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"G. CAPOREALE"

# **Veterinary Intelligence: From Zoonotic Threats to Global Health Preparedness**

**Alessio Lorusso, IZS-Teramo**

**9 Marzo 2024**

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National and International Ref Labs: EURL Rift, FAO CoVs, Exotic diseases

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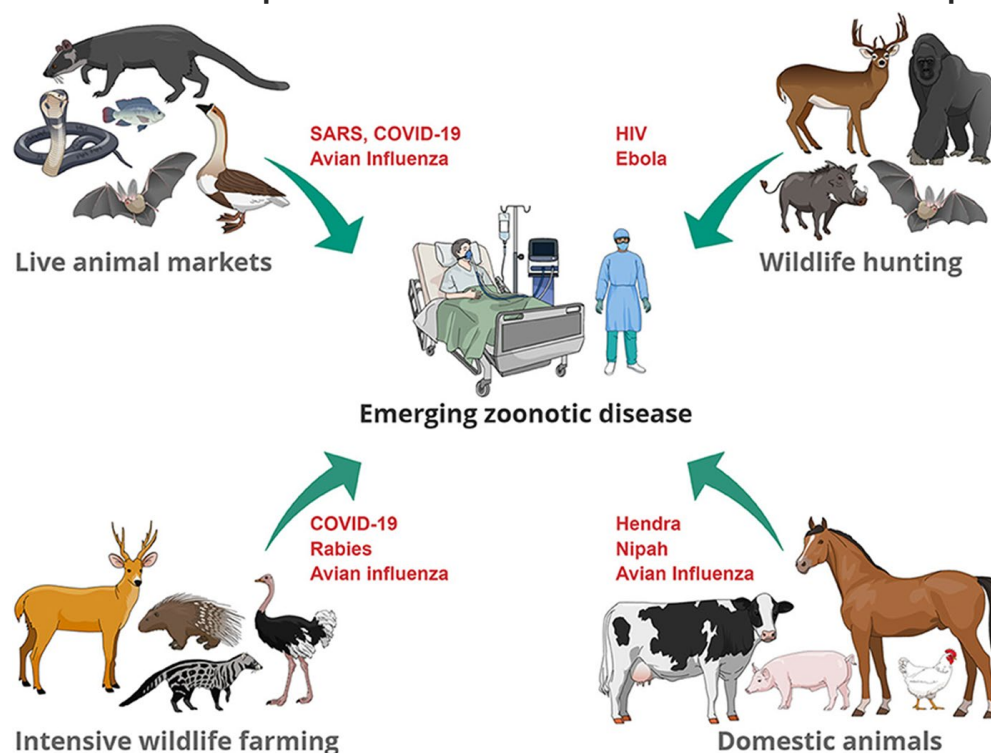
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## Outline

- Current scenario, One health
- Major driver: CoVs, NGS

- Major public health emergencies (SARS; 2002–2004), Ebola (2013–2016), Zika virus (2015–2016), (COVID-19) pandemic
- Since 1970, zoonotic diseases have accounted for more than 75% of emerging and re-emerging ID, leading to 2.5 billion infections and 2.7 million deaths each year
- Lack of cross-cooperation among human, animal and environmental/ecosystem health agencies: scarce prevention and containment of epidemics

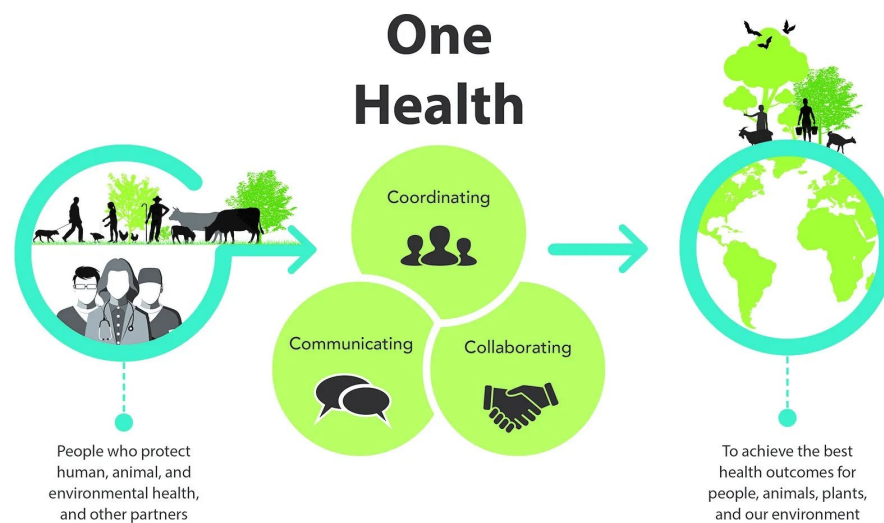


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CS302365-A



Centers for Disease  
Control and Prevention  
National Center for Emerging and  
Zoonotic Infectious Diseases

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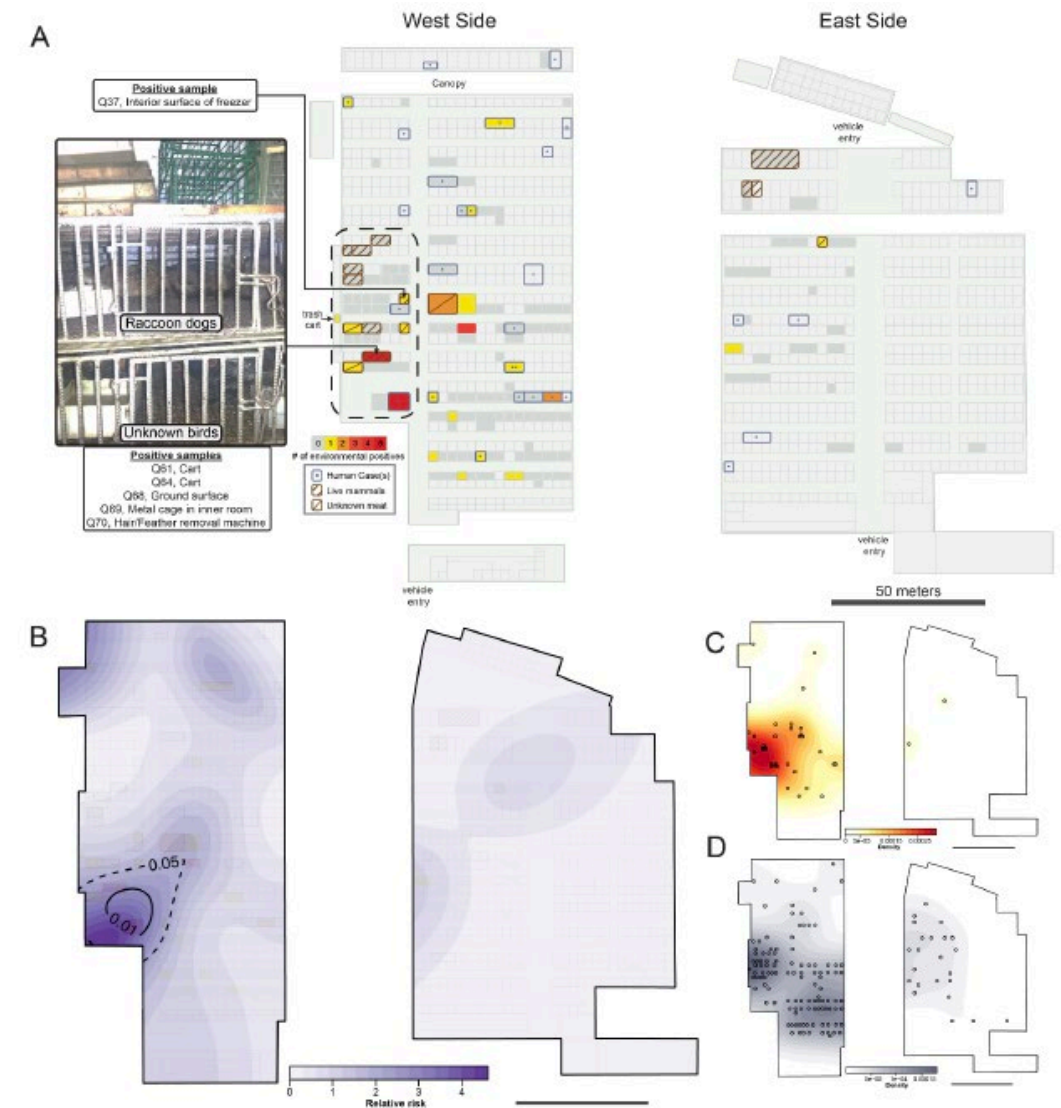
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# Susceptible Wildlife was Sold in the Huanan Market in 2019



