# Diverse hosts, diverse immune systems: evolutionary variation in bat immunology

Daniel J. Becker[1*], Amanda Vicente-Santos[1], Ashley B. Reers[2], B. R. Ansil[1], Mika O'Shea[2], Caroline A. Cummings[1], Alicia J. Roistacher[1], Rita M. Quintela-Tizon[3,4], Manuela M. T. Pereira[3,4], Juniper Rosen[2], Arinjay Banerjee[3–7], Hannah K. Frank[2]

[1] School of Biological Sciences, University of Oklahoma, Norman, OK, USA
[2] Department of Ecology and Evolutionary Biology, Tulane University, New Orleans, LA, USA
[3] Vaccine and Infectious Disease Organization, Saskatoon, Canada
[4] Department of Veterinary Microbiology, University of Saskatchewan, Saskatoon, Canada
[5] Department of Biology, University of Waterloo, ON, Canada
[6] Department of Laboratory Medicine and Pathobiology, University of Toronto, ON, Canada
[7] Department of Biochemistry and Molecular Biology, University of British Columbia, BC, Canada
*Corresponding author, danbeck@ou.edu

**Running head:** Bat diversity and immunology
**Keywords:** Chiroptera, phylogenetic comparative methods, ecoimmunology, SARS-CoV-2, phylogeography, white-nose syndrome, zoonotic spillover

## Abstract

The ability of multiple bat species to host zoonotic pathogens without showing disease has fostered growing interest in bat immunology, indicating ways immune systems may differ between bats and other vertebrates. However, interspecific variation in immunological diversity among bats has only begun to be recognized. The order Chiroptera accounts for over 20% of all mammal species and shows extreme diversity in a suite of correlated ecological traits, such that bats should not be expected to be immunologically homogenous. Here, we review the ecological and evolutionary diversity of chiropteran hosts and highlight case studies emphasizing the range of immune strategies thus far observed across bat species, including responses to SARS-CoV-2. Next, we synthesize and propose hypotheses to explain this immunological diversity, focused on pathogen exposure, biogeography, host energetics, and environmental stability. Lastly, we analyze immunology citations across bat species to motivate discussion of outstanding research priorities. Broad sampling is needed to remedy current biases, as only a fraction of bat species has been immunologically studied. Such work should integrate methodological advancements, *in vitro* and *in vivo* studies, and phylogenetic comparative methods to robustly test evolutionary hypotheses and understand the drivers and consequences of immunological diversity among bats.

## Introduction

Over the past decades, bats have been linked to numerous spillovers of zoonotic pathogens, including viruses such as Hendra and Nipah virus, SARS-like coronaviruses (CoVs), Marburg virus (MARV), and MERS-like CoVs; bacteria such as *Bartonella mayotimonensis*, *B. rousetti*, and *Candidatus* Mycoplasma haematohominis; and protozoa such as *Trypanosoma cruzi* [1–9]. These spillovers, alongside observations that bats often host such pathogens without signs of disease, have generated substantial interest in bat immunology and understanding mechanisms of host tolerance [10–14]. Bats are also exceptional among mammals in other ways; they are the only mammals with powered flight, are potentially resistant to cancer, and many have long lifespans for their body size [15–19]. The association of many bat species with multiple pathogens and their unique adaptations have led to hypotheses about how bats, as an order, may differ in their immune system from other mammals. The "flight as fever" hypothesis posits that the elevated body temperatures bats reach during powered flight could specifically dampen viral replication or select for viruses able to withstand the febrile responses of other mammals [20]. However, this hypothesis has received little empirical support [21,22], with growing evidence suggesting that flight has likely shaped bat immunity in other ways [23,24]. For example, metabolic demands of flight generate high oxidative stress [25], such that bats have evolved mechanisms to withstand subsequent DNA damage while avoiding pathology by downregulating inflammatory pathways [26,27]. These adaptations have been proposed to explain why bats typically tolerate intracellular infections and harbor more viruses than other mammals while also being susceptible to certain extracellular infections (e.g., *Pseudogymnoascus destructans*, the fungus causing white-nose syndrome [WNS], has decimated populations of hibernating North American bat species) [21,28].

Support for hypotheses about distinct immune adaptations of bats largely stems from a small but growing number of model systems in bat immunology [29–32]. However, while multiple immune adaptations are certainly present across bat species, immunological diversity within the order Chiroptera is also becoming increasingly acknowledged and characterized [17,27,33–35]. In this review, we highlight the diversity of immune systems across this hyper-diverse clade of mammals, emphasizing that bats—as an order—are far from immunologically homogenous. We also synthesize proposed evolutionary hypotheses underlying this diversity and suggest future directions to test such hypotheses. We do not exhaustively summarize the state of research on bat immunology or the immune characteristics that make bats distinct from other mammals, given previous reviews on these topics [36–38]. Our objectives are instead for this work to serve as an entry point for immunologists to consider variation within this group of flying mammals as well as a resource for both field and comparative biologists to test central evolutionary hypotheses.

## Ecological and evolutionary diversity among bats

Bats are the second largest mammalian order (after rodents), accounting for over 20% of all mammal species. The order Chiroptera originated during the Cretaceous–Tertiary boundary, approximately 65 million years ago (mya), followed by divergence into two monophyletic suborders: Yinpterochiroptera and Yangochiroptera [39,40]. This divergence was followed by a rapid radiation event during the early Eocene (52–50 mya), coinciding with global temperature rise and concurrent expansion of plant and insect diversity [41,42]. Multiple, subsequent radiations, such as those of the Phyllostomidae in the Western Hemisphere (30 mya) and the Pteropodidae in the Eastern Hemisphere (25 mya), were further driven by factors including niche partitioning, novel innovations (e.g., phytophagy), and geographic isolation [43,44]. These evolutionary processes generated the remarkable diversity of bats, resulting in 1,482 extant species across 21

families [45]. Underexplored tropical regions and unclear taxonomic boundaries (e.g., cryptic species) are expected to only further increase bat global diversity [46,47]. Bats inhabit a wide variety of terrestrial habitats on every continent except for Antarctica, with some species occupying up to seven or eight distinct habitat types (e.g., *Rousettus aegyptiacus* and *Taphozous nudiventris*, respectively), as defined by the International Union for the Conservation of Nature (IUCN) [48]. Bats accordingly exhibit a remarkable array of morphological (e.g., body mass), ecological (e.g., diet), and physiological adaptations (e.g., echolocation) that evolved to suit their ecological niches and life history strategies (Figure 1) [49]. For example, body mass varies over three orders of magnitude across bats, ranging from just a few grams in small insectivores (e.g., *Craseonycteris thonglongyai*, which weighs approximately two grams) to over a kilogram in larger frugivores (e.g., *Acerodon jubatus*) [48]. Frugivorous bats are generally larger with broader wingspans, while insectivorous bats tend to be smaller but with shorter wingspans to improve agility [50,51]. The specialized facial morphologies of bats also evolved as adaptations to their diverse dietary habits, including nectarivory (e.g., *Leptonycteris yerbabuenae*), frugivory (e.g., *Pteropus medius*), insectivory (e.g., *Myotis myotis*), carnivory (e.g., *Macroderma gigas*), piscivory (e.g., *Noctilio leporinus*), and hematophagy (e.g., *Desmodus rotundus*) [52,53].

Morphology and foraging ecology are only two of multiple axes of variation among the Chiroptera. Physiological adaptations such as metabolic rates, thermoregulation mechanisms, and sensory abilities vary widely across species, allowing bats to inhabit diverse habitats (Figure 1) [48,54]. For example, some bat species adjust their metabolic rate (i.e., torpor) to allow matching their activity level to environmental conditions [55]. Hibernation, a more extreme drop in metabolic rate, is used mostly by Neartic and Paleartic bats to avoid harsh winter temperatures [56], but this adaptation also occurs in tropical species and has evolved multiple times in bats [57,58]. Other bat species instead undertake long-distance latitudinal (e.g., *Tadarida brasiliensis*) or altitudinal (e.g., *Miniopterus natalensis*) migrations to escape extreme temperatures [59–61]. This metabolic flexibility is also one of the evolutionary drivers for the exceptional longevity seen in bats as compared to other small mammals [15]. Although bats overall have a slow life-history strategy, species vary substantially along the fast–slow continuum (Figure 1) [48,62]. For example, *Myotis brandtii* can live for up to 41 years [63], in contrast to the mean bat lifespan of 15 years [48]. Similarly, while most bat species have one breeding cycle per year with a single pup [48,64], some species are polyestrous (e.g., *Tadarida fulminans,* multiple phyllostomids [65,66]) and/or polytocous (e.g., mostly in the Vespertilionidae but also in other families such as the Pteropodidae [67,68]).

Bats also display substantial diversity in their associations with pathogens, with most data focused on viruses and bacteria [69–71]. For the former, approximately one-quarter of bat species are infected by at least one virus, with infected species hosting an average of three and up to 21 viral families (Figure 1) [71]. This viral pressure has imposed extreme selection within bat genomes for viral tolerance [72]. However, distinct coevolutionary histories between bats and their viruses [73,74], coupled with substantial variation in observed viral diversity among species [71], have likely also shaped distinct defense strategies and corresponding immune phenotypes among bats.

**Bats are not a monolith: interspecific variation in bat immunity**

Given substantial diversity in morphological, ecological, and physiological traits of bats; their long coevolutionary relationships with pathogens; and variance in pathogen diversity, the immune systems of bats are expected to be equally heterogeneous. Recent *in vitro* and *in vivo* studies have begun to reveal an array of species-specific immune responses, shedding light on the distinct immune strategies that bat species use against their viral pathogens. As one key

example, in the case of SARS-CoV-2 *in vivo* infections, both *Eptesicus fuscus* and *Myotis lucifugus* were resistant, while *Tadarida brasiliensis* was susceptible but likely not competent for onward transmission [75–78]. Similarly, *Rousettus aegyptiacus* challenged with SARS-CoV-2 demonstrated susceptibility but had transient infections [79,80]. Other *in vitro* studies have demonstrated that *Myotis myotis*, *Eptesicus serotinus*, *Tadarida brasiliensis*, and *Nyctalus noctula* wing cells were not permissive to SARS-CoV-2, due to low expression of the angiotensin-converting enzyme 2 (ACE2) receptor or to poor interactions between ACE2 and the viral S protein [81]. ACE2 receptor sequences and the selection acting on them also vary between bat species, further shaping differences in SARS-CoV-2 susceptibility [82]. Additionally, intestinal organoids of *Rhinolophus sinicus* were susceptible to SARS-CoV-2 and sustained viral replication [83], while fibroblasts of *Rhinolophus ferrumequinum* were resistant to infection [84]. Intestinal organoids of *Rousettus leschenaultii* were also resistant to infection [85], while both intestinal organoids and *in vivo* challenge of *Artibeus jamaicensis* show this species is susceptible but does not support SARS-CoV-2 replication [86,87]. Such case studies demonstrate substantial species-level heterogeneity in susceptibility and suitability for SARS-CoV-2 infection, even in species in the same genus (Figure 2). Importantly, the bat species involved in these diverse challenges originate from both hemispheres and include susceptible and resistant species in multiple families. This suggests differences in susceptibility are unlikely to stem only from coevolutionary history, as the current repertoire of sarbecoviruses and their known bat hosts are restricted to the Eastern Hemisphere, largely in the Paleartic and Indomalayan regions [88].

Interspecific differences in infection response have been observed for other viruses. *Eidolon helvum* cells were refractory to Ebola virus (EBOV) entry due to a single mutation in the filovirus receptor, Niemann-Pick C1; species without this mutation are likely susceptible to filovirus entry [89]. Further, *Rousettus aegyptiacus* were susceptible to MARV but resistant to EBOV, highlighting that even closely related viruses (both within *Filoviridae*) can have different outcomes in the same species [90]. In the case of rabies virus (RABV), outcomes can vary both across and within species, highlighting the complex nature of the relationships between bat immunity and infection [91–93]. Work on RABV has shown especially interesting differences in adaptive immunity. Following RABV infection, some *Eptesicus fuscus* failed to seroconvert and succumbed to infection [94]. In contrast, some *Desmodus rotundus* vaccinated against and challenged with RABV survived despite not producing detectable antibody titers [95].

Given the logistical challenges of *in vivo* or *in vitro* experiments using pathogens, antigen challenges that instead stimulate a more general acute phase response without true infection have illuminated additional interspecific differences in bat immune systems. For example, in response to lipopolysaccharide (LPS) challenge, mimicking a bacterial infection, *Molossus molossus* had no detectable inflammation while *Desmodus rotundus* experienced pronounced leukocytosis and behavioral changes [96,97]. In contrast, *Carollia perspicillata* challenged with LPS also displayed no fever or leukocytosis but did show decreased food intake and lost body mass [98]. *Desmodus* and *Carollia* are both in the family Phyllostomidae while *Molossus* is in the Molossidae, suggesting evolutionary and intra-family effects that could stem from species differences in ecology or life history. Similarly, while *in vitro* challenge with polyinosinic:polycytidylic acid (polyI:C), mimicking infection with an RNA virus, upregulated similar genes related to cytokine and inflammatory responses across phylogeographically diverse bats (i.e., *Rousettus aegyptiacus*, *Pipistrellus kuhlii*, *Eptesicus fuscus*, *Eptesicus nilsonii*), species-specific differences were also found (e.g., between *Rousettus aegyptiacus* and *Pipistrellus kuhlii*) [99,100]. Such challenges have also revealed intra-family differences in the bat antiviral response. For example, constitutive

expression of interferon alpha (IFN-α) has been observed in *Pteropus alecto* tissues but not in *Rousettus leschenaultii* kidney cells, despite both species belonging to the family Pteropodidae; stimulation with polyI:C increased IFN-α expression in the latter but not the former species [30,101].

Beyond viral and bacterial infections, bats also show varied susceptibility to fungal pathogens, notably *Pseudogymnoascus destructans*. The highly susceptible Nearctic *Myotis lucifugus* mounts a substantial transcriptomic response to infection, upregulating leukocyte activation and inflammatory pathways, whereas the tolerant Palearctic *Myotis myotis* has a nearly undetectable transcriptional response [102]. The less-susceptible Nearctic *Eptesicus fuscus* exhibits a similar gene expression profile to *Myotis lucifugus* but instead mounts a localized, non-systemic response. Across these three host–pathogen contexts, the fungal transcriptome is notably consistent, highlighting bat species–level differences that drive WNS outcomes [103].

