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Review Article

Some Insights into the Immune System of Bats that Makes them Harbour Various Human Viruses

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Abstract

In last two years, whole world has been fighting with a ravaging pandemic, COVID-19. The virus responsible for this pandemic is SARS-CoV-2, which was detected in bats. Bats shelter a range of viruses viz. Nipah, Ebolaviruses, Hendra, SARS, Marburg, MERS, etc. and these viruses shed from bats and transfer to other vertebrates. After spread of SARS-CoV-2 during last two years, the interest to study the bat biology has intensified. There are a number of coronaviruses harboured by bats, but it was only after the discovery of SARS-associated coronavirus in bats that the bat immune system attracted the attention of researchers. This article reviews our contemporary knowledge of immune system of bats and their unique ability to harbour various disease-causing viruses.

Keywords: Pandemic, COVID-19, Nipah, Ebolaviruses, Hendra

1. Introduction

Bats play a vital part in our biological system including pollination, insect control, seed dispersal, etc. [1]. They belong to Chiroptera, a diverse mammalian order consisting of over 1300 bat species with distribution ranging across every continent except Antarctica [1]. Chiroptera consists of two suborders: Yinpterochiroptera (which comprises megabats and several families of microbats) and Yangochiroptera (comprising all remaining microbat families) that are believed to have diverged over 50 million years ago [2,3,4]. Within these suborders, bats are tremendously diverse in morphology, size, food habits, ecological niches, social interactions, etc.

2. Bats as virus pool

The bats have attracted considerable research in last several years due to a number of viruses that bats harbour and also because of their ability to transmit these viruses to other living organisms [5]. effectively managing the host responses against infection, even though richness of species play important role [10]. Additionally, bats also defend against most of the viruses by avoiding mounting of exaggerated immune responses due to a number of ecological and biological factors. A large number of studies have raised questions about adaptations in bat's antiviral immune responses. It has been observed that viruses that are known to severely affect other mammals, including humans, are apparently non-pathogenic to bats [11]. This adaptability of bats to shelter many viruses without displaying an overt pathology suggests that in bats the immune mechanisms have evolved that allow for benign virus–host relationships.

3. Bat and SARS-CoV-2

The virus SARS-CoV-2 was reported in December 2019, in Wuhan city of China for the first time has greatly impacted the human lives and the lives of other animals. This virus causes mild to severe respiratory illness that might occasionally result in death. World Health Organization (WHO) termed it as COVID-19. This disease was first confined to China, and in no time, it turned into pandemic. After spread of this virus, the interest to study the bat biology intensified. There are a number of coronaviruses harboured by bats and, but it was only after the discovery of SARS-associated

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coronavirus in bats that the bat immune system attracted the attention of researchers [12,13,14,15,16,17].

3.1 Traits that make bat reservoirs of human viruses

These flying mammals have a number of traits that make them to act as the tremendous reservoirs of viruses [18,19,20,21,22]. These traits include an apparently decrease in viral load due to immune variation at low and higher temperatures that these animals sustain during flights [11]. But, a few of the studies have demonstrated decreased viral load has no association with high temperatures [23] and more studies have revealed that bats act as virus reservoirs primarily because of their tolerance to viral infection whereas as a decrease in viral load might be playing only a minor role.

The genomes and transcriptomes of at least 18 bat species are currently available in databases [24,25], that provide important insights into the evolution of their immune system and antiviral immunity. The evolution of antiviral immune system in bats is multifaceted and several factors, including the evolution of flight [26,24] and the co-evolution with their viruses, may have likely shaped their distinct immunological responses. By understanding how these bats control virus-mediated pathogenesis might help researchers in the identification of some novel therapeutic targets and molecules for the effective treatment of infections resulting because of these viruses in a number of other mammals, including humans and agricultural animals.

Anti-disease characteristic of bats makes them special rather their antiviral skill and a unique association between virus (especially coronavirus) and bats is maintained due to exceptional stability between host defence and immune tolerance. Tolerance against viral diseases in bats has been noticed when minimal or no signs of infection shown even when high viral load present in bat tissues [27,28,29,30].

4. Immune system of bats

Contemporary studies bring new insights to understand tolerate responses in bats against disease infection such as work on innate and adaptive immune system, metabolism and mitochondrial activity. This disease tolerance in bats may contribute to their long lifespans. Moreover, studies on variation in the expression of antiviral genes in IFN signalling, autophagy clearance of pathogen and production of heat shock proteins also helps bats to control viral load during infection [31,32,33,34]. Adaptive evolutionary variations in genes of nuclear and mitochondrial oxidative phosphorylation require fulfilling high energy demands associated with flight [35,36].

High concentration of genes involved in DNA-damage check points are present in bats which are also essential for cancer, innate immune system and ageing [26]. A recent work has manifested that bats show resistance against cancer because efflux of chemotherapeutic drugs through ABCB1 transporter blocked DNA disruption due these drugs such as doxorubicin and etoposide [36]. Furthermore, they have low level of reactive oxygen species (ROS) as compared to the other mammals of same size but hold similar activity of antioxidant superoxide dismutase [37,38]. A recent work revealed that in bat mitochondria there is low production of ROS [39]. Numerous studies have been investigated innate signalling mechanism in human and rodents, however, in recent studies similar mechanism have demonstrated in bats [16]. Pattern recognition receptors (PRRs) are molecules that recognise pathogen associated molecular patterns (PAMPs) that are originated from pathogens such as bacteria, viruses, parasites etc. [40,41,42]. Induction of signalling mechanism occurs after virus infection that leads to production of cytokines (proinflammatory and antiviral) [40,43,44]. Expression of IFN-stimulated genes (ISGs) can be induced by interferons (IFNs), an antiviral cytokine, this ISGs leads to inhibition of virus replication with various signalling pathways [45]. Data available on the whole genome and transcriptome sequences for handful bat species has facilitate to observe homologs of the innate immune pathway in mammals [16].

5. Perspectives

A few years back, nobody would have expected this high jump in understanding of bat biology, their ecological role, unique immune system, etc. as it has after COVID-19 pandemic. Bat is a unique mammal as it has ability to flight. The trait of flight in bats may evolve to support immune responses against viruses and inflammatory responses [16]. A homeostatic balance in bats is managed by key regulators and different signalling machinery. Understanding of host defence-immune tolerance system in bat may provide worthwhile lessons to guide and combat various inflammatory disorders in humans, viral infection, ageing and cancer. An additional research work on bats is required to establish the role of different species of bats in harbouring various viruses, and a holistic map of immune responses might help to draw a picture for translational results for humans. The delineation of the actual source and cause of spread of viruses can go a long way in the development of various approaches to ameliorate the global health status of serious viral diseases.

6. Competing interest

The authors declare that there are no conflicts of interest.

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