- Strong resemblance to the emergence of SARS-CoV-1 in 2002/2003



- Most positive environmental samples (Jan 2020) come from the south-west corner of the market that sold wildlife

# SARS-CoV-2-Like Viruses in *Rhinolophus* Bats

## Article

### Bat coronaviruses related to SARS-CoV-2 and infectious for human cells

<https://doi.org/10.1038/s41586-022-04532-4>

Received: 3 September 2021

Accepted: 8 February 2022

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Check for updates

Sarah Temman<sup>1,2\*</sup>, Khamsing Vongphayloth<sup>3,4\*</sup>, Eduard Baquero<sup>4,5\*</sup>, Sandie Munier<sup>4,6\*</sup>, Massimiliano Bonomi<sup>4,6\*</sup>, Béatrice Regnault<sup>1,2</sup>, Bounsavane Douangboubpha<sup>7</sup>, Yasaman Karami<sup>8</sup>, Delphine Chrétien<sup>1,2</sup>, Daosavanh Sanamxay<sup>7</sup>, Vilakhan Xayaphet<sup>7</sup>, Phetphoumin Paphaphanh<sup>1</sup>, Vincent Lacoste<sup>9</sup>, Somphavanh Somlor<sup>1</sup>, Khaithong Lakeomany<sup>1</sup>, Nothasin Phommavanh<sup>1</sup>, Philippe Pérot<sup>1,2</sup>, Océane Dehan<sup>4,6</sup>, Faustine Amara<sup>4</sup>, Flora Donati<sup>4,6</sup>, Thomas Bigot<sup>1,2</sup>, Michael Nilges<sup>4</sup>, Félix A. Rey<sup>4</sup>, Sylvie van der Werf<sup>4,5</sup>, Paul T. Brey<sup>7</sup> & Marc Eloit<sup>1,2,6,10</sup>

- Banal-20-52, from a *Rhinolophus* in bats from Laos, is the **closest** relative of SARS-CoV-2 (96.8%)
- Very close to SARS-CoV-2 in the receptor binding domain

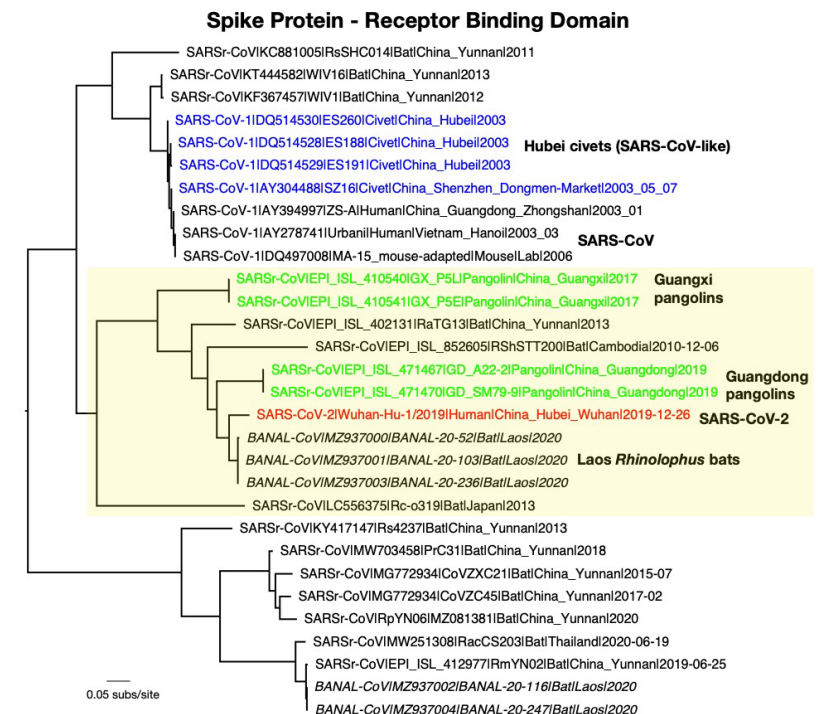
Horseshoe bat  
(*Rhinolophus affinis*)



By Jonathan Corum | Sources: Spyros Lytras et al., Science; Sarah Temman et al., Research Square

Courtesy of the New York Times

## Functional core of SARS-CoV-2 exists in nature



## REVIEWS

### Origin and evolution of pathogenic coronaviruses

Jie Cui<sup>1</sup>, Fang Li<sup>2</sup> and Zheng-Li Shi<sup>1</sup> \*

*....given the prevalence and great genetic diversity of bat SARSr-CoVs, their close coexistence and the frequent recombination of CoVs, it is expected that novel variants will emerge in the future.....*



## Severe Acute Respiratory Syndrome Coronavirus as an Emerging and Reemerging Infection

Vincent C. C. Cheng, Susanna K. P. Lau, Patrick C. Y. Woo, and Kwok Yu

*State Key Laboratory of Emerging Infectious Diseases, Department of Microbiology, Research Centre Immunology, The University of Hong Kong, Hong Kong Special Administrative Region, China*

SARS-CoV AS AN AGENT OF EMERGING/REEMERGING INFECTION 683

or immunization (Table 10). The Koch's postulates for SARS-CoV as a causative agent of SARS were tested in a primate model using cynomolgus macaques (*Macaca fascicularis*), which demonstrated clinical and pathological similarities to those found in humans. In contrast, African green monkeys (*Cercopithecus aethiops*) did not develop significant lung pathology with the SARS-CoV. The lack of consistency between models of rhesus, cynomolgus, and African green monkeys for experimental SARS was noted in another study. However, these large mammals are expensive and difficult to maintain. BALB/c mice demonstrated asymptomatic infection in lungs and nasal turbinates by intranasal inoculation, which was not significantly different from the findings in immunological Th1-biased C57BL/6 mice. BALB/c mice that were 12 to 14 months old developed pneumonia, which correlated with the susceptibility to acute SARS in humans (287). As expected, knockout-immunodeficient mice had fatal disease (143). Transgenic mice expressing ACE2 receptors also developed fatal disease, with dissemination to many organs including the brain. It is interesting that mouse-adapted SARS-

