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The quest for broad-spectrum coronavirus inhibitors

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Stellingen behorend bij het proefschrift

The quest for broad-spectrum coronavirus inhibitors

1. Based on its role as an error correction enzyme and the essential nature of the 3'-to-5' exoribonuclease and N7-guanine methyltransferase enzymes for viral replication, coronavirus nsp14 can be considered a good target for drug design. (*This thesis, chapters III to V*)
2. The efficacy of repurposed drugs as inhibitors of SARS-CoV-2 replication is underestimated when comparing their EC₅₀ values from cell-based assays with presumed golden standards like remdesivir. (*This thesis, chapter VII*)
3. The impact of substitution of nsp14 key residues on *Betacoronavirus* replication is likely similar, but disguised by differences in replication kinetics and interactions with other viral components. (*This thesis, chapters IV, V and VIII*)
4. For effective treatment of COVID-19, a combination therapy with different classes of drugs (antivirals, anti-inflammatory and/or immune modulators) may be a better choice path than the use of a single broad-spectrum antiviral. (*This thesis, chapters I, VII and VIII*)
5. To increase our understanding about the lack of effectiveness of antiviral drugs, the structural and biochemical characterization of coronavirus replicase proteins should be translated to the relevant context of the infected cell or the in vivo model. (*This thesis*)
6. Although mRNA technology has accelerated vaccine development, stockpiled antiviral drugs with broad-spectrum activity will remain the first possible response to newly emerging viruses. (*This thesis and Pardi et al., 2020*)
7. The actual number of MERS-CoV infections in the human population is underestimated, which reflects the uneven international distribution of diagnostic resources due to differences in economic and political power. (*Müller et al., 2015; El-Kafrawy et al., 2019*)
8. Translational and fundamental research should support each other to promote the development of both our technology and scientific knowledge.
9. The misinformation and fear promoted by different media and institutions during the COVID-19 pandemic highlights that scientists should consider outreach as one of their main responsibilities to society.
10. If you never ask, you may never know; if you ask, you may find out the answer.
11. You do not need to be big to make a difference, just consider the impact that a minimalistic microorganism like a virus can create.
12. After making a mistake, there are two options: to hide it and be part of the problem, or to admit it and potentially be part of the solution. (*modified from Tina Fey, comedian and actress*)