

Unlocking The Potential Of Micornas As Biomarkers Of Vector-borne Diseases

Tilini De Silva¹

John Stenos², Stephen Graves³, Tarka Bhatta³, Nathan Unsworth⁴, Cameron Stewart⁵, Ryan Farr⁵ and Simon Firestone⁶

¹ Department of Veterinary Biosciences, Melbourne Veterinary School, Faculty of Science, The University of Melbourne, Parkville, VIC 3052, Australia

² Australian Rickettsial Reference Laboratory

³ Australian Rickettsial Reference Laboratory, Bellerine St., University Hospital Geelong, Geelong, VIC 3220, Australia

⁴ Sensors and Effectors Division, Defence Science and Technology Organisation, 506 Lorimer Street, Fisherman's Bend, Melbourne, VIC 3207, Australia

⁵ CSIRO Health & Biosecurity, Australian Centre for Disease Preparedness, Geelong, VIC 3220, Australia

⁶ The University of Melbourne

Unlocking the Potential of MicroRNAs as Biomarkers of Vector-Borne Diseases

Vector-borne diseases (VBDs), such as q-fever, dengue, and Lyme disease pose substantial threats to veterinary public health, necessitating precise diagnostics. MicroRNAs (miRNAs) are regulatory RNAs that have emerged as promising biomarkers.

A systematic review was carried out to analyse the current research on miRNAs in arthropod vectors and humans. A comprehensive literature search across four databases resulted in 61 articles following stringent screening protocols.

Dengue (22%) and chikungunya virus (19%) were the most prominent VBDs assessed in the review. Notably, miR-1246 and miR-320a were differentially expressed in dengue⁽¹⁾, while miR-21 and miR-155 were linked to Japanese encephalitis⁽²⁾, and miR-4497 to malaria⁽³⁾. In arthropod vectors, tick saliva, and salivary glands were extensively studied, due to their pivotal role in pathogen transmission.

Furthermore, in a pilot investigation, the stability of miRNAs was investigated by evaluating degradation patterns from 0-, to 120-hours post-incubation of human serum at different temperatures (-80°C, 4°C, 22°C). The analytical pipeline consisted of RNA extraction, cDNA synthesis, and high-throughput Next-generation sequencing analysis. It is expected to observe stable miRNA levels at 4°C for 24 hours and a significant degradation after 72 hours incubation at 4°C. This pilot study will denote the miRNAs that are substantially stable, which could be chosen as biomarkers, should they be differentially expressed.

The systematic review underscores a significant knowledge gap in the application of miRNA biomarkers for VBD detection. Additional research is requisite to develop standardized protocols, and validate clinical utility, notwithstanding the promising potential of miRNAs in enhancing veterinary public health.

References

1. Martins SdT, Kuczera D, Lötvall J, Bordignon J, Alves LR. Characterization of dendritic cell-derived extracellular vesicles during dengue virus infection. *Frontiers in Microbiology*. 2018;9(August):1792.
2. Baluni M, Ghildiyal S, Fatima T, Tiwari R, Upadhyay S, Dhole TN, et al. Differential expression of circulating microRNAs in serum: Potential biomarkers to track Japanese encephalitis virus infection. *J Med Virol*. 2022;94(2):531-9.
3. Gupta H, Rubio M, Siteo A, Varo R, Cisteró P, Madrid L, et al. Plasma MicroRNA Profiling of *Plasmodium falciparum* Biomass and Association with Severity of Malaria Disease. *Emerg Infect Dis*. 2021;27(2):430-42.