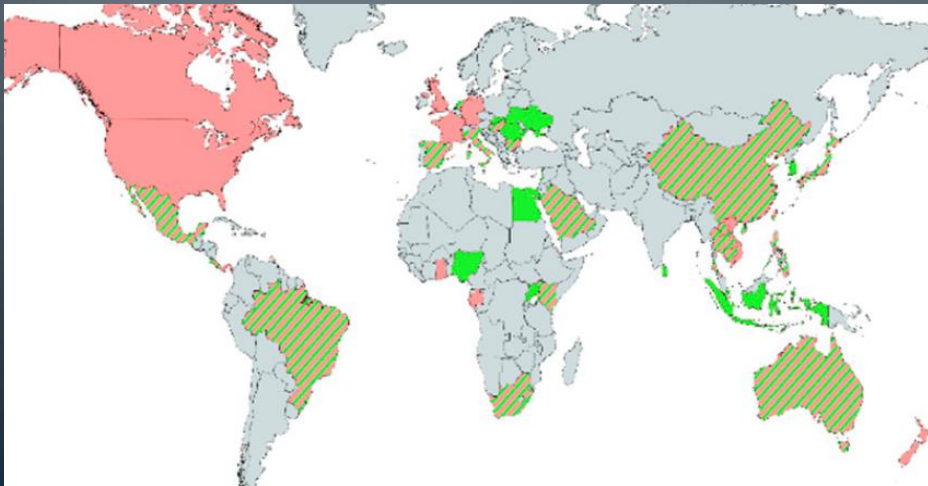
- ❖ CoV com **alta similaridade genética** e capaz de **utilizarem o mesmo recetor** de SARS e MERS já foram encontrados em morcegos



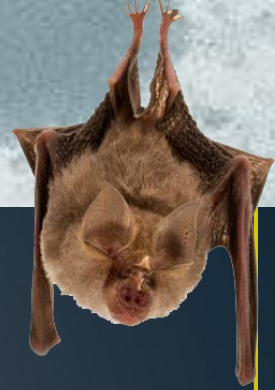
Coronavírus e Morcegos



- Até a descoberta do CoV-SARS em 2002 não era conhecido a relação entre coronavirus e morcegos.
- Após a epidemia de SARS novos coronavirus humanos foram descobertos, sendo dois endêmicos e não zoonóticos e 2 zoonóticos emergentes (CoV-MERS e New CoV 2019)
- Atualmente 7 CoV são capazes de infectar humanos
- Estudos de vigilância de CoV em morcegos foram realizados em diferentes morcegos do mundo e atualmente estes são reconhecidos como hospedeiros reservatórios de CoV e certamente comportaram CoV ancestrais de diferentes mamíferos.

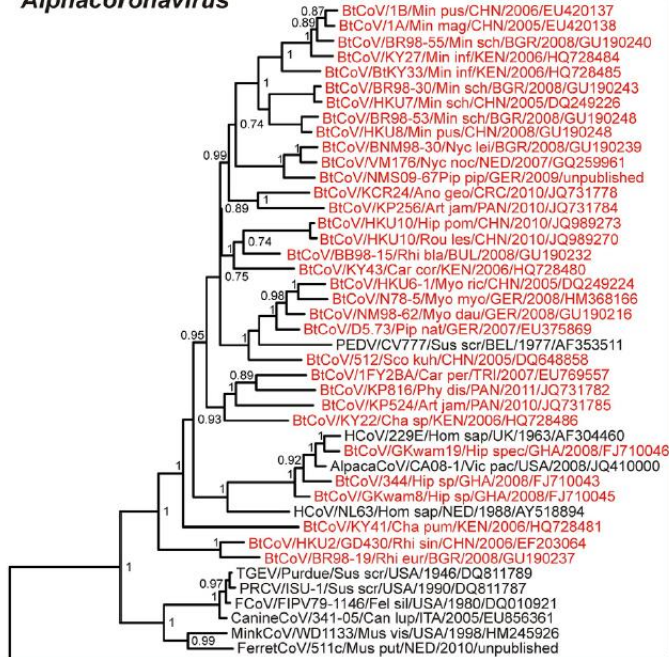


Coronavírus de Morcegos



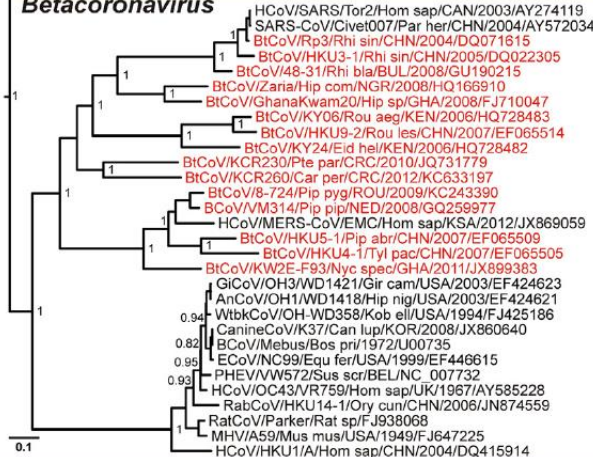
ICTV coronavirus species

Alphacoronavirus



- ↳ *Miniopterus bat coronavirus 1*
- ↳ *Miniopterus bat coronavirus HKU8*
- ↳ *Porcine epidemic diarrhea virus*
- ↳ *Scotophilus bat coronavirus 512*
- ↳ *Human coronavirus 229E*
- ↳ *Human coronavirus NL63*
- ↳ *Rhinolophus HKU2*
- ↳ *Alphacoronavirus 1*

Betacoronavirus



- ↳ *Severe acute respiratory syndrome-related coronavirus*
- ↳ *Roussettus bat coronavirus HKU9*
- ↳ *Middle East respiratory syndrome coronavirus*
- ↳ *Pipistrellus bat coronavirus HKU5*
- ↳ *Tylonycteris bat coronavirus HKU4*
- ↳ *Betacoronavirus 1*
- ↳ *Murine coronavirus*
- ↳ *Human coronavirus HKU1*



Drexler JF, et l. 2013.

Conclusões gerais

1. Morcegos apresentam a maior diversidade genética de coronavírus quando comparado a todos os outros mamíferos e são, provavelmente, os reservatórios naturais e ancestrais de todos coronavírus de mamíferos.
2. Alguns coronavírus de morcegos evoluem e infectam novas espécies.
3. Uma grande diversidade de CoV similares ao SARS-CoV circulam em morcegos da China e Europa e mutações em seu gene Spike permite a infecção de novos hospedeiros
4. Alguns Coronavírus de morcegos similares ao SARS-CoV utilizam o mesmo receptor deste (ex: New CoV 2019), o que pode permitir uma transmissão direta destes virus para humanos e outros animais.
5. Morcegos são os prováveis reservatórios do CoV-MERS e do novo Coronavírus 2019.
6. Uma grande diversidade de CoV com potencial zoonótico desconhecido já foram detectados em morcegos de diferentes espécies por todo o globo, incluindo no Brasil e um número maior aguarda ser descoberto.
7. A transmissão de coronavírus animais para humanos vai continuar ocorrendo . Estudos de vigilância e entendimento de eventos de spillover, assim como estratégias de diagnóstico rápido e avaliação da ocorrência destes eventos devem ser estimulados, inclusive em território nacional.