### SHOULD WE BE READY FOR THE REEMERGENCE OF SARS?

The medical and scientific community demonstrated marvelous efforts in the understanding and control of SARS within a short time, as evident by over 4,000 publications available online. Despite these achievements, gaps still exist in terms of the molecular basis of the physical stability and transmissibility of this virus, the molecular and immunological basis of disease pathogenesis in humans, screening tests for early or cryptic SARS cases, foolproof infection control procedures for patient care, effective antivirals or antiviral combinations, the usefulness of immunomodulatory agents for late presenters, an effective vaccine with no immune enhancement, and the immediate animal host that transmitted the virus to caged civets in the market at the beginning of the epidemic. Coronaviruses are well known to undergo genetic recombination (375), which may lead to new genotypes and outbreaks. The presence of a large reservoir of SARS-CoV-like viruses in horseshoe bats, together with the culture of eating exotic mammals in southern China, is a time bomb. The possibility of the reemergence of SARS and other novel viruses from animals or laboratories and therefore the need for preparedness should not be ignored.

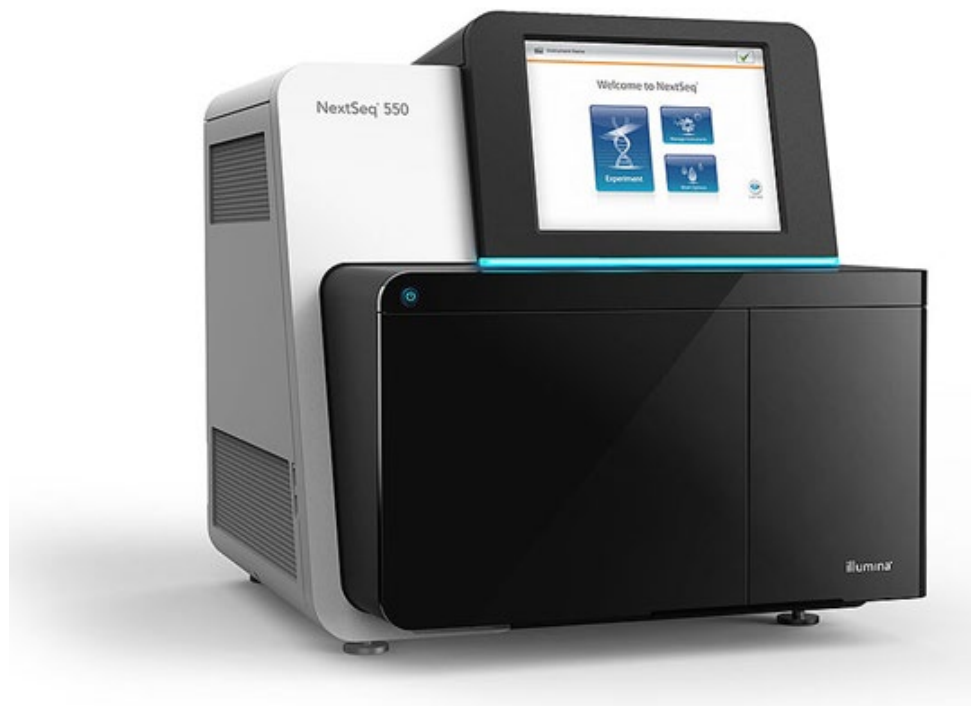
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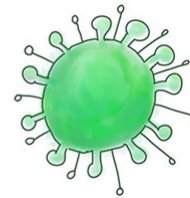
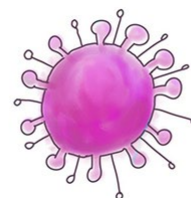
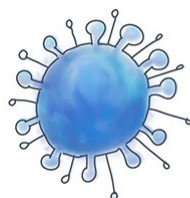
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## Diagnostic/Characterization





- **First CoV identified in bats, 2005; Minunacovirus subgenus**
- **35 % of the bat virome sequenced to date is composed of CoVs, 2014**
- **Recombinant origin of SARS-CoV-1, 2013**
- **No SARS-CoV-1 isolates from bats**

**IT'S NOT ROCKET  
SCIENCE!**  
**(OH WAIT, YES IT IS!)**



## A new member of the *Pteropine Orthoreovirus* species isolated from fruit bats imported to Italy

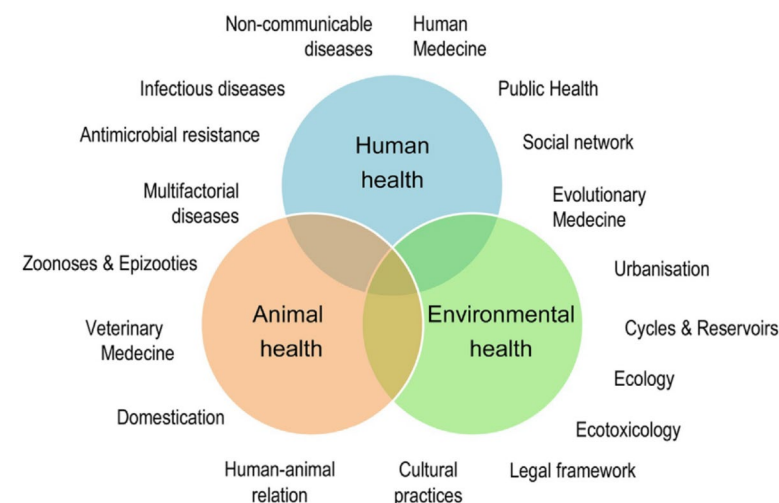
Alessio Lorusso\*, Liana Teodori, Alessandra Leone, Maurilia Marcacci, Iolanda Mangone, Massimiliano Orsini, Andrea Capobianco-Dondona, Cesare Camma', Federica Monaco, Giovanni Savini

*Istituto Zooprofilattico Sperimentale dell'Abruzzo e Molise, IZSAM, Teramo, Italy*



