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LEARNING FROM BATS: INSIGHTS INTO HOST–PATHOGEN INTERACTIONS AND HUMAN IMMUNITY

Biological Science

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ABSTRACT

Although humans and bats have many characteristics in common, they differ in their lifespans, metabolisms, and roles in the environment. Humans and bats are both mammals, but their immune systems are very different and are impacted by flight and longevity. Although many high-impact zoonotic viruses, such as SARS-CoV, Nipah, Ebola, and Marburg, naturally occur in bats, they hardly ever show signs of illness. Due to special immunological adaptations influenced by both flight and viral coexistence, this tolerance develops. By comparing the immune systems of humans and bats, new approaches to controlling inflammation, preserving viral tolerance, and preserving host fitness are revealed. This mini-review summarises recent findings in bat immunobiology, identifies important distinctions between bat and human immunity, and suggests how these findings might guide the development of new treatments for inflammatory and infectious diseases in humans.

KEYWORDS

Bat, Human, Viral, Disease, Therapeutics

1. INTRODUCTION

Bats and humans, although being mammals, represent two profoundly diverse evolutionary paths moulded by unique ecological pressures. Humans developed as terrestrial primates, focussing on bipedalism, brain development, and social cooperation, which resulted in complex language, tool usage, and civilisation [1]. Bats, the only mammals capable of sustained flight, have evolved nighttime adaptations such as echolocation, flying forelimbs, and upside-down roosting [2]. These adaptations are intimately related to energy efficiency, environmental navigation, and predator avoidance. Despite their diminutive size, several bat species have exceptional longevity, with some lasting for over 30 years, confounding the traditional inverse link between body size and lifespan seen in mammals[3]. According to Seim et al. (2013), this longevity is linked to effective DNA repair processes, reduced oxidative stress, and attenuated inflammatory reactions [4] . However, due to different life history strategies and metabolic constraints, humans are more likely to suffer from age-related diseases like cancer and neurodegeneration [5]. Additionally, as pollinators, insect predators, and seed dispersers, bats play a critical role in ecosystems, preserving biodiversity and bolstering agriculture [6]. Despite being essential to the biosphere, humans frequently interfere with natural systems through pollution, habitat loss, and climate change. Research in biomedicine and ecology can be inspired by examining the differences between these species, which can provide insights into metabolism, sensory biology, ageing, and environmental resilience.

2. Evolutionary Adaptations Shaping Bat Immunity

Bats' metabolic needs for flight have fuelled the development of effective DNA repair, antioxidant defences, and immune pathway modulation [7]. The signals of cellular damage that normally cause immune overactivation in other mammals are lessened by these adaptations. For example, the DNA sensor STING pathway is inhibited, which lowers inflammatory reactions to self-DNA without compromising antiviral protection [8]. Bat immunity has been further refined to balance tolerance and resistance due to their long lifespan and high viral exposure [9]. Bats are excellent models for researching immune regulation and pathogen persistence because of their evolutionary history.

3. How Bat Immunity Differs from Human and Other Mammalian Systems

Bat immune systems differ not only in quantity, but also in qualitative characteristics. Bats, for example, rely more on immunological tolerance mechanisms—a tactic that reduces tissue damage—than humans, who exhibit high inflammatory responses to viral infections [10, 11]. Modified interferon responses [12]decreased inflammasome activity [13, 14], and maybe changed T cell dynamics [15] are all components of this tolerance.

Table 1. Comparative Features of Bat, Human and Other Mammals Immune system

Immune Feature	Bats	Humans	Other Mammals	References
Type I Interferon Response	Constitutively expressed in some species, providing continuous antiviral state	Inducible only upon viral recognition	Inducible	[12, 15]
NLRP3 Inflammasome Activation	Dampened or absent; low IL-1β/IL-18 production	Strong activation; can cause cytokine storms	Active in most species	[10, 14]
STING Pathway (DNA sensing)	Suppressed activation to reduce DAMP-triggered inflammation	Active; detects cytosolic DNA and induces interferons	Fully functional	[8]
Antibody Kinetics and Longevity	Short-lived and lower titer; immunity may wane quickly	Long-lasting, high-titer antibody responses	Varies; often robust and memory-forming	[11, 16]
T Cell Exhaustion and Regulation	May be less prone to exhaustion during persistent infections	T cell exhaustion in chronic viral diseases is common	T cell exhaustion observed; varies by species	[11]
Viral Coexistence Strategy	Tolerant; allows viral persistence without disease	Clearance-focused; inflammation often damages host tissue	Clearance-driven with potential immuno-pathology	[17, 18]
DNA Damage Response and Oxidative Stress Tolerance	Enhanced DNA repair and ROS handling due to flight stress	Moderate; prone to damage-induced inflammation	Less adapted for chronic oxidative stress	[7, 9]

