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Safety and efficacy after immunization with *Plasmodium falciparum* sporozoites in the controlled human malaria infection model

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STELLINGEN

behorende bij het proefschrift

Safety and efficacy after immunization with *Plasmodium falciparum* sporozoites in the controlled human malaria infection model

- 1) Chemoprophylaxis and sporozoites immunisation (CPS) has proven to be a reproducible and robust strategy to induce sterile homologous protection against *P. falciparum* in healthy volunteers (this thesis)
- 2) The use of mefloquine to induce sterile protection in CPS, compared to chloroquine, has proven to be similarly safe, immunogenic and protective (this thesis)
- 3) The striking efficiency of homologous protection in CPS has yet to be demonstrated for heterologous protection required for use in malaria endemic areas (this thesis)
- 4) qPCR-based initiation of anti-malarial treatment in the controlled human malaria infection model, instead of microscopic examination of the thick smear, reduces symptoms and increases safety for volunteers (this thesis)
- 5) Plasmodium infected individuals change in human odor and produce greater amounts of aldehydes and enhances the attractiveness of mosquitoes [1]
- 6) Intradermal administration of sporozoites, compared to the intravenous route, provides less protective immunity due to increased regulatory immune responses and is independent of parasite liver load [2]
- 7) Malaria eradication will depend on the effective implementation of the combination of all current existing anti-malaria tools and a highly efficacious vaccine [3]
- 8) Don't be afraid to bite on a giant, learn from the mosquito (Bangambiki Habyarimana, Pearls of Eternity 2016)[#]
- 9) Two things are infinite. The universe and human stupidity; and I am not sure about the former (Albert Einstein 1947)^{*}
- 10) Wat er ook gebeurt, altijd blijven lachen... (Bas en Aad van Toor 1977)[§]

1. Robinson A, Busula AO, Voets MA, Beshir KB, Caulfield JC, Powers SJ, et al. Plasmodium-associated changes in human odor attract mosquitoes. *Proceedings of the National Academy of Sciences of the United States of America*. 2018;115(18):E4209-E18. doi: 10.1073/pnas.1721610115. PubMed PMID: 29666273; PubMed Central PMCID: PMC5939094.
 2. Haeberlein S, Chevalley-Maurel S, Ozir-Fazalalikhan A, Koppejan H, Winkel BMF, Ramesar J, et al. Protective immunity differs between routes of administration of attenuated malaria parasites independent of parasite liver load. *Sci Rep*. 2017;7(1):10372. doi: 10.1038/s41598-017-10480-1. PubMed PMID: 28871201; PubMed Central PMCID: PMC5583236.
 3. Chen I, Cooney R, Feachem RGA, Lal A, Mpanju-Shumbusho W. The Lancet Commission on malaria eradication. *Lancet*. 2018;391(10130):1556-8. doi: 10.1016/S0140-6736(18)30911-5. PubMed PMID: 29673872.
- # Addendum 8: If you ever think you might be too small or insignificant to make a difference, learn from the mosquito.
- * Addendum 9: 1947, Ego, Hunger, and Aggression: a Revision of Freud's Theory and Method by Frederick S. Perls, Page 111, George Allen and Unwin Ltd, London. 'This impatient, greedy attitude is responsible more than anything else for the excessive stupidity we find in the world'.
- \$ Addendum 10: De grootste kunst in het leven is te kunnen blijven lachen, ook als het (schijnbaar) tegenzit. Mind is the creator of happiness and suffering.

Remko Schats

12 november 2019