# One Health approach

## Rome, G20



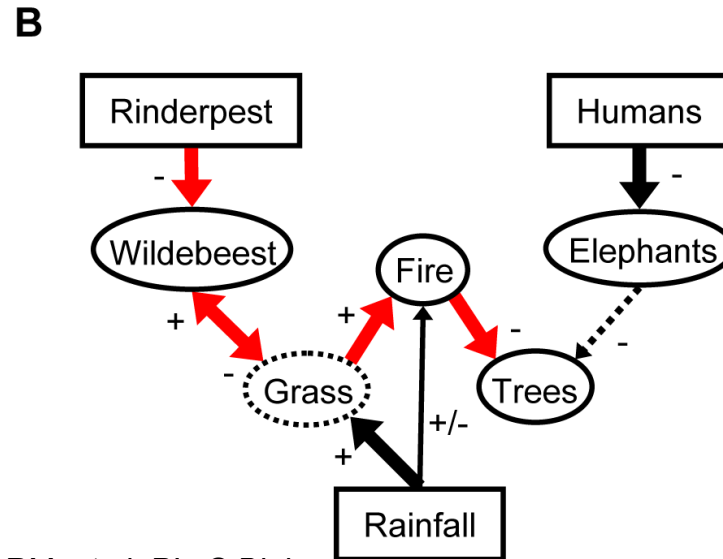
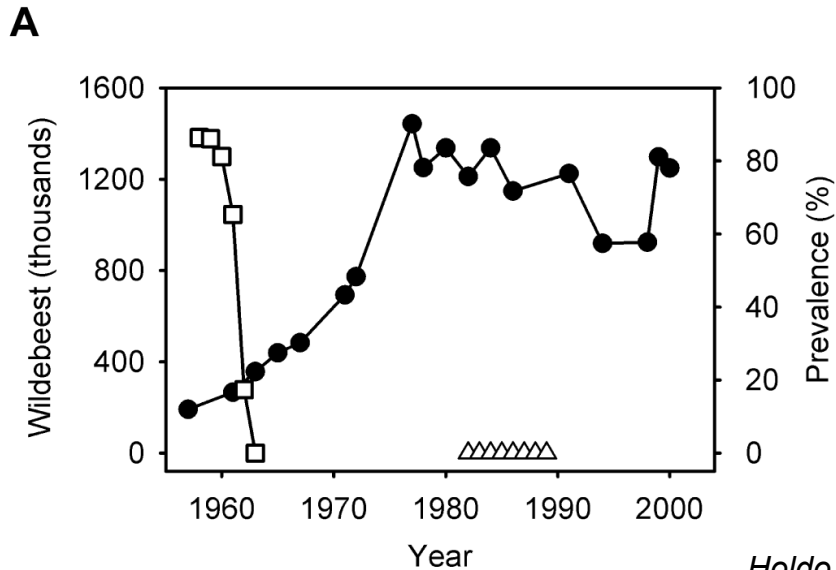
.....The Rome Declaration rightly emphasises **the importance of pursuing a One Health approach** - and here I'm coming to climate -, to preserve human, animal and environmental safety. **This is the key priority of Italy's G20 Presidency.**

The Scientific Expert Panel has stated how most infectious diseases are caused by **pathogens** that are **derived from animals**.

Their emergence is largely driven by **deforestation**, wildlife exploitation, and other **human activities**. Effective environmental action can help to defend animal welfare and ultimately mitigate the risk of new health threats.....

# Complex Ecological Interactions: Rinderpest

- Rinderpest (paramyxovirus) caused an epidemic in East Africa, leading to a reduction in the size of wildebeest and buffalo populations.
- This reduced grazing pressure, leading to more fires that suppressed the establishment of trees, reducing a major carbon sink and changing the ecosystem from woodland to grassland.
- The reduction in grazing mammals led to tsetse flies switching their prey to humans, resulting in an epidemic of African trypanosomiasis.
- The ecosystem reverted to a woodland state when rinderpest was eradicated through vaccination and the number of fires was reduced.



Holdo RM, et al. *PLoS Biol.*  
7:e1000210; 2009.



(A) Population size of wildebeest in the Serengeti and seroprevalence of rinderpest. (B) Relationships between ecosystem components, and particularly how they impact tree population dynamics, a major carbon sink. A causal pathway linking rinderpest with tree population numbers is shown in red.

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## Diagnostica

## Wildlife/Vectors/Food

Accettazione e Controllo campioni umani ed animali/

Attività di sorveglianza/Pathogen discovery



Attività di campo

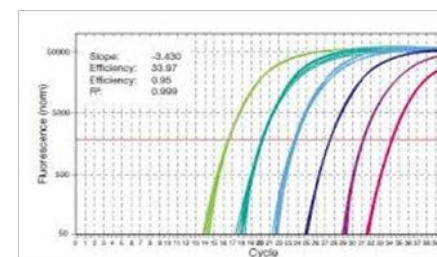


Illumina



Mini Ion

(patogeni ignoti)



Pannello Diagnostico (patogeni noti)

Results to Customer

Internal workflow for storage and R&D

Bionfo database

Studi epidemiologici  
Sviluppo di Test Diagnostici



Isolamento/Caratterizzazione

Studi di Patogenesi



WGS

Bioinfo database



Banca Antigeni

Vaccine

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Blue-med project



TeleVir Project

## Epizootic Haemorrhagic Disease virus serotype 8 in Tunisia, 2021

Soufien Sghaier<sup>1</sup>, Corinne Sailleau<sup>2</sup>, Maurilia Marcacci<sup>3</sup>, Sarah Thabet<sup>1</sup>, Valentina Curini<sup>3</sup>, Thameur Ben Hassin Liana Teodori<sup>3</sup>, Ottavio Portanti<sup>3</sup>, Salah Hammami<sup>5</sup>, Lucija Jurisic<sup>3,6</sup>, Massimo Spedicato<sup>3</sup>, Lydie Postic<sup>2</sup>, Ines Gazani<sup>7</sup>, Raja Ben Osman<sup>8</sup>, Stephan Zientara<sup>2</sup>, Emmanuel Breard<sup>2</sup>, Paolo Calistri<sup>3</sup>, Juergen A. Richt<sup>9</sup>, Edward C. Holmes<sup>10</sup>, Giovanni Savini<sup>3</sup>, Francesca Di Giallonardo<sup>11</sup>, and Alessio Lorusso<sup>3\*</sup>



*Epidemiology and Infection*

[www.cambridge.org/hyg](http://www.cambridge.org/hyg)

## Original Paper

**Cite this article:** Leopardi S, Desiato R, Mazzucato M, Orusa R, Obber F, Averaimo D, Berjaoui S, Canziani S, Capucchio MT, Conti R, di Bella S, Festa F, Garofalo L, Lelli D, Madrau MP, Mandola ML, Moreno Martin AM, Peletto S, Pirani S, Robetto S, Torresi C, Varotto M, Citterio C, Terregino C (2023). One health surveillance strategy for coronaviruses in Italian wildlife. *Epidemiology and Infection*, **151**, e96, 1–10  
<https://doi.org/10.1017/S095026882300081X>





Received: 27 January 2023

Accepted: 19 May 2023

### Keywords:

Coronaviruses; one health; surveillance;

# One health surveillance strategy for coronaviruses in Italian wildlife

Stefania Leopardi<sup>1,2</sup> , Rosanna Desiato<sup>3</sup>, Matteo Mazzucato<sup>1</sup>, Riccardo Orusa<sup>3,4</sup>, Federica Obber<sup>1</sup>, Daniela Averaimo<sup>5</sup>, Shadia Berjaoui<sup>5</sup>, Sabrina Canziani<sup>6</sup>, Maria Teresa Capucchio<sup>7</sup>, Raffaella Conti<sup>8</sup>, Santina di Bella<sup>9</sup>, Francesca Festa<sup>1</sup>, Luisa Garofalo<sup>8</sup> , Davide Lelli<sup>6,10</sup>, Maria Paola Madrau<sup>11</sup>, Maria Lucia Mandola<sup>3</sup>, Ana Maria Moreno Martin<sup>6</sup>, Simone Peletto<sup>3</sup>, Silvia Pirani<sup>12</sup> , Serena Robetto<sup>3</sup>, Claudia Torresi<sup>12</sup>, Maria Varotto<sup>1</sup>, Carlo Citterio<sup>1</sup>  and Calogero Terregino<sup>1</sup>

