The interplay between viruses and the host translation machinery – a novel antiviral therapeutic target

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The development of novel specific or broad-spectrum antiviral therapeutics depends on a deep understanding of the interplay between viruses and their host cells.

Viruses rely on the host-cell translation machinery to synthesize their own proteins. As RNA viruses do not encode tRNAs, they depend on host tRNAs for translation. However, as viral RNAs and host cell mRNAs may diverge significantly in terms of nucleotide composition (host cell genome is biased towards C/G-ending codons while the RNAs of many viruses are skewed towards A/U-ending codons), some viruses manipulate the host tRNA pool to decode viral skewed codons and optimize viral protein translation. Figure 1 depicts some of the strategies used by different viruses to manipulate the host tRNAs. We have recently published a manuscript discussing the importance of tRNA biology for viral infections (https://doi.org/10.1016/j.tibs.2020.05.007).

Our preliminary data indicates that the influenza A virus induces the specific deregulation of some of the host tRNA modifying enzymes (tRNAME) and consequently host tRNA modifications, in order to more efficiently translate its own viral proteins. Our research furthermore suggests that perturbing the host tRNA epitranscriptome machinery may unravel novel targets for single or broad-spectrum antiviral strategies. Our recently awarded H2020 Twinning grant will allow us to collaborate with world-renowned virologists from the Leiden University Medical Centre and Analytical Chemists from the Ludwig-Maximilians University in Munich and have the ideal setting to understand gene regulation during viral infection while identifying regulators of viral protein translation. We will not only unravel how the host tRNA epitranscriptome is regulated upon viral infection but, importantly, how it can be manipulated for antiviral targeting.

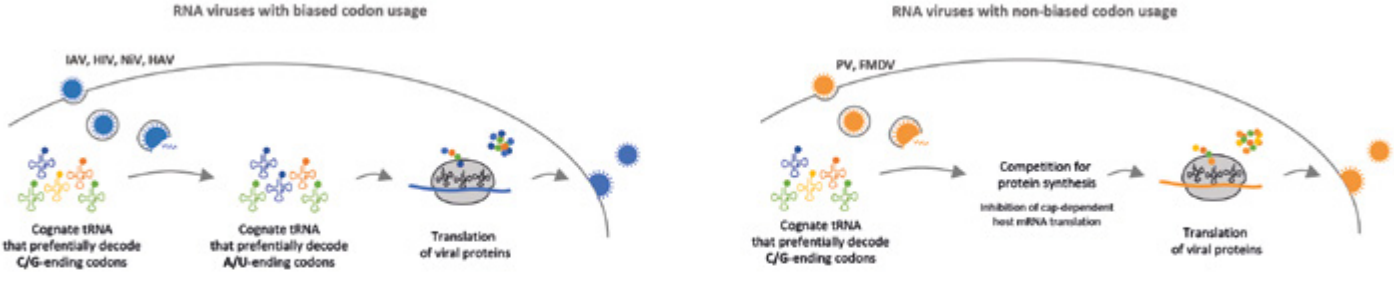

FIGURE 1
Manipulation of the host cell tRNA pool and codon usage adaptation upon viral infection. Viruses with biased codon usage, such as influenza A virus (IAV), HIV, Nipah virus (NiV), and hepatitis A virus (HAV), are able to exploit and manipulate the tRNA pool of the host to better match their codon usage and, therefore, favor the translation of their own proteins. On the other hand, viruses with nonbiased codon usage, such as poliovirus (PV) and foot-and-mouth disease virus (FMDV), compete for tRNAs for protein synthesis and inhibit host protein translation.