A larger body of work on immune profiles of wild bats at baseline has also revealed immunological differences among species, although such patterns are more difficult to interpret given the unknowns about pathogen exposure history [104]. For example, white blood cell counts varied substantially across a Neotropical bat community in Costa Rica, with larger bat species and carnivorous bat species characterized by more leukocytes [35]. Similarly, in Belize, neutrophil counts of a frugivore (*Sturnira parvidens*) decreased over time with land conversion, whereas those of hematophagous bats (*Desmodus rotundus*) increased and those of an insectivore bat (*Pteronotus mesoamericanus*) showed no response [105]. To compare cellular immunity at a finer resolution, single-cell RNA-Seq has revealed different proportions of B cells in bone marrow and natural killer cells in spleen between *Pteropus alecto* and *Eonycteris spelaea* [106,107]. Functional assays applied to sera samples have also found substantial interspecific differences in complement activity, with higher rates of lysis from *Eptesicus fuscus* than *Pteropus vampyrus* [108]. Extensions of these baseline approaches have also revealed immune differences within genera; among sympatric horseshoe bat species in China, RNA-Seq of organs found that *Rhinolophus siamensis* and *R. episcopus* differ in expression of immunoregulatory genes [109].

Lastly, comparative genomics have emphasized the genetic basis of interspecific differences in bat immunity. Considering innate immunity, the composition of the type I IFN locus varies across bats, with initial work showing this locus is contracted in *Pteropus alecto* but expanded in *Pteropus vampyrus*, *Myotis lucifigus*, and *Rousettus aegyptiacus* [30,110]. Recent work has suggested IFN-ω in bats may play an expanded antiviral role compared to other type I IFNs, given that several bat species have lost all IFN-α genes (i.e., *Pipistrellus kuhlii*, *Myotis myotis*, and *Pteronotus mesoamericanus*) [17]. Considering adaptive immunity, the immunoglobulin heavy chain (IGH) locus of bats is unusually variable between species. IGHV gene number varies substantially, with 132 genes in *Eptesicus fuscus*, 66 in *Rousettus aegyptiacus*, 41 in *Rhinolophus ferrumequinum*, 81 in *Phyllostomus discolor*, and 57 in *Pipistrellus pipistrellus* [111–113]. In comparison, humans and mice have 104 and 161 IGHV genes [114], respectively, and these species are over 60 million years further diverged than the most related bat species above (i.e., *Eptesicus fuscus* and *Pipistrellus pipistrellus*) [115]. Most strikingly, bats within the Vespertilionidae possess two distinct and functional IGH loci [111], an organization that has not been previously described in mammals but bears similarity to a more limited duplication in teleost fish [116,117].

**Evolutionary hypotheses in bat immunology**

As highlighted above, the pronounced diversity across bats is matched by substantial interspecific variation in immunity, as revealed by both experimental (e.g., Figure 2) and observational results. However, an outstanding need remains to identify the mechanisms

underlying these species-level differences. Here, we synthesize and propose hypotheses about the interspecific drivers of bat immunity: pathogen exposure, biogeography, host energetics, and environmental stability (Table 1). For each hypothesis, we present supporting research and outline potential directions for future studies. We note that while some trait drivers may lend themselves to testing a single hypothesis (e.g., pathogen richness to test hypotheses about pathogen exposure), others could shape immune diversity through multiple pathways (e.g., dietary diversity could test hypotheses about both pathogen exposure and host energetics).

*Pathogen exposure*

One of the central hypotheses to explain immune variation among bat species focuses on the long coevolutionary history between chiropteran hosts and many of their pathogens. Across host taxa, pathogens impose strong selection pressures that can shape immunological diversity [118,119]. For example, pathogen richness is positively associated with major histocompatibility complex (MHC) variability across primate, ungulate, and a small number of bat species [120,121]. Bat–virus associations display strong signals of phylogeography that should likewise shape immune strategies. For example, henipaviruses are highly diverse in Africa (suggesting their likely origin in this region) and are primarily associated with pteropodid bats found only in Africa, Asia, and Oceania [122,123]. Likewise, bat-associated filoviruses have only been found in Africa and Asia, despite potential favorable host conditions in the Americas [124,125]. As one case study of immune adaptations structured by viral phylogeography, bats in the genus *Eidolon,* whose range includes the known distribution of filoviruses, have a mutation in their host receptor to prevent EBOV entry [89]. Similarly, bat influenza A viruses (IAVs) have been detected in diverse bat species, including H17N10 and H18N11 from *Sturnira parvidens* and multiple *Artibeus* species in the Neotropics as well as an H9N2-like IAV from *Rousettus aegyptiacus* in Egypt [126–128]. In the Afrotropical host, H9N2-like IAV preferentially binds α2,3-sialic acid receptors, while the Neotropical H17N10 and H18N11 IAVs instead enter cells via the MHC class II DR protein [129].

Alongside expectations about coevolutionary histories shaping immunogenetics across bat species, pathogen diversity should also structure bat immune phenotypes. In other taxa such as birds, energetic investment into immune function is often elevated in areas of high pathogen richness (e.g., the tropics). For example, tropical bird species have more leukocytes in blood and larger spleen sizes than temperate bird species, with the latter indicating greater investment in adaptive immunity [130]. Indeed, as antigen exposure drives selection of specific cell populations and, in turn, the pool of B and T lymphocytes, greater exposure to pathogens should increase allocation to adaptive immunity [131]. Explicit tests of how immunity is associated with pathogen richness across bats are needed to fully assess this hypothesis, which can be facilitated by standardized species-level data on pathogen-host status and diversity (e.g., VIRION; Figure 1) [71].

Multiple behavioral and life-history traits of bat species could drive pathogen exposure, with subsequent effects on immune variation. For example, colony size varies several orders of magnitude across bats [132], with more colonial species possibly supporting pathogen transmission and thus investment into adaptive immunity. In birds, density-dependent pathogen transmission in colonial species results in stronger B and T cell responses than in solitary species [133]. However, support for density dependence in bat–pathogen systems is weak [134,135], with exposure more likely a function of social and metapopulation structure or arthropod vectors [136,137]. Sociality may thus possibly have stronger effects on immunity via this exposure mechanism; in other mammals, more promiscuous species show greater investment in white blood cells, likely driven through increased exposure to sexually transmitted infections [138,139]. However, bat

sociality is highly complex, with some species being characterized by seasonal maternity colonies [140] or fission-fusion societies [141]. This complexity in social behavior will thus likely complicate efforts to understand how sociality drives species differences in immunity. Other interspecific differences in bat behavior, such as co-roosting with other bat species, could also elevate pathogen exposure and have similar effects on interspecific variation in immunity [142–145].

The extreme dietary diversity observed across bats could also shape immune variation through pathogen exposure. Bat species that include more animals in their diets, particularly other vertebrates (e.g., phyllostomines including *Trachops cirrhosus*, *Chrotopterus auritus*, *Phyllostomus hastatus* and *Vampyrum spectrum*; both *Noctilio* species, all three members of the Desmodontinae, *Myotis vivesi, Cardioderma cor, Megaderma lyra, Macroderma gigas* [146]), could be exposed to pathogens hosted by prey [147], selecting for greater investment in defense. Initial support for this hypothesis has been found within Neotropical bat communities, using data on the cellular immune system [35]. Other foraging-related behaviors, such as large geographic ranges or high habitat breadth, as well as long-distance migration, could also expose bats to a wider array of pathogens, as shown in birds [148] and supported by select bat case studies (e.g., extreme MHC class I diversity in the geographically widespread *Carollia perspicillata* [149]). In birds, migratory species invest more in immune organ size than resident species, supporting links between habitat diversity, pathogen exposure, and immunity [150]; such comparisons have yet to be performed across bat species, despite known variation in migratory strategies [60]. Hypotheses about habitat breadth and geographic range more generally could be tested by comparing immunity among bat species in globally distributed taxa, such as the genus *Myotis* or several families (e.g., Figure 3). Lastly, longer-lived species can accumulate pathogen exposure across their lifespan, as seen in birds, bats, and some terrestrial mammals [151,152], which could also increase adaptive investment.

*Biogeography*

Alongside coevolutionary history with pathogens, the distinct biogeography of many bats has likely contributed to their immunological diversity. Prior work on bat–CoV interactions has shown that regions with more evolutionarily distinct host communities harbor more divergent viral assemblages, which should likewise generate strong selective pressure for specialized immune adaptations [74]. As one example, the historical biogeography of the Phyllostomidae and Pteropodidae resulted in their restriction to the Western and Eastern Hemispheres, respectively. Multiple gene families underwent expansion or contraction within the Pteropodidae, including those related to immunity, and this family has been characterized by loss of the inflammasome *NLRP*1 gene and attenuated Toll-like receptor 2 ability [153,154]. Similarly, genomic comparisons support expansion of the *PRDM9* gene, which governs meiotic recombination and can be upregulated during viral infection in Phyllostomidae compared to other bats [17]. Further, the sister family Mormoopidae (also only in the Western Hemisphere) display major expansions of heat-shock protein genes compared to other bats [17], indicating possibly unique adaptations involved in the stress response as well as in both innate and adaptive immunity [155].

Recent work on the phylogenetic distribution of viral virulence also suggests biogeographic drivers in bat–pathogen interactions. Whereas previous work has found bats are more likely than other mammalian and avian orders to host viruses with high virulence in humans [156,157], phylogenetic analyses agnostic to taxonomic order suggest that the Chiroptera do not emerge as a taxon more likely to harbor such viruses than other mammal clades [158]. Notably, a subclade of the Yangochiroptera consisting of the superfamilies Emballonuroidea and

Vespertilionoidea was more likely to host high-virulence viruses, with most included families being cosmopolitan (i.e., Emballonuridae, Vespertilionidae, and Molossidae; Figure 3). Shared ability to harbor otherwise virulent viruses in bat families that span both the Western and Eastern Hemisphere could suggest common immune adaptations that evolved with geographic divergence. For example, the Molossidae originated in the Paleocene, with Western (e.g., *Eumops*, *Molossus*) and Eastern Hemisphere (e.g., *Chaerephon*, *Mops*) clades diverging 29 million years ago [159]. Future comparisons between species in the genus found globally (i.e., *Tadarida*) and between molossid genera unique to each hemisphere could indicate which immune features are basal to the family and which originated with spread into the Americas [159].

Biogeography could also shape bat immune diversity via differences in geographic range size. A smaller geographic range is one criterion used by the IUCN to delineate conservation risk, as lower effective population size can facilitate inbreeding depression and reduce genetic diversity [160]. Species with smaller geographic ranges could thus show less immunogenetic diversity (e.g., in MHC loci). Island occupancy could help test this hypothesis; over 25% of bat species are island endemic, and many have small population sizes and face critical extinction risks [161,162]. Immune comparisons of island endemic and non-endemic species in select genera (e.g., *Pteropus*, *Natalus*) or families (e.g., Pteropodidae) could thus be fruitful. From a similar perspective, subspecies that occur exclusively in islands could allow analogous comparisons among endemics and with mainland populations (e.g., within *Pteropus medius*, *P. medius medius* occurs in mainland India and Sri Lanka, while *P. medius ariel* occurs in the Maldives) [163].

*Host energetics*

Different strategies in energy acquisition and allocation among bat species could affect immune investment, as developing and maintaining immune responses require substantial resources [164]. Innate immunity generally incurs low developmental but high maintenance costs, while adaptive immunity can be more costly to develop but less expensive to maintain [131,165]. The 'pace-of-life' hypothesis therefore posits that species with faster life histories, allocating more energy into reproduction at the expense of lifespan, will invest less into immunity and prioritize innate defenses [166,167]. In contrast, species with slower life histories, being more likely to encounter similar pathogens multiple times over their lifespan, invest more in adaptive immunity. While this hypothesis has been supported for some small mammals [168], it has yet to be evaluated for bats. Explicit tests of trade-offs between innate and adaptive immunity among bat species that vary along the fast–slow axis are needed. Focusing such comparisons on females across species would be especially informative [169], given the energetic costs of reproduction in bats [170,171].

Similarly, diet can impose significant energetic constraints in bat species, influencing the trade-offs observed between arms of the immune system [172,173]. Across phyllostomid bat species, nectarivores have greater mass-independent basal metabolic rate than other dietary guilds, although effects were sensitive to controlling for phylogeny [174]. Similarly, strictly phytophagous species (e.g., in the Pteropodidae) have relatively less protein in their diet than other species, including frugivores or nectarivores with more flexible foraging strategies (e.g., *Glossophaga soricina* will actively hunt insect prey [175]) as well as strict insectivores or carnivores [176,177]. Links between high-protein diets and investment in adaptive immunity are well-established in model mammalian systems (i.e., humans and mice [173]) as well as in both domestic and wild birds [172,178], although this has received little attention in bats[179,180]. Those bat species that rely on food with lower energetic content (e.g., obligate nectarivores and frugivores) are thus more likely to invest less in adaptive immunity when compared to species with energetically dense food (e.g.,

insectivores). Although this prediction mostly supports bat species at higher trophic levels investing more in adaptive defense, blood-feeding species (i.e., Desmodontinae) could serve as an exception owing to their unique diet of blood, which is high in protein but lacking in other macronutrients [181]. The low fat content of blood likely led to loss of genes governing fat storage in vampire bats [182], such that these species lethally starve within 72 hours of feeding [183,184]. The ability to invest in adaptive defenses may thus be diminished in blood-feeding bats. Given the importance of lipids in immune defense more generally [172,173,178], interspecific differences in fat reserves could serve as another useful source of dietary variation to test energetic hypotheses [185].

*Environmental stability*

Lastly, bat species inhabiting environments with more extreme seasonality in resources or climate, such as temperate zones or high elevations, could similarly differ in their ability to invest in immune defense. Periods of limited food availability could weaken the acute phase response [186] as well as immune factors that control pathogen shedding [180], manifesting in differences at the species level among bats that have seasonally varying versus stable resources. As one example relevant to immunity, seasonal patterns of cortisol concentrations differed between frugivorous *Carollia perspicillata* and blood-feeding *Desmodus rotundus*, likely driven by differences in resource stability [187]. Yet while seasonality in resources is particularly evident in phytophagous and insectivorous bat species [188–190], food availability can vary temporally across dietary guilds [191], such that such effects could be tested independently from foraging ecology. Given the relative costs of the two primary immunological arms noted above, species with more seasonal resources could also be expected to invest more in innate defenses [131,192].

Prolonged torpor or hibernation function as other strategies that bat species use to cope with environmental instability [193], which could also generate interspecific variation in immune strategies. These pronounced reductions in metabolic activity and body temperature allow such species to conserve energy but at the cost of a dampened innate and adaptive immune response [194,195]. Impaired immunity during hibernation can have important implications for susceptibility and persistence of infection. For example, lowered body temperature during hibernation allows RABV to go dormant in *Eptesicus fuscus*, allowing the virus to overwinter and persist in the spring as bats then emerge from hibernation [196]. Similarly, *Myotis myotis* cell lines challenged with the RABV-related European bat lyssavirus 1 showed an immune response under control conditions but no substantial immune gene expression under conditions simulating torpor [197]. Interspecific differences in torpor could thus serve as an important axis for partitioning immune variation [55], with particular relevance for susceptibility to and progression of WNS. Arousal from torpor contributes to the depletion of fat stores and in turn the severity of infection, although inflammatory responses during arousal also play a role in pathology [198,199]. Importantly, because immune responses to fungal infection display variation among bat species [200,201], future work evaluating how interspecific differences in torpor duration and body temperature affect immune response could be highly relevant for both hypothesis testing and conservation management.