<sup>1</sup>Istituto Zooprofilattico Sperimentale delle Venezie, Legnaro, Italy; <sup>2</sup>Department of Veterinary Medicine, Università Aldo Moro di Bari, Valenzano, Italy; <sup>3</sup>Istituto Zooprofilattico Sperimentale del Piemonte, Liguria e Valle d'Aosta, Quart, Italy;

<sup>4</sup>National Reference Center Wildlife Diseases, Aosta Valley, Quart, Italy; <sup>5</sup>Istituto Zooprofilattico Sperimentale di Abruzzo e Molise, Teramo, Italy; <sup>6</sup>Istituto Zooprofilattico Sperimentale della Lombardia ed Emilia Romagna, Brescia, Italy;

<sup>7</sup>Department of Veterinary Sciences, Centro Animali Non Convenzionali (C.A.N.C.), University of Turin, Turin, Italy;

<sup>8</sup>Istituto Zooprofilattico Sperimentale di Lazio e Toscana, Roma, Italy; <sup>9</sup>Istituto Zooprofilattico Sperimentale della Sicilia, Palermo, Italy; <sup>10</sup>Molecular Medicine PhD Program, Department of Medicine and Surgery, University of Parma, Parma, Italy; <sup>11</sup>Istituto Zooprofilattico Sperimentale della Sardegna, Cagliari, Italy and <sup>12</sup>Istituto Zooprofilattico Sperimentale di

Umbria e Marche, Perugia, Italy

“...survey carried out in Italy with the double objective of uncovering CoV diversity associated with wildlife and of excluding the establishment of a reservoir for SARS-CoV-2 in particularly susceptible or exposed species.....**Two novel viruses likely belonging to a novel CoV genus were found in mustelids.**”

## Novel Canine Coronavirus Isolated from a Hospitalized Patient With Pneumonia in East Malaysia

Anastasia N. Vlasova,<sup>1,a</sup> Annika Diaz,<sup>1,a</sup> Debasu Damtie,<sup>2,3</sup> Leshan Xiu,<sup>4,5,6</sup> Teck-Hock Toh,<sup>7,8</sup> Jeffrey Soon-Yit Lee,<sup>7,8</sup> Linda J. Saif,<sup>1</sup> and Gregory C. Gray<sup>4,5,9,10</sup>

<sup>1</sup>Food Animal Health Research Program, Ohio Agricultural Research and Development Center, College of Food, Agricultural and Environmental Sciences, Department of Veterinary Preventive Medicine, The Ohio State University, Wooster, Ohio, USA; <sup>2</sup>Department of Immunology and Molecular Biology, School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia; <sup>3</sup>The Ohio State University Global One Health LLC, Eastern Africa Regional Office, Addis Ababa, Ethiopia; <sup>4</sup>Division of Infectious Diseases, Duke University School of Medicine, Durham, North Carolina, USA; <sup>5</sup>Duke Global Health Institute, Duke University, Durham, North Carolina, USA; <sup>6</sup>NHC Key Laboratory of Systems Biology of Pathogens, Institute of Pathogen Biology, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China; <sup>7</sup>Clinical Research Center, Sibuh Hospital, Ministry of Health Malaysia, Sibuh, Sarawak, Malaysia; <sup>8</sup>Faculty of Medicine, SEGi University, Kota Damansara, Selangor, Malaysia; <sup>9</sup>Global Health Research Center, Duke Kunshan University, Kunshan, China; and <sup>10</sup>Program in Emerging Infectious Diseases, Duke-NUS Medical School, Singapore

### HEALTH AND MEDICINE

## Swine coronavirus shows potential to spread to humans



Lab tests at UNC-Chapel Hill Gillings School of Global Public Health demonstrate swine coronavirus replicates in human airway and intestinal cells.

### Article

## Independent infections of porcine deltacoronavirus among Haitian children

<https://doi.org/10.1038/s41586-021-04111-z>

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Published online: 17 November 2021

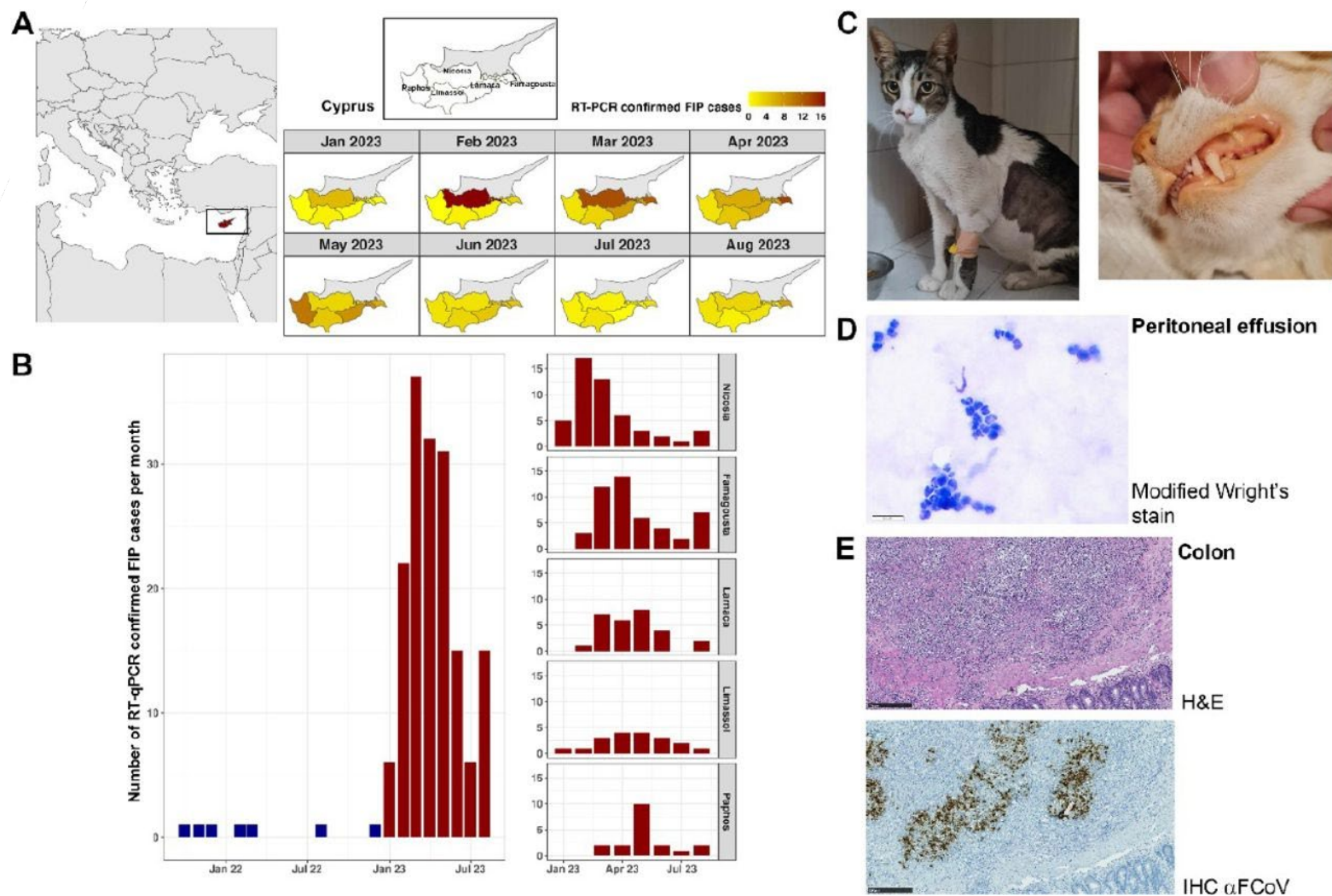
John A. Lednicky<sup>1,2,7</sup>, Massimiliano S. Tagliamonte<sup>1,3,7</sup>, Sarah K. White<sup>1,2</sup>, Maha A. Elbadry<sup>1,2</sup>, Md. Mahbubul Alam<sup>1,2</sup>, Caroline J. Stephenson<sup>1,2</sup>, Tania S. Bonny<sup>1,2</sup>, Julia C. Loeb<sup>1,2</sup>, Taina Telisma<sup>4</sup>, Sonese Chavannes<sup>4</sup>, David A. Ostrov<sup>1,3</sup>, Carla Mavian<sup>1,3</sup>, Valery Madsen Beau De Rochars<sup>1,5</sup>, Marco Salemi<sup>1,3,6</sup> & J. Glenn Morris Jr<sup>1,6</sup>