Ecology of zoonoses: natural and unnatural histories

William B Karesh, Andy Dobson, James O Lloyd-Smith, Juan Lubroth, Matthew A Dixon, Malcolm Bennett, Stephen Aldrich, Todd Harrington, Pierre Formenty, Elizabeth H Loh, Catherine C Machalaba, Mathew Jason Thomas, David L Heymann

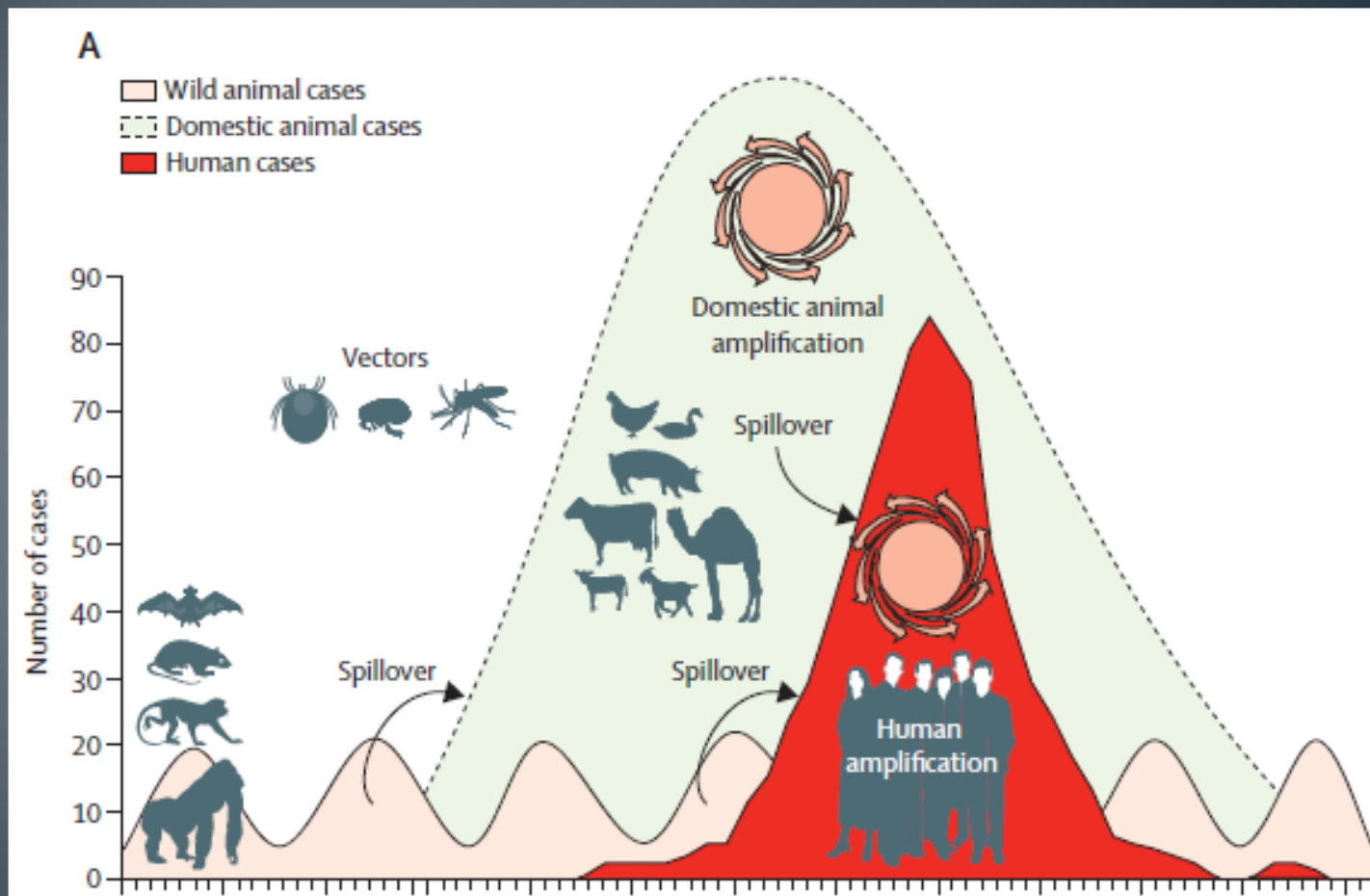
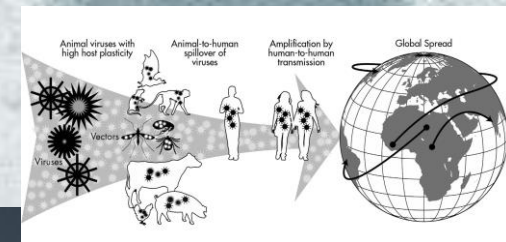


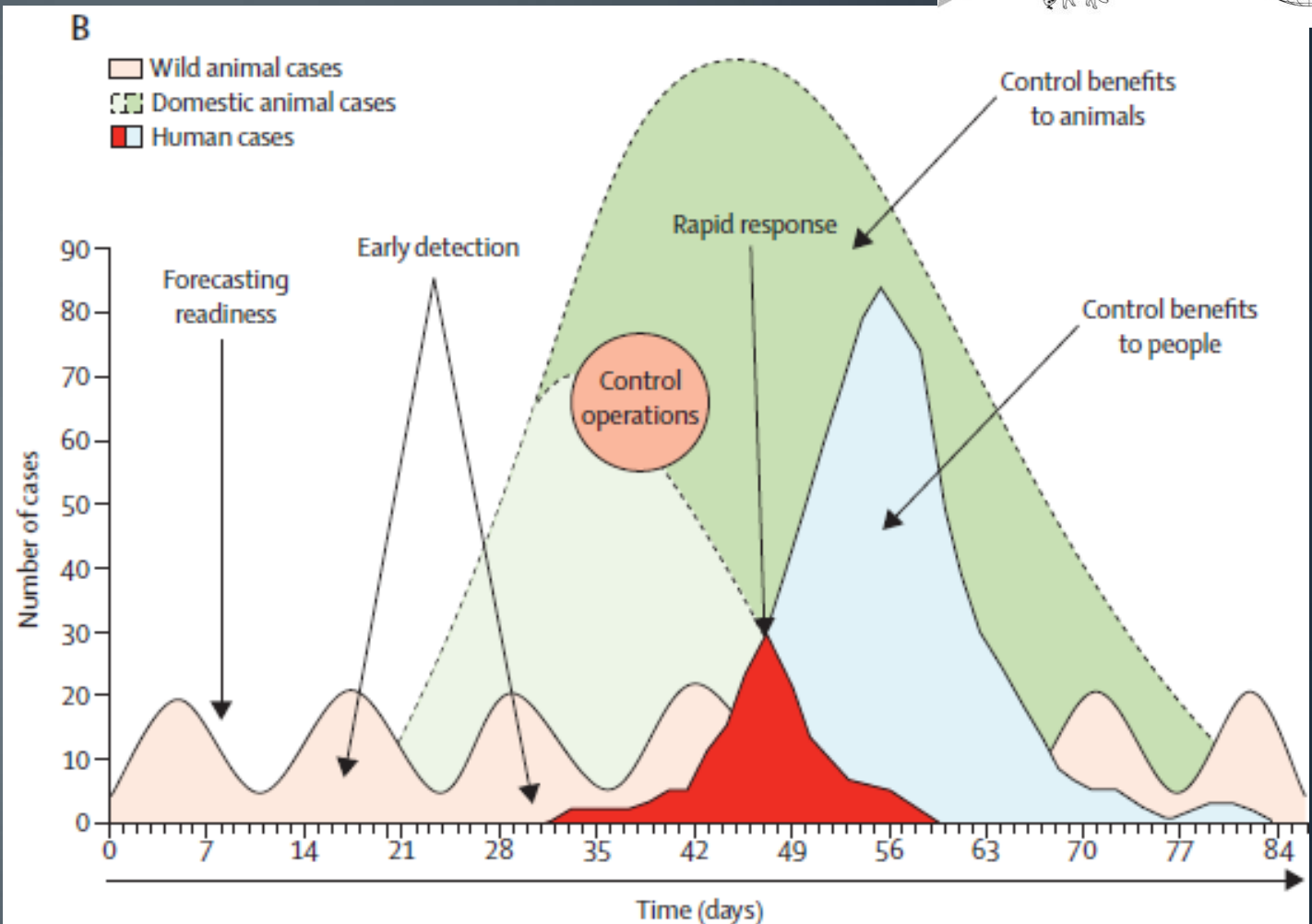
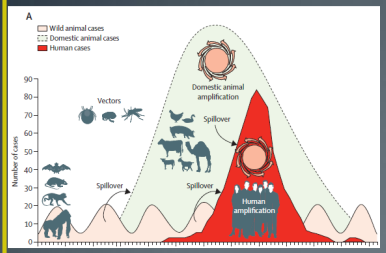
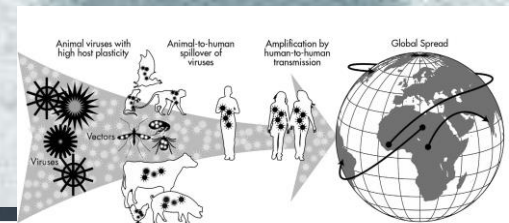
Figure: Clinical relevance of disease ecology

(A) Transmission of infection and amplification in people (bright red) occurs after a pathogen from wild animals (pink) moves into livestock to cause an outbreak (light green) that amplifies the capacity for pathogen transmission to people.

