ResearchGate

See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/353651573

A great ape perspective on the origins and evolution of human viruses

Chapter *in* Advances in Virus Research · January 2021

DOI: 10.1016/bs.aivir.2021.06.001

CITATIONS
0

READS
19

5 authors, including:

Sébastien Calvignac-Spencer
Robert Koch Institut
158 PUBLICATIONS **3,133** CITATIONS

SEE PROFILE

Ariane Düx
Robert Koch Institut
44 PUBLICATIONS **619** CITATIONS

SEE PROFILE

Jan Frederik Gogarten
Robert Koch Institut
84 PUBLICATIONS **1,094** CITATIONS

SEE PROFILE

Fabian H Leendertz
Robert Koch Institut
450 PUBLICATIONS **6,826** CITATIONS

SEE PROFILE

Some of the authors of this publication are also working on these related projects:

Project

Community health care initiatives and protected areas View project

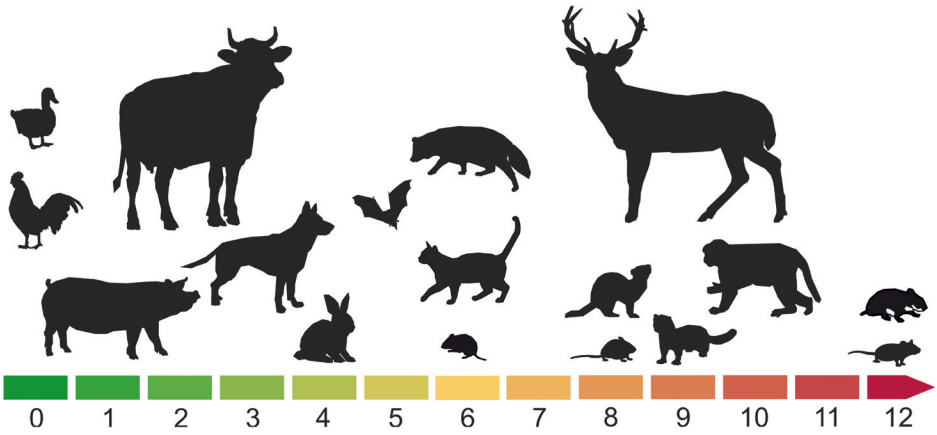
Project

Capacity building for the detection and prevention of neglected infectious zoonoses in tropical Africa View project

All content following this page was uploaded by Jan Frederik Gogarten on 09 August 2021.

The user has requested enhancement of the downloaded file.

Advances in VIRUS RESEARCH



110

Edited by
Margaret Kielian,
Thomas C. Mettenleiter
and Marilyn J. Roossinck

VOLUME ONE HUNDRED AND TEN

ADVANCES IN
VIRUS RESEARCH

Serial Editors

MARGARET KIELIAN

THOMAS C. METTENLEITER

MARILYN J. ROOSSINCK

ADVISORY BOARD

SHOUWEI DING

JOHN FAZAKERLY

KARLA KIRKEGAARD

JULIE OVERBAUGH

DAVID PRANGISHVILI

FÉLIX A. REY

JUERGEN RICHT

JOHN J. SKEHEL

GEOFFREY SMITH

MARC H.V. VAN REGENMORTEL

VERONIKA VON MESSLING

VOLUME ONE HUNDRED AND TEN

ADVANCES IN VIRUS RESEARCH

Edited by

MARGARET KIELIAN
Albert Einstein College of Medicine,
Bronx, New York, United States

THOMAS C. METTENLEITER
Friedrich-Loeffler-Institut,
Federal Research Institute for Animal Health,
Greifswald – Insel Riems, Germany

MARILYN J. ROOSSINCK
Department of Plant Pathology and
Environmental Microbiology,
Center for Infectious Disease Dynamics,
Penn State University, University Park,
PA, United States

ELSEVIER

ACADEMIC PRESS
An imprint of Elsevier

Academic Press is an imprint of Elsevier
50 Hampshire Street, 5th Floor, Cambridge, MA 02139, United States
525 B Street, Suite 1650, San Diego, CA 92101, United States
The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, United Kingdom
125 London Wall, London, EC2Y 5AS, United Kingdom

First edition 2021

Copyright © 2021 Elsevier Inc. All rights reserved.

No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or any information storage and retrieval system, without permission in writing from the publisher. Details on how to seek permission, further information about the Publisher's permissions policies and our arrangements with organizations such as the Copyright Clearance Center and the Copyright Licensing Agency, can be found at our website: www.elsevier.com/permissions.

This book and the individual contributions contained in it are protected under copyright by the Publisher (other than as may be noted herein).

Notices
Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

To the fullest extent of the law, neither the Publisher nor the authors, contributors, or editors, assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

ISBN: 978-0-12-824604-7
ISSN: 0065-3527

For information on all Academic Press publications
visit our website at https://www.elsevier.com/books-and-journals

Publisher: Zoe Kruze
Acquisitions Editor: Ashlie M. Jackman
Developmental Editor: Federico Paulo S. Mendoza
Production Project Manager: James Selvam
Cover Designer: Alan Studholme

Typeset by SPi Global, India

ELSEVIER Book Aid International Working together to grow libraries in developing countries
www.elsevier.com • www.bookaid.org

Contents

Contributors *vii*

1. A great ape perspective on the origins and evolution of human viruses **1**

Sébastien Calvignac-Spencer, Ariane Düx, Jan F. Gogarten, Fabian H. Leendertz, and Livia V. Patrono

1. A theoretical basis for comparative hominine molecular virology 2
2. An AGA perspective on the four hypotheses of the Paleolithic baseline 9
3. Conclusion 18

References 19

2. A holistic perspective on herpes simplex virus (HSV) ecology and evolution **27**

Molly M. Rathbun and Moriah L. Szpara

1. Introduction 28
2. Mechanisms for generating viral diversity at the molecular level 30
3. Clinical sampling and experimental design considerations 34
4. Integrating the whole body: Chronic infection, shedding patterns, and tissue compartmentalization 37
5. Extending beyond individual hosts, strains, and species 43
6. Summary and perspectives 49

Acknowledgments 50

References 50

3. SARS-CoV-2 in animals: From potential hosts to animal models **59**

Anna Michelitsch, Kerstin Wernike, Lorenz Ulrich, Thomas C. Mettenleiter, and Martin Beer

1. Introduction 60
2. Reservoir and intermediate hosts 62
3. Pet animals and their non-domesticated counterparts 68
4. Livestock animals 72
5. Animal models in SARS-CoV-2 research 75
6. Concluding remarks 81

References 83

Contributors

Martin Beer
Friedrich-Loeffler-Institut, Greifswald - Insel Riems, Germany

Sébastien Calvignac-Spencer
Epidemiology of Highly Pathogenic Microorganisms; Viral Evolution, Robert Koch-Institute, Berlin, Germany

Ariane Düx
Epidemiology of Highly Pathogenic Microorganisms; Viral Evolution, Robert Koch-Institute, Berlin, Germany

Jan F. Gogarten
Epidemiology of Highly Pathogenic Microorganisms; Viral Evolution, Robert Koch-Institute, Berlin, Germany

Fabian H. Leendertz
Epidemiology of Highly Pathogenic Microorganisms, Robert Koch-Institute, Berlin, Germany

Thomas C. Mettenleiter
Friedrich-Loeffler-Institut, Greifswald - Insel Riems, Germany

Anna Michelitsch
Friedrich-Loeffler-Institut, Greifswald - Insel Riems, Germany

Livia V. Patrono
Epidemiology of Highly Pathogenic Microorganisms, Robert Koch-Institute, Berlin, Germany

Molly M. Rathbun
Department of Biochemistry and Molecular Biology, Department of Biology, Center for Infectious Disease Dynamics, and Huck Institutes of the Life Sciences, Pennsylvania State University, University Park, PA, United States

Moriah L. Szpara
Department of Biochemistry and Molecular Biology, Department of Biology, Center for Infectious Disease Dynamics, and Huck Institutes of the Life Sciences, Pennsylvania State University, University Park, PA, United States

Lorenz Ulrich
Friedrich-Loeffler-Institut, Greifswald - Insel Riems, Germany

Kerstin Wernike
Friedrich-Loeffler-Institut, Greifswald - Insel Riems, Germany

CHAPTER ONE

A great ape perspective on the origins and evolution of human viruses

Sébastien Calvignac-Spencer[a,b,†,*], Ariane Düx[a,b,†], Jan F. Gogarten[a,b,†], Fabian H. Leendertz[a,*,†], and Livia V. Patrono[a,†]
[a]Epidemiology of Highly Pathogenic Microorganisms, Robert Koch-Institute, Berlin, Germany
[b]Viral Evolution, Robert Koch-Institute, Berlin, Germany
*Corresponding authors: e-mail address: calvignacs@rki.de; leendertzf@rki.de

Contents

1. A theoretical basis for comparative hominine molecular virology 2
   1.1 Deeper histories of codivergence and zoonotic transmission 2
   1.2 Changes in recent history and their impact on the human virome 7
2. An AGA perspective on the four hypotheses of the Paleolithic baseline 9
   2.1 Endemic viruses were "heirloom" parasites 9
   2.2 Viral zoonosis was common 11
   2.3 Human-adapted epidemic viral diseases did not exist 14
   2.4 Viral disease burden was limited 16
3. Conclusion 18
References 19

Abstract

Over the last two decades, the viromes of our closest relatives, the African great apes (AGA), have been intensively studied. Comparative approaches have unveiled diverse evolutionary patterns, highlighting both stable host-virus associations over extended evolutionary timescales and much more recent viral emergence events. In this chapter, we summarize these findings and outline how they have shed a new light on the origins and evolution of many human-infecting viruses. We also show how this knowledge can be used to better understand the evolution of human health in relation to viral infections.

African great apes (AGA), i.e., chimpanzees (*Pan troglodytes*), bonobos (*Pan paniscus*) and gorillas (*Gorilla gorilla* and *Gorilla beringei*), are our closest living relatives (Perelman et al., 2011). Their evolutionary proximity translates into

† All authors contributed equally and are alphabetically listed.

Advances in Virus Research, Volume 110
ISSN 0065-3527
https://doi.org/10.1016/bs.aivir.2021.06.001
Copyright © 2021 Elsevier Inc.
All rights reserved.

major similarities between their and our biology, from physiology over behavior to ecology. This has motivated comparative studies across many fields of research (Tattersall, 1999).

Microorganisms play an important role in the evolution and ecology of humans and AGA (i.e., hominines). Indeed, they existed long before the first multicellular organisms developed, and eukaryotes (including hominines) evolved in a world dominated by microbes (López-García et al., 2017; McFall-Ngai et al., 2013; Sogin, 1991). Among the diversity of microorganisms influencing eukaryotes, viruses are likely the most abundant entities (Sogin, 1991) and are well-known to have a considerable impact on host health and evolution. For example, some viruses can cause massive mortality in eukaryote populations, e.g., algae infecting viruses (Brussaard, 2004). Others have been key to the evolution of the placenta in all mammalian lineages, e.g., endogenized retroviruses (Villarreal, 2016). Clearly, understanding the viruses that infect us can greatly enhance our insight into human (evolutionary) history.

