

## Poster abstract submission

**Approval Status**

Not Started

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**Poster title**

Deciphering Host Signaling Alterations During Carbapenem-Resistant *Acinetobacter baumannii* Infection Using an Integrated Proteomics–Metabolomics Approach for Host-Directed Therapy

**Poster abstract**

Carbapenem-resistant *Acinetobacter baumannii* (CRAB) remains a WHO “critical priority” pathogen, responsible for severe hospital-acquired infections and rising global mortality. Innovative strategies such as host-directed therapy (HDT) are urgently needed. Our study aims to elucidate the dysregulated host signaling pathways associated with CRAB persistence within host cells using an integrated LC-MS–based proteomic and metabolomic approach. This study investigates host signaling alterations associated with CRAB infection through an integrated serum proteomics and metabolomics approach. Serum samples obtained from CRAB-infected subjects and healthy controls were analyzed to elucidate host signaling and metabolic alterations associated with bacterial persistence. For proteomic profiling, serum proteins were precipitated, digested with trypsin, and analyzed using LC–MS/MS. For metabolomic analysis, metabolites were extracted from serum using a Chloroform methanol-based precipitation method and analyzed via LC–MS. Protein identification was performed with MaxQuant, and metabolite profiling and pathway analysis were conducted using MetaboAnalyst and KEGG databases. Differential expression was determined using a fold-change threshold of  $\geq 2$  and  $p < 0.05$ . Key proteomic findings were validated using qPCR. A total of 357 proteins and 1970 metabolites were detected across the samples, out of which 124 proteins and 642 metabolites were identified as differentially expressed. Among these, 64 proteins and 366 metabolites were significantly downregulated while 60 proteins and 276 metabolites were upregulated. These findings suggest extensive metabolic reprogramming involving multiple pathways, highlighting the profound impact of CRAB infection on systemic metabolic homeostasis. Notably, proteins including NRP1, APOL1, FABP3, CALR, and CDH5 were linked to sphingolipid-enriched membrane domains and S1P signaling within the sphingolipid metabolism pathway, the pathway which was also validated by metabolomic analysis. This strong concordance between proteomic and metabolomic data underscores the significant impact of sphingolipid metabolism. These findings suggest that such pathways may serve as promising biomarkers or therapeutic targets for early diagnosis or intervention for CRAB infection.

## Research topic

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## Small molecule therapeutics