Zoonoses 1

Ecology of zoonoses: natural and unnatural histories

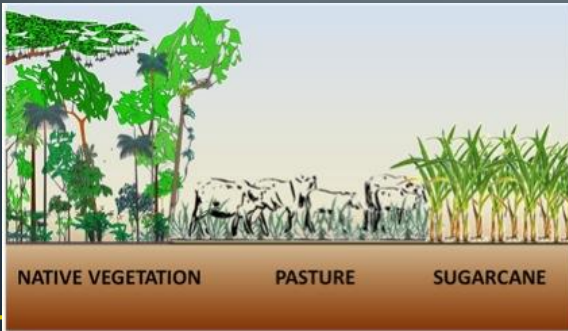
William B Karesh, Andy Dobson, James O Lloyd-Smith, Juan Lubroth, Matthew A Dixon, Malcolm Bennett, Stephen Aldrich, Todd Harrington, Pierre Formenty, Elizabeth H Loh, Catherine C Machalaba, Mathew Jason Thomas, David L Heymann



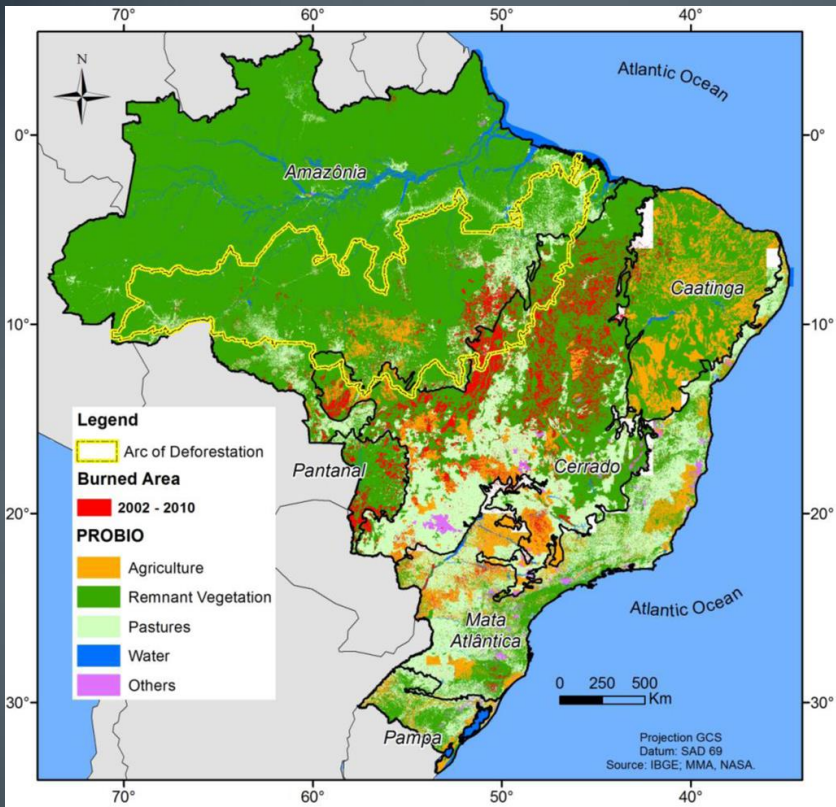
(B) Early detection and control efforts reduce disease incidence in people (light blue) and animals (dark green). Spillover arrows shows cross-species transmission.

Drivers of the Emergence of zoonotic EID

- **Emergence of virus from nature** are consequence of relation between:
 1. **Viral evolution factors** (ex: rate of mutation or replication aspects)
 2. **Increase of contact between humans, livestock and animal reservoirs**
Usually related with anthropogenic activities and environment changes as:
 - **Intensification of agriculture**
 - **Urbanization**
 - **Deforestation**
 - **Habitat alteration**
 - **Human encroachment on wildlife habitat**
 - **Wildlife animal consumption behavior**
 - **Others factors can increase the risk for emergence of zoonotic EID as local richness of mammals and biodiversity lost**



Drivers of the Emergence of zoonotic EID in Brazil



- Distinct biomes are under anthropogenic threatens
 1. Intensification of agriculture
 2. Intensification of livestock production
 3. Deforestation
- Brazil is in the map of local global hotspot for EID