Considerable efforts have already gone toward describing the virome of AGA. One major hope was (and still is) to use viral nucleic acid sequences (from short phylogenetically informative fragments to complete genomes) to understand the origins of the viruses associated with humans (Gogarten et al., 2021; Hoppe et al., 2015; Wertheim et al., 2014; Woolhouse et al., 2012). At the same time, our fellow hominines can serve as a model of early human societies and their relationship to the viral world (Gogarten et al., 2019). In this review, we summarize some of the progress made over the last two decades in this field of research. We first address the theoretical and practical bases of comparative hominine *molecular* virology. Revisiting a series of predictions derived from the hypothesis of a first epidemiological transition of humankind, we will then summarize what such comparative approaches have revealed about the origins of human viruses.

1. A theoretical basis for comparative hominine molecular virology

1.1 Deeper histories of codivergence and zoonotic transmission

It has long been hypothesized that humans and AGA are susceptible to similar viruses and that our closest living relatives host viruses that represent the closest relatives of our viruses. This idea was driven by an intuitive evolutionary scenario in which hominine viruses codiverged/cospeciated with

their hosts from a shared common ancestor (in the following we use the term codivergence, as the evolutionary units discussed here are not always recognized as viral species by the International Committee on Taxonomy of Viruses and many AGA-virus cophylogenetic analyses were conducted at the population/sub-species scale). In this scenario, divergence events of viral lineages infecting different hominine species are explained by the divergence events of their hosts. Therefore, viral and hominine phylogenetic trees should be largely congruent, both when considering their topologies and branch lengths, i.e., the order and dates of divergence events. Documenting such congruence in AGA provides evidence that a human virus has been with the human lineage since at least the time that it infected the last common ancestor of our species.

On the other hand, discordance in cophylogenetic analyses indicates that processes other than codivergence were at play (de Vienne et al., 2013). A virus may have gone extinct in one or several host lineages. Another may have undergone lineage duplication (i.e., intra-host speciation), where two viral lineages diverge and then coexist in the same host, e.g., by adapting to separate body compartments. And yet another virus may have failed to codiverge due to incomplete viral lineage sorting (Sharp and Simmonds, 2011). Last but certainly not least, discordance can also be a product of host switching events (i.e., between species transmission). This can lead to the unambiguous identification of nonhuman hominines as the reservoir from which a human virus emerged, e.g., when the diversity of a human virus nests within the diversity of an AGA virus.

Such a reasoning requires the detection of closely related viruses in humans and at least some AGA. Assuming effective tools are available and an appropriate detection effort is made, the failure to identify close relatives of a human virus in AGA is already a hint toward its zoonotic origin in a non-hominine reservoir (Box 1). Consequently, virus/hominine codivergence can be considered as a null model of evolution whose violation, whether due to the nonexistence of AGA viruses or discordant phylogenetic trees, can show the zoonotic origin of a human virus.

Box 1. A practical basis for comparative hominine molecular virology.

One way to study the viruses infecting AGA occurred when animals captured in the wild were used to establish laboratory colonies or to populate zoos. A number of viruses were discovered in invasive samples collected from these animals, often when clinical signs or lesions were observed. Some of these viruses had a resemblance to those already described in

humans or other species (e.g., adenoviruses and papillomaviruses; Asher et al., 1978; Hillis et al., 1969; Hollander and van Noord, 1972; Sundberg et al., 1992) and the accumulation of such case reports suggested AGA were infected with a broad range of viruses. Unfortunately, captivity introduced considerable uncertainty as to whether these viruses were truly AGA viruses, as opposed to newly introduced human viruses, and the capture of wild AGA has now stopped due to ethical and conservation concerns. Invasive sampling of semi-free ranging animals, for example those illegally caught for the pet trade and then reassigned to wildlife rescue centers, represented another way to explore the AGA virome (Lacoste et al., 2000b, 2001; Peeters et al., 1992), though these AGA also have a history of close contact with humans. A more systematic exploration of viral diversity in wild great apes presents a number of challenges, but when overcome, arguably provides the best insight into the AGA viromes.

While labor intensive, surveys of indirect signs of great ape presence (e.g., nests, feeding remains, vocalizations) can allow for the opportunistic collection of fecal samples from AGA. In a seminal work focused on SIVcpz, Santiago et al. showed that feces contain amplifiable viral genetic material (Santiago et al., 2002). Increasing evidence suggests that irrespective of tropism, most (if not all) viruses leave genetic traces in AGA feces, particularly with ever improving methods for sample preservation (Calvignac-Spencer et al., 2012a). While such opportunistic sampling enables the detection of viruses across large spatial scales (Heuverswyn et al., 2007; Seimon et al., 2015), it does not necessarily allow for the identification of those associated with morbidity and mortality in AGA.

The creation of long-term AGA research sites across ecosystems where animals are habituated to the presence of humans in an effort to study their behavior, has opened exciting new opportunities for studies of viruses that address these gaps (Boesch and Boesch-Achermann, 2000; Goodall, 1986). Researchers at these study sites can individually recognize animals, which allows for an intensification of non-invasive sampling, as well as the observation of clinical signs and mortality associated with particular viruses (Fig. B1-A). The long-term presence of researchers in association with AGA populations also creates many opportunities for necropsies to be performed on wild AGA carcasses (Fig. B1-B). For example, major die-offs in great ape populations in the Taï Forest in 1994 led to the identification of a novel ebolavirus species infecting chimpanzees (Formenty et al., 1999). Despite the promise of such approaches, conducting necropsies in the rainforest presents considerable challenges; carcasses rapidly decompose, scavengers quickly detect carcasses, samples degrade quick, and carcasses can contain viruses and bacteria that pose a significant risk to humans, necessitating very high safety precautions. Indeed, the Taï Forest ebolavirus

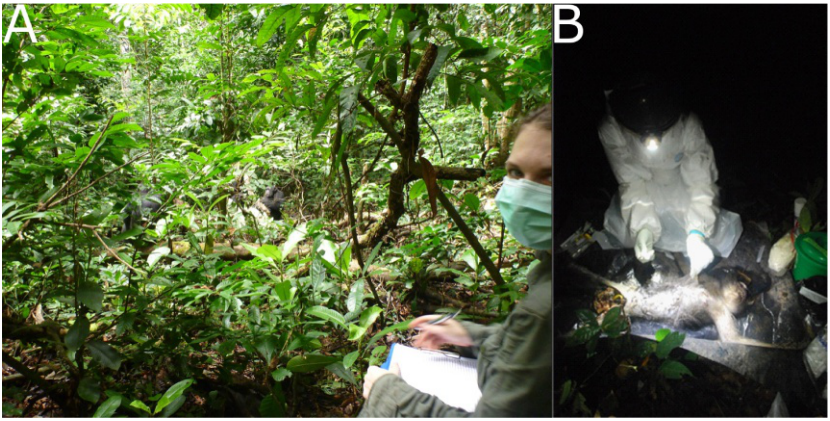


Fig. B1 (A) A researcher observing habituated wild chimpanzees in the Taï National Park (TNP), Côte d'Ivoire. Observations simultaneously allow researchers to identify potential health issues and to collect noninvasive samples (feces, urine, food leftovers). *Image courtesy of Jan F. Gogarten and the Taï Chimpanzee Project*. (B) A veterinarian performs a necropsy at night on a primate to collect samples for further laboratory analyses (also in TNP). *Image courtesy of Therese Löhrich and the Taï Chimpanzee Project.*

investigation led to the infection of a researcher that luckily survived. These experiences led to the adoption of rigorous safety standards and the development of protocols and training for field veterinarians at many field sites (Gilardi et al., 2015; Leendertz et al., 2006). The continuous observation of wild AGA populations by primatologists is increasingly coupled with longitudinal health monitoring programs providing new insights into the AGA virome.

Viral detection in AGA samples largely relies on standard molecular biology techniques, such as polymerase chain reaction (PCR). PCR has proven to be a robust method to amplify small fragments of viral genomes in both necropsy and non-invasive samples, for virus detection and acquiring short but phylogenetically informative sequences. Tools that allow for the retrieval of complete viral genomes can better characterize viruses and lead to a more accurate estimation of phylogenetic relationships. As virus isolation is often impossible from such samples (presumably because of decomposition state in necropsy samples, or because of low viral loads in feces), high throughput sequencing (HTS) approaches have increasingly been adopted. Direct shotgun sequencing typically results in the majority of information retrieved belonging to the host and other microbes. When a target is known, enrichment strategies based on either multiplex

PCR or hybridization capture allow sequencing effort to target the virus(es) of interest. Multiplex PCR amplifies the entire genome of a virus with overlapping PCR amplicons using primer schemes designed based on the genome of a close relative of the target virus. Hybridization capture uses customized probes (baits) to fish out viral RNA/DNA from the total nucleic acids contained in a HTS library prior to sequencing. Hybridization capture is efficient even when there is a 20–30% divergence between the bait and target, and is easily scaled up to viruses with large genomes (e.g., monkeypox virus), making it more versatile than typical multiplex PCR strategies; it is however generally a more expensive approach. These tools have been used to generate large amounts of genomic information from a diversity of wild AGA sample types.

Finally, ancient DNA and even RNA approaches are proving useful for generating sequence data on viruses from a diversity of museum specimen types (Calvignac et al., 2008; Düx et al., 2020), though to date this not been extensively applied to historic AGA collections. The marked global population decline experienced by all AGA, accompanied by a reduced connectivity between populations due to increasingly fragmented habitats, might well have resulted in a decreased or patchy prevalence of some viruses, and even the complete disappearance of others. In addition, recent contact to human populations may have resulted in transmission of human viruses to AGA that complicate the interpretation of data from contemporaneous wild AGA populations. The ability to study viral diversity in historic AGA samples, of which there are large collections in museums, will almost certainly provide further insights into the ancient and recent evolution of their viromes.

An important caveat is that methods to detect codivergence or discordance rely on our ability to accurately assess the topologies and branch lengths of both host and viral phylogenies. The AGA phylogeny is globally well resolved, although some uncertainty about the timing and the divergence of different sub-species remains (Castellano and Munch, 2020). By contrast, robust estimates for many viral phylogenies are still lacking. Reliably estimating the timing of viral divergence events has proven to be particularly challenging (notably due to time-dependent rates of evolution; Aiewsakun and Katzourakis, 2016; Duchêne et al., 2014; Wertheim and Kosakovsky Pond, 2011), though selection-aware molecular clock models do appear to provide better descriptions of the nucleotide substitution process and, accordingly, better estimates of divergence dates (Düx et al., 2020; Membrebe et al., 2019). Reevaluating datasets with ever-improving methods will continue to provide new insights and improve estimates.

