LOCATION-SPECIFIC HUMAN UTERINE TISSUE PROTEOMIC SIGNATURES ARE NOT AFFECTED BY LABOUR STATUS

Burté F[1], Browne B[2], Lai PF[2], Johnson MR[3], Tribe RM[2], Taggart M[1] on behalf of the **BUMP Collaborative**

[1]Biosciences Institute, Newcastle University, Newcastle upon Tyne, UK

[2]Institute of Reproductive and Developmental Biology, Imperial College London, London, UK

[3]Department of Women and Children's Health, School of Life Course and Population Sciences, King's College London, London, United Kingdom

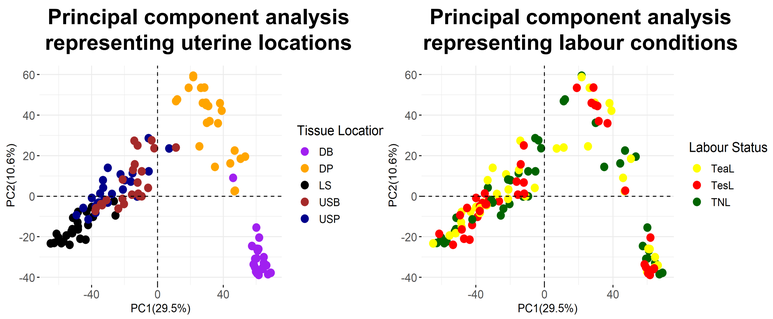
INTRODUCTION and AIM

Globally, preterm birth is a leading cause of childhood death and, for survivors, an increased risk of ill-health through their lifecourse[1]. Medicinal intervention targeted to prevent uterine contractions remains ineffective and is accompanied with a risk of maternal and fetal adverse effects[2]. A limiting factor in the quest for improved tocolytics is our incomplete understanding of the protein constituents of tissues of the uterus in pregnancy and how these may depend upon spatial location and/or labour status. **Our objective, therefore, was to quantify and compare the proteomes of human uterine tissues from different regions and labour conditions.**

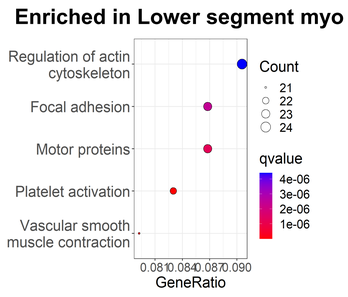
METHODS

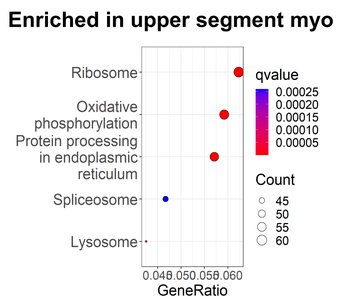
- Matched tissue biopsies were obtained from 24 healthy pregnant women undergoing elective Caesarean section (39-40 weeks gestation, LREC 10/H0801/10) from 5 spatial locations: myometrium of lower segment (LS), upper segment parietalis (UPS) and upper segment basalis (USB) and decidua parietalis (DP) and basalis (DB). The women were divided in three groups of labour conditions: at term not in labour (TNL); at term early labour (TEaL); and at term established labour (TIL).
- Tissues were homogenized, in-column trypsinized using S-trap™ columns (Protifi) and peptides analysed using liquid chromatography followed by Orbitrap Exploris™ 480 (ThermoFisher Scientific) mass spectrometer in data-independent acquisition (DIA) mode.
- Data analysis was performed using DIA-NN in library-free mode[3].
- Significant differences were identified using ANOVA followed by k-means clustering and t-test for pairwise analysis corrected for multiple comparison with FDR-permutation using R (version 4.2.2) and Perseus software (version 2.0.7.0).
- Pathway analyses were performed using ClusterProfiler (version 4.8.1) in R.

