Troublesome Ticks:

Determining the aetiology of DSCATT in Australia
(NHMRC: 1169949)

This study has approval from the Human Research Ethics Committees of Murdoch University (permit 2019/124), the Northern Sydney Local Health District (permit 2019_ETH12032) and the ARC Lifeblood (permit 2019-20).

Professor Emeritus Peter Irwin
90 South St, Murdoch WA6150

www.murdoch.edu.au

CRICOS Provider Code: 00125J
ABN 61 616 369 313

Sunday, 16 March 2025

Senate Standing Committees on Community Affairs
References Committee
Parliament House, Canberra ACT 2600

Dear Senators,

Inquiry into access to diagnosis and treatment for people in Australia with tick-borne diseases

Right of Reply to submission by:
Lyme Disease Association of Australia and Sarcoidosis Lyme Australia
Supplementary Submission - QON

We thank the Senate committee for the opportunity to respond to the LDAA submission. We emphasise that the study funded by the NHMRC Targeted Call for Research 'Troublesome Ticks: Determining the aetiology of DSCATT in Australia' (GNT 1169949) **is still in progress** and all **results are yet to be peer reviewed**.

In addition to the methodology published in 2022 (Barbosa et al., 2022) a series of pilot studies were conducted on a small sub-cohort for proof-of-concept of novel laboratory methods (Lee et al., 2023, 2024 & 2025). We anticipate the remainder of our studies **will be published during 2025**.

For senators' information, our NHMRC-funded research is the most comprehensive, coordinated and targeted investigation of tick-borne disease in Australia to date.

For your reference, our **broad research hypothesis** is that by tracking tick bite victims using a range of cutting-edge technologies to search for **infectious organisms, perturbations in gene expression and immune responses**, whilst also considering each individual's **psychological status**, compared with un-bitten controls, we might discover **potential causation, patterns, or differences** in people who became unwell, compared with those who did not. Such discoveries may lead to **exactly the outcomes wished for by patients and advocacy groups such as the LDAA**.

Our current research project follows many years' collective experience investigating Australian ticks and tick-associated organisms, and brings together an expert **multidisciplinary team** of scientists

with knowledge of **medicine, pathology, microbiology, infectious disease, immunology, parasitology, psychology, virology,** and **epidemiology.**

We have read the submissions from the LDAA and note these documents express concerns that we may misinterpret our own findings. We are conscious of the limitations of all scientific studies. We wish to reassure members of the Senate Committee that **we have approached our work in good faith** and emphasise that all such studies are designed to contribute to knowledge, but we acknowledge that single studies are rarely the last word in exploring new disease conditions.

We wish to provide responses to some of the comments within the LDAA section about "Overlooked and Misdirected" research (pages 13-23) and refer you to the **Appendix** that follows.

Ethical issues. We wish to reassure the committee that informed consent has been obtained from all patients.

Yours faithfully,

Peter J. Irwin
Chief Investigator (A)
NHMRC Grant: GNT1169949

List of Publications arising (to date):

- Barbosa et al. (2022) **The Troublesome Ticks Research Protocol**: Developing a Comprehensive, Multidiscipline Research Plan for Investigating Human Tick-Associated Disease in Australia. Pathogens 11:1290. https://doi.org/10.3390/pathogens11111290
- Lee et al. (2023) **A systems biology approach to better understand human tick-borne diseases.** *Trends in Parasitology*, *39*(1), 53–69. https://doi.org/10.1016/j.pt.2022.10.006
- Lee et al. (2024) **Molecular analysis of human tick-bitten skin yields signatures associated with distinct spatial and temporal trajectories - A proof-of-concept study.** *Heliyon*, 10(13), e33600. https://doi.org/10.1016/j.heliyon.2024.e33600
- Lee et al. (2025) **From Local to Systemic: The Journey of Tick Bite Biomarkers in Australian Patients.** *International Journal of Molecular Sciences* 26, 1520. https://doi.org/10.3390/ijms26041520

Appendix

Study Design

'Building on a flawed dataset'

1. Contrary to the LDAA assertion that our research was "building upon a flawed dataset" (p. 13) we took a new approach to the problem, and for the **first time in Australia** we have **studied persons with tick bite, within 72 hours of the bite, prospectively for twelve months**. We note that the LDAA calls for "new, well-designed prospective studies" (p. 14) and this is exactly what our approach has been. Our study has been conducted independently and is not based on any work conducted by Prof Kenaan.

'Exclusion of patients with pre-existing medical conditions such as 'Myalgic Encephalomyelitis (ME), chronic fatigue syndrome (CFS), fibromyalgia and chronic "Lyme-like" illness''

2. Excluding people with declared chronic illnesses provides a **robust opportunity** to study disease progression while **minimising confounding variables**.

'Control group matching'

3. Control group matching. Unmeasured confounding is always an issue in case control studies; the use of **two separate control groups was designed to mitigate, but not eliminate, this risk**.

Methodology

'Limited temporal scope'

4. This comment incorrectly states (p. 15) that patients were sampled up to 72 hours post-tick bite only. In fact, patients were re-examined at **1 week, 3 months and 1-year post tick-bite**, providing us ample opportunities to isolate organisms, and contributing prospectively to our understanding of the biological events after tick-bite.

'Overreliance on 16S rRNA & 18S rRNA sequencing'

5. In addition to 16S rRNA and 18S rRNA sequencing the methodology included **microscopy, cell culture, a wide range of serological testing, and other focused molecular methods including metagenomics, transcriptomics and targeted assays**.

Data Interpretation

'Risk of overinterpretation in psychometric profiling'

6. Results of psychometric profiling were not used to include or exclude patients. Clinical data and results from the many laboratory tests conducted are **analysed independently of any psychometric information**.

'Ambiguity in defining causality'

7. Patient symptoms and laboratory data were **analysed independently of any results from other cohorts**. Control groups were used.

'Limited exploration of non-infectious causes'

8. The study has utilised cutting-edge methods including micro-RNA analysis and transcriptomics to investigate **perturbations in the patients' immune responses** throughout the one-year study enrolment.

Ethical Matters

'Use of skin biopsy'

9. Patients gave informed consent prior to this procedure. **Skin biopsy is more sensitive than blood samples** for identification of tick-transmitted microorganisms. Declining consent for biopsy did not exclude the patient from participation in the study.

'Limited Indigenous and regional representation'

10. The study was open to **participation by patients nationwide**, regardless of ethnicity and location.