It has become clear that provided long-enough evolutionary timescales are considered, the phylogeny of any viral group shows evidence of discordance with that of their hosts. However, the relative frequency of codivergence/host switch events appears to vary across viral groups, and the nature of the viral genome has often been evoked as a predictor for this phenomenon. The theory behind this is that viruses with an RNA genome (RNA viruses) generally have higher mutation rates, which favors adaptation to novel environments allowing them to more successfully jump species. Reciprocally, DNA viruses tend to establish persistent and sometimes lifelong infections which favors long-term host associations (Duffy et al., 2008) and therefore also codivergence. The importance of the nature of the viral genome in shaping relative frequency of host switch events is supported by a large-scale analysis of 19 families of viruses infecting a diverse sample of eukaryotic hosts including mammals, birds, reptiles, amphibians, fish, plants and insects (Geoghegan et al., 2017). This study also suggests that DNA viruses switch hosts more than initially assumed (Geoghegan et al., 2017). The nature of viral genomes is expected to play a similar role in shaping the interaction of viruses and hominines at smaller evolutionary timescales, though tools to generate the data to facilitate a large-scale comparative analysis of AGA viruses to test these ideas have only recently become widely applied (Box 1).

1.2 Changes in recent history and their impact on the human virome

While much of what we have discussed so far pertains to the long-term evolution of hominine-virus associations which potentially reach back millions of years, the more recent history of humankind was marked by major changes in our species' ecology which are thought to have permanently altered the human virome. In his theory of the epidemiologic transition, Omran posited a first phase in the evolution of health and disease, which he coined the Age of Pestilence and Famine (Omran, 1971). During this Age, which Omran ascribes to premodern societies (before 1650), epidemics, wars, and famine were the primary causes of generally high levels of mortality. It was later proposed that the Age of Pestilence and Famine had begun as a consequence of the Neolithic transition (starting about 10,000 years ago in the Middle-East), which therefore represented the first epidemiologic transition (Armelagos et al., 2005). According to this model, the transition from a nomadic hunter-gatherer to a sedentary agricultural lifestyle resulted in increased opportunities of infectious agent transmission between domestic and peridomestic animals and humans. At the same time,

the sedentary lifestyle led to increased population densities which was a prerequisite for sustained human-to-human transmission of newly emerged agents and therefore favored the accumulation of new pathogens in humans. The advent of long-distance trade then allowed such pathogens to circulate globally. Indeed, during the agricultural demographic transition, increased fertility led to increased human population sizes, and average life expectancy and body condition dropped, in line with the combined effects of changes in nutrition and the rise of new infectious agents (Bocquet-Appel, 2011).

The notion of a first epidemiologic transition draws on a vision for what the landscape of infectious diseases in hunter-gatherer societies was like. Armelagos et al. described this Paleolithic baseline as characterized by: (i) endemic diseases caused by "heirloom" parasites, i.e., parasites that always accompanied our species, (ii) relatively frequent zoonotic diseases, notably due to occupying a trophic position of frequent hunters/scavengers in biodiverse ecosystems, (iii) rare or absent human-adapted epidemic diseases, because of the low population densities and relatively low inter group connectivity, and (iv) as a consequence of the prior hypotheses, overall little evolutionary significance of infectious diseases. While modern hunter-gatherer societies may offer an opportunity to test these predictions, these societies too have undergone many changes. Indeed, it has been hypothesized that rather than being completely isolated, hunter-gatherer populations (including many modern hunter-gatherer populations) have been interconnected with neighboring populations (including sedentary populations) since the Holocene (Headland and Reid, 1991). The spread of many infectious diseases into modern (even uncontacted) hunter-gatherer populations has further complicated the use of modern human populations to gain insights into human health in the distant past (Hurtado et al., 2001). Another possibility is the study of extant AGA communities as a proxy for Paleolithic human societies, although this approach also faces inherent limitations, particularly that, despite notable similarities, AGA societies still differ in many ways from any human society, past or present (e.g., they exhibit clearly distinct social structures and exploit unique ecological niches).

Below we explore the four aforementioned hypotheses about infectious diseases in the Paleolithic which if true, we would expect to largely apply to wild AGA populations as well. We recognize that these four hypotheses are certainly not universally accepted, but we hope an exploration of how they are supported by studies of wild AGA will be informative for the reader.

2. An AGA perspective on the four hypotheses of the Paleolithic baseline

In this section, we try to summarize most findings about AGA viruses while also examining whether they align well with predictions about Paleolithic hunter-gatherer societies.

2.1 Endemic viruses were "heirloom" parasites

Many viruses identified in AGA have been detected at relatively high rates across AGA ranges and, where AGA were habituated, from apparently healthy animals, suggesting enzootic circulation with little impact on AGA health (Calvignac-Spencer et al., 2012a). This is especially true for viruses with a double-stranded DNA genome, of which numerous lineages in multiple viral families have now been discovered.

Among those, herpesviruses (family *Herpesviridae*) have long been suspected to have a deep history of association with their hosts, with early observations suggesting codivergence at the scale of the entire mammalian phylogeny (McGeoch et al., 2006). Viruses closely related to all eight human-infecting herpesviruses except varicella zoster virus (*Human alphaherpesvirus 3*) have been detected in at least one AGA. Patterns compatible with almost strict codivergence were identified for relatives of human herpesvirus 7 (HHV-7; *Human betaherpesvirus 7*) (Lavergne et al., 2014) and Kaposi's sarcoma-associated herpesvirus (KSHV, *Human gammaherpesvirus 8*) (Lacoste et al., 2000a, 2001), providing solid evidence for the permanent association of these viruses and the hominine lineage. Herpes simplex viruses 1 and 2 (HSV-1 and -2; *Human alphaherpesvirus 1* and *2*), Epstein-Barr virus (EBV; *Human gammaherpesvirus 4*) and human cytomegalovirus (HCMV; *Human betaherpesvirus 5*) belong to lineages with more complicated histories involving potential cross-hominine jumps, including toward humans (see *Cross-species transmission between hominines*) (Ehlers et al., 2010; Leendertz et al., 2009; Murthy et al., 2019; Wertheim et al., 2014, 2021). Yet, hypothesis testing assuming scenarios combining specific codivergence and host switch events have also shown that HSV-1, EBV and HCMV are heirloom parasites of humans. HSV-2 likely resulted from a cross-species transmission from the ancestors of gorillas or bonobos but molecular clock analyses showed that this transmission event happened more than a million year ago (i.e., before our

species existed; Wertheim et al., 2014, 2021). This virus was therefore transmitted to another (now extinct) member of the human lineage (*Paranthropus boisei* was identified as this potential intermediate host; Underdown et al., 2017) but likely always infected *Homo sapiens*.

Observations consistent with a very long association of dsDNA viruses and hominines/humans are not restricted to herpesviruses; similar indications have been obtained about viruses from at least two other families (families *Adenoviridae* and *Polyomaviridae*). The diversification process of the human adenovirus C (HAdV-C; *Human Mastadenovirus C*) matches very closely that of their hominine hosts, including when it comes to the phylogenetic placement of human-infecting members (Duncan et al., 2013; Hoppe et al., 2015; Roy et al., 2009; Wevers et al., 2011). By contrast, the human-infecting Merkel cell polyomavirus (MCPyV; *Human polyomavirus 5*) occupies a basal position in an otherwise mostly codivergent lineage of hominine polyomaviruses (Madinda et al., 2016). The date to the last common ancestor of polyomaviruses is however consistent with the notion that MCPyV failed to codiverge. Both HAdV-C and MCPyV are also likely to represent ancestral companions of mankind. Other examples of heirloom dsDNA viruses are very likely to be formally identified in the future, as AGA-infecting viruses are already known to be the closest relatives of a number of human-infecting ones. This includes dsDNA viruses belonging to the aforementioned families, e.g., human herpesvirus 6 (*Human betaherpesvirus 6*; Lacoste et al., 2005) and New Jersey polyomavirus (*Human polyomavirus 13*; Mishra et al., 2014) but also papillomaviruses (family *Papillomaviridae*; Hoffmann et al., 2019; Mengual-Chuliá et al., 2012; Van Ranst et al., 1991).

Enzootic RNA viruses do not appear to be very common in wild AGA. For example, in a recent study of the gastrointestinal virome of chimpanzees from Kibale National Park (Uganda) no RNA virus very clearly associated with primate hosts could be detected (Negrey et al., 2020). Importantly, this general view may be the result of shared biological features of RNA viruses, including their tendency to mostly establish transient infections, which might complicate their detection. Two viral families are notable exceptions and comprise members which can be identified year-round in wild AGA. Enteroviruses (family *Picornaviridae*) have been detected frequently, including from samples of relatively modest size (Harvala et al., 2011, 2014; Mombo et al., 2017; Sadeuh-Mba et al., 2014). To our knowledge, enterovirus evolutionary timescales have not been well characterized, so it remains unknown whether some enteroviral types are long-term associates of humans or AGA. At least three distinct groups of exogenous retroviruses,

representing the genera *Deltaretrovirus*, *Lentivirus* and *Spumaretrovirus* in the family *Retroviridae*, can be considered enzootic in AGA. Among those, foamy viruses most certainly represent one of the viral groups for which the evidence in favor of very long-term association with vertebrate hosts, and among them primate hosts, is the most convincing (e.g., Khan et al., 2018; Switzer et al., 2005). Foamy viruses have been detected in all AGA and within these hosts their evolution seems to have been almost entirely compatible with a pure codivergence model (Liu et al., 2008; Schulze et al., 2011; Switzer et al., 2005). However, if AGA-infecting foamy viruses can be considered heirloom parasites, humans stand as clear outliers as they do not host any closely associated foamy virus, most likely reflecting an ancient virus extinction event.

In summary, the notion that most enzootic viruses of AGA and endemic viruses of pre-Neolithic humans would have a long history of association with their hosts seems to be well in line with our current knowledge, and particularly so when considering dsDNA viruses.

2.2 Viral zoonosis was common

2.2.1 Nonhominine-borne zoonoses

Hunting is considered one of the major behaviors that shaped early hominids' evolution and is a shared character of humans, chimpanzees and bonobos. It seems plausible that hunting might have led to virus emergence in these three species. Observations of chimpanzees and bonobos in their natural habitats have revealed that many populations hunt regularly, and sometimes heavily (Boesch and Boesch, 1989; Klein et al., 2021; Pika et al., 2019; Samuni et al., 2020). For example, in TNP it has been estimated that the average adult male chimpanzee consumes around 68 kg of red colobus meat annually (Leendertz et al., 2011). The particular prey species hunted and the amount of hunting performed by an AGA population appears to depend on a number of factors, including availability of prey, the cultural preference of particular groups, social factors, and the abundance of other foods (Mitani and Watts, 2001; Samuni et al., 2020; Stanford et al., 1994).