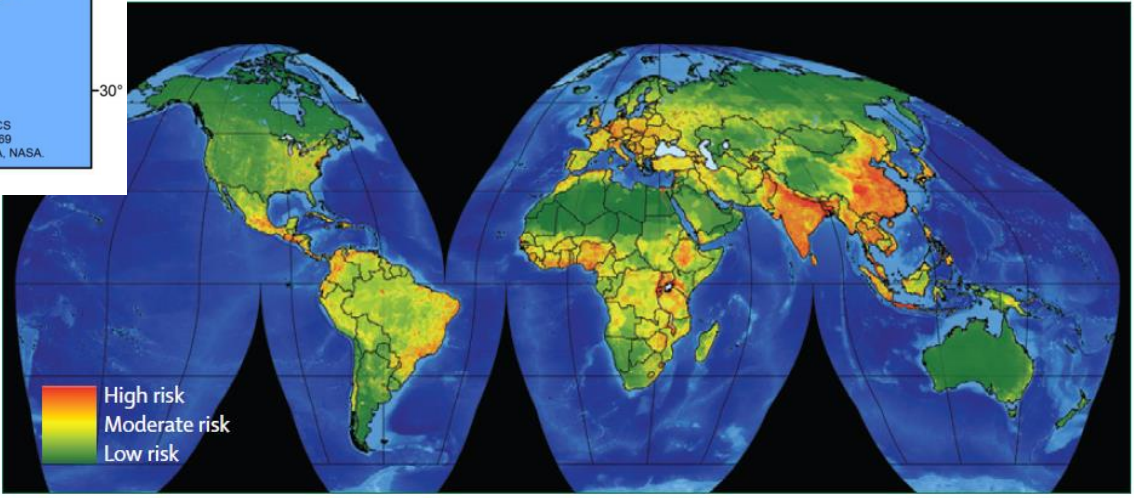
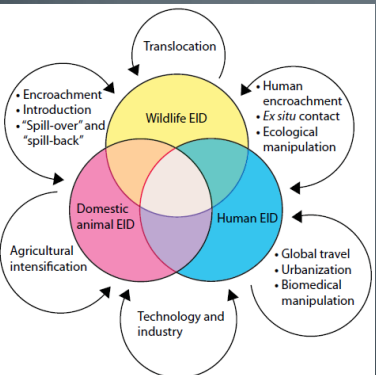
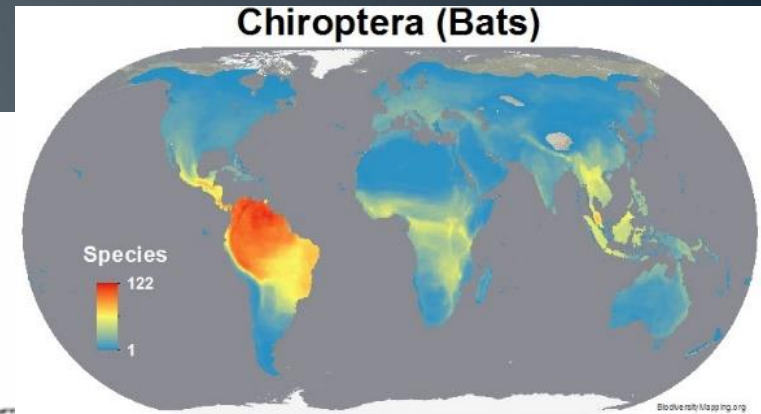
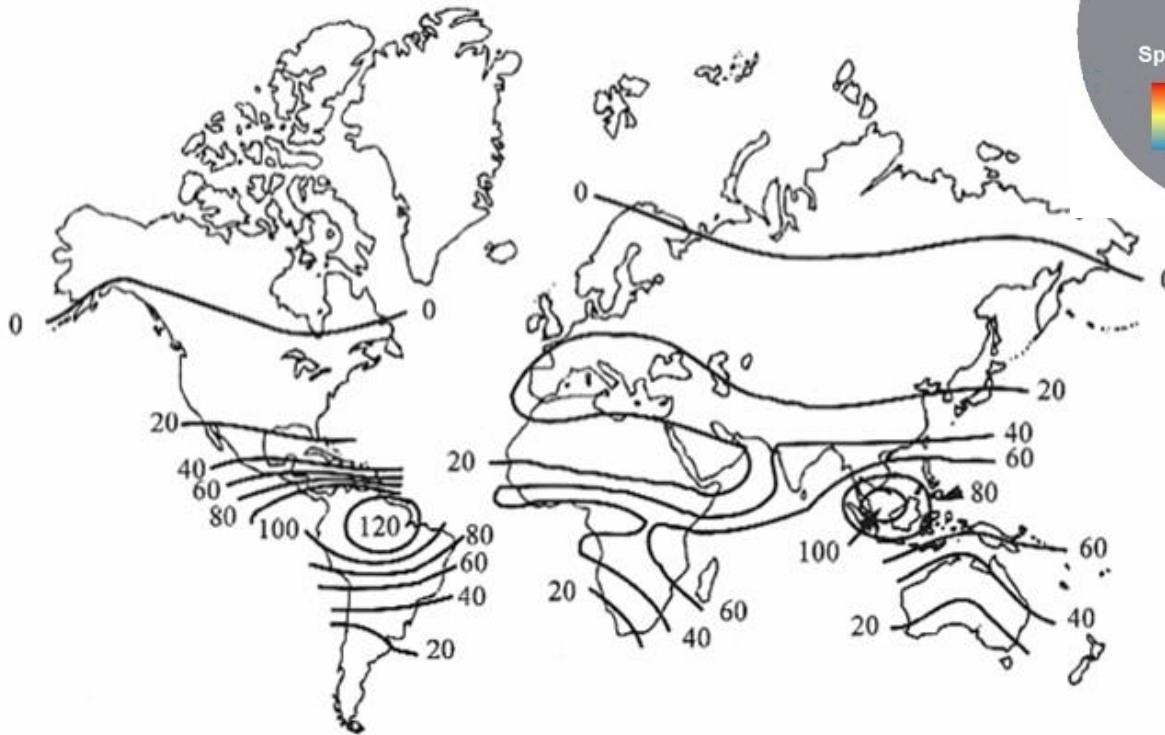


Figure 1: Global hotspots for emerging infectious diseases that originate in wildlife

Bat Diversity in Brazil

- Brazil host 183 bats species of the world (~15% world diversity)
 - 9 bat families
 - 68 genera

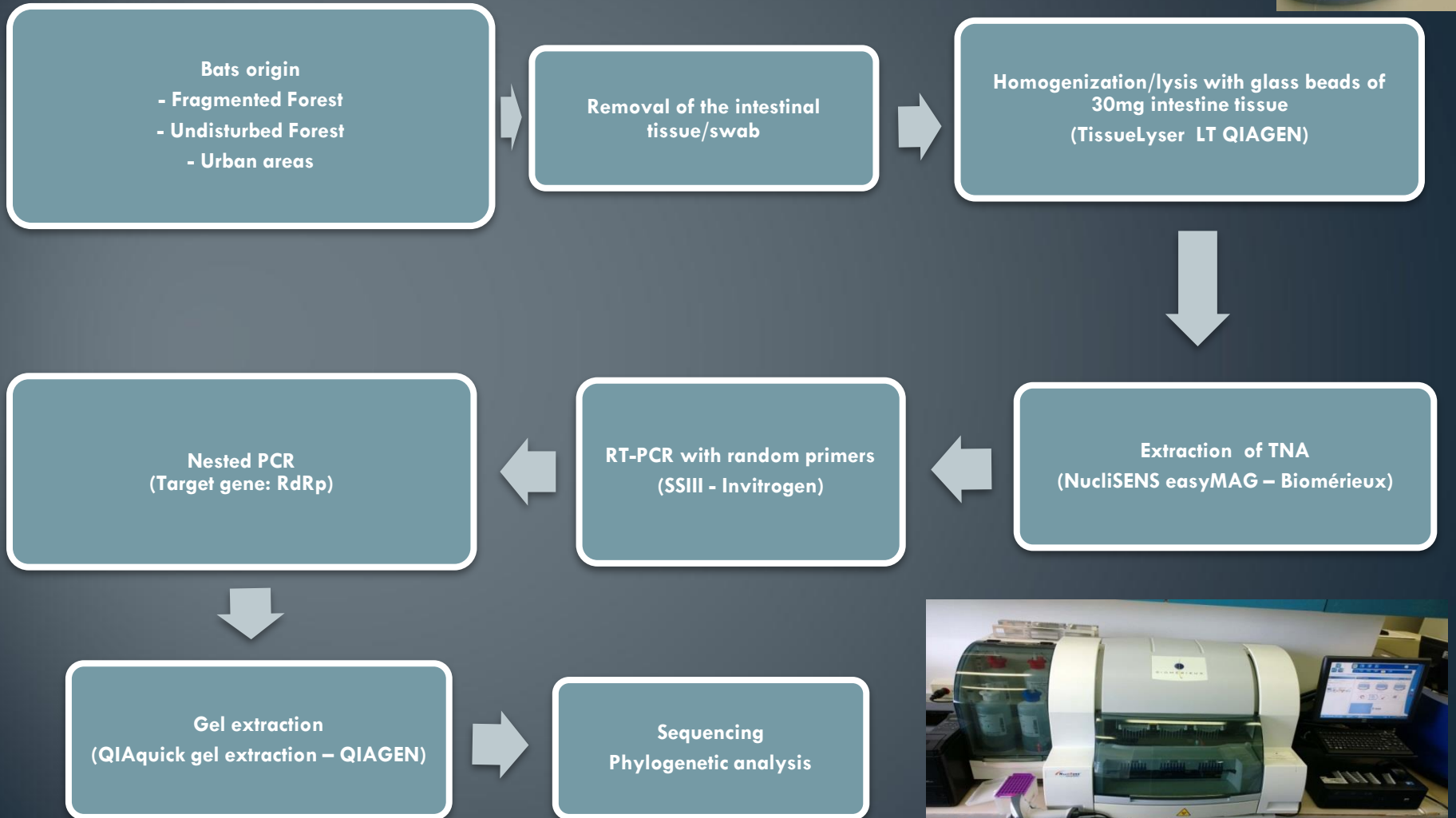
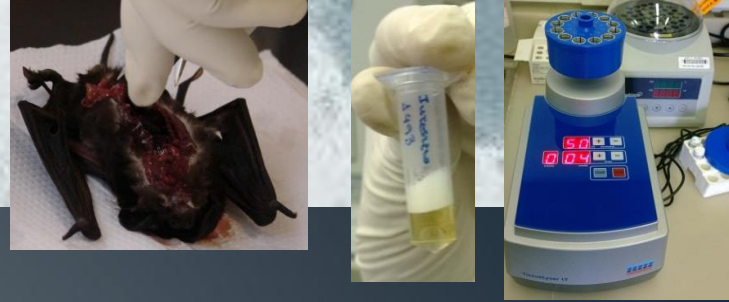
Bat species diversity