Seasonal migrations offer select bat species another approach to deal with seasonally varying temperature or resources. Short- and long-distance migrations occur across the bat phylogeny but are especially concentrated within the Vespertilionidae and Molossidae [59,60]. Across taxa, migratory species often redistribute resources from their immune systems to increase body fat and enhance metabolism prior to these long-distance movements, as these physiological changes sustain endurance [202]. Work in avian systems supports suppression of immune function prior to, during, and/or following migration [203,204], with consequences for

enhancing susceptibility to or reactivation of infections [205,206]. By contrast, research on the immunology of migratory bat species is still in its infancy [207–209] . Future work comparing immune phenotypes of migratory and non-migratory species, as well as species varying in their migratory strategies (e.g., average distance traveled), would test whether similar patterns of immunosuppression are observed within bats. Similarly, comparisons among subspecies that vary in their propensity to migrate (e.g., partially or fully migratory *Tadarida brasiliensis mexicana* versus resident *Tadarida brasiliensis cynocephala* [210]) would also be informative. Variation in mean migratory distance and dispersion among bat species, measures commonly used in comparative avian studies [211,212], could especially allow testing hypotheses of energy allocation, given that species with longer migrations should display weaker immune response.

**Future directions for illuminating species-level differences in bat immunity**

Current hypotheses on the drivers of interspecific variation in bat immunity (Table 1) are supported by select case studies as well as first principles in host–pathogen coevolution and ecological immunology. To robustly test and differentiate these competing hypotheses, the field of bat immunology must address outstanding data needs, methodological advancements, expansion of experimental studies, and phylogenetically informed statistical analyses.

First, broad sampling across bat species is essential to better characterize the diversity of immune components, function, and response to infection. To date, comparative tests of bat immunity have largely been limited to genomic comparisons or to analyses of phenotypes within single bat communities [23,35], with some exceptions [213]. At the genomic level, ongoing efforts are working to generate genome assemblies across bat species (e.g., the Bat1K Project) [214], and resulting comparative analyses have provided important insights into bat evolution (including of the immune system) [23,215–219]. However, of the currently recognized 1,482 bat species, genome assemblies are currently publicly available at the National Center for Biotechnology Information (NCBI) for only 92 species (Table S1). Further, only 47 of these species have chromosome-level assemblies, which are often required to properly characterize complex immune gene loci [111,220]. Additionally, while these genomes are invaluable resources, characterizing the diversity of bat immune systems requires more systematic evaluation of downstream phenotypes. For example, while genomic data indicate *Pteropus alecto* has a small type I IFN locus, qRT-PCR data show IFN-α is instead constitutively expressed [30]. Similar tests are needed across more bat species.

On a more general level, data syntheses of bat immunology as a field are lacking, resulting in a limited understanding of how research is distributed across the bat phylogeny. To provide an initial characterization of immunological studies conducted across bats, we used the *easyPubMed* package in R to obtain total and immunology-related citation counts for the 1,287 bat species in the recent mammal phylogeny [221]; citation counts are a common approximation of research effort in comparative analyses [222]. Despite the fact that most bats have been studied to some degree (i.e., 55% of species have greater than zero total citations), only 14% of bats have immunology-related citations (Figure 4). To understand the taxonomic distribution of research effort, we next applied phylogenetic factorization, a flexible graph-partitioning algorithm, to identify bat clades with distinct citation counts at varying taxonomic depths [223]. We used the *phylofactor* package to partition immunology-related citations relative to total citations as a binomial response in a series of generalized linear models for each edge in the bat phylogeny, determining the number of significant clades using Holm's sequentially rejective 5% cutoff for the family-wise error rate [223,224]. We identified seven clades with significantly different numbers of immunology-related citations, of which six had more immunology citations compared to the

remainder of the bat phylogeny (Figure 4). These clades included most of the Pteropodidae, a subclade of the Rhinolophidae, most members of the genus *Tadarida* and the Western Hemisphere molossids, a subclade of the tribe Eptesicini, the whole genus *Myotis*, and the clade containing the genera *Artibeus* and *Dermanura*; in contrast, Eastern Hemisphere molossids (i.e., the genera *Mops* and *Chaerephon*) had relatively fewer immunology citations. This assessment highlights the substantial gaps in immunological characterization across bats as a whole, noting clades that could be up- or down-prioritized for future immune profiling (e.g., Afrotropical molossids and most pteropodids, respectively). In contrast, application of this algorithm to the presence of NCBI genome assemblies showed no phylogenetic clustering (Figure 4), suggesting that genomic characterization efforts to date have been evenly distributed across bat species.

Second, methodological expansion is necessary to better characterize immunological variation across bat species and fill these global data gaps. In wild bats, relatively simple assays such as total and differential white blood cell counts, bacterial killing ability of plasma, and antibody titers have provided key starting points to profile bat immunity [35,208,225,226]. However, these assays require most of the small blood volumes that can be safely obtained from the majority of bat species (Figure 5), limiting the number of assays that can be performed while yielding information on single components of the immune system. Further, the coarse nature of these measurements, and the lack of knowledge about prior or existing immune challenges in wild bats, also restricts mechanistic insights into immunity. Flow cytometry holds promise for quantifying many immune cell subsets beyond that allowed by typical hematology, but analyses remain restricted by the larger blood volumes required, the need to process samples relatively soon after collection, and limited availability of cross-reactive antibodies for bats [106,227–229]. Alternatively, the increasing adoption of -omics approaches can investigate hundreds or even thousands of immune components at once (e.g., transcripts, proteins) without species-specific or cross-reactive reagents. In particular, proteomics can provide data on hundreds of proteins from very small volumes of plasma or sera, making the most of the limited samples non-lethally obtained from wild bats [230,231]. Between more historic and newly applied methodologies for characterizing immunity of wild bats especially, an outstanding need is the development of comparable and accessible protocols for collecting and storing biological samples, conducting assays, and analyzing raw data to standardize approaches and enable comparisons among studies.

Third, the expansion of experimental studies will be central to advance the tools used in bat immunology and to mechanistically test evolutionary hypotheses. Increased representation of major bat families in captive systems is needed to develop bat-specific immunological tools [29], including but not limited to monoclonal antibodies [228]. Such captive systems will be especially important for better characterizing and comparing parts of bat immunity that remain elusive, such as adaptive defense [10,111,232]. Several studies have shown variation in the B cell and antibody response among bat species [94,95], although the drivers behind these differences remain poorly understood. Studies have also focused on neutralizing antibodies, such that our understanding of other aspects of the humoral immune response, including the role of non-neutralizing antibodies and Fc receptor functions, likewise remains limited. However, given the challenges associated with maintaining captive bat colonies [233,234], greater adoption of *in vitro* models should especially enhance mechanistic insights into the patterns of immunity and infection observed in the wild. For example, persistence of a novel α-CoV was observed in *Myotis lucifugus* for at least four months during hibernation without detectable pathology [235]. Infection of cell lines derived from another vesper bat, *Eptesicus fuscus*, with MERS-CoV recapitulated this duration of viral persistence but further demonstrated this phenomenon was

associated with an IFN regulatory factor 3–dependent antiviral response [236]. Organoid models in particular could be especially informative given their ability to model whole immunological tissue [83,85,87,237]. Immunological differences in wild bat species could then be interrogated with focused tests in these *in vitro* models (e.g., via mock or actual infection between bat species) [238].

Finally, application of phylogenetic comparative methods and other statistical tools are central to test support for correlated evolution of bat species traits and immunological outcomes. Phylogenetic generalized linear models (PGLMs) or phylogenetic generalized linear mixed models (PGLMMs) should be a primary approach to control for evolutionary history, depending on the use of species-level (i.e., mean or binary immune outcomes) or individual-level data, respectively. For PGLMs, weighting strategies can allow accounting for variation in sample size or even measures of precision for species means, providing more robust estimates of model coefficients and ability to test hypotheses [239,240]. For PGLMMs, inclusion of both phylogenetic and non-phylogenetic random effects can reduce bias and improve inference [241,242]. Such analyses have been applied to comparative studies of avian and terrestrial mammal immunology [211,243–247], and addressing immunological data gaps across bat species (Figure 4) will enable greater adoption of these methods to the Chiroptera. Additional statistical methods, such as ancestral state reconstruction, state-dependent diversification, and phylogenetic factorization would facilitate improved understanding of the evolution of bat immune systems, their relation to speciation and extinction, and identification of distinct lineages of immune strategies [158,211,248].

To statistically differentiate multiple, competing evolutionary hypotheses about the drivers of interspecific variation in bat immunology, we suggest greater adoption of frameworks for causal inference [249,250], such as causal mediation analysis (CMA) [251]. Similar to structural equation modelling, CMA decomposes a hypothesized causal relationship between a predictor and a response into the direct effect and the indirect effect mediated through a third variable. This approach could be especially useful in cases where a given trait driver is hypothesized to affect immunity through multiple mechanisms, such as for diet (Table 1). Here, CMA would estimate the direct effect of diet on immunity (representing energetic hypotheses) as well as the indirect effect of diet on pathogen exposure (Figure 6). Importantly, PGLMs or PGLMMs can be used in these analyses, and both the mediator and outcome models can adjust for relevant precision covariates, such as citation counts (i.e., for species-level analyses) or time between capture and blood collection (i.e., for individual-level analyses). Controlling for such variables, especially those well-known to introduce artifacts into immunology data [252,253], will more generally be important for accurate estimation of effects when testing evolutionary hypotheses.

**Acknowledgements**

This project was supported by the National Science Foundation (DBI 2515340; RAPID 2032157), National Institutes of Health (5R21AI169548-02, P20GM134973), Edward Mallinckrodt, Jr. Foundation, Human Frontier Science Program (RGP002/2023, LT0017/2024-L), Government of Canada's New Frontiers in Research Fund (NFRFE-2023-00025), and Natural Sciences and Engineering Research Council of Canada (RGPIN-2022-03010). The Vaccine and Infectious Disease Organization also receives operational funding from the Government of Saskatchewan through Innovation Saskatchewan and the Ministry of Agriculture and from the Canada Foundation for Innovation through the Major Science Initiatives.

## Figures and legends

Figure 1. Representative axes of ecological and epidemiological variation among bat species using the most recent mammal phylogeny (1,287 bat species, colored by family) [221]. Body mass, phytophagy, thermoregulation (torpor or hibernation), and maximum lifespan were obtained from the COalesced Mammal dataBase of INtrinsic and Extrinsic traits (COMBINE) database of mammalian traits [48]. Viral family richness data were obtained from the Global Virome in One Network (VIRION) database [71], simplified to only those records detected through sequencing or isolation, resolved by NCBI, and aligned to the tree taxonomy. Missing data are shown in white.

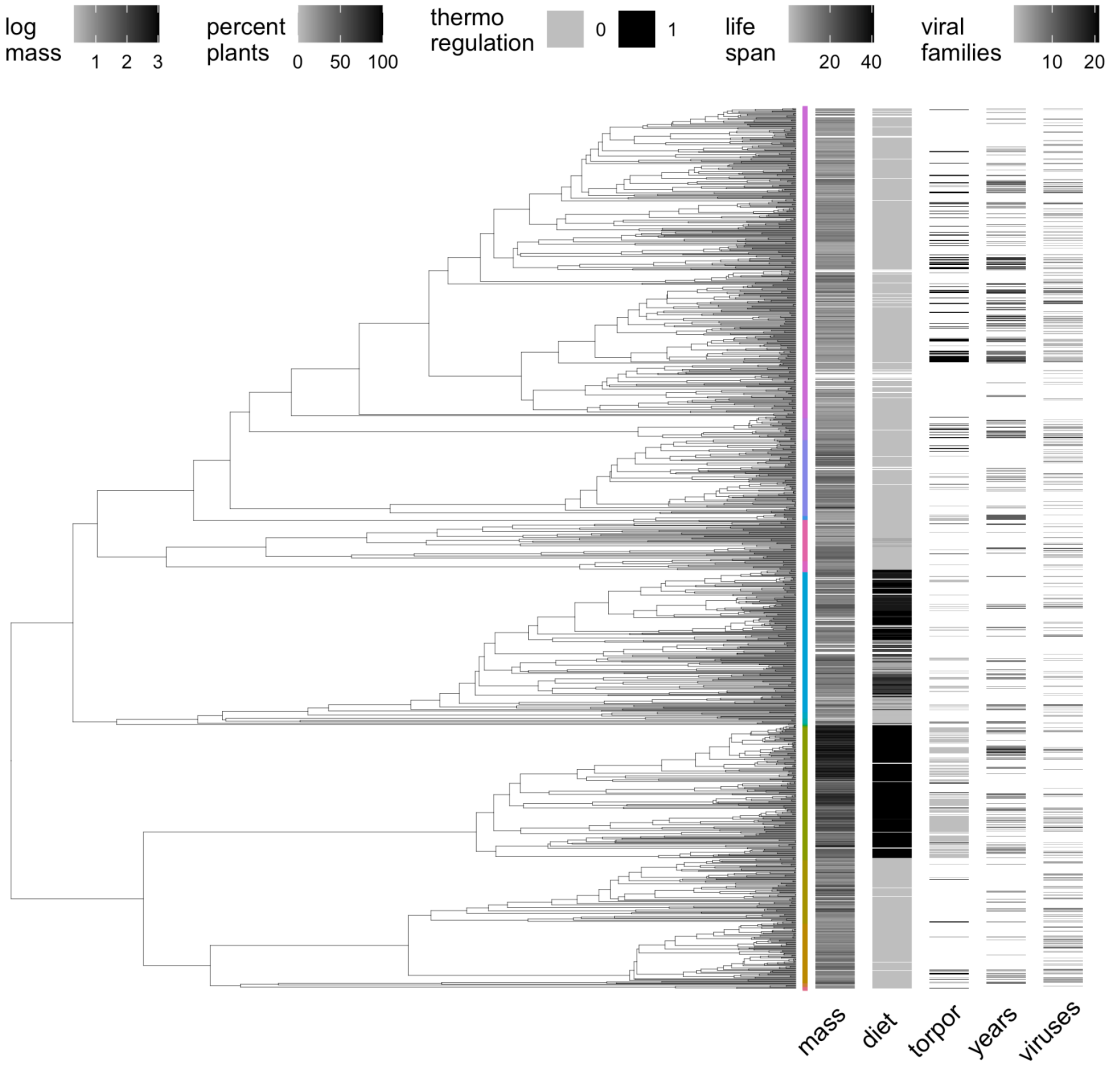

Figure 2. Phylogeography of bat species shown to be susceptible or resistant to SARS-CoV-2 infection through *in vivo* or *in vitro* challenge, using the most recent mammal phylogeny [221], experimental data [75–81,83], and species distributions from the IUCN. Subgenera of the genus *Eptesicus* were recently elevated to full genus rank, such that species in the Eastern Hemisphere have been reclassified into the genus *Cnephaeus* [254]. We note that SARS-CoV-2 isolates used in these experimental studies were derived from humans and thus do not represent interactions of bats or their cells with bonafide bat-derived SARS-CoV-2–like viruses, such as BANAL-236 [255].

