Evolutionarily missing and conserved tRNA genes in human and avian

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A B S T R A C T

Viral infection heavily relies on host transfer RNA (tRNA) for viral RNA decoding. Counterintuitively, not all tRNA species based on anticodon are matched to all 64-triplet codons during evolution. Life solves this problem by cognate tRNA species via wobbling decoding. We found that 14 out of 64 tRNA genes in humans and the main avian species (chicken and duck) were parallelly missing, including 8 tRNA-\textsuperscript{A34NN} and 6 tRNA-\textsuperscript{G34NN} species. By analyzing the conservation of key motifs in tRNA genes, we found that box A and B served as intragenic tRNA promoters that were evolutionally conserved among human, chicken, and duck. Thus, decoding viral RNA by similar wobbling strategies and tRNA transcripts may be parallelly used by human, chicken, and duck. We envisioned that many basic mechanisms regarding viral RNA decoding were possibly conserved in these hosts and may consequently promote cross-species infection.

Transfer RNAs (tRNAs) are essentially required for gene decoding. Despite the universal nature of genetic codon, not all tRNA genes are common to all organisms. Here, we would like to discuss fundamental problems and possible effects arising from the evolutionarily missing and conserved tRNA genes in human, chicken, and duck (Alkatib et al., 2012; Ou et al., 2019; Rogalski et al., 2008). Among these three organisms, viruses especially the avian influenza virus can cross infect (Pepin et al., 2010). For multi-host viruses, similar viral RNA decoding strategies may be parallelly used by different hosts. Because viral cross-species infection heavily relies on host tRNAs of different species for viral RNA decoding (Ou et al., 2020; van Weringh et al., 2011). We envisioned that many basic mechanisms regarding viral RNA decoding were possibly conserved in these three hosts and may consequently promote cross-species infection.

1. Evolutionarily missing tRNA genes in human and avian

In the ribosome, 61 amino acid charging tRNAs and 3 suppress tRNAs are theoretically needed to decode 64 genetic codons that specify 20 amino acids (Ou et al., 2019). However, we found that certain types of tRNA in humans and the main species of avian are missing during evolution. This triggers an interesting question that how the 64 genetic codons of cellular mRNA or viral RNA can be decoded by partially missing tRNAs. Recently, it has been verified that the number of obligatory tRNA species (based on anticodons) for decoding is substantially less than 64. Life solves this problem by wobbling that the unpaired codons are decoded by cognate tRNA species otherwise misdecoding (Ou et al., 2019; Rogalski et al., 2008). It has been proven in humans that 15 out of theoretically necessary 64 tRNA species, including 8 tRNA-\textsuperscript{A34NN} and 7 tRNA-\textsuperscript{G34NN} species, are missing confirmed by humans that 15 out of theoretically necessary 64 tRNA species, in-
comparing the conservation of key motifs in tRNA, we found that box A and B are evolutionarily conserved among human and avian (Vassetzky and Kramerov, 2013) (Fig. 1B). Specifically, box A and B of tRNA genes in human and avian are TGGNNNAG(A)TGG and GGGTTCGANNCC, respectively (Vassetzky and Kramerov, 2013). Strikingly, these two boxes are identical in chicken and duck, in which box A is TGGGCTAATGG and GGGTTCGATCCC for box B. Conservation of tRNA genes (chicken & duck: 272: 361) were generated by multiple alignments and visualized by WebLogo 3.1. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
3. The implication of evolutionarily missing and conserved tRNA genes for viral decoding

Viral decoding is regulated by the landscape of tRNA – viral codons, probably through adapting to host codon usage or modulating the host tRNAome (Ou et al., 2020). It has been reported that codon usage bias is generally distinct between virus and host due to translational selection (Chen et al., 2020). For viral decoding in human, chicken, and duck, because the same tRNA species (based on the anticodon) are parallelly missing, the unpaired codons of viruses are obliviously decoded by the cognate tRNA species through similar wobbling decoding strategies (Ou et al., 2019). Due to the difference in codon usage bias between virus and host, we speculate that efficient viral translation may require rewiring the host tRNAome. Supportively, we recently found that the expression landscape of hepatic tRNAome was remodeled by infection of the zoonotic hepatitis E virus (HEV) (Ou et al., 2020). Because of the conservation of the D loop and TΨC loop (Box A and B) of tRNA species, regulation of tRNAome at the transcriptional level is well possible though not all tRNA species are equally transcribed. Using similar wobbling decoding strategies or host tRNAome remodeling, viruses may adapt two or more hosts like human, chicken, and duck thus may contribute to viral cross-species infection. For the avian influenza virus, the evolutionally missing and conserved tRNA genes between human, chicken, and duck can possibly explain why this virus can crossly infect among these hosts. Because the similar tRNA transcripts and wobbling decoding strategies are used for RNA decoding of the avian influenza virus. Besides, the viral cross-species infection also links to the development of live attenuated vaccines, such as the Sabin vaccine, dengue vaccine, influenza vaccine, and mumps vaccine (Bhamarapravati and Sutee, 2000; Koprowski, 1960). Because they were developed through a series of passages from one host to another. As tested in chicken and duck, we developed a live attenuated vaccine by serial passage of the virulent strain of duck hepatitis A virus in the chicken embryo (Ou et al., 2017; Ou et al., 2018).

Collectively, we found those tRNA genes in humans and the main avian species were parallelly missing and evolutionally conserved. We envisioned that many basic mechanisms regarding viral RNA decoding were possibly conserved in these hosts. For viral cross-species infection in humans and avian, the investigation from the standpoint of tRNA-codon interaction will define novel mechanisms in this respect and decipher viral translation in many aspects (Schimmel, 2018).

Supplementary data to this article can be found online at https://doi.org/10.1016/j.meegid.2020.104460.

Declaration of Competing Interest

The authors have declared that no competing interests exist.

Acknowledgments

This work was supported by grants from the National Key Research and Development Program of China (2017YFD0500800), China Agricultural Research System (CARS-42-17), Sichuan Veterinary Medicine and Drug Innovation Group of China Agricultural Research System (CARS-SVDIP), Science and Technology Program of Sichuan Province (2020YJ0396), and Integration and Demonstration of Key Technologies for Goose Industrial Chain in Sichuan Province (2018NZ0005).

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