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Chikungunya virus nonstructural protein 1 as an antiviral target

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STELLINGEN

behorende bij het proefschrift getiteld

Chikungunya virus nonstructural protein 1 as an antiviral target

1. Past and recent outbreaks have showed us the importance of continuing further research in the arbovirus field, as arboviruses will continue to (re)emerge in the future due to their unpredictable epidemiology. *This thesis, chapters 1 and 7*
2. The methylation of GTP precedes its transfer onto the 5' end of viral RNA, making alphavirus RNA capping an attractive target for antiviral drug development. *This thesis, chapters 4, 5 and 6*
3. Given the current absence of a licensed vaccine, a clinically approved Chikungunya virus small-molecule inhibitor would be especially advantageous in outbreak containment. Alternatively, it could be prescribed as a form of prophylaxis to local citizens in affected areas or to travelers at-risk. *This thesis, chapter 2*
4. Validation of compounds originating from in silico virtual screens in enzymatic assays with purified proteins is especially important for confirmation of target specificity. *This thesis, chapters 2 and 6*
5. A Chikungunya virus small-molecule inhibitor should be administered early in infection since residual viral material (RNA/protein) in joint tissue, rather than replicating virus, seems to contribute to Chikungunya virus-induced immunopathology. (Poo et al., PLoS Negl Trop Dis, 2014)
6. The production of noncapped genomic RNAs, which can be modulated by point mutations in nonstructural protein 1, is critical for alphaviral virulence and pathogenicity. This should be considered during preclinical development of compounds targeting the alphavirus RNA capping. (LaPointe et al., mBio, 2018 & LaPointe et al., mBio, 2020)
7. The recent elucidation of the structure of the Chikungunya virus nonstructural protein 1, which is assembled into a membrane-bound dodecameric complex, has not only improved our functional understanding of alphavirus replication complexes, but is also instrumental for rational design of inhibitors. (Jones et al., Nature, 2020)
8. The pursuit of elegance can improve the quality of our science, but we should pursue it with caution, as the truth is sometimes inelegant. (Casadevall and Fang, mBio, 2018)
9. A successful vaccination campaign is the result of a team effort between biomedical scientists who develop a vaccine and social scientists who enhance vaccine acceptance among the hesitant population.
10. Infectious diseases don't discriminate between the rich and the poor, yet their prevention and treatment often comes at a price only a few can afford to pay.
11. The COVID-19 pandemic has reminded us to appreciate the little joys in life.
12. Those who know many languages live as many lives as the languages they know. *Czech proverb*