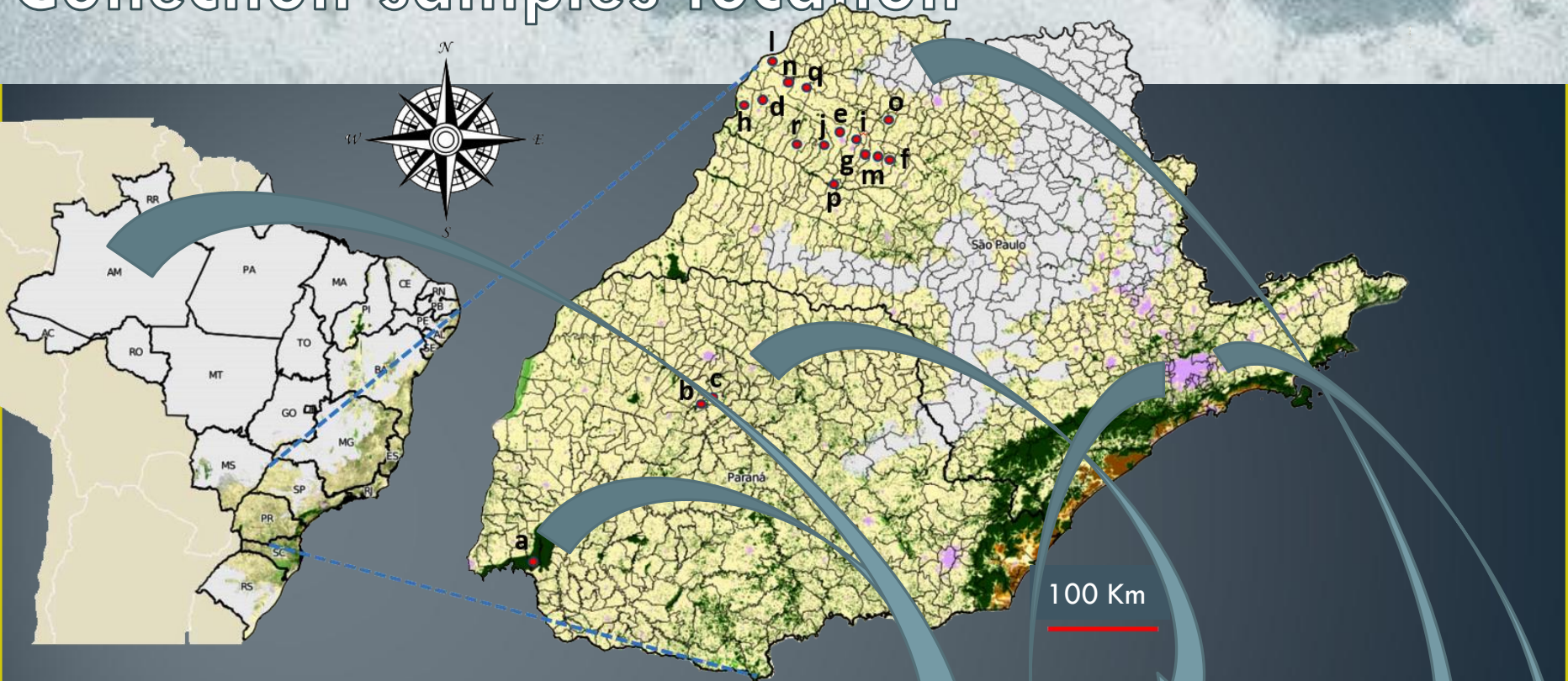
- 113 of bat species are found in the area of Atlantic Forest.

Fig. 1.11. The number of bat species in 500 km² quadrats in different parts of the world (adapted from Findley, 1993).

Materials and Methods



Collection samples location



Undisturbed forest remnant area

1. Iguaçu National Park-PR (185,262.5 ha)
2. Amazon forest

Fragmented forests areas

3. Central of PR state (Farms and sugar cane plantations)
4. Forest fragments inside São Paulo city

Urban areas

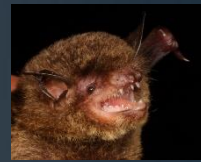
5. Northwest of SP state
6. Urbans areas for Metropolitan area of São Paulo



List of Bats species screened for CoV



Bat species	N° of ind. Analyzed	Diet	Family	N° of Positives	Biome	Urban Area		Urban Frag. forest-SP / N Pos	Frag Forest - PR / N Pos	Continuous forest AF/N Pos	Continuous forest AM. /N Pos
						NW SP / N Pos	SE SP / N Pos				
<i>Ametrida centurio</i>	1	Frugivorous	Phyllostomidae	0	AM	0	0	0	0	0	1
<i>Anoura caudifer</i>	1	Frugivorous	Phyllostomidae	0	AM	0	0	0	0	0	1
<i>Artibeus concolor</i>	1	Frugivorous	Phyllostomidae	0	AM	0	0	0	0	0	1
<i>Artibeus fimbriatus</i>	6	Frugivorous	Phyllostomidae	0	AF	0	0	3	0	3	0
<i>Artibeus lituratus</i>	149	Frugivorous	Phyllostomidae	4 (2,7%)	AM / AF	6	3	18/1	59/1	61/2	2
<i>Artibeus obscurus</i>	2	Frugivorous	Phyllostomidae	0	AF	1	0	1	0	0	0
<i>Artibeus planirostris</i>	11	Frugivorous	Phyllostomidae	0	AM / AF	1	0	4	1	2	3
<i>Carollia benkeithi</i>	1	Frugivorous	Phyllostomidae	0	AM	0	0	0	0	0	1
<i>Carollia brevicauda</i>	2	Frugivorous	Phyllostomidae	0	AM	0	0	0	0	0	2
<i>Carollia perspicillata</i>	120	Frugivorous	Phyllostomidae	5 (4,2%)	AM / AF	0	0	10	32/3	12	66/2
<i>Chropterus auritus</i>	2	Carnivorous	Phyllostomidae	0	AM	0	0	0	0	0	2
<i>Cynomops planirostris</i>	6	Insectivorous	Molossidae	0	AF	0	6	0	0	0	0
<i>Dermanura gnoma</i>	1	Frugivorous	Phyllostomidae	0	AM	0	0	0	0	0	1
<i>Desmodus rotundus</i>	19	Hematophagous	Phyllostomidae	0	AM / AF	10	5	2	0	0	2
<i>Diphylla ecaudata</i>	1	Hematophagous	Phyllostomidae	0	AF	0	0	1	0	0	0
<i>Eptesicus furinalis</i>	9	Insectivorous	Vespertilionidae	0	AF	5	3	1	0	0	0
<i>Eumops auripendulus</i>	1	Insectivorous	Molossidae	0	AF	0	1	0	0	0	0
<i>Eumops glaucinus</i>	43	Insectivorous	Molossidae	1 (2,3%)	AF	27/1	16	0	0	0	0
<i>Eumops laucinus</i>	1	Insectivorous	Molossidae	0	AF	0	1	0	0	0	0
<i>Eumops perotis</i>	8	Insectivorous	Molossidae	0	AF	0	8	0	0	0	0
<i>Glossophaga soricina</i>	55	Nectivorous	Phyllostomidae	3 (5,5%)	AF/AM	3/1	24	27/2	0	0	1
<i>Histiotus velatus</i>	1	Nectivorous	Phyllostomidae	0	AF	0	0	1	0	0	0
<i>Lasiurus cinereus</i>	1	Insectivorous	Vespertilionidae	0	AF	1	0	0	0	0	0
<i>Lasiurus ega</i>	1	Insectivorous	Vespertilionidae	0	AF	0	1	0	0	0	0
<i>Lonchophylla thomasi</i>	1	Omnivorous	Phyllostomidae	0	AM	0	0	0	0	0	1
<i>Lophostoma silviculum</i>	3	Nectivorous	Phyllostomidae	0	AM	0	0	0	0	0	1
<i>Micronycteris hirsuta</i>	2	Insectivorous	Phyllostomidae	0	AM	0	0	0	0	0	2