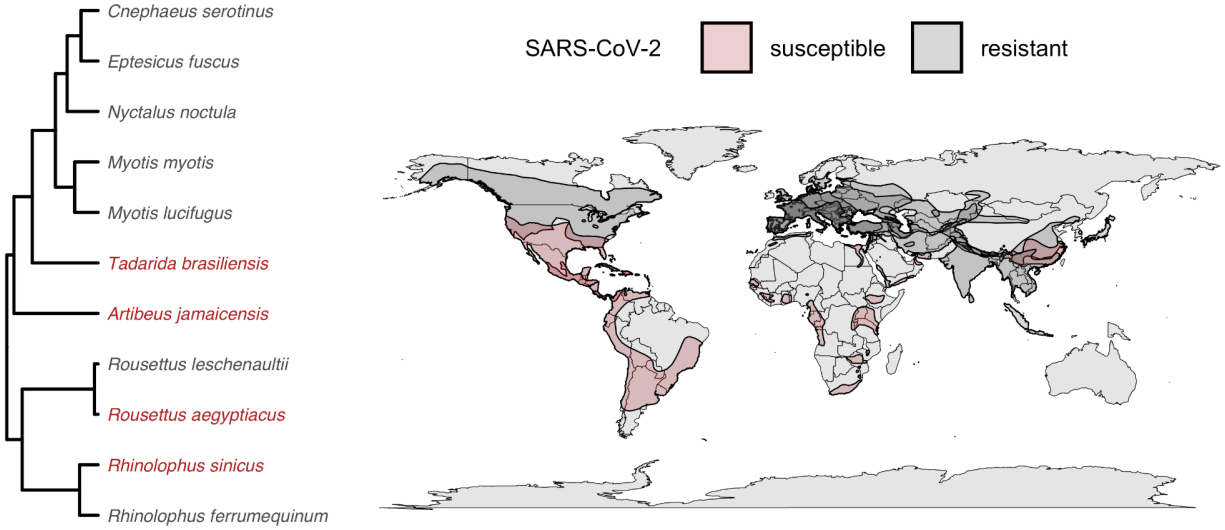

Figure 3. Geographic and behavioral distributions of global bat families: the Emballonuridae, Vespertilionidae, and Molossidae. Species distributions were drawn from the IUCN and merged per bat family using the *rgeos* package in R. Inset plots display the relationships between habitat breadth and geographic range size (left) as well as between geographic range size and viral family richness (right) across 565 species (not all species have matching trait data). Trait data are from COMBINE [48], PanTHERIA [256], and VIRION [71]. Data are overlaid with the posterior mean slope and 95% credible interval (CI) band from each phylogenetic generalized linear model (PGLM) fit using the *brms* package [257], each using four chains including 2,000 iterations and 50% burn-in for a total 4,000 samples (both models converged, given inspection of traces and Rhat values). Within these three bat families, habitat breadth predicts $\log_{10}$-geographic range size ($\beta = 0.30$, 95% CI: 0.21–0.39; PGLM with gaussian response), and $\log_{10}$-geographic range size predicts viral diversity ($\beta = 1.19$, 95% CI: 0.94–1.46; PGLM with negative binomial response).

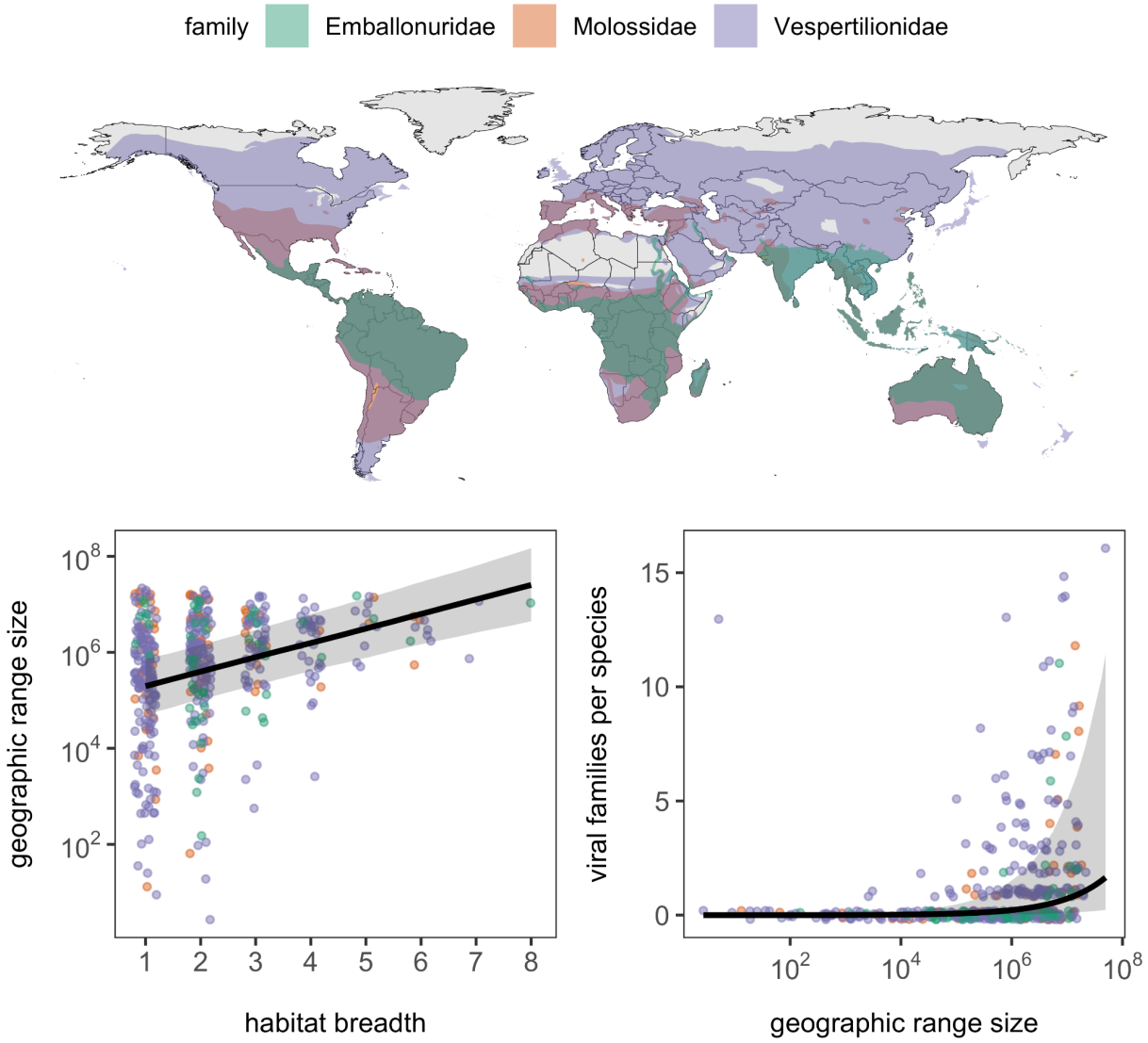

Figure 4. Taxonomic patterns in the relative number of immunology-related citations and public availability of genome assemblies per bat species (Table S1), as two measures of data coverage. The phylogeny ($n$ = 1,287 species)[221] is presented with seven clades identified from phylogenetic factorization of immunology citations, modeled with the *phylofactor* package as a binomial response to account for the total citation count per species [223]. Clades with proportionally greater or fewer immunology citations compared to the rest of the phylogeny are shown in red and blue, respectively, with segments showing the raw counts of total citations (grey) and immunity citations (black). Asterisks are provided for those species with an NCBI genome assembly.

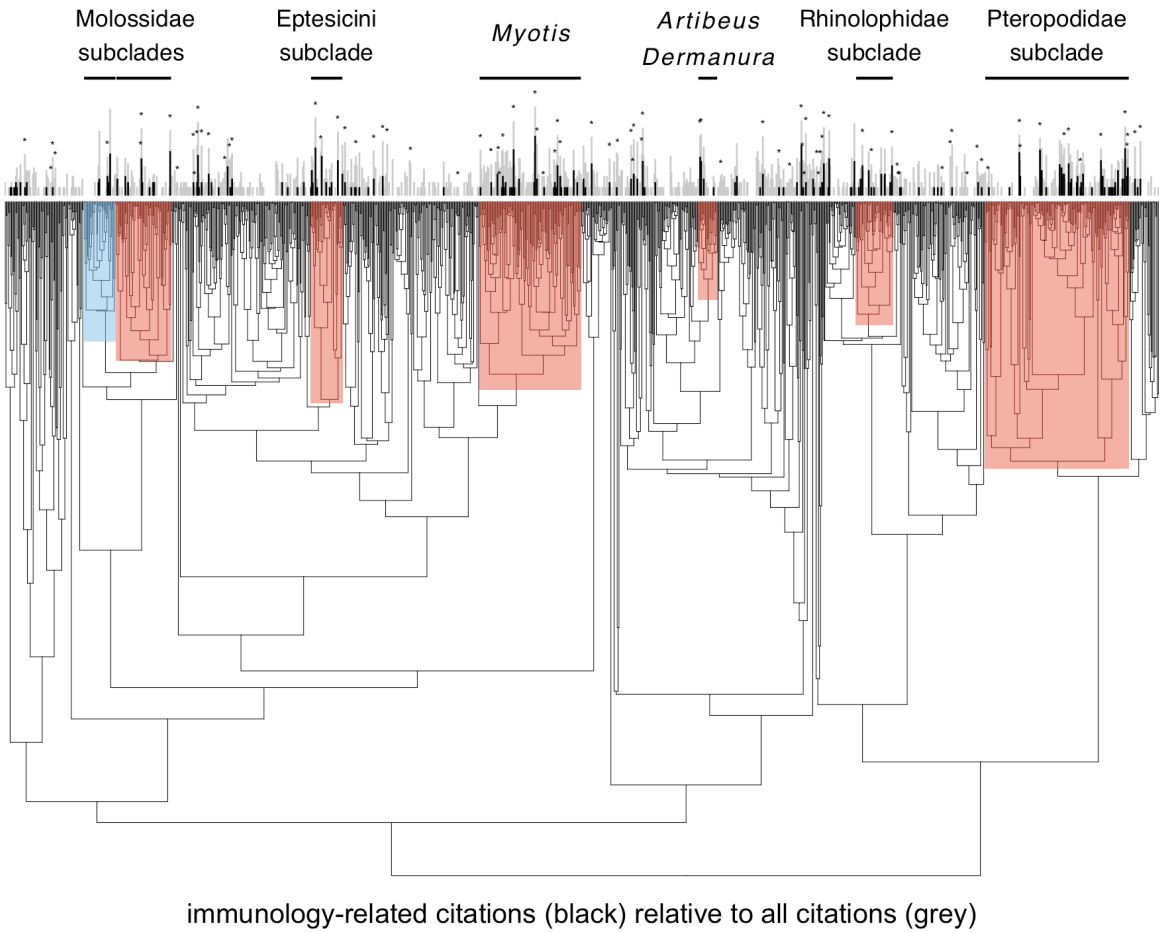

Figure 5. Distribution of average body mass across bat species ($n$ = 1,217) [48,221]. Overlaid are the minimum body masses for which varying small blood volumes can be safely and non-lethally obtained (representing approximately 0.5% body mass as a highly conservative limit) [258,259].

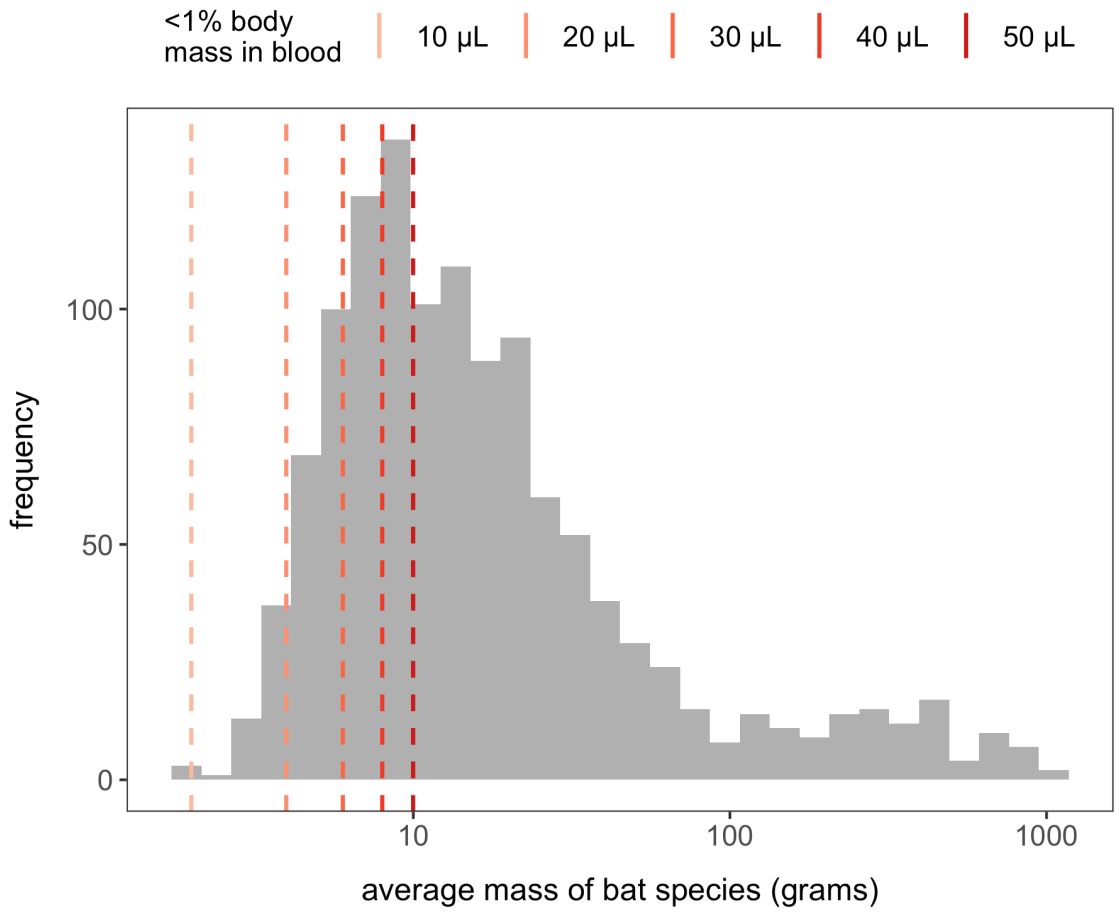

Figure 6. Example of how CMA can differentiate hypotheses about the drivers of interspecific variation in bat immunology, considering alternative mechanisms of pathogen exposure and host energetics. Here, CMA estimates the total indirect relationship between a dietary trait and pathogen exposure (*a*) and pathogen exposure and immunity (*b*) as well as the direct relationship between a dietary trait and immunity (*c'*). The total effect (*c*) is then the sum of the indirect effect (*ab*) and the direct effect (*c'*). The proportion mediated by pathogen exposure ($P_M$) is derived as the indirect effect (*ab*) divided by the estimated total effect (*c*): *ab*/*c*. High estimates of $P_M$ support the indirect relationship (i.e., pathogen-mediated selection), whereas negligible $P_M$ estimates better support the direct relationship between diet and immunity (i.e., host energetics).