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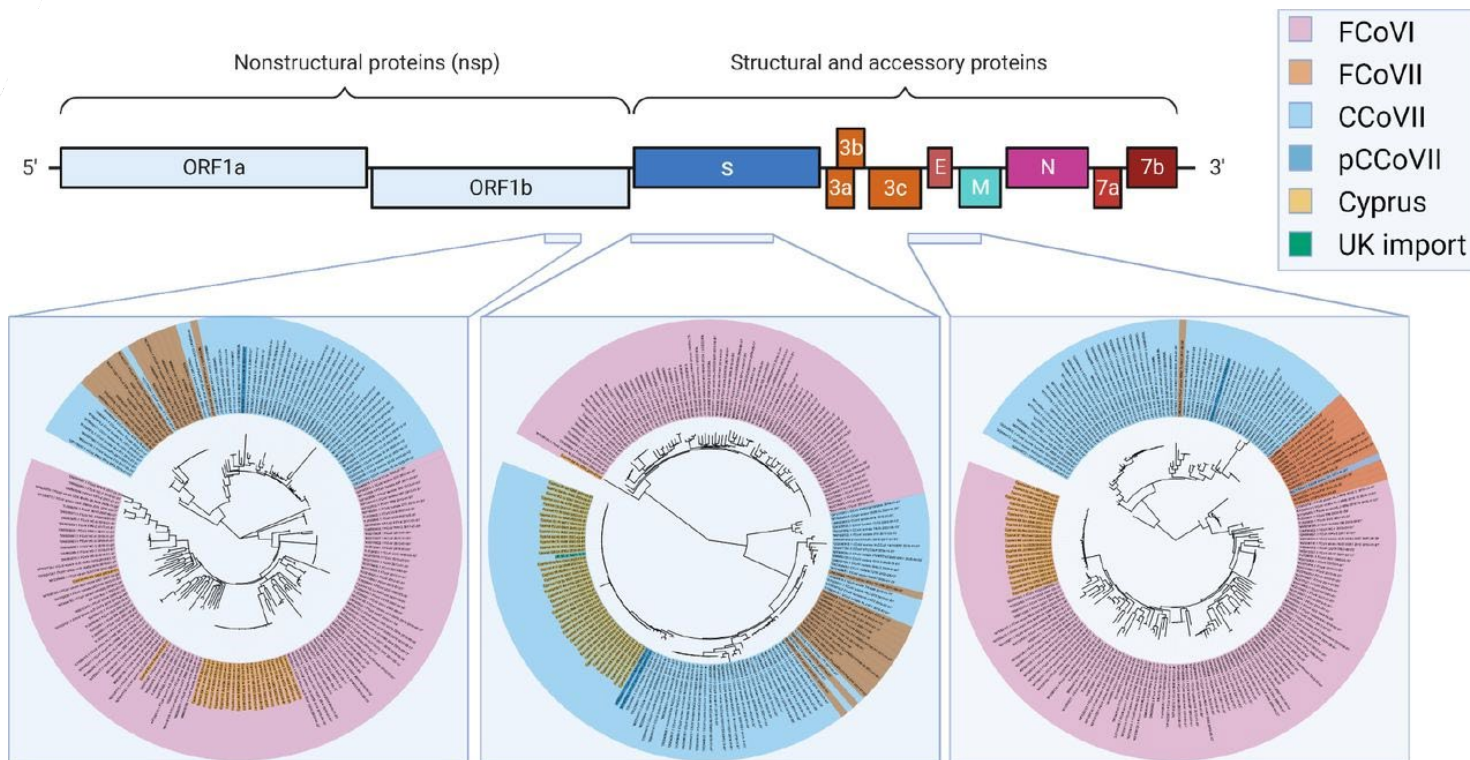
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## A novel recombinant canine/feline alphacoronavirus




# Virus diversity, wildlife-domestic animal circulation and potential zoonotic viruses of small mammals, pangolins and zoo animals

Received: 27 February 2023

Accepted: 20 April 2023

Published online: 29 April 2023

 Check for updates

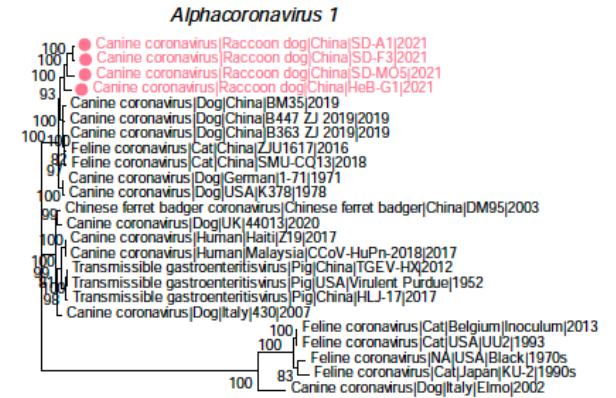
Xinyuan Cui<sup>1,20</sup>, Kewei Fan<sup>2,20</sup>, Xianghui Liang<sup>1,20</sup>, Wenjie Gong<sup>3,4,20</sup>, Wu Chen<sup>5,20</sup>, Biao He<sup>4,20</sup>, Xiaoyuan Chen<sup>1</sup>, Hai Wang<sup>1</sup>, Xiao Wang<sup>1</sup>, Ping Zhang<sup>1</sup>, Xingbang Lu<sup>1</sup>, Rujian Chen<sup>1</sup>, Kaixiong Lin<sup>6</sup>, Jiameng Liu<sup>1</sup>, Junqiong Zhai<sup>5</sup>, Ding Xiang Liu<sup>7,8</sup>, Fen Shan<sup>5</sup>, Yuqi Li<sup>2</sup>, Rui Ai Chen<sup>8</sup>, Huifang Meng<sup>1</sup>, Xiaobing Li<sup>1,2</sup>, Shijiang Mi<sup>3,4</sup>, Jianfeng Jiang<sup>3,4</sup>, Niu Zhou<sup>5</sup>, Zujin Chen<sup>5</sup>, Jie-Jian Zou<sup>9</sup>, Deyan Ge<sup>10</sup>, Qisen Yang<sup>10</sup>, Kai He<sup>11</sup>, Tengting Chen<sup>6</sup>, Ya-Jiang Wu<sup>5</sup>, Haoran Lu<sup>12</sup>, David M. Irwin<sup>13,14</sup>, Xuejuan Shen<sup>1</sup>, Yuanjia Hu<sup>1</sup>, Xiaoman Lu<sup>1</sup>, Chan Ding<sup>15,16</sup>✉, Yi Guan<sup>17,18</sup>✉, Changchun Tu<sup>4,16</sup>✉ & Yongyi Shen<sup>1,19</sup>✉