List of Bats species screened for CoV



Bat species	Nº of ind. Analyzed	Diet	Family	Nº of Positives	Biome	Urban Area	Urban Area	Urban	Continuous		Continuous
						NW SP / N Pos	SE SP / N Pos	forest-SP / N Pos	Frag Forest forest AF/N forest AM.	forest AF/N forest AM.	
<i>Mimon crenulatum</i>	20	Insectivorous	Phyllostomidae	1 (5%)	AM	0	0	0	0	0	20/1
<i>Molossops neglectus</i>	1	Insectivorous	Molossidae	0	AF	0	0	1	0	0	0
<i>Molossus molossus</i>	115	Insectivorous	Molossidae	0	AF	80	35	0	0	0	0
<i>Molossus rufus</i>	63	Insectivorous	Molossidae	2 (3,2%)	AF	56/2	7	0	0	0	0
<i>Myotis nigricans</i>	24	Insectivorous	Verperilionidae	1 (4,2%)	AM / AF	8/1	5	6	0	0	5
<i>Myotis riparius</i>	1	Insectivorous	Verperilionidae	1 (100%)	AF	1/1	0	0	0	0	0
<i>Myotis ruber</i>	3	Insectivorous	Verperilionidae	0	AF	0	0	3	0	0	0
<i>Nyctinomops laticaudatus</i>	3	Insectivorous	Molossidae	0	AF	0	3	3	3	3	3
<i>Nyctinomops macrotis</i>	1	Insectivorous	Molossidae	0	AF	0	1	0	0	0	0
<i>Phyllostomus discolor</i>	5	Omnivorous	Phyllostomidae	1 (20%)	AM	0	2/1	0	0	0	3
<i>Phyllostomus elongatus</i>	5	Frugivorous	Phyllostomidae	0	AM	0	0	0	0	0	5
<i>Phyllostomus hastatus</i>	2	Omnivorous	Phyllostomidae	0	AM	0	0	0	0	0	2
<i>Platyrrhinus lineatus</i>	11	Frugivorous	Phyllostomidae	0	AF	3	1	7	0	0	0
<i>Platyrrhinus sp.</i>	1	Frugivorous	Phyllostomidae	0	AM	0	0	0	0	0	1
<i>Promops nasutus</i>	1	Insectivorous	Molossidae	0	AF	0	1	0	0	0	0
<i>Pteronotus parnellii</i>	36	Insectivorous	Mormoopidae	0	AM	0	0	0	0	0	36
<i>Pygoderma bilabiatum</i>	5	Frugivorous	Phyllostomidae	0	AF	0	0	5	0	0	0
<i>Rhinophylla fischeræ</i>	5	Frugivorous	Phyllostomidae	0	AM	0	0	0	0	0	5
<i>Rhinophylla pumillio</i>	12	Frugivorous	Phyllostomidae	0	AM	0	0	0	0	0	12
<i>Saccopteryx bilineata</i>	1	Insectivorous	Emballonuridae	0	AM	0	0	0	0	0	1
<i>Sturnira lilium</i>	56	Frugivorous	Phyllostomidae	7 (12,4%)	AF	0	0	24/4	6/1	22/2	4
<i>Sturnira tildæ</i>	5	Frugivorous	Phyllostomidae	0	AM/AF	0	0	3	0	0	2
<i>Tadarida brasiliensis</i>	9	Insectivorous	Molossidae	0	AF	0	9	0	0	0	0
<i>Tonatia saurophila</i>	2	Omnivorous	Phyllostomidae	0	AM	0	0	0	0	0	2
<i>Trachops cirrhosus</i>	1	Carnivorous	Phyllostomidae	0	AM	0	0	0	0	0	1
<i>Vampyressa pusilla</i>	1	Frugivorous	Phyllostomidae	0	AF	0	0	0	1	0	0
TOTAL	840	5	5	26 (3,1%)	2	202/6	132/1	119/7	99/5	100/4	188/3

- 840 samples analyzed (intestine_533, rectal and oral swabs_307)
- 54 bat species (14 species N samples > 10), 5 distinct diets
- 5 bat families (Phyllostomidae, Vespertilionidae, Molossidae, Mormoopidae, Emballonuridae)

List and information's of CoV positive bat samples detected in our study.



Sample ID	Bat species	CoV Genus	Bat family	Gender	Ecol. Chact.	Year
2064	<i>Artibeus lituratus</i>	β-CoV "C"	Phyllostomidae	F	Continuous forest - PR	2011
1816	<i>Artibeus lituratus</i>	α-CoV	Phyllostomidae	F	Fragmented forest - PR	2010
2294	<i>Artibeus lituratus</i>	α-CoV	Phyllostomidae	F	Continuous forest - PR	2012
157	<i>Artibeus lituratus</i>	α-CoV	Phyllostomidae	M	Urban fragmented forest - SP	2013
1514	<i>Carollia perspicillata</i>	α-CoV	Phyllostomidae	M	Fragmented forest - PR	2011
1516	<i>Carollia perspicillata</i>	α-CoV	Phyllostomidae	M	Fragmented forest - PR	2011
1599	<i>Carollia perspicillata</i>	α-CoV	Phyllostomidae	F	Fragmented forest - PR	2012
2079	<i>Carollia perspicillata</i>	α-CoV	Phyllostomidae	?	Continuous forest-AM	2014
2087	<i>Carollia perspicillata</i>	α-CoV	Phyllostomidae	?	Continuous forest-AM	2014
242	<i>Eumops glaucinus</i>	β-CoV "C"	Molossidae	F	Urban area – NW SP	2013
100	<i>Glossophaga soricina</i>	α-CoV	Phyllostomidae	M	Urban area – NW SP	2013
158	<i>Glossophaga soricina</i>	α-CoV	Phyllostomidae	M	Urban fragmented forest - SP	2013
163	<i>Glossophaga soricina</i>	α-CoV	Phyllostomidae	M	Urban fragmented forest - SP	2013
2111	<i>Mimon crenulatum</i>	α-CoV	Phyllostomidae	?	Continuous forest-AM	2014
92	<i>Molossus rufus</i>	α-CoV	Molossidae	F	Urban area – NW SP	2013
63	<i>Molossus rufus</i>	α-CoV	Molossidae	M	Urban area – NW SP	2014
117	<i>Myotis nigricans</i>	α-CoV	Vespertilionidae	M	Urban area – NW SP	2013
259	<i>Myotis riparus</i>	α-CoV	Vespertilionidae	F	Urban area – NW SP	2013
2442	<i>Phyllostomus discolor</i>	α-CoV	Phyllostomidae	F	Urban area – SE SP	2014
1573	<i>Sturnira lilium</i>	α-CoV	Phyllostomidae	F	Fragmented forest - PR	2012
1613	<i>Sturnira lilium</i>	α-CoV	Phyllostomidae	F	Continuous forest - PR	2012
1617	<i>Sturnira lilium</i>	α-CoV	Phyllostomidae	F	Continuous forest - PR	2012
150	<i>Sturnira lilium</i>	α-CoV	Phyllostomidae	F	Urban fragmented forest - SP	2013
152	<i>Sturnira lilium</i>	α-CoV	Phyllostomidae	M	Urban fragmented forest - SP	2013
313	<i>Sturnira lilium</i>	α-CoV	Phyllostomidae	M	Urban fragmented forest - SP	2014
314	<i>Sturnira lilium</i>	α-CoV	Phyllostomidae	M	Urban fragmented forest - SP	2014

