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Driving innovation from discovery to access

Lymph nodes as niches for *Mycobacterium tuberculosis* infection in humans and profiling of associated host immune responses

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Development of new tuberculosis (TB) vaccines is hindered, in part, by our incomplete understanding of host-pathogen interactions in human tissues. Initiation and orchestration of adaptive immunity against pulmonary bacterial infections largely occur in lung-draining lymph nodes (LNs). However, LNs are also potential niches of Mycobacterium tuberculosis (Mtb) persistence and common sites of extrapulmonary disease. Therefore, LNs are potentially major determinants of the outcome of Mtb infection.

Our objectives are to investigate the prevalence of Mtb in human LNs and better understand immune responses in human LNs.

We accrued a cohort of recently deceased individuals with clinical presentations along the TB spectrum, from healthy individuals who died of trauma with no TB pathology to those with confirmed TB pathology. With consent from next-of-kin, samples were collected during forensic autopsies, including thoracic lung-draining LNs, non-thoracic LNs, and blood. Mtb nucleic acid was detected by multiplex targeting of RD9 and IS6110 genomic DNA and ETS1 and 23S ribosomal RNA using droplet digital PCR. Immune response profiles and transcriptomic signatures in LNs and blood were characterized by single-cell RNA sequencing (scRNAseq).

Of 58 decedents, 11 exhibited confirmed (n=10) or possible (n=1) TB pathology at autopsy. Of the 47 without TB pathology, Mtb nucleic acid was detected in 29 individuals (~62%) within thoracic LNs (n=5), non-thoracic LNs (n=6), or both (n=18). Preliminary findings from scRNAseq data indicate marked differences in immune cell composition and functional gene expression profiles between LN and blood. Detailed analyses are underway and will be reported at the conference.

Our results suggest Mtb is highly prevalent in the population served by the Western Cape Forensic Pathology Services in a high TB-burden setting and underscore the value of investigating LNs to better understand the tissue-level spectrum of Mtb infection and TB pathology.

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Conflicts of Interest
None