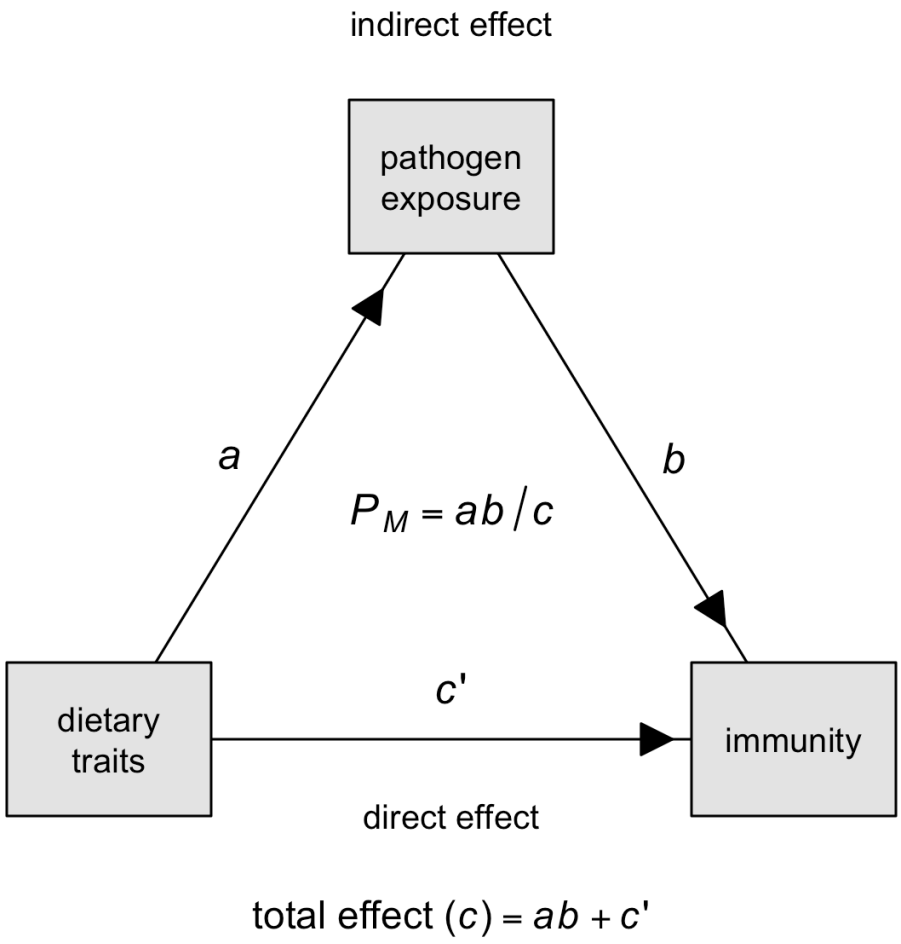

Table 1. Proposed hypotheses that predict interspecific differences in bat immunology.

| Mechanism | Driver | Prediction |
|---|---|---|
| Pathogen exposure | Coevolution | Host immune genes will show signatures of positive selection in response to pathogen pressure. |
| | Pathogen richness | Species with high pathogen diversity will invest more in adaptive immunity than those with few pathogens. |
| | Colony size | Species with large colonies will invest more in adaptive immunity, if pathogens mainly follow density-dependent transmission. |
| | Co-roosting | Species that share roosts with more bat and non-bat species will invest more in adaptive immunity. |
| | Diet | Species that consume other animals should invest more in defense and have greater immunogenetic diversity |
| | Habitat diversity | Greater habitat diversity (including large geographic range size and migratory distances) will promote immunogenetic diversity due to pathogen exposure. |
| | Longevity | Long-lived species will invest more in adaptive immunity owing to accumulated pathogen exposure. |
| Biogeography | Speciation | Speciation events will correlate with diversification in immune strategies in both innate and adaptive arms. |
| | Genetic drift | Small and isolated populations will show reduced immune diversity due to drift and inbreeding. |
| Host energetics | Pace of life | Fast-lived species will prioritize defenses with lower developmental costs (i.e., innate immunity). |
| | Diet | Species with low-energy food will invest less in adaptive immunity than those with high-energy food. |
| Environmental stability | Food seasonality | For species that do not hibernate or migrate, those with more seasonal food will invest more in innate defenses. |
| | Hibernation | Hibernating species will on average have lower baseline measures and weaker immune responses to conserve energy. |
| | Migration | Species with longer migrations between wintering and maternity grounds will show weaker immune responses. |

## References


1. Descloux E., O. Mediannikov, A.-C. Gourinat, *et al.* 2021. Flying Fox Hemolytic Fever, Description of a New Zoonosis Caused by Candidatus Mycoplasma haemohominis. *Clin. Infect. Dis.* **73**: e1445–e1453.
2. Amman B.R., S.A. Carroll, Z.D. Reed, *et al.* 2012. Seasonal pulses of Marburg virus circulation in juvenile Rousettus aegyptiacus bats coincide with periods of increased risk of human infection. *PLoS Pathog.* **8**: e1002877.
3. Eby P., A.J. Peel, A. Hoegh, *et al.* 2022. Pathogen spillover driven by rapid changes in bat ecology. *Nature*. https://doi.org/10.1038/s41586-022-05506-2
4. McKee C.D., A. Islam, M.Z. Rahman, *et al.* 2022. Nipah virus detection at bat roosts after spillover events, Bangladesh, 2012-2019. *Emerg. Infect. Dis.* **28**: 1384–1392.
5. Anthony S.J., K. Gilardi, V.D. Menachery, *et al.* 2017. Further Evidence for Bats as the Evolutionary Source of Middle East Respiratory Syndrome Coronavirus. *MBio* **8.**: https://doi.org/10.1128/mBio.00373-17
6. Bai Y., M.O.V. Osinubi, L. Osikowicz, *et al.* 2018. Human Exposure to Novel Bartonella Species from Contact with Fruit Bats. *Emerg. Infect. Dis.* **24**: 2317–2323.
7. Ramírez J.D., C. Hernández, M. Montilla, *et al.* 2014. First report of human Trypanosoma cruzi infection attributed to TcBat genotype. *Zoonoses Public Health* **61**: 477–479.
8. Wang N., S.-Y. Li, X.-L. Yang, *et al.* 2018. Serological Evidence of Bat SARS-Related Coronavirus Infection in Humans, China. *Virol. Sin.* **33**: 104–107.
9. Frank H.K., S.D. Boyd & E.A. Hadly. 2018. Global fingerprint of humans on the distribution of Bartonella bacteria in mammals. *PLoS Negl. Trop. Dis.* **12**: e0006865.
10. Gonzalez V., A.M. Hurtado-Monzón, S. O'Krafka, *et al.* 2024. Studying bats using a One Health lens: bridging the gap between bat virology and disease ecology. *J. Virol.* e0145324.
11. Subudhi S., N. Rapin & V. Misra. 2019. Immune System Modulation and Viral Persistence in Bats: Understanding Viral Spillover. *Viruses* **11.**: https://doi.org/10.3390/v11020192
12. Mandl J.N., C. Schneider, D.S. Schneider, *et al.* 2018. Going to Bat(s) for Studies of Disease Tolerance. *Front. Immunol.* **9.**: https://doi.org/10.3389/fimmu.2018.02112
13. Schountz T., M.L. Baker, J. Butler, *et al.* 2017. Immunological Control of Viral Infections in Bats and the Emergence of Viruses Highly Pathogenic to Humans. *Front. Immunol.* **8**: 1098.
14. Irving A.T., M. Ahn, G. Goh, *et al.* 2021. Lessons from the host defences of bats, a unique viral reservoir. *Nature* **589**: 363–370.
15. Wilkinson G.S. & J.M. South. 2002. Life history, ecology and longevity in bats. *Aging Cell* **1**: 124–131.
16. Anderson S.C. & G.D. Ruxton. 2020. The evolution of flight in bats: a novel hypothesis. *Mamm. Rev.* **50**: 426–439.
17. Scheben A., O.M. Ramos, M. Kramer, *et al.* 2023. Long-read sequencing reveals rapid evolution of immunity- and cancer-related genes in bats. *Genome Biol. Evol.* **15**: evad148.
18. Hua R., Y.-S. Ma, L. Yang, *et al.* 2024. Experimental evidence for cancer resistance in a bat species. *Nat. Commun.* **15**: 1401.
19. Cooper L.N., M.Y. Ansari, G. Capshaw, *et al.* 2024. Bats as instructive animal models for studying longevity and aging. *Ann. N. Y. Acad. Sci.* https://doi.org/10.1111/nyas.15233
20. O'Shea T.J., P.M. Cryan, A.A. Cunningham, *et al.* 2014. Bat flight and zoonotic viruses. *Emerg. Infect. Dis.* **20**: 741–745.
21. Brook C.E. & A.P. Dobson. 2015. Bats as "special"reservoirs for emerging zoonotic

pathogens. *Trends Microbiol.*
22. Levesque D.L., J.G. Boyles, C.J. Downs, *et al.* 2020. High Body Temperature Is an Unlikely Cause of High Viral Tolerance in Bats. *J. Wildl. Dis.*
23. Moreno Santillán D.D., T.M. Lama, Y.T. Gutierrez Guerrero, *et al.* 2021. Large-scale genome sampling reveals unique immunity and metabolic adaptations in bats. *Mol. Ecol.* **30**: 6449–6467.
24. Zhang G., C. Cowled, Z. Shi, *et al.* 2013. Comparative analysis of bat genomes provides insight into the evolution of flight and immunity. *Science* **339**: 456–460.
25. Brunet-Rossinni A.K. 2004. Reduced free-radical production and extreme longevity in the little brown bat (Myotis lucifugus) versus two non-flying mammals. *Mech. Ageing Dev.* **125**: 11–20.
26. Ahn M., D.E. Anderson, Q. Zhang, *et al.* 2019. Dampened NLRP3-mediated inflammation in bats and implications for a special viral reservoir host. *Nat Microbiol* **4**: 789–799.
27. Xie J., Y. Li, X. Shen, *et al.* 2018. Dampened STING-Dependent Interferon Activation in Bats. *Cell Host Microbe* **23**: 297–301.e4.
28. Luis A.D., D.T.S. Hayman, T.J. O'Shea, *et al.* 2013. A comparison of bats and rodents as reservoirs of zoonotic viruses: are bats special? *Proc. Biol. Sci.* **280**: 20122753.
29. Wang L.-F., A.M. Gamage, W.O.Y. Chan, *et al.* 2021. Decoding bat immunity: the need for a coordinated research approach. *Nat. Rev. Immunol.* **21**: 269–271.
30. Zhou P., M. Tachedjian, J.W. Wynne, *et al.* 2016. Contraction of the type I IFN locus and unusual constitutive expression of IFN-α in bats. *Proc. Natl. Acad. Sci. U. S. A.* **113**: 2696–2701.
31. Guito J.C., S.G.M. Kirejczyk, A.J. Schuh, *et al.* 2024. Coordinated inflammatory responses dictate Marburg virus control by reservoir bats. *Nat. Commun.* **15**: 1826.
32. Kessler S., P. Stegen, S. Zhan, *et al.* 2024. Jamaican fruit bats mount a stable and highly neutralizing antibody response after bat influenza virus infection. *Proc. Natl. Acad. Sci. U. S. A.* **121**: e2413619121.
33. Pei G., A. Balkema-Buschmann & A. Dorhoi. 2024. Disease tolerance as immune defense strategy in bats: One size fits all? *PLoS Pathog.* **20**: e1012471.
34. Ahn M., V.C.-W. Chen, P. Rozario, *et al.* 2023. Bat ASC2 suppresses inflammasomes and ameliorates inflammatory diseases. *Cell* **186**: 2144–2159.e22.
35. Schneeberger K., G.Á. Czirják & C.C. Voigt. 2013. Measures of the constitutive immune system are linked to diet and roosting habits of neotropical bats. *PLoS One* **8**: e54023.
36. Baker M.L., T. Schountz & L.-F. Wang. 2013. Antiviral immune responses of bats: a review. *Zoonoses Public Health* **60**: 104–116.
37. Gonzalez V. & A. Banerjee. 2022. Molecular, ecological, and behavioral drivers of the bat-virus relationship. *iScience* **25**: 104779.
38. Banerjee A., M.L. Baker, K. Kulcsar, *et al.* 2020. Novel Insights Into Immune Systems of Bats. *Front. Immunol.* **11**: 26.
39. Springer M.S., W.J. Murphy, E. Eizirik, *et al.* 2003. Placental mammal diversification and the Cretaceous-Tertiary boundary. *Proc. Natl. Acad. Sci. U. S. A.* **100**: 1056–1061.
40. Teeling E.C., M.S. Springer, O. Madsen, *et al.* 2005. A molecular phylogeny for bats illuminates biogeography and the fossil record. *Science* **307**: 580–584.
41. Simmons N.B., K.L. Seymour, J. Habersetzer, *et al.* 2008. Primitive Early Eocene bat from Wyoming and the evolution of flight and echolocation. *Nature* **451**: 818–821.
42. *Phylogenetic relationships of Icaronycteris, Archaeonycteris, Hassianycteris, and*

