A plasmodium falciparum sporozoite's journey: through organs and across CD8+ T-cell challenges

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Stellingen behorende bij het proefschrift getiteld

A *Plasmodium falciparum* sporozoite's journey, through organs and across CD8$^+$ T-cell challenges

1. A key question in the development of effective malaria vaccines is whether CD8$^+$ T-cell priming is primarily driven by infected hepatocytes or by antigen-presenting cells that cross-present parasite-derived antigens. Clarifying their roles is crucial for understanding the mechanisms of protective immunity (this thesis).

2. Functional memory CD8$^+$ T-cells usually require repeated antigen exposure. Protection after a single immunization with late-arresting attenuated sporozoites suggests these parasites may persist in hepatocytes, serving as an internal booster to sustain CD8$^+$ T-cell responses (this thesis).

3. Protective efficacy of late-arresting genetically attenuated sporozoites depends not only on the presence of immune responses, but also on sporozoite viability, age and dose (this thesis).

4. Late-arresting attenuated sporozoite vaccines elicit strong CD8$^+$ T-cell responses in both lungs and liver, suggesting a key role for the lungs in immune priming. Understanding organ-specific responses is vital for improving vaccine efficacy (this thesis).

5. Ultra-low volume intradermal administration significantly enhances liver homing and invasion of radiation-attenuated sporozoites, suggesting that the same approach may improve liver invasion, CD8$^+$ T-cell activation and protective efficacy in the context of late-arresting attenuated sporozoite vaccination (adapted from Watson et al., 2024, Scientific reports).

6. Generating a diverse repertoire of epitope-specific memory CD8$^+$ T-cell populations, rather than maximizing their quantity, may be key to achieving robust protective immunity (adapted from Lefebvre et al., 2020, Trends in Parasitology).

7. While circumsporozoite protein persists during the liver stage, other antigens with sustained hepatic expression may offer superior vaccine targets and are equally important for achieving protection (adapted from Chakravarty et al., 2007, Nature Medicine).

8. Protective efficacy of malaria vaccines in endemic regions is lower than in non-endemic areas, possibly due to immune tolerance and antigenic variation (adapted from Chen et al., 2025, Vaccines).

9. Academic culture has traditionally emphasized positive findings, often leaving negative results unpublished. Embracing the idea that all well-conducted research contributes valuable knowledge, regardless of outcome, can foster a more transparent, collaborative, and productive scientific system.

10. While life presents challenges beyond our control, how we respond shapes our freedom and purpose. Growth comes not from controlling circumstances, but from choosing how to face them and the meaning we give them (after Maya Angelou and J.R.R. Tolkien).

11. Determination and courage allow individuals to overcome barriers and achieve what others might consider impossible. As demonstrated by Kathrine Switzer, the first woman to officially finish a marathon in 1967 despite attempts to stop her, no matter your gender, nationality, or who you love, everyone is equally strong, capable, and unstoppable.

12. Happiness and purpose are found when we take risks, follow our passions, and embrace new experiences. As Steve Irwin said, "That's what life's about, mate. Just getting out there, having fun, following your passion and just being enthusiastic".