. 26/840 positive samples (3,1%)

. 10 bat species positive for CoV RNA

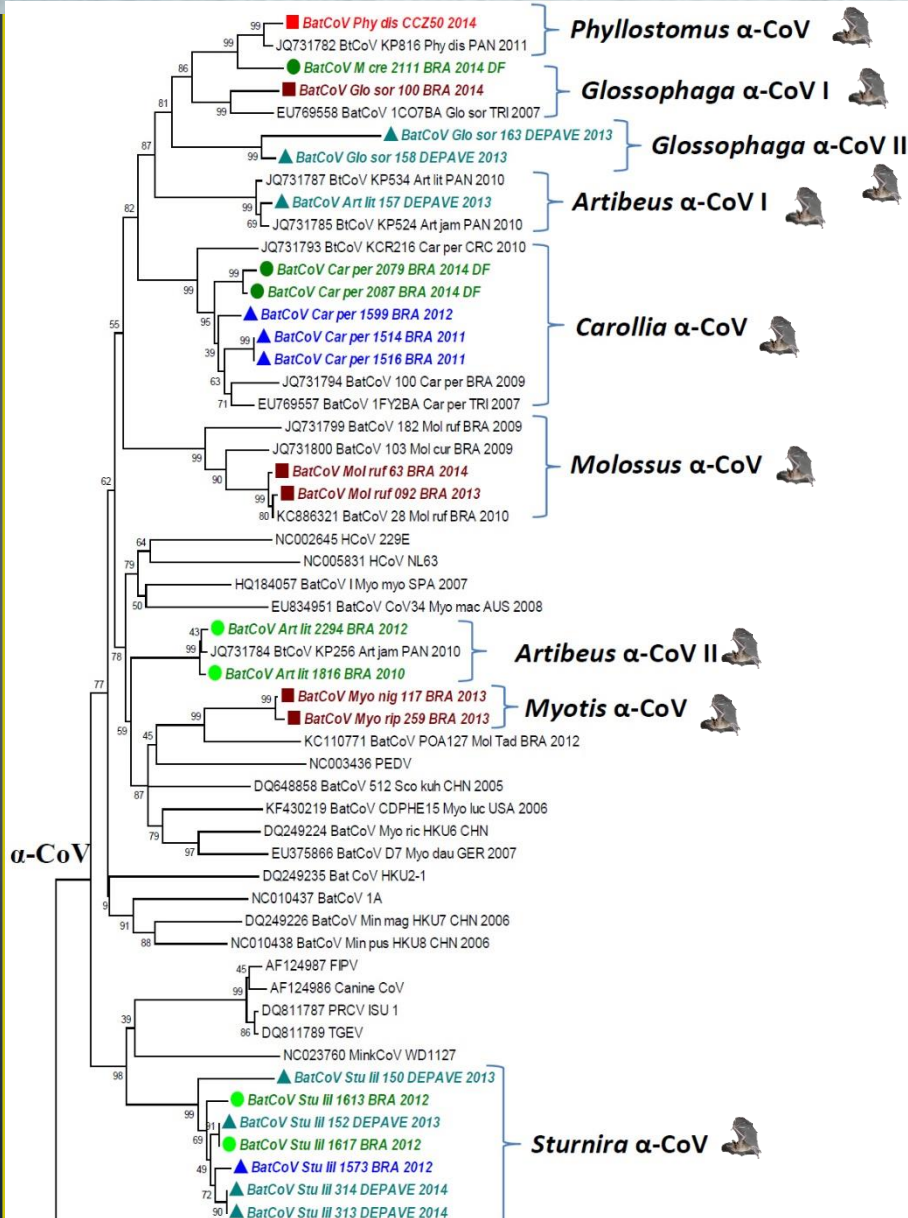
. BatCoVs circulate in all ecologic gradients analyzed

. 11 CoV genotypes (3 potential new CoVs)

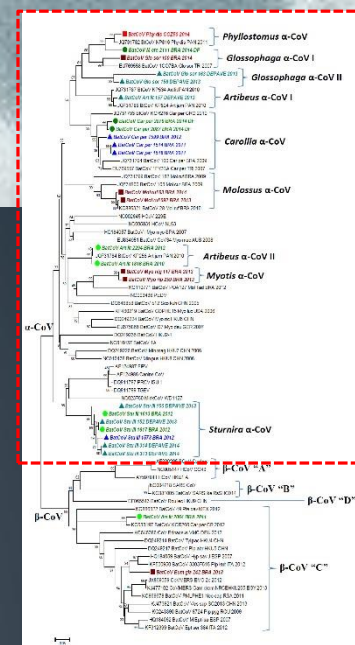
. 24 α-CoV / 2 β-CoV "c"



α- BatCoVs detected



- 8 bat genus pos. for CoV
- 2 distincts α-CoV Artibeus
- 24 samples pos for α-CoV



Amplicon: **394 bp** (440 less the primers)

The evolutionary history was inferred using the **Neighbor-Joining method**

The percentage of replicate trees in which the associated taxa clustered together in the **bootstrap test** (1000 replicates)

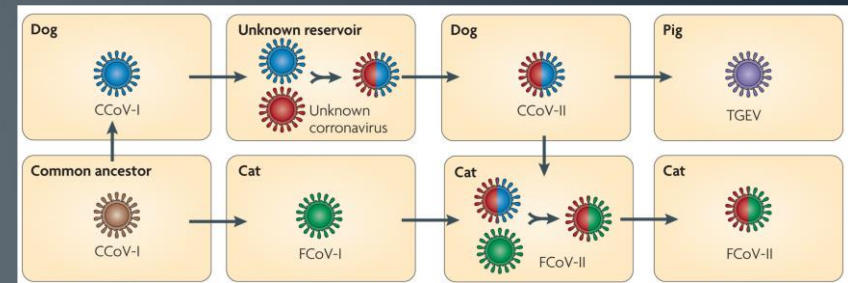
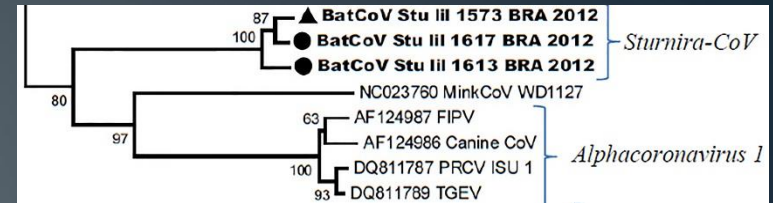
The evolutionary distances were computed using the **Maximum Composite Likelihood method**.

Program: **Mega 7**

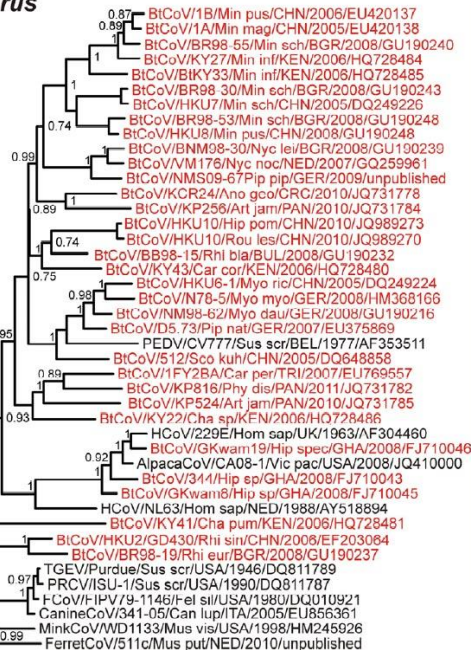
- Continuous Forest/Atlantic Forest (PR)
- Continuous Forest/Amazon (AM)
- ▲ Forest Fragment/Atlantic Forest (PR)
- ▲ Urban Forest Fragment/ Atlantic Forest (SP)
- Urban area/Northwest São Paulo state (SP)
- Urban area/Southeast São Paulo state (SP)

Bat Alphacoronavirus 1? Possible missing link?