*Palaeochiropteryx to extant bat lineages, with comments on the evolution of echolocation and foraging strategies*.
43. Grossnickle D.M., A. Sadier, E. Patterson, *et al.* 2024. The hierarchical radiation of phyllostomid bats as revealed by adaptive molar morphology. *Curr. Biol.* **34**: 1284–1294.e3.
44. Almeida F.C., L.I. Amador & N.P. Giannini. 2021. Explosive radiation at the origin of Old World fruit bats (Chiroptera, Pteropodidae). *Org. Divers. Evol.* **21**: 231–243.
45. Simmons, N B, A L Cirranello. 2024. "*Bat Species of the World: A taxonomic and geographic database*." https://doi.org/10.5281/zenodo.10580176
46. Chaverri G., I. Garin, A. Alberdi, *et al.* 2016. Unveiling the Hidden Bat Diversity of a Neotropical Montane Forest. *PLoS One* **11**: e0162712.
47. Ladle R.J., J.V.L. Firmino, A.C.M. Malhado, *et al.* 2012. Unexplored diversity and conservation potential of neotropical hot caves. *Conserv. Biol.* **26**: 978–982.
48. Soria C.D., M. Pacifici, M. Di Marco, *et al.* 2021. COMBINE: a coalesced mammal database of intrinsic and extrinsic traits. *Ecology* **102**: e03344.
49. Fenton M.B. & N.B. Simmons. 2020. "*Bats: a world of science and mystery*." University of Chicago Press.
50. Moyers Arévalo R.L., L.I. Amador, F.C. Almeida, *et al.* 2020. Evolution of body mass in bats: Insights from a large supermatrix phylogeny. *J. Mamm. Evol.* **27**: 123–138.
51. Marinello M.M. & E. Bernard. 2014. Wing morphology of Neotropical bats: a quantitative and qualitative analysis with implications for habitat use. *Can. J. Zool.* **92**: 141–147.
52. Arbour J.H., A.A. Curtis & S.E. Santana. 2019. Signatures of echolocation and dietary ecology in the adaptive evolution of skull shape in bats. *Nat. Commun.* **10**: 2036.
53. Monteiro L.R. & M.R. Nogueira. 2011. Evolutionary patterns and processes in the radiation of phyllostomid bats. *BMC Evol. Biol.* **11**: 137.
54. Russo D. & M.B. Fenton. 2023. "*A Natural History of Bat Foraging: Evolution, Physiology, Ecology, Behavior, and Conservation*." Elsevier Science & Technology.
55. Stawski C., C.K.R. Willis & F. Geiser. 2014. The importance of temporal heterothermy in bats. *J. Zool.* **292**: 86–100.
56. Norquay K.J.O. & C.K.R. Willis. 2014. Hibernation phenology of*Myotis lucifugus*. *J. Zool. (1987)* **294**: 85–92.
57. Lazzeroni M.E., F.T. Burbrink & N.B. Simmons. 2018. Hibernation in bats (Mammalia: Chiroptera) did not evolve through positive selection of leptin. *Ecol. Evol.* **8**: 12576–12596.
58. Geiser F. & C. Stawski. 2011. Hibernation and torpor in tropical and subtropical bats in relation to energetics, extinctions, and the evolution of endothermy. *Integr. Comp. Biol.* **51**: 337–348.
59. Fleming T.H., P. Eby, T.H. Kunz, *et al.* 2003. Ecology of bat migration. *Bat ecology* **156**: 164–165.
60. Bisson I.-A., K. Safi & R.A. Holland. 2009. Evidence for repeated independent evolution of migration in the largest family of bats. *PLoS One* **4**: e7504.
61. Voigt C.C., M. Helbig-Bonitz, S. Kramer-Schadt, *et al.* 2014. The third dimension of bat migration: evidence for elevational movements of Miniopterus natalensis along the slopes of Mount Kilimanjaro. *Oecologia* **174**: 751–764.
62. Barclay R.M.R., L.D. Harder, T.H. Kunz, *et al.* 2003. Life histories of bats: life in the slow lane. *Bat ecology*.
63. Podlutsky A.J., A.M. Khritankov, N.D. Ovodov, *et al.* 2005. A new field record for bat

longevity. *J. Gerontol. A Biol. Sci. Med. Sci.* **60**: 1366–1368.
64. Racey P. & A. Entwistle. 2000. Life-history and reproductive strategies of bats. *Reproductive biology of bats* 363–414.
65. Cotterill F.P.D. & R.A. Fergusson. 1993. Seasonally Polyestrous Reproduction in a Free-Tailed Bat Tadarida fulminans (Microchiroptera: Molossidae) in Zimbabwe. *Biotropica* **25**: 487.
66. Reid. 2009. "*A field guide to the mammals of central America and southeast Mexico*," , 2nd ed. New York, NY: Oxford University Press.
67. Happold D.C.D. & M. Happold. 1990. Reproductive strategies of bats in Africa. *J. Zool. (1987)* **222**: 557–583.
68. Garbino G.S.T., A. Feijó, R. Beltrão-Mendes, *et al.* 2021. Evolution of litter size in bats and its influence on longevity and roosting ecology. *Biol. J. Linn. Soc. Lond.* **132**: 676–684.
69. Letko M., S.N. Seifert, K.J. Olival, *et al.* 2020. Bat-borne virus diversity, spillover and emergence. *Nat. Rev. Microbiol.* **18**: 461–471.
70. Szentivanyi T., C. McKee, G. Jones, *et al.* 2023. Trends in Bacterial Pathogens of Bats: Global Distribution and Knowledge Gaps. *Transbound. Emerg. Dis.* **2023.**: https://doi.org/10.1155/2023/9285855
71. Carlson C.J., R.J. Gibb, G.F. Albery, *et al.* 2022. The Global Virome in One Network (VIRION): an Atlas of Vertebrate-Virus Associations. *MBio* **13**: e0298521.
72. Morales A, Dong Y, Brown T, Baid K, Kontopoulos D, Gonzalez V, Huang Z, Ahmed A, Hilgers L, Winkler S, Hughes G, Li X, Kirilenko B, Devanna P, Lama Tm, Nissan Y, Pippel M, Dávalos L, Vernes S, Puechmaille S, Rossiter S, Yovel Y, Prescott J, Kurth A, Ray D, Lim B, Myers E, Teeling E, Banerjee A, Irving A, Hiller M. Reference-quality bat genomes illuminate adaptations to viral tolerance and disease resistance. *Research Square*. https://doi.org/10.21203/rs.3.rs-2557682/v1
73. Liang J., C. Zhu & L. Zhang. 2021. Cospeciation of coronavirus and paramyxovirus with their bat hosts in the same geographical areas. *BMC Ecol Evol* **21**: 148.
74. Forero-Muñoz N.R., R.L. Muylaert, S.N. Seifert, *et al.* The coevolutionary mosaic of bat betacoronavirus emergence risk. *Virus Evol*. https://doi.org/10.1093/ve/vead079
75. Bosco-Lauth A.M., S.M. Porter, K.A. Fox, *et al.* 2022. Experimental Infection of Brazilian Free-Tailed Bats (Tadarida brasiliensis) with Two Strains of SARS-CoV-2. *Viruses* **14.**: https://doi.org/10.3390/v14081809
76. Hall J.S., E. Hofmeister, H.S. Ip, *et al.* 2023. Experimental Infection of Mexican Free-Tailed Bats (Tadarida brasiliensis) with SARS-CoV-2. *mSphere* e0026322.
77. Hall J.S., S. Knowles, S.W. Nashold, *et al.* 2021. Experimental challenge of a North American bat species, big brown bat (Eptesicus fuscus), with SARS-CoV-2. *Transbound. Emerg. Dis.* **68**: 3443–3452.
78. Hall J.S., S. Nashold, E. Hofmeister, *et al.* 2024. Little brown bats (Myotis lucifugus) are resistant to SARS-CoV-2 infection. *J. Wildl. Dis.* **60**: 924–930.
79. Schlottau K., M. Rissmann, A. Graaf, *et al.* 2020. SARS-CoV-2 in fruit bats, ferrets, pigs, and chickens: an experimental transmission study. *Lancet Microbe* **1**: e218–e225.
80. Mohl B.-P., C. Blaurock, A. Breithaupt, *et al.* 2024. Increased susceptibility of Rousettus aegyptiacus bats to respiratory SARS-CoV-2 challenge despite its distinct tropism for gut epithelia in bats. *Viruses* **16.**: https://doi.org/10.3390/v16111717
81. Aicher S.-M., F. Streicher, M. Chazal, *et al.* 2022. Species-Specific Molecular Barriers to SARS-CoV-2 Replication in Bat Cells. *J. Virol.* **96**: e0060822.

82. Frank H.K., D. Enard & S.D. Boyd. 2022. Exceptional diversity and selection pressure on coronavirus host receptors in bats compared to other mammals. *Proc. Biol. Sci.* **289**: 20220193.
83. Zhou J., C. Li, X. Liu, *et al.* 2020. Infection of bat and human intestinal organoids by SARS-CoV-2. *Nat. Med.* **26**: 1077–1083.
84. Bisht P., M.D. Gallagher, M.I. Barrasa, *et al.* 2024. Abortive infection of bat fibroblasts with SARS-CoV-2. *Proc. Natl. Acad. Sci. U. S. A.* **121**: e2406773121.
85. Elbadawy M., Y. Kato, N. Saito, *et al.* 2021. Establishment of intestinal organoid from Rousettus leschenaultii and the susceptibility to bat-associated viruses, SARS-CoV-2 and Pteropine Orthoreovirus. *Int. J. Mol. Sci.* **22**: 10763.
86. Port J.R., J.C. Riopelle, S. van Tol, *et al.* 2024. Jamaican fruit bat (Artibeus jamaicensis) insusceptibility to mucosal inoculation with SARS-CoV-2 Delta variant is not caused by receptor compatibility. *npj Viruses* **2.**: https://doi.org/10.1038/s44298-024-00037-1
87. Hashimi M., T.A. Sebrell, J.F. Hedges, *et al.* 2023. Antiviral responses in a Jamaican fruit bat intestinal organoid model of SARS-CoV-2 infection. *Nat. Commun.* **14**: 6882.
88. Muylaert R.L., T. Kingston, J. Luo, *et al.* 2022. Present and future distribution of bat hosts of sarbecoviruses: implications for conservation and public health. *Proc. Biol. Sci.* **289**: 20220397.
89. Ng M., E. Ndungo, M.E. Kaczmarek, *et al.* 2015. Filovirus receptor NPC1 contributes to species-specific patterns of ebolavirus susceptibility in bats. *Elife* **4.**: https://doi.org/10.7554/eLife.11785
90. Paweska J.T., N. Storm, A.A. Grobbelaar, *et al.* 2016. Experimental Inoculation of Egyptian Fruit Bats (Rousettus aegyptiacus) with Ebola Virus. *Viruses* **8**: 29.
91. Aguilar-Setien A., E. Loza-Rubio, M. Salas-Rojas, *et al.* 2005. Salivary excretion of rabies virus by healthy vampire bats. *Epidemiol. Infect.* **133**: 517–522.
92. Abbott R.C., L. Saindon, E.A. Falendysz, *et al.* 2020. Rabies outbreak in captive big brown bats (Eptesicus fuscus) used in a white-nose syndrome vaccine trial. *J. Wildl. Dis.* **56**: 197–202.
93. Turmelle A.S., F.R. Jackson, D. Green, *et al.* 2010. Host immunity to repeated rabies virus infection in big brown bats. *J. Gen. Virol.* **91**: 2360–2366.
94. Jackson F.R., A.S. Turmelle, D.M. Farino, *et al.* 2008. Experimental rabies virus infection of big brown bats (Eptesicus fuscus). *J. Wildl. Dis.* **44**: 612–621.
95. Aguilar-Setién A., Y.C. Leon, E.C. Tesoro, *et al.* 2002. Vaccination of vampire bats using recombinant vaccinia-rabies virus. *J. Wildl. Dis.* **38**: 539–544.
96. Stockmaier S., D.K.N. Dechmann, R.A. Page, *et al.* 2015. No fever and leucocytosis in response to a lipopolysaccharide challenge in an insectivorous bat. *Biol. Lett.* **11**: 20150576.
97. Stockmaier S., D.I. Bolnick, R.A. Page, *et al.* 2018. An immune challenge reduces social grooming in vampire bats. *Anim. Behav.* **140**: 141–149.
98. Melhado G., L.G. Herrera M & A.P. da Cruz-Neto. 2020. Bats respond to simulated bacterial infection during the active phase by reducing food intake. *J. Exp. Zool. A Ecol. Integr. Physiol.* **333**: 536–542.
99. Schneor L., S. Kaltenbach, S. Friedman, *et al.* 2023. Comparison of antiviral responses in two bat species reveals conserved and divergent innate immune pathways. *iScience* **26**: 107435.
100. Lin H.-H., M. Horie & K. Tomonaga. 2022. A comprehensive profiling of innate immune responses in Eptesicus bat cells. *Microbiol. Immunol.* **66**: 97–112.

101. Omatsu T., E.-J. Bak, Y. Ishii, *et al.* 2008. Induction and sequencing of Rousette bat interferon alpha and beta genes. *Vet. Immunol. Immunopathol.* **124**: 169–176.
102. Lilley T.M., J.M. Prokkola, A.S. Blomberg, *et al.* 2019. Resistance is futile: RNA-sequencing reveals differing responses to bat fungal pathogen in Nearctic Myotis lucifugus and Palearctic Myotis myotis. *Oecologia* **191**: 295–309.
103. Davy C.M., M.E. Donaldson, H. Bandouchova, *et al.* 2020. Transcriptional host-pathogen responses of Pseudogymnoascus destructans and three species of bats with white-nose syndrome. *Virulence* **11**: 781–794.
104. Demas G.E., D.A. Zysling, B.R. Beechler, *et al.* 2011. Beyond phytohaemagglutinin: assessing vertebrate immune function across ecological contexts. *J. Anim. Ecol.* **80**: 710–730.
105. DeAnglis I.K., B.R. Andrews, L.R. Lock, *et al.* 2024. Bat cellular immunity varies by year and dietary habit amidst land conversion. *Conserv Physiol* **12**: coad102.
106. Periasamy P., P.E. Hutchinson, J. Chen, *et al.* 2019. Studies on B Cells in the Fruit-Eating Black Flying Fox (Pteropus alecto). *Front. Immunol.* **10**: 489.
107. Gamage A.M., W.O.Y. Chan, F. Zhu, *et al.* 2022. Single-cell transcriptome analysis of the in vivo response to viral infection in the cave nectar bat Eonycteris spelaea. *Immunity* **55**: 2187–2205.e5.
108. Hatten B.A., J.H. Lutskus & S.E. Sulkin. 1973. A serologic comparison of bat complements. *J. Exp. Zool.* **186**: 193–206.
109. Li J., K. Sun, W. Dai, *et al.* 2023. Divergence in interspecific and intersubspecific gene expression between two closely related horseshoe bats (Rhinolophus). *J. Mammal.* **104**: 62–75.
110. Pavlovich S.S., S.P. Lovett, G. Koroleva, *et al.* 2018. The Egyptian Rousette Genome Reveals Unexpected Features of Bat Antiviral Immunity. *Cell* **173**: 1098–1110.e18.
111. Pursell T., A. Reers, A. Mikelov, *et al.* 2024. Genetically and functionally distinct immunoglobulin heavy chain locus duplication in bats. *bioRxivorg*. https://doi.org/10.1101/2024.08.09.606892
112. Larson P.A., M.L. Bartlett, K. Garcia, *et al.* 2021. Genomic features of humoral immunity support tolerance model in Egyptian rousette bats. *Cell Rep.* **35**: 109140.
113. Ma L., L. Liu, J. Li, *et al.* 2024. Landscape of IGH germline genes of Chiroptera and the pattern of Rhinolophus affinis bat IGH CDR3 repertoire. *Microbiol. Spectr.* **12**: e0376223.
114. Das S., M. Nozawa, J. Klein, *et al.* 2008. Evolutionary dynamics of the immunoglobulin heavy chain variable region genes in vertebrates. *Immunogenetics* **60**: 47–55.
115. Kumar S., M. Suleski, J.M. Craig, *et al.* 2022. TimeTree 5: An expanded resource for species divergence times. *Mol. Biol. Evol.* **39.**: https://doi.org/10.1093/molbev/msac174
116. Yasuike M., J. de Boer, K.R. von Schalburg, *et al.* 2010. Evolution of duplicated IgH loci in Atlantic salmon, Salmo salar. *BMC Genomics* **11**: 486.
117. Bradshaw W.J. & D.R. Valenzano. 2020. Extreme genomic volatility characterizes the evolution of the immunoglobulin heavy chain locus in cyprinodontiform fishes. *Proc. Biol. Sci.* **287**: 20200489.
118. Marques J.T. & R.W. Carthew. 2007. A call to arms: coevolution of animal viruses and host innate immune responses. *Trends Genet.* **23**: 359–364.
119. Vinkler M., S.R. Fiddaman, M. Těšický, *et al.* 2023. Understanding the evolution of immune genes in jawed vertebrates. *J. Evol. Biol.* **36**: 847–873.
120. Garamszegi L.Z. & C.L. Nunn. 2011. Parasite-mediated evolution of the functional part of