Wildlife is reservoir of emerging viruses. Here we identified 27 families of mammalian viruses from 1981 wild animals and 194 zoo animals collected from south China between 2015 and 2022, isolated and characterized the pathogenicity of eight viruses. Bats harbor high diversity of coronaviruses, picornaviruses and astroviruses, and a potentially novel genus of *Bornaviridae*. In addition to the reported SARSr-CoV-2 and HKU4-CoV-like viruses, picornavirus and respiroviruses also likely circulate between bats and pangolins. Pikas harbor a new clade of Embecovirus and a new genus of arenaviruses. Further, the potential cross-species transmission of RNA viruses (paramyxovirus and astrovirus) and DNA viruses (pseudorabies virus, porcine circovirus 2, porcine circovirus 3 and parvovirus) between wildlife and domestic animals was identified, complicating wildlife protection and the prevention and control of these diseases in domestic animals. This study provides a nuanced view of the frequency of host-jumping events, as well as assessments of zoonotic risk.

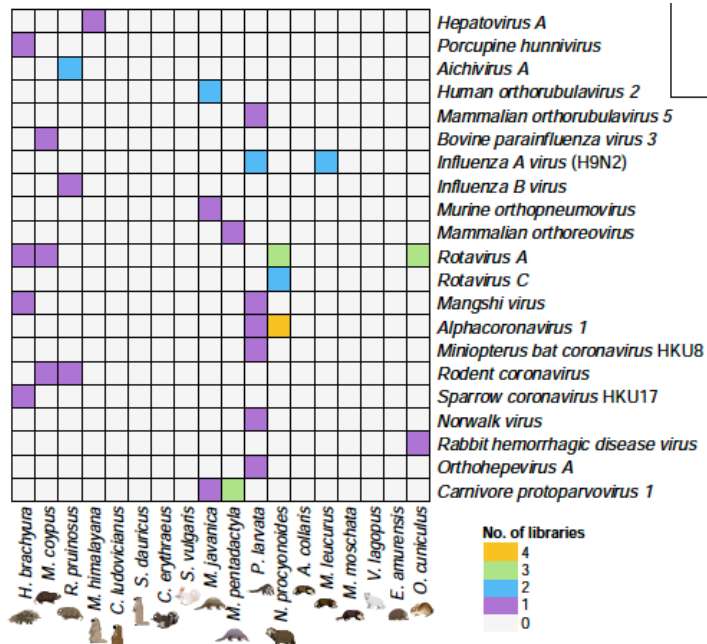
# Viromes of Game Animals in China



## Canine $\alpha$ -CoV in a racoon dog (gastric)



- Sampled 1941 game animals from 5 mammalian orders
- 102 mammalian viruses discovered: 21 of potential human risk
- Bat HKU8 coronavirus in a civet
- Avian H9N2 influenza virus in a civet and an Asian badger



# Goals of Our Animal-Human Interface (and human) Studies

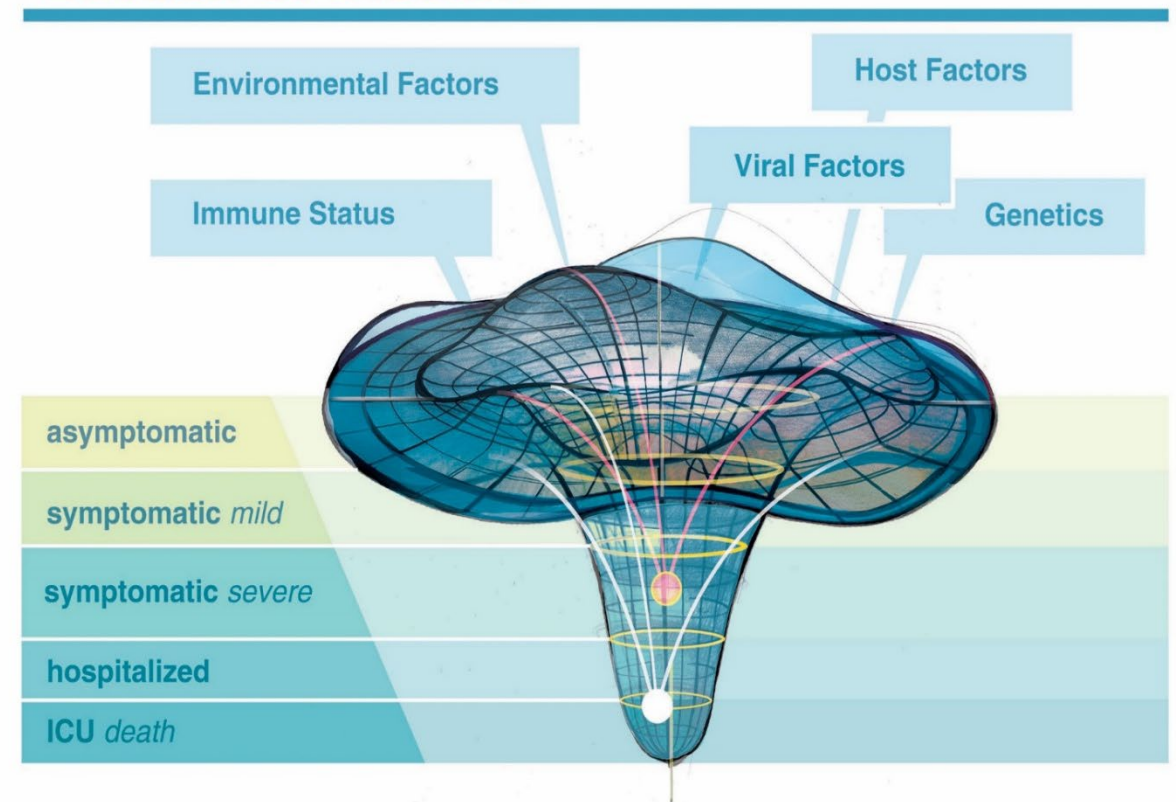
What viruses present a zoonotic risk?

What host factors (biological, behavioral, environmental) increase the risk of zoonotic transmission?

Immunological and other host factor associations with clinical disease

What factors determine poor clinical outcomes? Can these outcomes be predicted? Prevented? Treated?