Examinations of these predator-prey relationships, particularly of AGA and their sympatric monkeys, have revealed clear examples of between-species transmission of viruses. As an example, we discuss three retroviruses circulating in Tai National Park at high prevalence: simian T-cell leukemia viruses type 1 (STLV-1), simian foamy viruses (SFV), and simian immunodeficiency viruses (SIV; Gogarten et al., 2014).

To date, STLV-1 has been detected in sooty mangabeys, red colobus monkeys, and chimpanzees, and the STLV-1 strains circulating are not strictly species-specific; STLV-1 infecting sooty mangabeys on the one hand (which are not hunted by chimpanzees) and red colobus and chimpanzees on the other, form largely homogeneous clades (Calvignac-Spencer et al., 2012b). While this is clear evidence for ongoing cross-species transmission, no cases of further transmission in chimpanzees have been documented, suggesting these are (at least largely) dead end transmission events. Similar observations have been made regarding SFV, in the context of the aforementioned very strong codivergence signal of these viruses. It was indeed shown that some chimpanzees were coinfected by their species-adapted foamy virus as well as by the red colobus-specific foamy virus (Leendertz et al., 2010). In contrast, SIV, which has been detected at high prevalence in sooty mangabeys, western red colobus and olive colobus, showed a very strict host specificity, suggesting very rare or absent ongoing transmission (Courgnaud et al., 2003; Leendertz et al., 2011; Liégeois et al., 2009). Like other *Pan troglodytes* vs populations (Gao et al., 1999; Prince et al., 2002; Santiago et al., 2002) the chimpanzees of TNP are not infected by SIV (Leendertz et al., 2011). Central West African chimpanzees (*Pan troglodytes troglodytes*) on the other hand, are infected with SIV; the virus infecting chimpanzees is a mosaic of SIVs from at least two of its prey species, the red-capped mangabeys (*Cercocebus torquatus*) and either mustached guenons (*Cercopithecus cephus*), mona monkeys (*Cercopithecus mona*) or greater spot-nosed monkeys (*Cercopithecus nictitans*) or an ancestor of these cercopithecines (Courgnaud et al., 2003; Sharp et al., 2005). The 5′ part of the virus genome might even come from a third, as yet unidentified host (Bell and Bedford, 2017). This suggests that given the right conditions, SIV lineages infecting different hosts can recombine in a predator in ways that allow the virus to thrive. It appears that the hunting behavior of chimpanzees creates opportunities for transmission and recombination of viruses, but that not all viruses are able to establish in AGA.

At least two other viruses are known to cause sporadic outbreaks in AGA populations and are likely to arise from a zoonotic reservoir. Ebolaviruses (family *Filoviridae*) have caused outbreaks in chimpanzees and gorillas, yet the source of these spillover events remains unknown. These outbreaks quickly burned themselves out, presumably due to the high mortality caused by this virus (ebolavirus outbreaks in AGA are dealt with in greater detail in Section 2.4). Similarly, there were repeated emergence events of monkeypox virus (family *Poxviridae*) in chimpanzees in TNP, though the reservoir remains unknown and these outbreaks also quickly came to an end (Patrono et al., 2020).

2.2.2 Cross-species transmission between hominines

The range of humans overlaps with that of all AGA, and the ranges of many AGA also overlap. There are no good reasons to believe this did not apply for most of the evolutionary history of this group. Therefore, humans and AGA very often use(d) the same habitats, which has provided the opportunity for virus exchanges via a number of direct or indirect interactions, e.g., hunting/aggression or resource sharing (Walsh et al., 2007). Because phylogenetic proximity is a predictor of successful cross-species transmission (Streicker et al., 2010), it can be expected that cross-hominine virus transmission played a significant role in shaping their viromes.

As a matter of fact, there is good evidence that AGA have transmitted their viruses to humans all along their evolutionary history. The most ancient known transmission event gave rise to HSV-2, whose ancestor probably originated in gorillas and was transmitted to humans more than one million year ago (Wertheim et al., 2014, 2021). The human adenovirus B (HAdV-B; *Human mastadenovirus B*), another virus whose original host was gorillas, was transmitted twice to humans more than 100,000 years ago, while human adenovirus E (HAdV-E; *Human mastadenovirus E*) probably emerged from chimpanzees slightly more recently (Hoppe et al., 2015). Much more recently and prominently, the various groups of HIV-1 have emerged in humans as the result of transmission events from chimpanzees (groups M and N) and gorillas (groups O and P) during the 20th century (D'Arc et al., 2015; Sharp and Hahn, 2011). Individual transmission events of SFV from chimpanzees and gorillas to humans have also been documented, although contrary to the aforementioned examples they never led to human-to-human transmission and a *fortiori* long-term endemic circulation (Betsem et al., 2011; Calattini et al., 2007; Heneine et al., 1998).

Strikingly, cross-hominine transmission histories are often complicated by networks of transmission between multiple hominine species. This is the case for all of the aforementioned examples. The simplexvirus lineage originating in gorillas which caused the emergence of HSV-2 also came to infect bonobos and chimpanzees (Wertheim et al., 2021). One of the HAdV-B lineages currently circulating in humans actually emerged from chimpanzees which had themselves been infected by gorillas (Hoppe et al., 2015). Finally, if gorillas have transmitted their SIV to humans, they initially acquired them from chimpanzees. Another example of complicated transmission history was recently confirmed for cytomegaloviruses; while HCMV appears to be the expected codivergent virus, the gorilline and panine lineages exchanged their respective CMV more than one million years ago. This was later followed by codivergence with their hosts, leading to an

apparent lineage duplication and the circulation of two independent CMV lineages in all modern AGA (Murthy et al., 2019).

Importantly, humans can also transmit their viruses to AGA. While this is obvious from ongoing observations of respiratory virus transmission in the context of long-term habituation programs of wild great apes (see next section), hepatitis B viruses enzootically infecting wild AGA (Hu et al., 2001; MacDonald et al., 2000; Njouom et al., 2010; Takahashi et al., 2000) were likely transmitted from humans a few thousand years ago (Mühlemann et al., 2018).

In line with the expectations of the Paleolithic baseline model, the zoonotic emergence of viruses appears as a relatively common (and still ongoing) process in the hominine lineage. Ancient transmission events have even led to the establishment of a number of human endemic viruses. Perhaps surprisingly, a high proportion of these zoonotic events have involved cross-hominine jumps, highlighting both frequent interactions between our species and enhanced likelihood of successful adaptation to the new host.

2.3 Human-adapted epidemic viral diseases did not exist

As highlighted above, zoonotic transmissions to AGA are quite common, and in some cases (e.g., ebolaviruses) can cause epizootics. In contrast, we are not aware of any epizootic in AGA that was caused by an AGA-adapted virus rather than a zoonotic spill over. To investigate the hypothesis that AGA populations are not permissive to the long-term establishment of epizootic agents, the inadvertent transmission of human respiratory viruses to wild, human-habituated AGA can serve as an interesting model.

Since the early 2000s', common human endemic viruses have been responsible for mild to severe respiratory disease outbreaks across AGA species and habitats. Viruses of the family *Pneumoviridae*, such as the human orthopneumovirus (type A and B) and the human metapneumovirus (HMPV) were among the first to be identified in necropsy samples collected during lethal outbreaks (Köndgen et al., 2008), and have since been detected repeatedly. Infections with human orthopneumoviruses were reported in western chimpanzees in Ivory Coast (Köndgen et al., 2008, 2017), in western lowland gorillas in Central African Republic (Grützmacher et al., 2016), and in bonobos in the Democratic Republic of the Congo (Grützmacher et al., 2018). HMPV has been transmitted to western chimpanzees in Ivory Coast (Köndgen et al., 2008), eastern chimpanzees in Tanzania

(Kaur et al., 2008) and Uganda (Negrey et al., 2019), and mountain gorillas in Rwanda (Palacios et al., 2011). Thanks to the awareness raised by these first reports, other human viruses have been reported in association with acute disease in AGA, such as the human rhinovirus C (family *Picornaviridae*; Scully et al., 2018), the human respirovirus 3 (family *Paramyxoviridae*; Negrey et al., 2019) and the human coronavirus OC43 (family *Coronaviridae*; Patrono et al., 2018). Phylogenetic analyses consistently placed the viral strains found in the AGA within the diversity of human lineages, though a lack of data on the circulation of these pathogens in local human populations precluded a more precise determination of the geographical origins of the strains transmitted.

Morbidity varied greatly among these different outbreaks but was generally high, reaching up to 100% during an HMPV outbreak in western chimpanzees (Köndgen et al., 2010). Mortality was often attributed to secondary bacterial infections and the highest rate reported was 18% (Köndgen et al., 2010). Thus far, re-emergence of the same virus has not been reported in any instance, pointing toward isolated spillover events. Studies in the Taï chimpanzees have shown that in between two independent outbreaks of orthopneumovirus B, occurring 7 months apart in the same group, no viral shedding could be detected (Köndgen et al., 2010). These findings suggest that once a virus has spread within a group, conditions that would support endemicity do not subsist.

Several factors may contribute to the lack of persistence of these viruses in these populations. Following infection, AGA likely develop some degree of immunity as has been observed in humans (González et al., 2017), though this has not yet been formally demonstrated in wild populations. AGA population densities are naturally low and this has been amplified over the last centuries/decades due to hunting, habitat encroachment, and infectious diseases (Greer et al., 2018). Combined with the insurgence of immunity, these small numbers may not allow the presence of enough susceptible individuals that would be required to maintain the virus in the population. Understanding how rates of contact between groups, including intergroup encounters and rates of immigration influence the spread of disease in wild populations represents an important area of future research.

Overall, the evidence gathered from many episodes of (human introduced) acute viral disease in AGA supports the theory that also in ancient human populations community size likely did not support the persistence of such infections.

2.4 Viral disease burden was limited

An examination of mortality patterns in wild AGA populations reveals that mortality is not random or primarily driven by food abundance. Rather mortality occurs in patterns that suggest an important role of infectious diseases. In the chimpanzees of TNP, mortality cycled in a way that was not well explained by environmental factors, rather mortality cycles were driven by the ontogeny of social play. Cycles started when diseases led to the death of multiple infants, which synchronized the reproductive cycles of their mothers and a subsequent pulse of births ultimately led to increasing social connectivity as the large birth cohort approached the peak of social play. The high social connectivity at this play peak then appeared to facilitate disease outbreaks and mortality (Kuehl et al., 2008). A comparative analysis of adult and juvenile mortality across many non-human primate species, including AGA populations, revealed that those living in more seasonal environments have more seasonal mortality patterns, often with elevated mortality during the rainy season when disease burden is increased due to arthropod abundance and parasite transmission rates, not when food availability was scarce. In mountain gorillas specifically, mortality was markedly seasonal, with increased deaths during the pronounced rainy season rather than when preferred foods were least abundant (Gogarten et al., 2012). These studies suggest that infectious diseases likely play an important role in the mortality of AGA.

