## Lipidomic biomarkers and QTL discovery for transition cow diseases: foundation for a multi-omics approach

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The transition period, defined as three weeks before to three weeks after calving, is the most critical stage in a dairy cow's production cycle. Major metabolic shifts predispose cows to diseases including mastitis, metritis, retained foetal membranes, milk fever, and ketosis. These conditions reduce productivity, increase treatment costs, and contribute to early culling. This study aimed to identify serum-based biomarkers and associated genomic regions, or quantitative trait loci (QTL) for transition cow diseases using a multi-omics approach. Lipidomics is presented here as the initial dataset, with proteomics, metabolomics, and transcriptomics to follow. In a case-control study, blood samples were collected from 200 clinically diseased and 331 healthy transition cows within 70 days after calving across 15 pasture-based farms in Victoria, Australia. Lipidomic profiling was performed using liquid chromatography tandem mass spectrometry (LC-MS/MS). Differential analysis compared lipid concentrations between groups, and genome-wide association studies (GWAS) mapped lipid-associated QTLs. Among 238 assayed lipids, 173 were differentially abundant between diseased and healthy cows (154 decreased, 19 increased). Lysophosphatidylcholines (LPC), lipids involved in immune and inflammatory pathways, were the most significantly altered class. Eight LPC species demonstrated strong predictive capacity (area under the curve [AUC] >0.73), with LPC 14:0 and LPC 18:3 achieving AUC of 0.78. GWAS identified 35 lipids associated with three QTLs on chromosomes 11 and 19; 20 of these lipids were also differentially abundant and their classes linked to membrane structure and stability, antioxidant protection, and cell signaling, highlighting multiple physiological pathways affected in transition cow disease. These findings demonstrate that lipidomic biomarkers reflect key physiological disruptions during transition diseases. Integrating molecular biomarkers with genomic markers through multi-omics enables discovery of both disease indicators and causative genetic variants, supporting development of genomic breeding values for improved transition health and enhancing animal welfare and farm profitability.

Keywords: transition cow, lipidomics, GWAS, biomarkers