4. Innate Immune Features in Bats

Constitutive Interferon Expression: Bats like Rousettus aegyptiacus and Pteropus alecto constitutively express type I IFNs, in contrast to humans [12, 15]. Due to the simultaneous suppression of downstream inflammatory pathways, this pre-activated state offers ongoing antiviral protection without causing detrimental inflammation.

Suppression of NLRP3 Inflammasome: According to Ahn et al. (2019), the NLRP3 inflammasome is downregulated in a number of bat species, which lowers the secretion of pro-inflammatory cytokines like IL-1β and IL-18 [14]. This modification stops immunopathology while the virus is replicating.

Pattern Recognition and Viral Sensing: Although bats still have conserved pathogen recognition receptors (PRRs), such as TLRs, RIG-I,

and MDA5, downstream signalling is frequently inhibited or regulated differently, as evidenced by decreased IRF3 phosphorylation [8].

5. Adaptive Immunity in Bats

Antibody Kinetics: Despite the fact that bats produce immunoglobulins, antibody titers are frequently low and transient after infection. In Eidolon helvum, for example, antibodies against the Lagos bat virus diminish in a matter of months [19], indicating that humoral memory plays a limited role in long-term viral control.

T Cell Responses and Regulation: According to new research, bat T cells might produce different cytokines and experience less fatigue than human T cells [11]. Comprehensive phenotyping of the CD4+ and CD8+ subsets of bats is still scarce, though.

Viral Tolerance and Long-Term Coexistence: Often asymptomatic, bats carry zoonotic viruses including Ebola, Hendra, and SARS-related CoVs [20]. This tolerance entails keeping the virus contained while reducing overzealous immune activity. Unlike human chronic infections, which frequently result in fibrosis or immunological fatigue, viral RNA and proteins may remain in tissues without causing any associated disease [18].

Translational Insights: How Bat Immunity Can Guide Human Therapeutics.By studying bats, we gain a blueprint for modulating immune responses, particularly in diseases characterized by dysregulated inflammation such as COVID-19, influenza, viral encephalitis, and even autoimmune conditions [10, 11].

6. Future Directions and Challenges

Table 2. How Insights from Bat Immunity Can Aid in Combating Human Pathogens

Bat Immune Feature	Human Relevance	Therapeutic Application	References
Constitutive Type I IFN expression	Enhances rapid antiviral defense	Development of IFN-based antivirals or gene therapy to pre-arm host defenses	[12, 15]
Suppressed NLRP3 inflammasome	Limits cytokine storms and tissue damage	NLRP3 inhibitors (e.g., MCC950) for diseases like COVID-19 or influenza	[10, 21]
Dampened STING pathway	Reduces harmful IFN responses to self-DNA	Targeting STING in autoimmune diseases or to reduce vaccine side effects	[8]
Low but functional antibody titers	Suggests role of non-antibody immunity	Alternative vaccine designs that emphasize T cell or innate responses	[11, 19]
Viral tolerance mechanisms	Disease without damage (tolerance > clearance)	Shift focus from sterilizing immunity to host resilience	[17, 18]
Balanced redox environment and DNA repair	Prevents inflammation from DAMPs during stress	Antioxidant and DNA repair-targeting therapies for chronic inflammation	[7, 9]
Altered T cell activation/exhaustion	Avoids immune exhaustion in persistent infections	Novel checkpoint inhibitors or T cell modulators	[11]

Key challenges in bat immunology include species diversity, limited immunological reagents, and difficulty in maintaining colonies for experimental work [9]. Yet advances in single-cell RNA-seq, CRISPR screening, and in vitro bat cell culture models are accelerating discovery. Synthetic immunology, such as engineering human cells with bat immune genes (e.g., modulated STING or IFN pathways), holds promise for creating new immunotherapies and vaccine adjuvants [11, 15].

7. CONCLUSION

Bats offer profound insights into immune regulation, viral persistence, and host tolerance. Understanding how bats avoid immune overactivation while controlling pathogens may reshape how we approach infectious disease treatment in humans. As we face increasing risks of viral spillover, decoding bat immunity is not just of academic interest—it is a public health imperative.

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