To specifically assess the viral disease burden of AGA, a number of approaches have been used. Because of the slow life history of AGA, to understand the health implications of naturally occurring viral infections, long-term studies are required that include data on viral infections, and such data are only slowly becoming available. Perhaps the best examples of such a long-term demographic assessment of the impact of naturally occurring chronic viral infections, are studies of SIV infections in East African chimpanzees (*Pan troglodytes schweinfurthii*). While it was long assumed that SIV in AGA are non-pathogenic, there was considerable interest from the medical community to understand how this might be possible. These studies revealed that in reality infections with SIV led to a 10- to 16-fold higher age-corrected death hazard and that infected females had lower birth rates and a higher infant mortality rate than uninfected females. SIV infections were further shown to cause clinical manifestations very similar to human AIDS (Keele et al., 2009). To assess the impact of SIV infections on chimpanzee population dynamics, these studies were expanded to include a neighboring non-habituated community, and found SIV infections were

likely responsible for a major decline in the size of the non-habituated community. Surprisingly, simulations parameterized with these data suggest that even when SIV infections are at a low prevalence in a particular chimpanzee community, they increased the risk of community extinction considerably (Rudicell et al., 2010). These SIV studies represent the culmination of huge efforts in terms of testing and following chimpanzees for many years; to date they have not been attempted for other viral infections, but that such a strong effect was found in the one system studied extensively suggests that chronic viral infections may play a more predominant role in AGA health than previously appreciated.

For those viruses that cause sporadic outbreaks in AGA populations arising from an unknown zoonotic reservoir, ebolaviruses represent perhaps the best example highlighting the massive impact such outbreaks can have. In the Republic of Congo, several ebolavirus outbreaks have caused massive mortality in Western lowland gorillas, as well as to a lesser extent in Central chimpanzee populations (Bermejo et al., 2006; Walsh et al., 2003). While exact estimates are difficult to obtain for wild populations of AGA, the numbers of gorillas killed in the outbreak in 2002 and 2003 in the Lossi Sanctuary in northwest Republic of Congo is estimated to be around 5000, with population losses exceeding 90% observed in habituated gorillas (Bermejo et al., 2006). Wildlife surveys in the Minkebé and Mwagne forest blocks suggested a similarly dramatic reduction (90–98%) in the gorilla and chimpanzee populations that have been attributable to the outbreaks over large spatial scales (Lahm et al., 2007). To date, it remains largely unclear how between-group transmission occurs, though emigration of infected animals or contact with carcasses from neighboring groups represent possible routes of transmission. Alternatively, these outbreaks may be driven by repeated spillover from an unknown reservoir or transmission from some other susceptible wildlife (Leendertz et al., 2017).

AGA have evolved resistance to some viral infections, and studies are increasingly revealing the mechanisms by which they do and how these are evaded by different viral genes. The evolution of such specific defense mechanisms is further evidence for the strong selection pressure posed by these viruses. Again, some of the best evidence comes from studies of SIV; the lack of SIV infections observed in TNP chimpanzees might be driven in part by the host defense protein APOBEC3G, which viruses attempt to outwit through the lentiviral viral integration factor (Vif). APOBEC3G is an intracellular cytidine deaminase which restricts

retroviruses by hypermutating their genomes; retroviruses in turn counteract APOBEC3G with Vif, which promotes APOBEC3G degradation by the proteasome. Evidence suggests that the binding site of Vif in a diversity of NHP's APOBEC3G is well conserved among cercopithecines and that the sequence is under strong positive selection (Compton and Emerman, 2013). Surprisingly, the binding site of Vif in colobine's APOBEC3G has shifted in a way that allows their SIVs to deal with the insertion in their host's APOBEC3G sequence (Compton and Emerman, 2013). Colobine SIVs appear to be susceptible to the activity of non-colobine APOBEC3G; all of this suggests that colobine SIVs are efficiently restricted by chimpanzee APOBEC3G, preventing infections from propagating, despite extremely high levels of exposure due to chimpanzee hunting of colobines.

More broadly, mammalian (and AGA) genomes bear strong marks of brutal battles with viral infections. Viruses interact with many proteins when they infect a host and viruses appear to target proteins in the host that are evolutionarily constrained; surprisingly, a study by Enard and colleagues found that virus-interacting proteins seem to represent an extremely high proportion of all protein adaptations observed in mammals. Their minimum estimate suggests that viruses drove close to 30% of all adaptive amino acid changes in the part of the human proteome conserved within mammals. These studies strongly suggest that viruses actually represent one of the most important drivers of evolutionary change across mammalian and human proteomes (Enard et al., 2016).

Overall, the prediction that viral disease burden was of limited evolutionary significance prior to the first epidemiological transition of humankind seems to be the only of the four hypotheses we revisited in this review that is not widely supported by evidence garnered from studies of AGA. Rather, viruses seem to influence mortality in wild AGA populations in a profound way and these viruses have left a considerable mark in the genomes of AGA.

3. Conclusion

The study of viruses infecting AGA has progressed immensely over the last two decades, taking advantage of technological revolutions, big (like the advent of high-throughput sequencing) and small (with the realization of the detectability of many viruses in fecal material). Although much remains to be discovered, this has already allowed for the identification of many viral lineages, whose often complex evolutionary histories could only

be disentangled with the help of ever improving statistical inference tools. Now, well-established frameworks to ethically conduct this type of research (and beyond, bona fide health monitoring) in wild populations create opportunities to scale up such activities across the entire range of AGA. As we hope this review illustrated, intensifying these efforts will simultaneously provide meaningful information about the viral determinants of our closest relatives' health and lay the foundations of a better understanding of the evolution of human health in general, and human-infecting viruses in particular.

References

Aiewsakun, P., Katzourakis, A., 2016. Time-dependent rate phenomenon in viruses. J. Virol. 90 (16), 7184–7195.

Armelagos, G.J., Brown, P.J., Turner, B., 2005. Evolutionary, historical and political economic perspectives on health and disease. Soc. Sci. Med. 61 (4), 755–765.

Asher, D.M., Hooks, J.J., Amyx, H.L., Luber, N.P., Asher, L.V., Gibbs, C.J., Gajdusek, D.C., 1978. Persistent shedding of adenovirus in urine of chimpanzees. Infect. Immun. 21 (1), 129–134.

Bell, S.M., Bedford, T., 2017. Modern-day SIV viral diversity generated by extensive recombination and cross-species transmission. PLoS Pathog. 13 (7), e1006466.

Bermejo, M., Rodríguez-Teijeiro, J.D., Illera, G., Barroso, A., Vilà, C., Walsh, P.D., 2006. Ebola outbreak killed 5000 gorillas. Science 314 (5805), 1564.

Betsem, E., Rua, R., Tortevoye, P., Froment, A., Gessain, A., 2011. Frequent and recent human acquisition of simian foamy viruses through apes' bites in Central Africa. PLoS Pathog. 7 (10), e1002306.

Bocquet-Appel, J.-P., 2011. The agricultural demographic transition during and after the agriculture inventions. Curr. Anthropol. 52 (S4), S497–S510.

Boesch, C., Boesch, H., 1989. Hunting behavior of wild chimpanzees in the Tai National Park. Am. J. Phys. Anthropol. 78 (4), 547–573.

Boesch, C., Boesch-Achermann, H., 2000. The Chimpanzees of the Taï Forest: Behavioural Ecology and Evolution. Oxford University Press, USA.

Brussaard, C.P., 2004. Viral control of phytoplankton populations—a review 1. J. Eukaryot. Microbiol. 51 (2), 125–138.

Calattini, S., Betsem, E.B.A., Froment, A., Mauclère, P., Tortevoye, P., Schmitt, C., Njouom, R., Saib, A., Gessain, A., 2007. Simian foamy virus transmission from apes to humans, rural Cameroon. Emerg. Infect. Dis. 13 (9), 1314–1320.

Calvignac, S., Terme, J.-M., Hensley, S.M., Jalinot, P., Greenwood, A.D., Hänni, C., 2008. Ancient DNA identification of early 20th century simian T-cell leukemia virus type 1. Mol. Biol. Evol. 25 (6), 1093–1098.

Calvignac-Spencer, S., Leendertz, S.A., Gillespie, T.R., Leendertz, F.H., 2012a. Wild great apes as sentinels and sources of infectious disease. Clin. Microbiol. Infect. 18 (6), 521–527.

Calvignac-Spencer, S., Adjogoua, E.V., Akoua-Koffi, C., Hedemann, C., Schubert, G., Ellerbrok, H., Leendertz, S.A.J., Pauli, G., Leendertz, F.H., 2012b. Origin of human T-lymphotropic virus type 1 in rural Côte d'Ivoire. Emerg. Infect. Dis. 18 (5), 830–833.

Castellano, D., Munch, K., 2020. Population genomics in the great apes. In: Statistical Population Genomics. Humana, New York, NY, pp. 453–463.

Compton, A.A., Emerman, M., 2013. Convergence and divergence in the evolution of the APOBEC3G-Vif interaction reveal ancient origins of simian immunodeficiency viruses. PLoS Pathog. 9 (1), e1003135.

Courgnaud, V., Formenty, P., Akoua-Koffi, C., Noe, R., Boesch, C., Delaporte, E., Peeters, M., 2003. Partial molecular characterization of two simian immunodeficiency viruses (SIV) from African colobids: SIVwrc from Western red colobus (Piliocolobus badius) and SIVolc from olive colobus (Procolobus verus). J. Virol. 77 (1), 744–748.

D'Arc, M., Ayouba, A., Esteban, A., Learn, G.H., Boué, V., Liegeois, F., Etienne, L., Tagg, N., Leendertz, F.H., Boesch, C., Madinda, N.F., Robbins, M.M., Gray, M., Cournil, A., Ooms, M., Letko, M., Simon, V.A., Sharp, P.M., Hahn, B.H., Delaporte, E., Mpoudi Ngole, E., Peeters, M., 2015. Origin of the HIV-1 group O epidemic in western lowland gorillas. Proc. Natl. Acad. Sci. U. S. A. 112 (11), E1343–E1352.

de Vienne, D.M., Refrégier, G., López-Villavicencio, M., Tellier, A., Hood, M.E., Giraud, T., 2013. Cospeciation vs host-shift speciation: methods for testing, evidence from natural associations and relation to coevolution. New Phytol. 198 (2), 347–385.

Duchêne, S., Holmes, E.C., Ho, S.Y., 2014. Analyses of evolutionary dynamics in viruses are hindered by a time-dependent bias in rate estimates. Proc. R. Soc. B Biol. Sci. 281 (1786), 20140732.

Duffy, S., Shackelton, L.A., Holmes, E.C., 2008. Rates of evolutionary change in viruses: patterns and determinants. Nat. Rev. Genet. 9 (4), 267–276.

Duncan, M., Cranfield, M.R., Torano, H., Kuete, H.M., Lee, G.P., Glenn, A., Bruder, J.T., Rangel, D., Brough, D.E., Gall, J.G., 2013. Adenoviruses isolated from wild gorillas are closely related to human species C viruses. Virology 444 (1–2), 119–123.

