

Human Milk Metabolomics Across Lactation: Bioactive Compound Dynamics and Perspectives for Maternal and Infant Health

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Women's health during pregnancy and lactation is very important to prevent complications and support optimal foetal and baby growth. Optimal nutritional intake, as well as attention to physical and mental health are crucial steps that can reduce the risk of premature birth, low birth weight and non-communicable diseases development, which have a significant impact on the child's long-term health. Conditions such as malnutrition, anaemia, gestational diabetes, and mental health issues have been associated with adverse birth outcomes like low birth weight, preterm delivery, and developmental delays in children. These complications can lead to long-term health and developmental challenges, underscoring the need for comprehensive maternal care. Although lot of research has been done linking the maternal health and nutrition with the lactation, no attention has been paid to the study of maternal factors as diet and health complications with bioactive metabolites composition of breastmilk and their role in shaping infant's health.

Our study aims to link mother's health and diet with bioactive compounds dynamics of breast milk and infant health in a small longitudinal mother-infant cohort (NEMO, n=55) applying a multi-omics approach. Firstly, we wanted to understand the metabolome (the complete set of metabolites) in human milk, with particular interest in bioactive compounds of human milk, and its changes throughout the different phases of lactation (colostrum, 1 month, 6 months and 1 year). The targeted metabolomics (UHPLC-Q-TOF-MS) retrieved 330 metabolites, 58 showed significant overall variation between phases (FDR $q < 0.05$). Strictly phase-specific metabolites were scarce, indicating that lactation dynamics are mainly reflected in changes in metabolite abundance throughout lactation. Curiously, colostrum showed a higher relative abundance of polyamines (spermidine and putrescine), tryptophan derivatives (kynurenine and indoles), neurotransmitters (GABA), and folates, with enrichment of pathways such as tryptophan metabolism, aminoacyl-tRNA biosynthesis, as well as arginine and proline metabolism.

This observational study describes the application of metabolomics to understand the dynamics of poorly characterized bioactive compounds, including tryptophan derivatives and neurotransmitters, which may participate in the metabolic, immune, and neuronal programming of the infant. Future analysis will explore the association among maternal nutrition and health status with relevant changes in bioactive compounds profiles during lactation and child's health and development, with the aim of supporting mother's health during the critical period of pregnancy and lactation.

Primary author: SÁEZ, Andrea

Co-authors: CIMBALO, Alessandra; MOLINA RODRIGUEZ, Alonso; MORENO, Ana; J RUIZ, Antonio; LUZ, Carlos; MECA, Giuseppe; BLESA, Jesús; NÚÑEZ-SÁNCHEZ, Maria A; ESTEBAN-TORRES, Maria; ESTEVE, Maria José; SUÁREZ CORTES, Maria; CASTAÑO MOLINA, Maria Ángeles

Presenter: SÁEZ, Andrea

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