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The analysis of exosomal micro-RNAs in peripheral blood mononuclear cell-derived macrophages after infection with bacillus Calmette–Guérin by RNA sequencing

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ABSTRACT

Objective/Background: Tuberculosis (TB) is a major global threat to human health, especially in low-income countries. The diagnosis of TB is challenging because of the limitations of specificity and sensitivity with the current diagnostics. Novel, selective biomarkers for TB would be of great practical value. Exosomes are bioactive vesicles with 30–100 nm in diameter, which are secreted from almost all cell types and are found in virtually every human body fluid. Exosomes transport micro-RNAs (miRNAs), which are post-transcriptional regulators of gene expression, around the body and allow miRNAs to modulate biological pathways in target cells. Our aim was to investigate the potential of exosomal miRNAs as biomarkers by examining their release from human monocyte-derived macrophages (MDMs) after infection with Mycobacterium using miRNA sequencing.

Methods: Human monocytes were obtained from blood and driven to an MDM phenotype using standard protocols. MDMs were infected with *Mycobacterium bovis* Bacillus Calmette–Guérin (BCG) or left uninfected as control. Exosomes were collected 72 h postinfection from the cell culture medium and subjected to RNA isolation. Small RNA libraries were constructed and RNA sequencing performed. The raw reads were filtered to eliminate adaptor and primer sequences, and the sequences in FASTQ format were run against the mature human miRNA sequences available in miRBase using BLAST software using a Linux operating system. Micro-RNAs were identified using $E = 0.01$ or 1.

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Results: Infection of MDMs with BCG lead to the release of a number of exosomal miRNAs. These mainly consisted with Let-7 family members, miR-155, miR-146a, miR-145, and miR-21 all of which were predicted to target important immune-related genes and pathways.

Conclusion: This study provides evidence for the release of specific miRNAs from BCG-infected MDMs. These results need to be confirmed and the presence of this panel of miRNAs tested in the blood of patients to determine their selectivity and specificity as a diagnostic in patients with TB.

Conflict of interest

All authors declare no conflicts of interest.