Düx, A., Lequime, S., Patrono, L.V., Vrancken, B., Boral, S., Gogarten, J.F., Hilbig, A., Horst, D., Merkel, K., Prepoint, B., 2020. Measles virus and rinderpest virus divergence dated to the sixth century BCE. Science 368 (6497), 1367–1370.

Ehlers, B., Spiess, K., Leendertz, F., Peeters, M., Boesch, C., Gatherer, D., McGeoch, D.J., 2010. Lymphocryptovirus phylogeny and the origins of Epstein-Barr virus. J. Gen. Virol. 91 (Pt. 3), 630–642.

Enard, D., Cai, L., Gwennap, C., Petrov, D.A., 2016. Viruses are a dominant driver of protein adaptation in mammals. elife 5, e12469.

Formenty, P., Boesch, C., Wyers, M., Steiner, C., Donati, F., Dind, F., Walker, F., Le Guenno, B., 1999. Ebola virus outbreak among wild chimpanzees living in a rain forest of Côte d'Ivoire. J. Infect. Dis. 179 (Suppl. 1), S120–S126.

Gao, F., Bailes, E., Robertson, D.L., Chen, Y., Rodenburg, C.M., Michael, S.F., Cummins, L.B., Arthur, L.O., Peeters, M., Shaw, G.M., Sharp, P.M., Hahn, B.H., 1999. Origin of HIV-1 in the chimpanzee Pan troglodytes troglodytes. Nature 397 (6718), 436–441.

Geoghegan, J.L., Duchêne, S., Holmes, E.C., 2017. Comparative analysis estimates the relative frequencies of co-divergence and cross-species transmission within viral families. PLoS Pathog. 13 (2), e1006215.

Gilardi, K.V., Gillespie, T.R., Leendertz, F.H., Macfie, E.J., Travis, D.A., Whittier, C.A., Williamson, E.A., 2015. Best Practice Guidelines for Health Monitoring and Disease Control in Great Ape Populations. IUCN SSC Primate Specialist Group, Gland, Switzerland.

Gogarten, J.F., Brown, L.M., Chapman, C.A., Cords, M., Doran-Sheehy, D., Fedigan, L.M., Grine, F.E., Perry, S., Pusey, A.E., Sterck, E.H., Wich, S.A., Wright, P.C., 2012. Seasonal mortality patterns in non-human primates: implications for variation in selection pressures across environments. Evolution 66 (10), 3252–3266.

Gogarten, J.F., Akoua-Koffi, C., Calvignac-Spencer, S., Leendertz, S.A.J., Weiss, S., Couacy-Hymann, E., Koné, I., Peeters, M., Wittig, R.M., Boesch, C., Hahn, B.H.,

Leendertz, F.H., 2014. The ecology of primate retroviruses—an assessment of 12 years of retroviral studies in the Taï national park area, Côte d'Ivoire. Virology 460–461, 147–153.
Gogarten, J.F., Schubert, G., Leendertz, F.H., Calvignac-Spencer, S., 2019. The chimpanzees of the Taï Forest as models for hominine microorganism ecology and evolution. In: The Chimpanzees of the Taï Forest: 40 Years of Research. Cambridge University Press.
Gogarten, J.F., Rühlemann, M., Archie, E., Tung, J., Akoua-Koffi, C., Bang, C., Deschner, T., Muyembe-Tamfun, J.-J., Robbins, M.M., Schubert, G., Surbeck, M., Wittig, R.M., Zuberbühler, K., Baines, J.F., Franke, A., Leendertz, F.H., Calvignac-Spencer, S., 2021. Primate phageomes are structured by superhost phylogeny and environment. Proc. Natl. Acad. Sci. 118 (15), e2013535118.
González, A.E., Lay, M.K., Jara, E.L., Espinoza, J.A., Gómez, R.S., Soto, J., Rivera, C.A., Abarca, K., Bueno, S.M., Riedel, C.A., Kalergis, A.M., 2017. Aberrant T cell immunity triggered by human respiratory syncytial virus and human Metapneumovirus infection. Virulence 8 (6), 685–704.
Goodall, J., 1986. The Chimpanzees of Gombe: Patterns of Behavior. Harvard University Press, Cambridge, MA.
Greer, D., Humle, T., Kormos, R., Kühl, H., Macfie, E., Maisels, F., Oates, J., Robbins, M., Sherman, J., Sop, T., 2018. Great Apes Status Report.
Grützmacher, K.S., Köndgen, S., Keil, V., Todd, A., Feistner, A., Herbinger, I., Petrzelkova, K., Fuh, T., Leendertz, S.A., Calvignac-Spencer, S., Leendertz, F.H., 2016. Codetection of respiratory syncytial virus in habituated wild western lowland gorillas and humans during a respiratory disease outbreak. EcoHealth 13 (3), 499–510.
Grützmacher, K.S., Keil, V., Metzger, S., Wittiger, L., Herbinger, I., Calvignac-Spencer, S., Mätz-Rensing, K., Haggis, O., Savary, L., Köndgen, S., Leendertz, F.H., 2018. Human respiratory syncytial virus and Streptococcus pneumoniae infection in wild bonobos. EcoHealth 15 (2), 462–466.
Harvala, H., Sharp, C.P., Ngole, E.M., Delaporte, E., Peeters, M., Simmonds, P., 2011. Detection and genetic characterization of enteroviruses circulating among wild populations of chimpanzees in Cameroon: relationship with human and simian enteroviruses. J. Virol. 85 (9), 4480–4486.
Harvala, H., Van Nguyen, D., McIntyre, C., Ahuka-Mundeke, S., Ngole, E.M., Delaporte, E., Peeters, M., Simmonds, P., 2014. Co-circulation of enteroviruses between apes and humans. J. Gen. Virol. 95 (Pt. 2), 403.
Headland, T.N., Reid, L.A., 1991. Holocene foragers and interethnic trade: a critique of the myth of isolated independent hunter-gatherers. In: Between Bands and States 9, pp. 333–340.
Heneine, W., Switzer, W.M., Sandstrom, P., Brown, J., Vedapuri, S., Schable, C.A., Khan, A.S., Lerche, N.W., Schweizer, M., Neumann-Haefelin, D., Chapman, L.E., Folks, T.M., 1998. Identification of a human population infected with simian foamy viruses. Nat. Med. 4 (4), 403–407.
Heuverswyn, F.V., Li, Y., Bailes, E., Neel, C., Lafay, B., Keele, B.F., Shaw, K.S., Takehisa, J., Kraus, M.H., Loul, S., Butel, C., Liegeois, F., Yangda, B., Sharp, P.M., Mpoudi-Ngole, E., Delaporte, E., Hahn, B.H., Peeters, M., 2007. Genetic diversity and phylogeographic clustering of SIVcpzPtt in wild chimpanzees in Cameroon. Virology 368 (1), 155–171.
Hillis, W.D., Garner, A.C., Hillis, A.I., 1969. A new simian adenovirus serologically related to human adenovirus type 2 and a chimpanzee with "viral hepatitis". Am. J. Epidemiol. 90 (4), 344–353.
Hoffmann, M., Schütze, E., Bernhard, A., Schlaphoff, L., Kaul, A., Schöniger, S., Pöhlmann, S., 2019. Disease manifestation and viral sequences in a bonobo more than 30 years after papillomavirus infection. Pathogens 8 (1), 13.

Hollander, C.F., van Noord, M.J., 1972. Focal epithelial hyperplasia: a virus-induced oral mucosal lesion in the chimpanzee. Oral Surg. Oral Med. Oral Pathol. 33 (2), 220–226.
Hoppe, E., Pauly, M., Gillespie, T.R., Akoua-Koffi, C., Hohmann, G., Fruth, B., Karhemere, S., Madinda, N.F., Mugisha, L., Muyembe, J.-J., 2015. Multiple cross-species transmission events of human adenoviruses (HAdV) during hominine evolution. Mol. Biol. Evol. 32 (8), 2072–2084.
Hu, X.-L., Javadian, A., Gagneux, P., Robertson, B.H., 2001. Paired chimpanzee hepatitis B virus (ChHBV) and mtDNA sequences suggest different ChHBV genetic variants are found in geographically distinct chimpanzee subspecies. Virus Res. 79 (1), 103–108.
Hurtado, M., Hill, K., Kaplan, H., Lancaster, J., 2001. The epidemiology of infectious diseases among South American Indians: a call for guidelines for ethical research. Curr. Anthropol. 42 (3), 425–432.
Kaur, T., Singh, J., Tong, S., Humphrey, C., Clevenger, D., Tan, W., Szekely, B., Wang, Y., Li, Y., Alex Muse, E., Kiyono, M., Hanamura, S., Inoue, E., Nakamura, M., Huffman, M.A., Jiang, B., Nishida, T., 2008. Descriptive epidemiology of fatal respiratory outbreaks and detection of a human-related metapneumovirus in wild chimpanzees (Pan troglodytes) at Mahale Mountains National Park, Western Tanzania. Am. J. Primatol. 70 (8), 755–765.
Keele, B.F., Jones, J.H., Terio, K.A., Estes, J.D., Rudicell, R.S., Wilson, M.L., Li, Y., Learn, G.H., Beasley, T.M., Schumacher-Stankey, J., Wroblewski, E., Mosser, A., Raphael, J., Kamenya, S., Lonsdorf, E.V., Travis, D.A., Mlengeya, T., Kinsel, M.J., Else, J.G., Silvestri, G., Goodall, J., Sharp, P.M., Shaw, G.M., Pusey, A.E., Hahn, B.H., 2009. Increased mortality and AIDS-like immunopathology in wild chimpanzees infected with SIVcpz. Nature 460 (7254), 515–519.
Khan, A.S., Bodem, J., Buseyne, F., Gessain, A., Johnson, W., Kuhn, J.H., Kuzmak, J., Lindemann, D., Linial, M.L., Löchelt, M., 2018. Spumaretroviruses: updated taxonomy and nomenclature. Virology 516, 158–164.
Klein, H., Bocksberger, G., Baas, P., Bunel, S., Théleste, E., Pika, S., Deschner, T., 2021. Hunting of mammals by central chimpanzees (pan troglodytes troglodytes) in the Loango National Park, Gabon. Primates 62 (2), 267–278.
Köndgen, S., Kühl, H., N'Goran, P.K., Walsh, P.D., Schenk, S., Ernst, N., Biek, R., Formenty, P., Mätz-Rensing, K., Schweiger, B., Junglen, S., Ellerbrok, H., Nitsche, A., Briese, T., Lipkin, W.I., Pauli, G., Boesch, C., Leendertz, F.H., 2008. Pandemic human viruses cause decline of endangered great apes. Curr. Biol. 18 (4), 260–264.
Köndgen, S., Schenk, S., Pauli, G., Boesch, C., Leendertz, F.H., 2010. Noninvasive monitoring of respiratory viruses in wild chimpanzees. EcoHealth 7 (3), 332–341.
Köndgen, S., Calvignac-Spencer, S., Grützmacher, K., Keil, V., Mätz-Rensing, K., Nowak, K., Metzger, S., Kiyang, J., Lübke-Becker, A., Deschner, T., Wittig, R.M., Lankester, F., Leendertz, F.H., 2017. Evidence for human Streptococcus pneumoniae in wild and captive chimpanzees: a potential threat to wild populations. Sci. Rep. 7 (1), 14581.
Kuehl, H.S., Elzner, C., Moebius, Y., Boesch, C., Walsh, P.D., 2008. The price of play: self-organized infant mortality cycles in chimpanzees. PLoS One 3 (6), e2440.
Lacoste, V., Kadyrova, E., Chistiakova, I., Gurtsevitch, V., Judde, J.-G., Gessain, A., 2000a. Molecular characterization of Kaposi's sarcoma-associated herpesvirus/human herpesvirus-8 strains from Russia. Microbiology 81 (5), 1217–1222.
Lacoste, V., Mauclère, P., Dubreuil, G., Lewis, J., Georges-Courbot, M.C., Gessain, A., 2000b. KSHV-like herpesviruses in chimps and gorillas. Nature 407 (6801), 151–152.
Lacoste, V., Mauclère, P., Dubreuil, G., Lewis, J., Georges-Courbot, M.-C., Gessain, A., 2001. A novel gamma 2-herpesvirus of the Rhadinovirus 2 lineage in chimpanzees. Genome Res. 11 (9), 1511–1519.

