Zoonotic viruses must express efficiently its protein in different organisms. It’s widely accepted that the main interspecies barrier is the recognition of cellular receptors, however, is still unknown why some viruses can effectively replicate and propagate in a new host and another not. Several viral and cellular determinant at protein level has been identified, however, exception are found suggesting that another factor is present. As efficient protein expression also depends of codon usage, we proposed that viral codon adaptation to the host is a key factor that precludes the protein determinants. Using a bioinformatic approach we analyze the translational and codon adaptation of the orthomyxoviruses to its respective hosts through the CAI, TAI and TW (developed in this work) indexes. The analysis of >6000 orthomyxoviruses, showed that ISAV is the orthomyxovirus and viral Salmo salar pathogens less host-adapted confirming its emerging pathogens nature. A negative correlation between PB1-TW score and ISAV pathogenicity, and coevolution among the CAI or TW values of polymerase encoding genes were found. In silico cross the Interspecies Barrier showed that IAVs are better adapted to Chicken>Human>Duck>Swine Hosts. Temporal evolution of CAI showed an increment in pandemic viruses that decrease across the time. We found that an increment in the adaptation to one host redounded in the adaptation to all others. In conclusion, our analyses suggest that Pathogen-Host relationship leave trace in viral codon usage that can be applied to analyze the evolution of viruses and could be used to detect new potential pandemic viruses.

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