- New α -CoV related to AlphaCoV 1 virus specie was detected in bats (representing the BatCoV with higher sequence homology with α -CoV lineage 1 described until this moment)
- α -CoV lineage 1 present a history of recombination and cross-species transmission between domestic and livestock animals



Alphacoronavirus



Miniopterus bat coronavirus 1

Miniopterus bat coronavirus HKU8

Porcine epidemic diarrhea virus
Scotophilus bat coronavirus 512

Human coronavirus 229E

Human coronavirus NL63

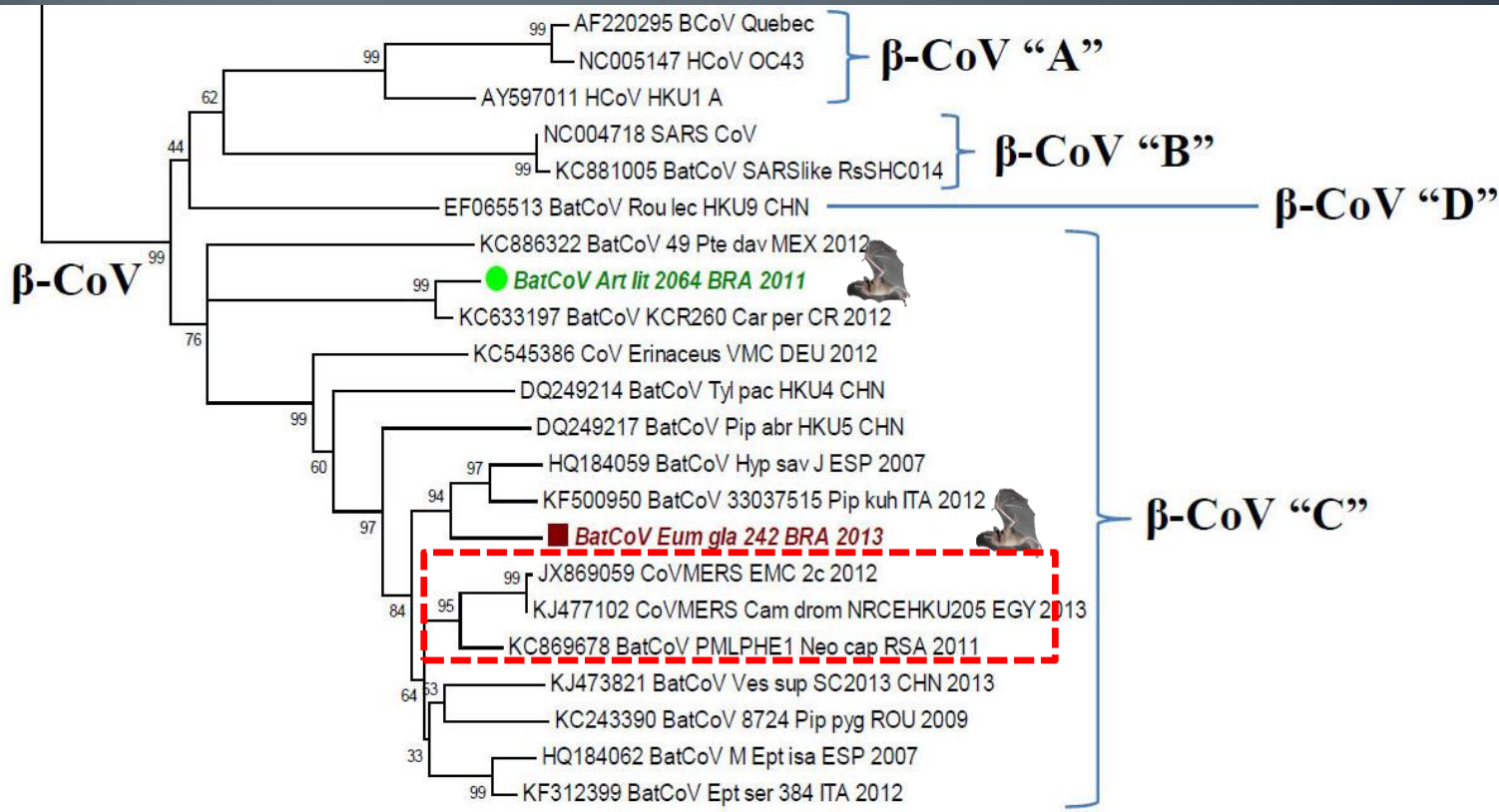
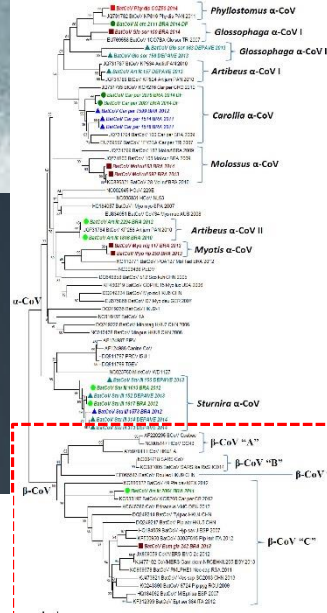
Rhinolophus HKU2

Alphacoronavirus 1

- This result indicate a possible origin of AlphaCoV 1 lineage from bats ancestor CoV

β- BatCoV detected

- . 2 bat genus positive for β-CoV
- . Both β-CoV clade “C”, similar to CoV-MERS



0.05

Lineage C β -CoV in *Eumops*

- First detection of β -CoV lineage C in South America
- Bat positive was found after predated by domestic cat



List of bat species positives for B-CoV C lineage

Bat specie	Family	Local
Pipistrellus pipistrellus	Vespertilionidae	Netherlands
Pipistrellus pigmaeus	Vespertilionidae	Romania
Pipistrellus pigmaeus	Vespertilionidae	Romania
Pipistrellus nathusii	Vespertilionidae	Ukraine
Eptesicus serotinus	Vespertilionidae	Italy
Hypsugo savii	Vespertilionidae	Italy
Nyctalus noctula	Vespertilionidae	Italy
Pipistrellus khuii	Vespertilionidae	Italy
Hypsugo savii	Vespertilionidae	Spain
Nyctalus noctula	Vespertilionidae	Italy
Eptesicus isabellinus	Vespertilionidae	Spain
Vespertilio superans	Vespertilionidae	China
Tylonycteris pachypus	Vespertilionidae	China
Neoromicia capensis	Vespertilionidae	South Africa
Neoromicia cf. zuluensis	Vespertilionidae	South Africa
Nycteris cf. gambiensis	Nycteridae	Gana
Nyctinomops lacticaudatus	Molossidae	Mexico
Tylonycteris pachypus	Vespertilionidae	China
Pipistrellus abramus	Vespertilionidae	China
Taphozous perforatus	Emballonuridae	KSA
Pteronotus davyi	Mormoopidae	Mexico
Carollia perspicillata	Phyllostomidae	Costa Rica
Artibeus lituratus	Phyllostomidae	Brazil
Eumops glaucinus	Molossidae	Brazil

[Infect Genet Evol.](#) 2016 Oct;44:510-513. doi: 10.1016/j.meegid.2016.07.034. Epub 2016 Jul 26.

Genetic diversity of bats coronaviruses in the Atlantic Forest hotspot biome, Brazil.

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Muito Obrigado!

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