Lacoste, V., Verschoor, E.J., Nerrienet, E., Gessain, A., 2005. A novel homologue of human herpesvirus 6 in chimpanzees. J. Gen. Virol. 86 (Pt. 8), 2135–2140.
Lahm, S.A., Kombila, M., Swanepoel, R., Barnes, R.F.W., 2007. Morbidity and mortality of wild animals in relation to outbreaks of Ebola haemorrhagic fever in Gabon, 1994–2003. Trans. R. Soc. Trop. Med. Hyg. 101 (1), 64–78.
Lavergne, A., Donato, D., Gessain, A., Niphuis, H., Nerrienet, E., Verschoor, E.J., Lacoste, V., 2014. African great apes are naturally infected with roseoloviruses closely related to human herpesvirus 7. J. Virol. 88 (22), 13212–13220.
Leendertz, F.H., Pauli, G., Maetz-Rensing, K., Boardman, W., Nunn, C., Ellerbrok, H., Jensen, S.A., Junglen, S., Christophe, B., 2006. Pathogens as drivers of population declines: the importance of systematic monitoring in great apes and other threatened mammals. Biol. Conserv. 131 (2), 325–337.
Leendertz, F.H., Deckers, M., Schempp, W., Lankester, F., Boesch, C., Mugisha, L., Dolan, A., Gatherer, D., McGeoch, D.J., Ehlers, B., 2009. Novel cytomegaloviruses in free-ranging and captive great apes: phylogenetic evidence for bidirectional horizontal transmission. J. Gen. Virol. 90 (Pt. 10), 2386–2394.
Leendertz, S.A.J., Junglen, S., Hedemann, C., Goffe, A., Calvignac, S., Boesch, C., Leendertz, F.H., 2010. High prevalence, coinfection rate, and genetic diversity of retroviruses in wild red colobus monkeys (Piliocolobus badius badius) in Taï National Park, Côte d'Ivoire. J. Virol. 84 (15), 7427–7436.
Leendertz, S.A.J., Locatelli, S., Boesch, C., Kücherer, C., Formenty, P., Liegeois, F., Ayouba, A., Peeters, M., Leendertz, F.H., 2011. No evidence for transmission of SIVwrc from western red colobus monkeys (Piliocolobus badius badius) to wild West African chimpanzees (Pan troglodytes verus) despite high exposure through hunting. BMC Microbiol. 11 (1), 1–11.
Leendertz, S.A.J., Wich, S.A., Ancrenaz, M., Bergl, R.A., Gonder, M.K., Humle, T., Leendertz, F.H., 2017. Ebola in great apes—current knowledge, possibilities for vaccination, and implications for conservation and human health. Mammal Rev. 47 (2), 98–111.
Liégeois, F., Lafay, B., Formenty, P., Locatelli, S., Courgnaud, V., Delaporte, E., Peeters, M., 2009. Full-length genome characterization of a novel simian immunodeficiency virus lineage (SIVolc) from olive colobus (Procolobus verus) and new SIVwrcPbb strains from Western red colobus (Piliocolobus badius badius) from the Taï Forest in Ivory Coast. J. Virol. 83 (1), 428–439.
Liu, W., Worobey, M., Li, Y., Keele, B.F., Bibollet-Ruche, F., Guo, Y., Goepfert, P.A., Santiago, M.L., Ndjango, J.-B.N., Neel, C., 2008. Molecular ecology and natural history of simian foamy virus infection in wild-living chimpanzees. PLoS Pathog. 4 (7), e1000097.
López-García, P., Eme, L., Moreira, D., 2017. Symbiosis in eukaryotic evolution. J. Theor. Biol. 434, 20–33.
MacDonald, D.M., Holmes, E.C., Lewis, J.C.M., Simmonds, P., 2000. Detection of hepatitis B virus infection in wild-born chimpanzees (Pan troglodytes verus): phylogenetic relationships with human and other primate genotypes. J. Virol. 74 (9), 4253–4257.
Madinda, N.F., Ehlers, B., Wertheim, J.O., Akoua-Koffi, C., Bergl, R.A., Boesch, C., Akonkwa, D.B.M., Eckardt, W., Fruth, B., Gillespie, T.R., 2016. Assessing host-virus codivergence for close relatives of Merkel cell polyomavirus infecting African great apes. J. Virol. 90 (19), 8531–8541.
McFall-Ngai, M., Hadfield, M.G., Bosch, T.C., Carey, H.V., Domazet-Lošo, T., Douglas, A.E., Dubilier, N., Eberl, G., Fukami, T., Gilbert, S.F., 2013. Animals in a bacterial world, a new imperative for the life sciences. Proc. Natl. Acad. Sci. 110 (9), 3229–3236.
McGeoch, D.J., Rixon, F.J., Davison, A.J., 2006. Topics in herpesvirus genomics and evolution. Virus Res. 117 (1), 90–104.

Membrebe, J.V., Suchard, M.A., Rambaut, A., Baele, G., Lemey, P., 2019. Bayesian inference of evolutionary histories under time-dependent substitution rates. Mol. Biol. Evol. 36 (8), 1793–1803.

Mengual-Chuliá, B., García-Pérez, R., Gottschling, M., Nindl, I., Bravo, I.G., 2012. Novel animal papillomavirus sequences and accurate phylogenetic placement. Mol. Phylogenet. Evol. 65 (3), 883–891.

Mishra, N., Pereira, M., Rhodes, R.H., An, P., Pipas, J.M., Jain, K., Kapoor, A., Briese, T., Faust, P.L., Lipkin, W.I., 2014. Identification of a novel polyomavirus in a pancreatic transplant recipient with retinal blindness and vasculitic myopathy. J. Infect. Dis. 210 (10), 1595–1599.

Mitani, J.C., Watts, D.P., 2001. Why do chimpanzees hunt and share meat? Anim. Behav. 61 (5), 915–924.

Mombo, I.M., Lukashev, A.N., Bleicker, T., Brünink, S., Berthet, N., Maganga, G.D., Durand, P., Arnathau, C., Boundenga, L., Ngoubangoye, B., 2017. African non-human primates host diverse enteroviruses. PLoS One 12 (1), e0169067.

Mühlemann, B., Jones, T.C., Damgaard, P.D.B., Allentoft, M.E., Shevnina, I., Logvin, A., Usmanova, E., Panyushkina, I.P., Boldgiv, B., Bazartseren, T., Tashbaeva, K., Merz, V., Lau, N., Smrčka, V., Voyakin, D., Kitov, E., Epimakhov, A., Pokutta, D., Vicze, M., Price, T.D., Moiseyev, V., Hansen, A.J., Orlando, L., Rasmussen, S., Sikora, M., Vinner, L., Osterhaus, A.D.M.E., Smith, D.J., Glebe, D., Fouchier, R.A.M., Drosten, C., Sjögren, K.-G., Kristiansen, K., Willerslev, E., 2018. Ancient hepatitis B viruses from the bronze age to the medieval period. Nature 557 (7705), 418–423.

Murthy, S., O'Brien, K., Agbor, A., Angedakin, S., Arandjelovic, M., Ayimisin, E.A., Bailey, E., Bergl, R.A., Brazzola, G., Dieguez, P., Eno-Nku, M., Eshuis, H., Fruth, B., Gillespie, T.R., Ginath, Y., Gray, M., Herbinger, I., Jones, S., Kehoe, L., Kühl, H., Kujirakwinja, D., Lee, K., Madinda, N.F., Mitamba, G., Muhindo, E., Nishuli, R., Ormsby, L.J., Petrzelkova, K.J., Plumptre, A.J., Robbins, M.M., Sommer, V., Ter Heegde, M., Todd, A., Tokunda, R., Wessling, E., Jarvis, M.A., Leendertz, F.H., Ehlers, B., Calvignac-Spencer, S., 2019. Cytomegalovirus distribution and evolution in hominines. Virus Evol. 5 (2), vez015.

Negrey, J.D., Reddy, R.B., Scully, E.J., Phillips-Garcia, S., Owens, L.A., Langergraber, K.E., Mitani, J.C., Emery Thompson, M., Wrangham, R.W., Muller, M.N., Otali, E., Machanda, Z., Hyeroba, D., Grindle, K.A., Pappas, T.E., Palmenberg, A.C., Gern, J.E., Goldberg, T.L., 2019. Simultaneous outbreaks of respiratory disease in wild chimpanzees caused by distinct viruses of human origin. Emerg. Microbes Infect. 8 (1), 139–149.

Negrey, J.D., Thompson, M.E., Langergraber, K.E., Machanda, Z.P., Mitani, J.C., Muller, M.N., Otali, E., Owens, L.A., Wrangham, R.W., Goldberg, T.L., 2020. Demography, life-history trade-offs, and the gastrointestinal virome of wild chimpanzees. Philos. Trans. R. Soc. B 375 (1811), 20190613.

Njouom, R., Mba, S.A.S., Nerrienet, E., Foupouapouognigni, Y., Rousset, D., 2010. Detection and characterization of hepatitis B virus strains from wild-caught gorillas and chimpanzees in Cameroon, Central Africa. Infect. Genet. Evol. 10 (6), 790–796.

Omran, A.R., 1971. The epidemiologic transition: a theory of the epidemiology of population change. Milbank Mem. Fund Q. 49, 509–538.

