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## **Comparative genomics of nidoviruses: towards understanding the biology and evolution of the largest RNA viruses**

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### **Citation**

Gulyaeva, A. (2020, June 2). *Comparative genomics of nidoviruses: towards understanding the biology and evolution of the largest RNA viruses*. Retrieved from <https://hdl.handle.net/1887/92365>

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**Title:** Comparative genomics of nidoviruses: towards understanding the biology and evolution of the largest RNA viruses

**Issue Date:** 2020-06-02

**Comparative genomics of nidoviruses:  
towards understanding the biology and evolution  
of the largest RNA viruses**

- 1. Nidovirus RdRp-associated nucleotidyltransferase (NiRAN) is the fifth, most recently discovered replicative domain universally conserved in all nidoviruses. Based on tertiary structure similarity, NiRAN might have evolved its activity from protein kinase.**

This thesis, chapters 3 and 6

Kirchdoerfer and Ward 2019, Nat Commun 10(1):2342

- 2. Duplication and gene acquisition play an important role in the evolutionary innovation of the nidovirus genome 5'- and 3'-terminus.**

This thesis, chapters 2, 4 and 6

Luytjes et al. 1988, Virology 166(2):415-422

Gorbalenya et al. 2006, Virus Res 117(1):17-37

- 3. Recent discoveries of variation in genome organization and genome expression mechanisms of nidoviruses leave synteny of five universally conserved replicative domains as the main hallmark of nidoviruses.**

This thesis, chapters 3, 4 and 6

Cowley et al. 2002, J Gen Virol 83(Pt 4):927-935

Gorbalenya et al. 2006, Virus Res 117(1):17-37

- 4. Identification of a disproportionately large ORF1b-like region in the 41.1 kb genome of planarian secretory cell nidovirus indicates that nidoviruses with even larger genomes may be discovered in the future.**

This thesis, chapter 4

Lauber et al. 2013, PLoS Pathog 9(7):e1003500

- 5. Splitting sequence of a large multidomain polyprotein in a biologically reasonable manner during annotation by homology can facilitate accurate estimation of hits' statistical significance and expand annotation coverage.**

This thesis, chapter 5

Söding 2005, Bioinformatics 21(7):951-960

- 6. High mutation rate makes RNA viruses a valuable model for studying evolution. Events on microevolutionary scale can be witnessed in real time. Enormous divergence of genomes and proteins during macroevolution informs about the limits of sequence variation in life forms.**

Domingo et al. 1978, Cell 13(4):735-744

Lauber et al. 2013, PLoS Pathog 9(7):e1003500

Geoghegan and Holmes 2018, Genetics 210(4):1151-1162

- 7. The entire known diversity of (+)ssRNA virus families can be characterized by a very limited number of syntenies of invariably encoded replicative domains.**  
Gorbalenya and Koonin 1993, Sov Sci Rev D Physicochem Biol 11:1-84
- 8. Greater diversity of eukaryotic, compared to prokaryotic RNA viruses, may be explained by the protection against antiviral responses targeting 'alien' RNA, offered by the endomembrane system of eukaryotic cell.**  
Dolja and Koonin 2018, Virus Res 244:36-52
- 9. Advancement of NGS technologies prompted the ongoing massive expansion of the known virosphere. Many newly discovered viruses are now characterized based solely on their genome sequences, making comparative genomics an indispensable tool of virosphere exploration.**  
Simmonds et al. 2017, Nat Rev Microbiol 15(3):161-168  
Shi et al. 2018, Virus Res 243:83-90  
Koonin and Dolja 2018, Virus Res 246:A1-A3
- 10. Explosive growth in virus discovery by NGS calls for development of automated user-friendly tools and a centralized online platform allowing virologists to easily access existing virus classification, as well as to classify new viruses simultaneously with their discovery.**  
Lauber and Gorbalenya 2012, J Virol 86(7):3905–3915  
Kuhn et al. 2019, Nature 566(7744):318-320
- 11. As industrialization, international trade and human mobility intensify around the globe, the world becomes more connected and prone to the emergence and spread of viral infections.**  
Morse et al. 2012, Lancet 380(9857):1956-1965  
Pybus et al. 2015, Proc Biol Sci 282(1821):20142878
- 12. Genius is simplicity.**

Anastasia Gulyaeva, March 2020