## Burden of Disease

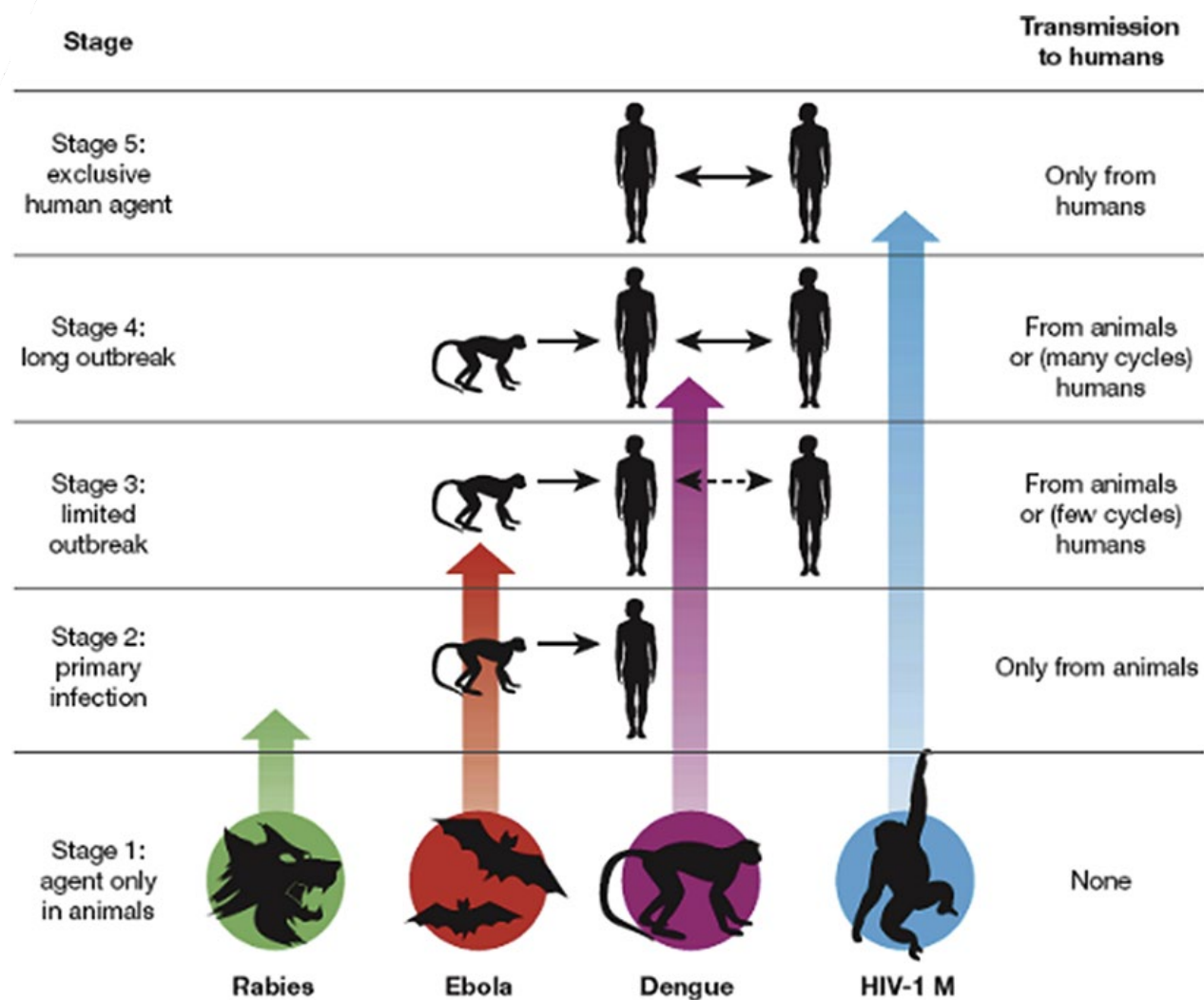


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*Ministero della Salute*

Direzione Generale della Prevenzione Sanitaria

## **Piano Nazionale della Prevenzione 2020-2025**

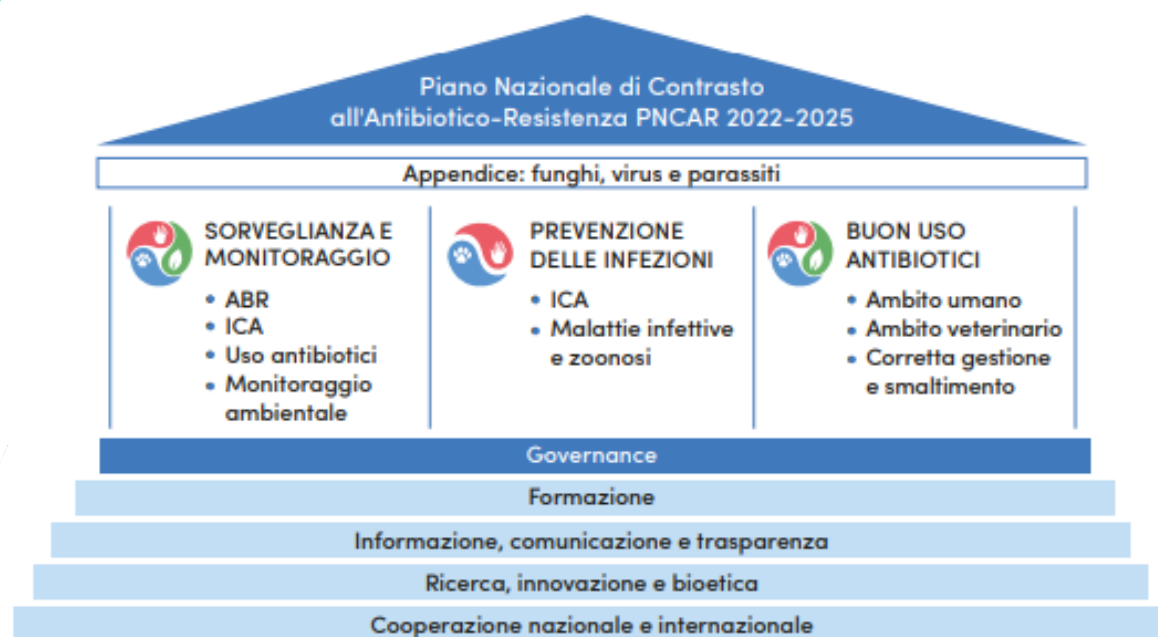
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## NGS: Next Generation Sequencing..Next Generation Strategies!



## Identifying and prioritizing potential human-infecting viruses from their genome sequences

Nardus Mollentze , Simon A. Babayan, Daniel G. Streicker

Published: September 28, 2021 • <https://doi.org/10.1371/journal.pbio.3001390>

« *Determining which animal viruses may be capable of infecting humans is currently intractable at the time of their discovery, precluding prioritization of high-risk viruses for early investigation and outbreak preparedness. Given the **increasing use of genomics** in virus discovery and the otherwise sparse knowledge of the biology of newly discovered viruses, we developed **machine learning models** that identify candidate **zoonoses** solely using signatures of host range encoded in viral genomes* »

# IZS

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- **Training**
- **Develop a novel generation of scientists**
- **Core of the pandemic preparedness**

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## Bushmeat and animal trade

### IL PIANO MATTEI PRENDE FORMA

Sviluppo comune, sostenibile e duraturo

- ✓ politico
- ✓ economico
- ✓ sociale
- ✓ culturale
- ✓ di sicurezza

#### AMBITI

- Energia
- Istruzione
- Formazione
- Ricerca
- Salute
- Agricoltura
- Sicurezza alimentare
- Lotta al cambiamento climatico
- Gestione risorse
- Contrasto immigrazione irregolare

#### CABINA DI REGIA



#### Durata del piano



#### Stato di attuazione



FONTE: Bozza decreto sulla governance del 'Piano Mattei'

GEA - WITHUB

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# Thank you