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Spotlight

The Expanding
Diversity of RNA
Viruses in VertebratesWenqiang Wang¹ and
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The diversity of RNA viruses in vertebrates remains largely unexplored. The discovery of 214 novel vertebrate-associated RNA viruses will likely help us to understand the diversity and evolution of RNA viruses in vertebrates.

RNA viruses infect vertebrates and lead to a variety of diseases. Many emerging or re-emerging infectious diseases, such as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and Ebola hemorrhagic fever, are caused by RNA viruses. Our current knowledge of the diversity of RNA viruses in vertebrates is rather fragmentary and biased. A large proportion of known vertebrate RNA viruses were isolated from humans or species of economical or medical importance, mainly mammals and birds. Relatively few viruses have been documented in other vertebrate species. With the advent of next-generation sequencing (NGS) techniques, more and more novel RNA viruses have been found through meta-genomic or meta-transcriptomic approaches [1]. Moreover, paleovirological studies discovered a large number of ancient RNA viral relics, namely endogenous RNA viral elements, within vertebrate genomes, providing important insights into the deep history of RNA viruses [2]. However, much remains unknown about the diversity of RNA viruses in vertebrates. A recent study by Shi *et al.* [3] greatly expands our understanding of the diversity of RNA viruses in vertebrates.

Shi *et al.* [3] performed a meta-transcriptomic screening of RNA viruses in 186

species from the previously undersampled chordate lineages, including lancelets (Leptocardii), jawless fish (Agnatha), cartilaginous fish (Chondrichthyes), ray-finned fish (Actinopterygii), lobe-finned fish (Sarcopterygii), amphibians (Amphibia), and reptiles (Reptilia). They identified a total of 214 novel RNA viruses and found that many viral families or genera that had been known to infect mammals, birds, and/or reptiles were also present in fishes and/or amphibians. The identification of these RNA viruses greatly extends the host distribution of vertebrate-associated RNA viruses (Figure 1). For example, the host distribution of the *Astroviridae* family was extended from mammals and birds to nearly all the major lineages of vertebrates; viruses related to influenza viruses were identified in jawless fish, ray-finned fish, and amphibians; the *Filoviridae* and *Arenaviridae* families were found to infect fish. Moreover, Shi *et al.* [3] discovered two novel viral groups that infect vertebrates: one distantly related to *Astroviridae* and plant viral family *Potyviridae* and the other falling within the diversity of a putative new viral family *Chuviridae* that is thought to infect arthropods [4].

Shi *et al.*'s study [3] reveals two paradoxical aspects of the evolution of RNA viruses in vertebrates. First, RNA viruses underwent more co-divergence with their vertebrate hosts than simply expected by chance; but they also underwent frequent host-switching. Second, the genome organizations among RNA viruses of the same family or genus appear to be generally conserved; but they also exhibit certain degree of variation, ranging from change in genome length to change in segment numbers. Therefore, the evolution of RNA viruses in vertebrates might be more complex than previously appreciated.

It remains mysterious how RNA viruses that infect tetrapods originated. There are

several possible evolutionary scenarios: i) RNA virus underwent water-to-land transition simultaneously with the colonization of terrestrial environments by their vertebrate hosts [5]; ii) RNA viruses of fish infected tetrapods through host-switching well after the conquest of land by vertebrates; or iii) tetrapod RNA viruses arose through cross-species transmission from these of non-vertebrate origin. Phylogenetic analyses show that fish viruses tend to fall basal to tetrapod viruses, indicating possibly aquatic origins of tetrapod RNA viruses [3]. However, viruses from lungfish are more closely related to these from ray-finned fish, which is inconsistent with the host evolutionary relationship and thus makes the scenario of simultaneous terrestrialization less likely. However, based on the data available, we still have no definite answer for the mystery of tetrapod RNA virus origin.

Our understanding of the diversity of RNA viruses in vertebrates, even in mammals and birds [6], remains far from complete. The RNA viruses identified by Shi *et al.* [3] might only represent a very small proportion of the vertebrate RNA virosphere. The reasons are as following: i) the species surveyed so far account for only a minority of described vertebrate species; ii) the individuals sampled are not infected by all the viruses that infect this species; iii) some viruses might be not globally distributed [7], and nearly all the samples surveyed by Shi *et al.* [3] are from China; iv) virus discovery through direct NGS might be inefficient due to low abundance of certain viruses [8]; v) the virus discovery strategy used by Shi *et al.* [3] relies on homology with the current known RNA viruses, but there could be many unknown divergent RNA viruses, the so-called viral "dark matter" [1].