the MHC in primates. *J. Evol. Biol.* **24**: 184–195.
121. Winternitz J.C., S.G. Minchey, L.Z. Garamszegi, *et al.* 2013. Sexual selection explains more functional variation in the mammalian major histocompatibility complex than parasitism. *Proc. Biol. Sci.* **280**: 20131605.
122. Drexler J.F., V.M. Corman, M.A. Müller, *et al.* 2012. Bats host major mammalian paramyxoviruses. *Nat. Commun.* **3**: 796.
123. Breed A.C., J. Meers, I. Sendow, *et al.* 2013. The distribution of henipaviruses in Southeast Asia and Australasia: is Wallace's line a barrier to Nipah virus? *PLoS One* **8**: e61316.
124. Han B.A., J.P. Schmidt, L.W. Alexander, *et al.* 2016. Undiscovered bat hosts of filoviruses. *PLoS Negl. Trop. Dis.* **10**: e0004815.
125. Taylor D.J., K. Dittmar, M.J. Ballinger, *et al.* 2011. Evolutionary maintenance of filovirus-like genes in bat genomes. *BMC Evol. Biol.* **11**: 336.
126. Tong S., Y. Li, P. Rivailler, *et al.* 2012. A distinct lineage of influenza A virus from bats. *Proc. Natl. Acad. Sci. U. S. A.* **109**: 4269–4274.
127. Tong S., X. Zhu, Y. Li, *et al.* 2013. New world bats harbor diverse influenza A viruses. *PLoS Pathog.* **9**: e1003657.
128. Campos A.C.A., L.G.B. Góes, A. Moreira-Soto, *et al.* 2019. Bat influenza A(HL18NL11) virus in fruit bats, Brazil. *Emerg. Infect. Dis.* **25**: 333–337.
129. Yang W., T. Schountz & W. Ma. 2021. Bat influenza viruses: Current status and perspective. *Viruses* **13**: 547.
130. Møller A.P. & A.P. Moller. 1998. Evidence of larger impact of parasites on hosts in the tropics: Investment in immune function within and outside the tropics. *Oikos* **82**: 265.
131. McDade T.W., A.V. Georgiev & C.W. Kuzawa. 2016. Trade-offs between acquired and innate immune defenses in humans. *Evol. Med. Public Health* **2016**: 1–16.
132. Santana S.E., T.O. Dial, T.P. Eiting, *et al.* 2011. Roosting ecology and the evolution of pelage markings in bats. *PLoS One* **6**: e25845.
133. Møller A.P., S. Merino, C.R. Brown, *et al.* 2001. Immune defense and host sociality: a comparative study of swallows and martins. *Am. Nat.* **158**: 136–145.
134. Streicker D.G., S. Recuenco, W. Valderrama, *et al.* 2012. Ecological and anthropogenic drivers of rabies exposure in vampire bats: implications for transmission and control. *Proc. Biol. Sci.* **279**: 3384–3392.
135. Gentles A.D., S. Guth, C. Rozins, *et al.* 2020. A review of mechanistic models of viral dynamics in bat reservoirs for zoonotic disease. *Pathog. Glob. Health* **114**: 407–425.
136. Blackwood J.C., D.G. Streicker, S. Altizer, *et al.* 2013. Resolving the roles of immunity, pathogenesis, and immigration for rabies persistence in vampire bats. *Proc. Natl. Acad. Sci. U. S. A.* **110**: 20837–20842.
137. Becker D.J., L.M. Bergner, A.B. Bentz, *et al.* 2018. Genetic diversity, infection prevalence, and possible transmission routes of Bartonella spp. in vampire bats. *PLoS Negl. Trop. Dis.* **12**: e0006786.
138. Nunn C.L., J.L. Gittleman & J. Antonovics. 2003. A comparative study of white blood cell counts and disease risk in carnivores. *Proc. Biol. Sci.* **270**: 347–356.
139. Nunn C.L. 2002. A comparative study of leukocyte counts and disease risk in primates. *Evolution* **56**: 177–190.
140. Frick W.F., P.A. Heady III, A.D. Earl, *et al.* 2018. Seasonal ecology of a migratory nectar-feeding bat at the edge of its range. *J. Mammal.* **99**: 1072–1081.
141. Willis C.K.R. & R.M. Brigham. 2004. Roost switching, roost sharing and social cohesion:

forest-dwelling big brown bats, Eptesicus fuscus, conform to the fission–fusion model. *Anim. Behav.* **68**: 495–505.
142. McKee C.D., A.I. Krawczyk, A.D. Sándor, *et al.* 2019. Host phylogeny, geographic overlap, and roost sharing shape parasite communities in European bats. *Front. Ecol. Evol.* **7.**: https://doi.org/10.3389/fevo.2019.00069
143. Willoughby A.R., K.L. Phelps & K.J. Olival. 2017. A comparative analysis of viral richness and viral sharing in cave-roosting bats. *Diversity* .
144. Simonis M.C. & D.J. Becker. 2023. A general framework for modeling pathogen transmission in co-roosting host communities. *bioRxiv* 2023.11.21.568148. https://doi.org/10.1101/2023.11.21.568148
145. Patterson B.D., C.W. Dick & K. Dittmar. 2007. Roosting Habits of Bats Affect Their Parasitism by Bat Flies (Diptera: Streblidae). *J. Trop. Ecol.* **23**: 177–189.
146. Santana S.E. & E. Cheung. 2016. Go big or go fish: morphological specializations in carnivorous bats. *Proc. Biol. Sci.* **283**: 20160615.
147. Malmberg J.L., L.A. White & S. VandeWoude. 2021. Bioaccumulation of pathogen exposure in top predators. *Trends Ecol. Evol.* **36**: 411–420.
148. Qiu Y., C. Lv, J. Chen, *et al.* 2024. The global distribution and diversity of wild-bird-associated pathogens: An integrated data analysis and modeling study. *Med (N. Y.)* 100553.
149. Qurkhuli T., N. Schwensow, S.D. Brändel, *et al.* 2019. Can extreme MHC class I diversity be a feature of a wide geographic range? The example of Seba's short-tailed bat (Carollia perspicillata). *Immunogenetics* **71**: 575–587.
150. Møller A.P. & J. Erritzøe. 1998. Host immune defence and migration in birds. *Evolutionary Ecology* **12**: 945–953.
151. Xu Y., V.N. Laine, K. Meramo, *et al.* 2024. Slow-lived birds and bats carry higher pathogen loads. *One Earth* **7**: 1121–1132.
152. Cooper N., J.M. Kamilar & C.L. Nunn. 2012. Host longevity and parasite species richness in mammals. *PLoS One* **7**: e42190.
153. Tsu B.V., C. Beierschmitt, A.P. Ryan, *et al.* 2021. Diverse viral proteases activate the NLRP1 inflammasome. *Elife* **10.**: https://doi.org/10.7554/eLife.60609
154. Tian S., J. Zeng, H. Jiao, *et al.* 2023. Comparative analyses of bat genomes identify distinct evolution of immunity in Old World fruit bats. *Sci. Adv.* **9**: eadd0141.
155. Srivastava P. 2002. Roles of heat-shock proteins in innate and adaptive immunity. *Nat. Rev. Immunol.* **2**: 185–194.
156. Guth S., E. Visher, M. Boots, *et al.* 2019. Host phylogenetic distance drives trends in virus virulence and transmissibility across the animal–human interface. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **374**: 20190296.
157. Guth S., N. Mollentze, K. Renault, *et al.* 2022. Bats host the most virulent—but not the most dangerous—zoonotic viruses. *Proceedings of the National Academy of Sciences* **119**: e2113628119.
158. Cummings C.A., A. Vicente-Santos, C.J. Carlson, *et al.* 2024. Viral epidemic potential is not uniformly distributed across the bat phylogeny. *bioRxiv*. https://doi.org/10.1101/2024.09.26.615197
159. Ammerman L., D.N. Lee & T. Tipps. 2012. First molecular phylogenetic insights into the evolution of free-tailed bats in the subfamily Molossinae (Molossidae, Chiroptera). *Journal of Mammalogy* **93**: 12–28.
160. Willoughby J.R., M. Sundaram, B.K. Wijayawardena, *et al.* 2015. The reduction of genetic

diversity in threatened vertebrates and new recommendations regarding IUCN conservation rankings. *Biol. Conserv.* **191**: 495–503.
161. Conenna I., R. Rocha, D. Russo, *et al.* 2017. Insular bats and research effort: a review of global patterns and priorities. *Mamm. Rev.* **47**: 169–182.
162. Frick W.F., T. Kingston & J. Flanders. 2020. A review of the major threats and challenges to global bat conservation. *Ann. N. Y. Acad. Sci.* **1469**: 5–25.
163. Charles Anderson R., R. Chakravarty & S. Raman. 2022. Bats in the Maldives: a review of historical data and first record of a vagrant Long-winged Tomb Bat (Emballonuridae: Taphozous longimanus). *Journal of Bat Research & Conservation* **15**: 78–83.
164. Lochmiller R.L. & C. Deerenberg. 2000. Trade-offs in evolutionary immunology: just what is the cost of immunity? *Oikos* **88**: 87–98.
165. Rauw W.M. 2012. Immune response from a resource allocation perspective. *Front. Genet.* **3**: 267.
166. Albery G.F. & D.J. Becker. 2021. Fast-lived Hosts and Zoonotic Risk. *Trends Parasitol.* **37**: 117–129.
167. Lee K.A. 2006. Linking immune defenses and life history at the levels of the individual and the species. *Integr. Comp. Biol.* **46**: 1000–1015.
168. Previtali M.A., R.S. Ostfeld, F. Keesing, *et al.* 2012. Relationship between pace of life and immune responses in wild rodents. *Oikos* **121**: 1483–1492.
169. Metcalf C.J.E., O. Roth & A.L. Graham. 2020. Why leveraging sex differences in immune trade-offs may illuminate the evolution of senescence. *Funct. Ecol.* **34**: 129–140.
170. Mellado B., L. de O. Carneiro, M.R. Nogueira, *et al.* 2024. Developmental instability, body mass, and reproduction predict immunological response in short-tailed bats. *Curr. Zool.* https://doi.org/10.1093/cz/zoae034
171. Kurta A., G.P. Bell, K.A. Nagy, *et al.* 1989. Energetics of pregnancy and lactation in freeranging little brown bats (*Myotis lucifugus*). *Physiol. Zool.* **62**: 804–818.
172. Strandin T., S.A. Babayan & K.M. Forbes. 2018. Reviewing the effects of food provisioning on wildlife immunity. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **373.**: https://doi.org/10.1098/rstb.2017.0088
173. Chandra R.K. 1997. Nutrition and the immune system: an introduction. *Am. J. Clin. Nutr.* **66**: 460S–463S.
174. Cruz-Neto A.P., T. Garland Jr & A.S. Abe. 2001. Diet, phylogeny, and basal metabolic rate in phyllostomid bats. *Zoology (Jena)* **104**: 49–58.
175. Clare E.L., H.R. Goerlitz, V.A. Drapeau, *et al.* 2014. Trophic niche flexibility in *Glossophaga soricina*: how a nectar seeker sneaks an insect snack. *Funct. Ecol.* **28**: 632–641.
176. Herrera G.L., E. Gutierrez, K.A. Hobson, *et al.* 2002. Sources of assimilated protein in five species of New World frugivorous bats. *Oecologia* **133**: 280–287.
177. Voigt C.C., A. Zubaid, T.H. Kunz, *et al.* 2011. Sources of assimilated proteins in old and new world phytophagous bats. *Biotropica* **43**: 108–113.
178. Klasing K.C. 1998. Nutritional modulation of resistance to infectious diseases. *Poult. Sci.* **77**: 1119–1125.
179. Falvo C., D. Crowley, E. Benson, *et al.* 2023. Diet-induced changes in metabolism influence immune response and viral shedding dynamics in Jamaican fruit bats. *bioRxivorg* 2023.12.01.569121. https://doi.org/10.1101/2023.12.01.569121
180. Becker D.J., P. Eby, W. Madden, *et al.* 2022. Ecological conditions predict the intensity of