Palacios, G., Lowenstine, L.J., Cranfield, M.R., Gilardi, K.V.K., Spelman, L., Lukasik-Braum, M., Kinani, J.F., Mudakikwa, A., Nyirakaragire, E., Bussetti, A.V., Savji, N., Hutchison, S., Egholm, M., Lipkin, W.I., 2011. Human metapneumovirus infection in wild mountain gorillas, Rwanda. Emerg. Infect. Dis. 17 (4), 711–713.

Patrono, L.V., Samuni, L., Corman, V.M., Nourifar, L., Rothemeier, C., Wittig, R.M., Drosten, C., Calvignac-Spencer, S., Leendertz, F.H., 2018. Human coronavirus OC43 outbreak in wild chimpanzees, Cote d Ivoire, 2016. Emerg. Microbes Infect. 7 (1), 118.

Patrono, L.V., Pléh, K., Samuni, L., Ulrich, M., Röthemeier, C., Sachse, A., Muschter, S., Nitsche, A., Couacy-Hymann, E., Boesch, C., Wittig, R.M., Calvignac-Spencer, S., Leendertz, F.H., 2020. Monkeypox virus emergence in wild chimpanzees reveals distinct clinical outcomes and viral diversity. Nat. Microbiol. 5 (7), 955–965.

Peeters, M., Fransen, K., Delaporte, E., Van den Haesevelde, M., Gershy-Damet, G.M., Kestens, L., van der Groen, G., Piot, P., 1992. Isolation and characterization of a new chimpanzee lentivirus (simian immunodeficiency virus isolate cpz-ant) from a wild-captured chimpanzee. AIDS 6 (5), 447–451.

Perelman, P., Johnson, W.E., Roos, C., Seuánez, H.N., Horvath, J.E., Moreira, M.A., Kessing, B., Pontius, J., Roelke, M., Rumpler, Y., 2011. A molecular phylogeny of living primates. PLoS Genet. 7 (3), e1001342.

Pika, S., Klein, H., Bunel, S., Baas, P., Théleste, E., Deschner, T., 2019. Wild chimpanzees (Pan troglodytes troglodytes) exploit tortoises (Kinixys erosa) via percussive technology. Sci. Rep. 9 (1), 1–7.

Prince, A.M., Brotman, B., Lee, D.-H., Andrus, L., Valinsky, J., Marx, P., 2002. Lack of evidence for HIV type 1-related SIVcpz infection in captive and wild chimpanzees (Pan troglodytes verus) in West Africa. AIDS Res. Hum. Retrovir. 18 (9), 657–660.

Roy, S., Vandenberghe, L.H., Kryazhimskiy, S., Grant, R., Calcedo, R., Yuan, X., Keough, M., Sandhu, A., Wang, Q., Medina-Jaszek, C.A., 2009. Isolation and characterization of adenoviruses persistently shed from the gastrointestinal tract of non-human primates. PLoS Pathog. 5 (7), e1000503.

Rudicell, R.S., Holland Jones, J., Wroblewski, E.E., Learn, G.H., Li, Y., Robertson, J.D., Greengrass, E., Grossmann, F., Kamenya, S., Pintea, L., Mjungu, D.C., Lonsdorf, E.V., Mosser, A., Lehman, C., Collins, D.A., Keele, B.F., Goodall, J., Hahn, B.H., Pusey, A.E., Wilson, M.L., 2010. Impact of simian immunodeficiency virus infection on chimpanzee population dynamics. PLoS Pathog. 6 (9), e1001116.

Sadeuh-Mba, S.A., Bessaud, M., Joffret, M.-L., Zanga, M.-C.E., Balanant, J., Ngole, E.M., Njouom, R., Reynes, J.-M., Delpeyroux, F., Rousset, D., 2014. Characterization of enteroviruses from non-human primates in cameroon revealed virus types widespread in humans along with candidate new types and species. PLoS Negl. Trop. Dis. 8 (7), e3052.

Samuni, L., Wegdell, F., Surbeck, M., 2020. Behavioural diversity of bonobo prey preference as a potential cultural trait. elife 9, e59191.

Santiago, M.L., Rodenburg, C.M., Kamenya, S., Bibollet-Ruche, F., Gao, F., Bailes, E., Meleth, S., Soong, S.J., Kilby, J.M., Moldoveanu, Z., Fahey, B., Muller, M.N., Ayouba, A., Nerrienet, E., McClure, H.M., Heeney, J.L., Pusey, A.E., Collins, D.A., Boesch, C., Wrangham, R.W., Goodall, J., Sharp, P.M., Shaw, G.M., Hahn, B.H., 2002. SIVcpz in wild chimpanzees. Science 295 (5554), 465.

Schulze, A., Lemey, P., Schubert, J., McClure, M.O., Rethwilm, A., Bodem, J., 2011. Complete nucleotide sequence and evolutionary analysis of a gorilla foamy virus. J. Gen. Virol. 92 (3), 582–586.

Scully, E.J., Basnet, S., Wrangham, R.W., Muller, M.N., Otali, E., Hyeroba, D., Grindle, K.A., Pappas, T.E., Thompson, M.E., Machanda, Z., Watters, K.E., Palmenberg, A.C., Gern, J.E., Goldberg, T.L., 2018. Lethal respiratory disease associated with human rhinovirus C in wild chimpanzees, Uganda, 2013. Emerg. Infect. Dis. 24 (2), 267–274.

Seimon, T.A., Olson, S.H., Lee, K.J., Rosen, G., Ondzie, A., Cameron, K., Reed, P., Anthony, S.J., Joly, D.O., McAloose, D., Lipkin, W.I., 2015. Adenovirus and herpesvirus diversity in free-ranging great apes in the Sangha region of the republic of Congo. PLoS One 10 (3), e0118543.

Sharp, P.M., Hahn, B.H., 2011. Origins of HIV and the AIDS pandemic. Cold Spring Harb. Perspect. Med. 1 (1), a006841.

Sharp, P.M., Simmonds, P., 2011. Evaluating the evidence for virus/host co-evolution. Curr. Opin. Virol. 1 (5), 436–441.
Sharp, P.M., Shaw, G.M., Hahn, B.H., 2005. Simian immunodeficiency virus infection of chimpanzees. J. Virol. 79 (7), 3891–3902.
Sogin, M.L., 1991. Early evolution and the origin of eukaryotes. Curr. Opin. Genet. Dev. 1 (4), 457–463.
Stanford, C.B., Wallis, J., Mpongo, E., Goodall, J., 1994. Hunting decisions in wild chimpanzees. Behaviour 131 (1–2), 1–18.
Streicker, D.G., Turmelle, A.S., Vonhof, M.J., Kuzmin, I.V., McCracken, G.F., Rupprecht, C.E., 2010. Host phylogeny constrains cross-species emergence and establishment of rabies virus in bats. Science 329 (5992), 676–679.
Sundberg, J.P., Shima, A.L., Adkison, D.L., 1992. Oral papillomavirus infection in a pygmy chimpanzee (Pan Paniscus). J. Vet. Diagn. Investig. 4 (1), 70–74.
Switzer, W.M., Salemi, M., Shanmugam, V., Gao, F., Cong, M.-e., Kuiken, C., Bhullar, V., Beer, B.E., Vallet, D., Gautier-Hion, A., 2005. Ancient co-speciation of simian foamy viruses and primates. Nature 434 (7031), 376–380.
Takahashi, K., Brotman, B., Usuda, S., Mishiro, S., Prince, A.M., 2000. Full-genome sequence analyses of hepatitis B virus (HBV) strains recovered from chimpanzees infected in the wild: implications for an origin of HBV. Virology 267 (1), 58–64.
Tattersall, I., 1999. Becoming Human: Evolution and Human Uniqueness. Houghton Mifflin Harcourt.
Underdown, S.J., Kumar, K., Houldcroft, C., 2017. Network analysis of the hominin origin of Herpes Simplex virus 2 from fossil data. Virus Evol. 3 (2), vex026.
Van Ranst, M., Fuse, A., Sobis, H., De Meurichy, W., Syrjänen, S.M., Billiau, A., Opdenakker, G., 1991. A papillomavirus related to HPV type 13 in oral focal epithelial hyperplasia in the pygmy chimpanzee. J. Oral Pathol. Med. 20 (7), 325–331.
Villarreal, L.P., 2016. Viruses and the placenta: the essential virus first view. APMIS 124 (1–2), 20–30.
Walsh, P.D., Abernethy, K.A., Bermejo, M., Beyers, R., De Wachter, P., Akou, M.E., Huijbregts, B., Mambounga, D.I., Toham, A.K., Kilbourn, A.M., Lahm, S.A., Latour, S., Maisels, F., Mbina, C., Mihindou, Y., Ndong Obiang, S., Effa, E.N., Starkey, M.P., Telfer, P., Thibault, M., Tutin, C.E.G., White, L.J.T., Wilkie, D.S., 2003. Catastrophic ape decline in western equatorial Africa. Nature 422 (6932), 611–614.
Walsh, P.D., Breuer, T., Sanz, C., Morgan, D., Doran-Sheehy, D., 2007. Potential for Ebola transmission between gorilla and chimpanzee social groups. Am. Nat. 169 (5), 684–689.
Wertheim, J.O., Kosakovsky Pond, S.L., 2011. Purifying selection can obscure the ancient age of viral lineages. Mol. Biol. Evol. 28 (12), 3355–3365.
Wertheim, J.O., Smith, M.D., Smith, D.M., Scheffler, K., Kosakovsky Pond, S.L., 2014. Evolutionary origins of human herpes simplex viruses 1 and 2. Mol. Biol. Evol. 31 (9), 2356–2364.
Wertheim, J.O., Hostager, R., Ryu, D., Merkel, K., Angedakin, S., Arandjelovic, M., Ayimisin, E.A., Babweteera, F., Bessone, M., Brun-Jeffery, K.J., Dieguez, P., Eckardt, W., Fruth, B., Herbinger, I., Jones, S., Kuehl, H., Langergraber, K.E., Lee, K., Madinda, N.F., Metzger, S., Ormsby, L.J., Robbins, M.M., Sommer, V., Stoinski, T., Wessling, E.G., Wittig, R.M., Yuh, Y.G., Leendertz, F.H., Calvignac-Spencer, S., 2021. Discovery of novel herpes simplexviruses in wild gorillas, bonobos, and chimpanzees supports zoonotic origin of HSV-2. Mol. Biol. Evol. 38 (7), 2818–2830.
Wevers, D., Metzger, S., Babweteera, F., Bieberbach, M., Boesch, C., Cameron, K., Couacy-Hymann, E., Cranfield, M., Gray, M., Harris, L.A., 2011. Novel adenoviruses in wild primates: a high level of genetic diversity and evidence of zoonotic transmissions. J. Virol. 85 (20), 10774–10784.
Woolhouse, M., Scott, F., Hudson, Z., Howey, R., Chase-Topping, M., 2012. Human viruses: discovery and emergence. Philos. Trans. R. Soc., B 367 (1604), 2864–2871.

View publication stats