

# A Short Communication on Multiplatform Metabolomics Provide Insights into the Molecular Basis of Tick-Borne Encephalitis

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## Description

Patients with Tick-Borne Encephalitis (TBE) may experience a sudden onset of symptoms, including in the central nervous system. Elucidating tick biology and pathogen transmission associated with TBE will help improve disease screening, diagnosis, and prognosis. Identifying the potential metabolites related to phenotype would be a clinical breakthrough [1,2].

Recent studies have shed light on underlying disease mechanisms. A multi-omics study of essential metabolic pathways involved in tick responses to *Anaplasma phagocytophilum* infection demonstrated the complexity of host-agent dynamics and provided new multitarget strategies for diagnosis, prevention, and control of infections [3]. A metabolomics study developed a more accurate test for early Lyme disease detection and outlined the requirements for new diagnostic approaches [4]. Our team used multi-omics to track metabolic and lipid changes during disease progression in patients infected with tick-borne encephalitis virus (TBEV) and provided important insights into the pathology of TBE [5].

We analyzed serum samples with untargeted metabolomic and lipidomic methods to identify metabolic pathways associated with disease progression and the mechanisms of TBEV infection. Lipidomics can reveal the lipid components involved in signaling and infection processes of pathogenic invasion [6]. For metabolomics, we used both a low-polarity column (HSS T3) and high-polarity column (Amide) to obtain a wide range of metabolites and thus provide a general understanding of TBEV infection. Thus, both methods can provide a comprehensive view of metabolites and offer valuable insights into the underlying mechanisms of diseases.

We analyzed the relationship between anti- and pro-inflammatory processes, metabolites and lipids using mass spectrometry (MS) and flow cytometry. Notably, TBEV infection in humans was associated with initial pro-inflammatory and subsequent anti-inflammatory responses that prevented excessive pathological injury to the host [7]. Biochemical reactions occurred throughout the body alongside the responses to anti- and pro-inflammatory processes. Triglycerides (TAGs) can provide energy storage in human metabolic processes. Viral infection can drive intracellular biochemical reactions with high energy needs, resulting in hydrolysis of TAGs [8]. Sphingomyelin (SM) mediates the host response to TBEV and immune cells, such as dendritic cells and B-lymphocytes, play primary roles in viral clearance. Therefore, we explored relationships between SM concentrations and immune cells [9] and further elucidated these metabolic mechanisms. We also found that arachidonic acid and its derivations are involved in inflammatory response.

Data pretreatment and statistical analysis is crucial in metabolomics research. For lipidomics datasets, we used information-dependent acquisition coupled with a dynamic background subtraction mode to acquire MS and MS/MS spectra and deducted the background spectrum to filter redundant information [10]. SWATH to MRM, an untargeted method that can profile pooled biological samples and reveal MS/MS spectra for all metabolites [11], was used to verify potential metabolites.

Our study underscores the need to expand the targets used for diagnosis and prognosis of TBE patients, which can be achieved through immunological detection based on antigen-antibody specificity and sensitivity, the duration of illness, and the type of syndrome. An accurate and visual approach to the management of such patients is critical. After 1-year of follow-up with patients recruited in TBEV research, our team will be able to provide comprehensive evidence regarding the pathology of TBE.

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