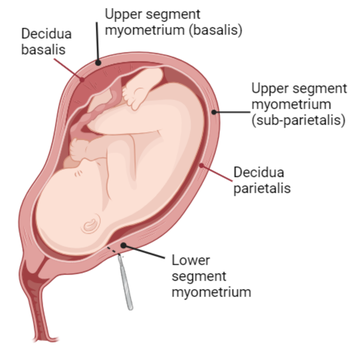
Uterine spatial locations have different proteome profiles (6,015 proteins quantified) that are unaffected by labour status.



Lower segment myometrium has a contractile-like phenotype, upper segment is more proliferatory





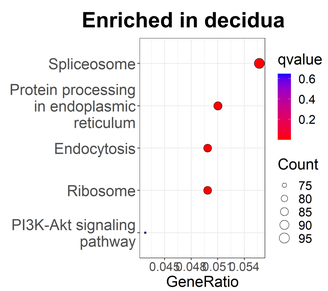


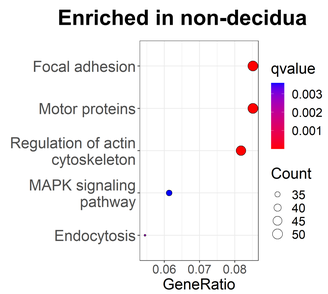
Myofilament-associated protein changes between lower and upper segment myometrium

Protein symbol	Fold-change LS versus USP	Fold-change LS versus USB
MYH11	1.2	↑ **1.4**
MYL6	↑ **1.4**	↑ **1.5**
MYL9	1.2	↑ **1.3**
MYLK	↑ **1.6**	↑ **1.8**
SMTN	1.3	↑ **1.5**
ACTA2	1.3	↑ **1.6**
ACTG2	1.3	↑ **1.7**
ACTN1	↑ **1.3**	↑ **1.4**
FLNA	1.2	↑ **1.3**
LMOD1	↑ **1.2**	↑ **1.4**
PALLD	↑ **1.3**	↑ **1.5**
CNN1	1.2	↑ **1.4**
ITPR1	↑ **1.3**	↑ **1.3**
PPP1R12A	1.1	↑ **1.3**
PPP1R12B	1.2	↑ **1.3**
PPP1R12C	↑ **2.0**	0.3
ROCK1	↑ **1.3**	1.0

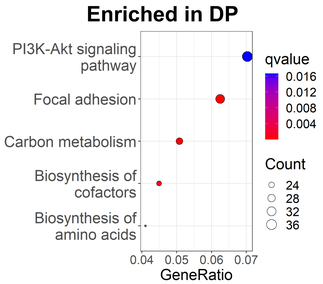
↑ significantly increased in lower segment

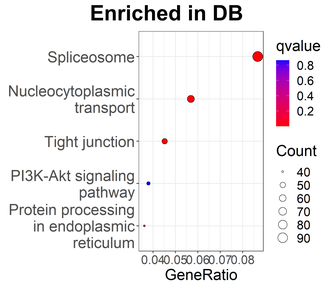
Decidual proteomes show proliferatory phenotypes compared to contractile non-decidual tissues





Decidua Pareatalis is highly metabolic whilst Decidua Basalis is enriched in transcriptional/translational surveillance





Conclusion

Human uterine tissue proteomes vary depending upon location. There are notable differences between lower and upper segment myometrium, decidua and myometrial tissues and decidua basalis and parietalis. Labour progression had no effect on the proteome in any tissue location investigated. The results have implications for our understanding of (i) location-dependent tissue phenotypes and thereby (ii) how uterine organ-level signalling is co-ordinated during pregnancy and labour onset.

BORNE-2021-0005

References

[1]Taggart, M. J., & Tribe, R. M. (2022) *Experimental Physiology*, **107**(5), 395-397.

[2]Wilson, A. *et al.* (2022) *Cochrane Database of Systematic Reviews,* **Issue 8**. Art. No.: CD014978.

[3]Demichev, V. *et al.* (2020) *Nature Methods,* **17** (1): 41-44.