Hendra virus excretion over space and time from bat reservoir hosts. *Ecol. Lett.* https://doi.org/10.1111/ele.14007
181. Breidenstein C.P. 1982. Digestion and assimilation of bovine blood by a vampire bat (Desmodus rotundus). *J. Mammal.* **63**: 482–484.
182. Blumer M., T. Brown, M.B. Freitas, *et al.* 2022. Gene losses in the common vampire bat illuminate molecular adaptations to blood feeding. *Sci. Adv.* **8**: eabm6494.
183. Wilkinson G.S. 1984. Reciprocal food sharing in the vampire bat. *Nature* **308**: 181–184.
184. Freitas M.B., A.F. Welker, S.F. Millan, *et al.* 2003. Metabolic responses induced by fasting in the common vampire bat Desmodus rotundus. *J. Comp. Physiol. B* **173**: 703–707.
185. McNab B.K. 1976. Seasonal fat reserves of bats in two tropical environments. *Ecology* **57**: 332–338.
186. Cabrera-Martinez L.V., L.G. Herrera M & A.P. Cruz-Neto. 2019. Food restriction, but not seasonality, modulates the acute phase response of a Neotropical bat. *Comp. Biochem. Physiol. A Mol. Integr. Physiol.* **229**: 93–100.
187. Lewanzik D., D.H. Kelm, S. Greiner, *et al.* 2012. Ecological correlates of cortisol levels in two bat species with contrasting feeding habits. *Gen. Comp. Endocrinol.* **177**: 104–112.
188. Ramos Pereira M.J., J.T. Marques & J.M. Palmeirim. 2010. Ecological responses of frugivorous bats to seasonal fluctuation in fruit availability in amazonian forests. *Biotropica* **42**: 680–687.
189. Zahn A., L. Rodrigues, A. Rainho, *et al.* 2007. Critical times of the year for Myotis myotis, a temperate zone bat: roles of climate and food resources. *Acta Chiropt.* **9**: 115–125.
190. Páez D.J., O. Restif, P. Eby, *et al.* 2018. Optimal foraging in seasonal environments: implications for residency of Australian flying foxes in food-subsidized urban landscapes. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **373.**: https://doi.org/10.1098/rstb.2017.0097
191. Gual-Suárez F. & R.A. Medellín. 2021. We eat meat: a review of carnivory in bats. *Mamm. Rev.* **51**: 540–558.
192. Nelson R.J., G.E. Demas, S.L. Klein, *et al.* 2002. "*Seasonal Patterns of Stress, Immune Function, and Disease*." Cambridge University Press.
193. Auteri G.G. 2022. A conceptual framework to integrate cold-survival strategies: torpor, resistance and seasonal migration. *Biol. Lett.* **18**: 20220050.
194. Speakman J.R. & A. Rowland. 1999. Preparing for inactivity: How insectivorous bats deposit a fat store for hibernation. *Proc. Nutr. Soc.* **58**: 123–131.
195. Bouma H.R., H.V. Carey & F.G.M. Kroese. 2010. Hibernation: the immune system at rest? *J. Leukoc. Biol.* **88**: 619–624.
196. George D.B., C.T. Webb, M.L. Farnsworth, *et al.* 2011. Host and viral ecology determine bat rabies seasonality and maintenance. *Proc. Natl. Acad. Sci. U. S. A.* **108**: 10208–10213.
197. Harazim M., J. Perrot, H. Varet, *et al.* 2023. Transcriptomic responses of bat cells to European bat lyssavirus 1 infection under conditions simulating euthermia and hibernation. *BMC Immunol.* **24**: 7.
198. Meteyer C.U., D. Barber & J.N. Mandl. 2012. Pathology in euthermic bats with white nose syndrome suggests a natural manifestation of immune reconstitution inflammatory syndrome. *Virulence* **3**: 583–588.
199. Fuller N.W., L.P. McGuire, E.L. Pannkuk, *et al.* 2020. Disease recovery in bats affected by white-nose syndrome. *J. Exp. Biol.* **223.**: https://doi.org/10.1242/jeb.211912
200. Mayberry H.W., L.P. McGuire & C.K.R. Willis. 2018. Body temperatures of hibernating little brown bats reveal pronounced behavioural activity during deep torpor and suggest a

fever response during white-nose syndrome. *J. Comp. Physiol. B* **188**: 333–343.
201. Fritze M., D. Costantini, J. Fickel, *et al.* 2019. Immune response of hibernating European bats to a fungal challenge. *Biol. Open* **8.**: https://doi.org/10.1242/bio.046078
202. McGuire L. & C. Guglielmo. 2009. What can birds tell us about the migration physiology of bats? *J. Mammal.* **90**: 1290–1297.
203. Owen J.C. & F.R. Moore. 2008. Swainson's thrushes in migratory disposition exhibit reduced immune function. *J. Ethol.* **26**: 383–388.
204. Nebel S., U. Bauchinger, D.M. Buehler, *et al.* 2012. Constitutive immune function in European starlings, Sturnus vulgaris, is decreased immediately after an endurance flight in a wind tunnel. *J. Exp. Biol.* **215**: 272–278.
205. Risely A., M. Klaassen & B.J. Hoye. 2018. Migratory animals feel the cost of getting sick: A meta-analysis across species. *J. Anim. Ecol.* **87**: 301–314.
206. Gylfe A., S. Bergström, J. Lundström, *et al.* 2000. Reactivation of Borrelia infection in birds. *Nature* **403**: 724–725.
207. Rogers E.J., L. McGuire, F.J. Longstaffe, *et al.* 2022. Relating wing morphology and immune function to patterns of partial and differential bat migration using stable isotopes. *J. Anim. Ecol.* **91**: 858–869.
208. Rivera-Ruiz D.A., J.J. Flores-Martínez, C. Rosales, *et al.* 2023. Constitutive Innate Immunity of Migrant and Resident Long-Nosed Bats (Leptonycteris yerbabuenae) in the Drylands of Mexico. *Diversity* **15**: 530.
209. Voigt C.C., M. Fritze, O. Lindecke, *et al.* 2020. The immune response of bats differs between pre-migration and migration seasons. *Sci. Rep.* **10**: 17384.
210. McCracken G.F. & M.F. Gassel. 1997. Genetic Structure in Migratory and Nonmigratory Populations of Brazilian Free-Tailed Bats. *J. Mammal.* **78**: 348–357.
211. Minias P. 2019. Evolution of heterophil/lymphocyte ratios in response to ecological and life-history traits: A comparative analysis across the avian tree of life. *J. Anim. Ecol.* **88**: 554–565.
212. Becker D.J. & B.A. Han. 2021. The macroecology and evolution of avian competence for*Borrelia burgdorferi*. *Glob. Ecol. Biogeogr.* **30**: 710–724.
213. Cornelius Ruhs E., D.J. Becker, S.J. Oakey, *et al.* 2021. Body size affects immune cell proportions in birds and non-volant mammals, but not bats. *J. Exp. Biol.* **224.**: https://doi.org/10.1242/jeb.241109
214. Teeling E.C., S.C. Vernes, L.M. Dávalos, *et al.* 2018. Bat Biology, Genomes, and the Bat1K Project: To Generate Chromosome-Level Genomes for All Living Bat Species. *Annu Rev Anim Biosci* **6**: 23–46.
215. Jebb D., Z. Huang, M. Pippel, *et al.* 2020. Six reference-quality genomes reveal evolution of bat adaptations. *Nature* **583**: 578–584.
216. Gutierrez E.G. & J. Ortega. 2025. Uncovering selection pressures on the IRF gene family in bats' immune system. *Immunogenetics* **77**: 10.
217. Foley N.M., A.J. Harris, K.R. Bredemeyer, *et al.* 2024. Karyotypic stasis and swarming influenced the evolution of viral tolerance in a species-rich bat radiation. *Cell Genom.* **4**: 100482.
218. Pinheiro A., J.R. Borges, J.V. Côrte-Real, *et al.* 2024. Evolution of guanylate binding protein genes shows a remarkable variability within bats (Chiroptera). *Front. Immunol.* **15**: 1329098.
219. Morales A.E., Y. Dong, T. Brown, *et al.* 2025. Bat genomes illuminate adaptations to viral

tolerance and disease resistance. *Nature* 1–10.
220. Peel E., L. Silver, P. Brandies, *et al.* 2022. Best genome sequencing strategies for annotation of complex immune gene families in wildlife. *Gigascience* **11.**: https://doi.org/10.1093/gigascience/giac100
221. Upham N.S., J.A. Esselstyn & W. Jetz. 2019. Inferring the mammal tree: Species-level sets of phylogenies for questions in ecology, evolution, and conservation. *PLoS Biol.* **17**: e3000494.
222. Nunn C.L. 2011. "*The comparative approach in evolutionary anthropology and biology*." Chicago, IL: University of Chicago Press.
223. Washburne A.D., J.D. Silverman, J.T. Morton, *et al.* 2019. Phylofactorization: a graph partitioning algorithm to identify phylogenetic scales of ecological data. *Ecol. Monogr.* **89**: e01353.
224. Holm S. 1979. A Simple Sequentially Rejective Multiple Test Procedure. *Scand. Stat. Theory Appl.* **6**: 65–70.
225. Becker D.J., M.M. Chumchal & A.B. Bentz. 2017. Predictors and immunological correlates of sublethal mercury exposure in vampire bats. *R. Soc. Health J.*
226. Johnson J.S., D.M. Reeder, T.M. Lilley, *et al.* 2015. Antibodies to Pseudogymnoascus destructans are not sufficient for protection against white-nose syndrome. *Ecol. Evol.* **5**: 2203–2214.
227. Martínez Gómez J.M., P. Periasamy, C.-A. Dutertre, *et al.* 2016. Phenotypic and functional characterization of the major lymphocyte populations in the fruit-eating bat Pteropus alecto. *Sci. Rep.* **6**: 37796.
228. Chen S., W.R. Sia, L.J.W. Tang, *et al.* 2024. Application of a bespoke monoclonal antibody panel to characterize immune cell populations in cave nectar bats. *Cell Rep.* **43**: 114703.
229. Friedrichs V., C. Toussaint, A. Schäfer, *et al.* 2022. Landscape and age dynamics of immune cells in the Egyptian rousette bat. *Cell Rep.* **40**: 111305.
230. Neely B.A., M.G. Janech, M.B. Fenton, *et al.* 2021. Surveying the vampire bat (Desmodus rotundus) serum proteome: A resource for identifying immunological proteins and detecting pathogens. *J. Proteome Res.* **20**: 2547–2559.
231. Vicente-Santos A., L.R. Lock, M. Allira, *et al.* 2023. Serum proteomics reveals a tolerant immune phenotype across multiple pathogen taxa in wild vampire bats. *Front. Immunol.* **14**: 1281732.
232. Roffler A.A., D.P. Maurer, T.J. Lunn, *et al.* 2024. Bat humoral immunity and its role in viral pathogenesis, transmission, and zoonosis. *Front. Immunol.* **15**: 1269760.
233. Schountz T. 2014. Immunology of Bats and Their Viruses: Challenges and Opportunities. *Viruses* **6**: 4880–4901. https://doi.org/10.3390/v6124880
234. Banerjee A., V. Misra, T. Schountz, *et al.* 2018. Tools to study pathogen-host interactions in bats. *Virus Res.* **248**: 5–12.
235. Subudhi S., N. Rapin, T.K. Bollinger, *et al.* 2017. A persistently infecting coronavirus in hibernating Myotis lucifugus, the North American little brown bat. *J. Gen. Virol.* **98**: 2297–2309.
236. Banerjee A., S. Subudhi, N. Rapin, *et al.* 2020. Selection of viral variants during persistent infection of insectivorous bat cells with Middle East respiratory syndrome coronavirus. *Sci. Rep.* **10**: 7257.
237. Su A., M. Yan, S. Pavasutthipaisit, *et al.* 2023. Infection studies with airway organoids from Carollia perspicillata indicate that the respiratory epithelium is not a barrier for interspecies

transmission of influenza viruses. *Microbiol. Spectr.* e0309822.
238. Becker D.J. & A. Banerjee. 2023. Coupling field and laboratory studies of immunity and infection in zoonotic hosts. *Lancet Microbe*. https://doi.org/10.1016/S2666-5247(23)00032-0
239. Garamszegi L.Z. & A.P. Møller. 2010. Effects of sample size and intraspecific variation in phylogenetic comparative studies: a meta-analytic review. *Biol. Rev. Camb. Philos. Soc.* **85**: 797–805.
240. Garamszegi L.Z. 2014. "*Modern Phylogenetic Comparative Methods and Their Application in Evolutionary Biology: Concepts and Practice*," Garamszegi, L.Z., Ed. Springer, Berlin, Heidelberg.
241. Housworth E.A., E.P. Martins & M. Lynch. 2004. The phylogenetic mixed model. *Am. Nat.* **163**: 84–96.
242. Cinar O., S. Nakagawa & W. Viechtbauer. 2022. Phylogenetic multilevel meta-analysis: A simulation study on the importance of modelling the phylogeny. *Methods Ecol. Evol.* **13**: 383–395.
243. Minias P., W.-X.V.-H. Peng & K.D. Matson. 2023. Evolutionary trade-off between innate and acquired immune defences in birds. *Front. Zool.* **20**: 32.
244. Minias P., P.L. Pap, O. Vincze, *et al.* 2024. Correlated evolution of oxidative physiology and MHC-based immunosurveillance in birds. *Proc. Biol. Sci.* **291**: 20240686.
245. Downs C.J., N.A. Dochtermann, R. Ball, *et al.* 2020. The Effects of Body Mass on Immune Cell Concentrations of Mammals. *Am. Nat.* **195**: 107–114.
246. McMinds R., R.H.Y. Jiang, S.R. Adapa, *et al.* 2024. Bacterial sepsis triggers stronger transcriptomic immune responses in larger primates. *Proc. Biol. Sci.* **291**: 20240535.
247. Addison B., K.C. Klasing, W.D. Robinson, *et al.* 2009. Ecological and life-history factors influencing the evolution of maternal antibody allocation: a phylogenetic comparison. *Proc. Biol. Sci.* **276**: 3979–3987.
248. Betke B.A., N.L. Gottdenker, L.A. Meyers, *et al.* 2023. Ecological and Evolutionary Characteristics of Anthropogenic Roosting Ability in Bats of the World. *bioRxiv* 2023.10.15.562433. https://doi.org/10.1101/2023.10.15.562433
249. Grace J.B. & K.M. Irvine. 2020. Scientist's guide to developing explanatory statistical models using causal analysis principles. *Ecology* **101**: e02962.
250. Laubach Z.M., E.J. Murray, K.L. Hoke, *et al.* 2021. A biologist's guide to model selection and causal inference. *Proc. Biol. Sci.* **288**: 20202815.
251. Imai K., L. Keele & D. Tingley. 2010. A general approach to causal mediation analysis. *Psychol. Methods* **15**: 309–334.
252. Claunch N.M., C.J. Downs, L.A. Schoenle, *et al.* 2022. Snap-freezing in the field: Effect of sample holding time on performance of bactericidal assays. *Integr. Comp. Biol.* **62**: 1693–1699.
253. Davis A.K. 2005. Effect of handling time and repeated sampling on avian white blood cell counts. *J. Field Ornithol.* **76**: 334–338.
254. Cláudio V.C., R.L.M. Novaes, A.L. Gardner, *et al.* 2023. Taxonomic re-evaluation of New World Eptesicus and Histiotus (Chiroptera: Vespertilionidae), with the description of a new genus. *Zoologia (Curitiba)* **40**: e22029.
255. Temmam S., K. Vongphayloth, E. Baquero, *et al.* 2022. Bat coronaviruses related to SARS-CoV-2 and infectious for human cells. *Nature* **604**: 330–336.
256. Jones K.E., J. Bielby, M. Cardillo, *et al.* 2009. PanTHERIA: a species-level database of life

history, ecology, and geography of extant and recently extinct mammals. *Ecology* **90**: 2648–2648.
257. Bürkner P.-C. 2017. brms: An R Package for Bayesian Multilevel Models Using Stan. *Journal of Statistical Software, Articles* **80**: 1–28.
258. Sikes R.S. & W.L. Gannon. 2011. Guidelines of the American Society of Mammalogists for the use of wild mammals in research. *J. Mammal.* **92**: 235–253.
259. Ott Joslin J. 2009. Blood collection techniques in exotic small mammals. *J. Exot. Pet Med.* **18**: 117–139.