

Differences between Arterial and Venous Umbilical Cord Plasma Metabolome and Association with Parity

Background/introduction/summary

Analysis of umbilical cord blood is important for assessing neonatal health. Sampling is normally performed by squeezing out blood after severing the cord, which leads to mixing of arterial and venous blood. Furthermore, additional variance may also be induced by traits not related to the present study question. In order to reduce variance in studies of umbilical cord blood we aimed to:

- Identify key differences between arterial and venous cord blood to determine the potential impact of sampling on the observed metabolic profile.
- Find associations between the maternal and infant traits gestational length, parity, birth weight, sex, maternal age and maternal BMI and the venous and arterial umbilical cord metabolomes.

Materials and Methods

48 paired venous and arterial cord plasma from the NICE-cohort [1] were analysed using a combination of targeted and untargeted GC-QqQ-MS. Multilevel random forest analysis with unbiased variable selection and repeated double cross-validation [2] was used as a discriminant analysis for differentiating venous and arterial umbilical cord. Random forest regression analyses were performed for the continuous variables; gestational length, birth weight, maternal age and maternal BMI while random forest classification was used for the dichotomous outcome variables sex and parity. Variables selected by the algorithms were further processed using the Mann-Whitney U-test

Results

A classification rate of 79% was achieved for arteriovenous differences ($p = 0.004$). Several monosaccharides had higher concentrations in the arterial cord plasma while amino acids were higher in venous plasma, suggesting that the main differences in the measured arterial and venous plasma metabolomes are related to amino acid and energy metabolism.

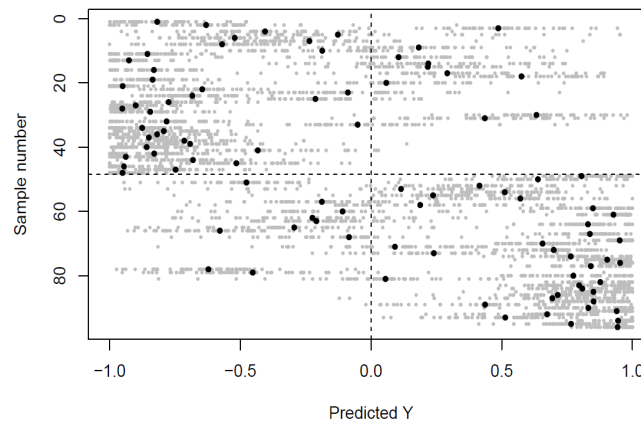


Fig. 1. Prediction results from multilevel RF analysis of metabolome differences of venous and arterial umbilical cord plasma. Black dots in top right and top left corners indicating correctly classified samples.

Venous cord plasma metabolites related to energy metabolism were positively associated with parity (77% classification rate, $p = 0.004$) while arterial cord plasma metabolites were not. Differences mainly driven by organic acids involved in energy metabolism.

No further associations between infant and maternal traits and the metabolomes were found

Conclusions

This study underlines the importance of selecting the appropriate sample matrix depending on study question. Moreover, the use of mixed, arterial, or venous cord blood could contribute to difficulties when trying to compare studies, especially given the potential for differing proportions of arterial and venous blood in mixed cord blood samples. We further found that parity associated with metabolites in the venous umbilical cord plasma related to energy metabolism, meaning that whether the mother has undergone previous deliveries affects the umbilical cord plasma metabolome. This may be an important factor to account for when matching case-control pairs and for outcomes that may be related to energy metabolism

Reference

- [1] Barman M, et al. "Nutritional impact on Immunological maturation during Childhood in relation to the Environment (NICE): a prospective birth cohort in northern Sweden." *BMJ open* 8.10 (2018): e022013.
- [2] Shi L, et al. "Variable selection and validation in multivariate modelling." *Bioinformatics* 35.6 (2018): 972-980.

Acknowledgements

We want to give a big thank you to all of the participating families within the NICE-cohort. Study nurses Marjut Larsson and Ulrika Börlin, study midwives Lisa Sundén and Louise Lindgren and the delivery ward at Sunderby hospital.

Contact

Olle Hartvigsson: ollehar@chalmers.se