Our biased understanding is not limited to RNA viruses, as illustrated by *Hepadnaviridae*, a family of reverse-transcribing

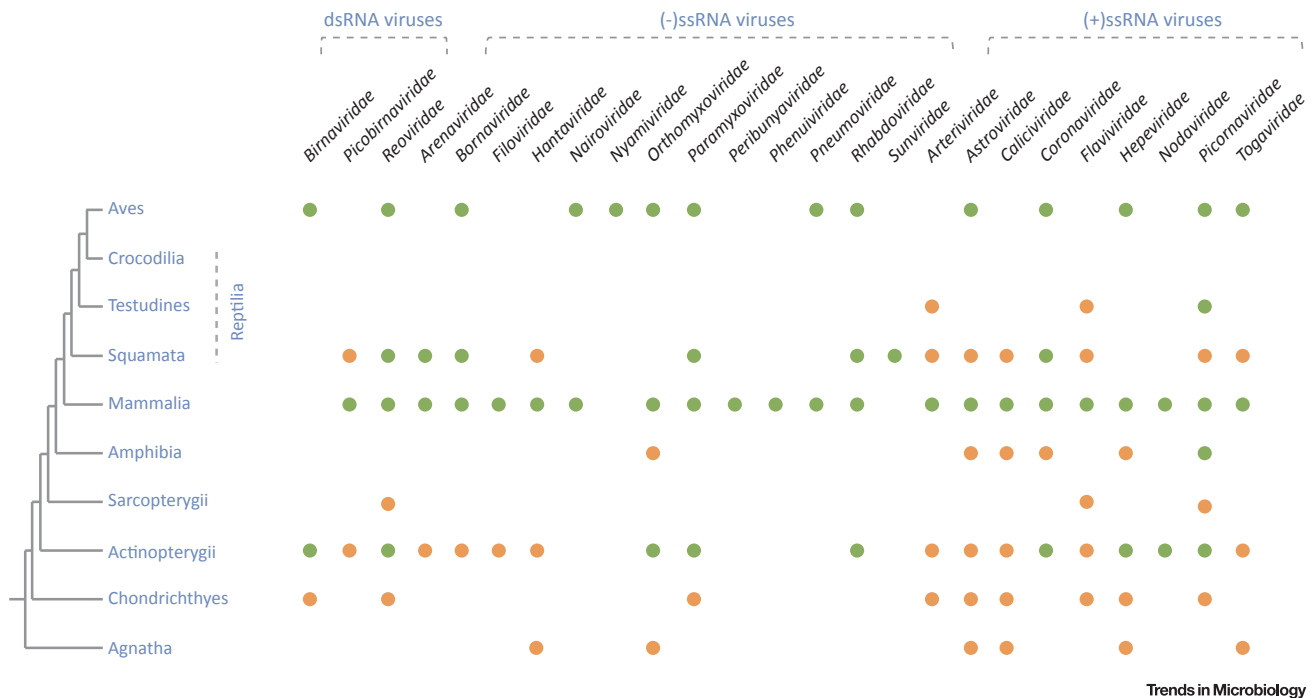


Figure 1. The Host Distribution of RNA Viral Families in Vertebrates. The host distribution of RNA viral families in vertebrates is based on the 10th report of the International Committee on Taxonomy of Viruses (ICTV) (<http://ictv.global/report>). The viruses known previously and identified by Shi *et al.* [3] are labelled by green and orange circles, respectively. Abbreviations: dsRNA viruses, double-stranded RNA viruses; (-)ssRNA viruses, negative-sense single-stranded RNA viruses; (+)ssRNA viruses, positive-sense single-stranded RNA viruses.

DNA viruses to which human hepatitis B virus belongs. Until recently, hepadnaviruses were thought to only infect mammals and birds. Recent paleovirological and meta-transcriptomic analyses reveal their presence in fish, amphibians, and reptiles [9,10]. Further sampling of more species worldwide might reveal the complete picture for the diversity, origin, and evolution of viruses in vertebrates.

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Forum

Bat-Origin Coronaviruses Expand Their Host Range to Pigs

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Infections with bat-origin coronaviruses have caused severe illness in humans by ‘host jump’. Recently, novel bat-origin coronaviruses were found in pigs. The large number of mutations on the receptor-binding domain allowed the viruses to infect the new host, posing a potential threat to both agriculture and public health.