The RNA landscape of the human placenta in health and disease

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Introduction

Motivations

1. Placental dysfunction underlies a large proportion of maternal and perinatal morbidity and mortality, which is a half the total burden due to cancer.
2. The placental tissues are under-represented (or none) in multi-omics projects (e.g. GTEx; RoadMap).
3. Publicly available placenta transcrptome data lack the depth of coverage and the sample number.

Materials & Methods

1. 302 placental biopsies of the POP Study cohort(Pasupathy et al. 2008; Sovio et al. 2015; Gaccioli et al. 2017), of which 94 and 56 are from cases of preeclampsia (PE) and fetal growth restriction (FGR).
2. 324 total RNA-Seq datasets (~102 million reads per sample)
3. 328 small RNA-Seq datasets (~20 million per sample)
4. TopHat2, StringTie and Cuffcompare
5. featureCount and DESeq2

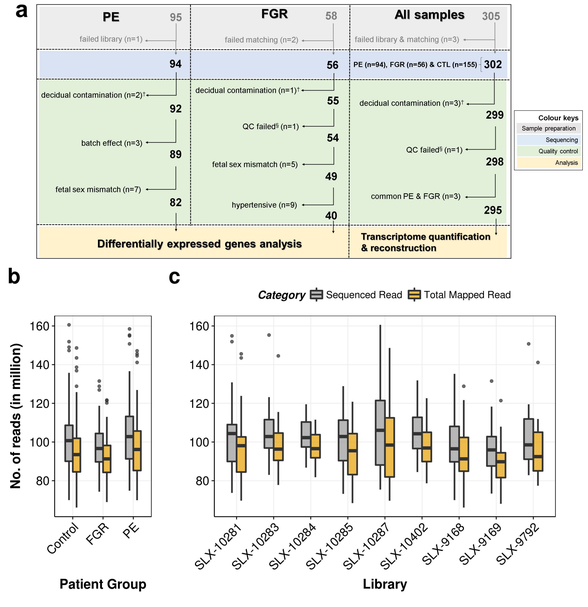

Figure 1: Number of placental biopsies and sequencing reads

Results

1. Relative abundance and complexity of long and short RNAs in the placenta

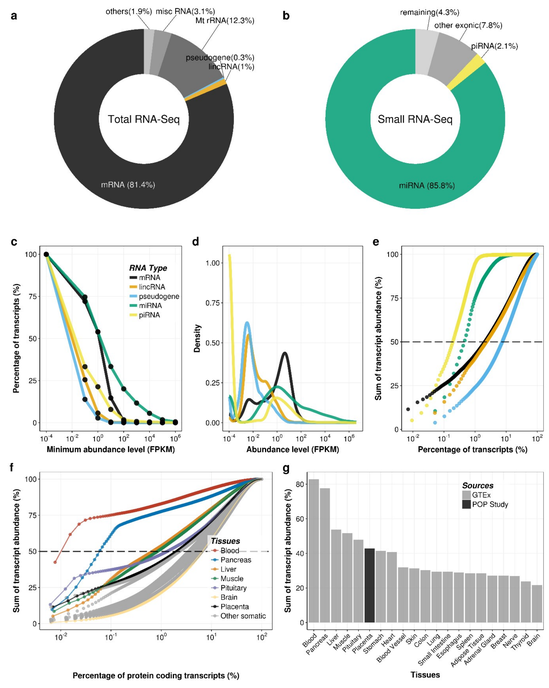

Figure 2: Complexity of RNA transcripts in the placenta

2. Genes expressed specifically in the placenta

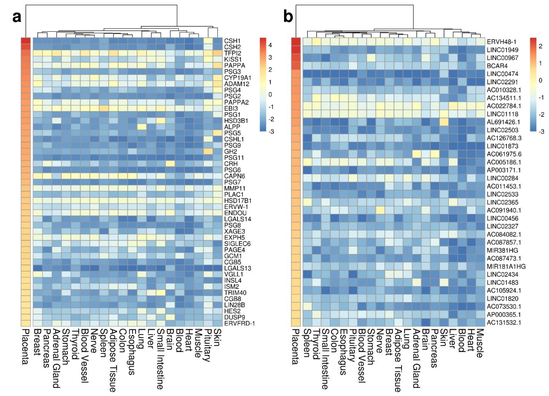

Figure 3: Abundance level of genes expressed specifically in the placenta (a: protein-coding, b: lincRNA)

3. Highly abundant circular RNAs and short RNAs

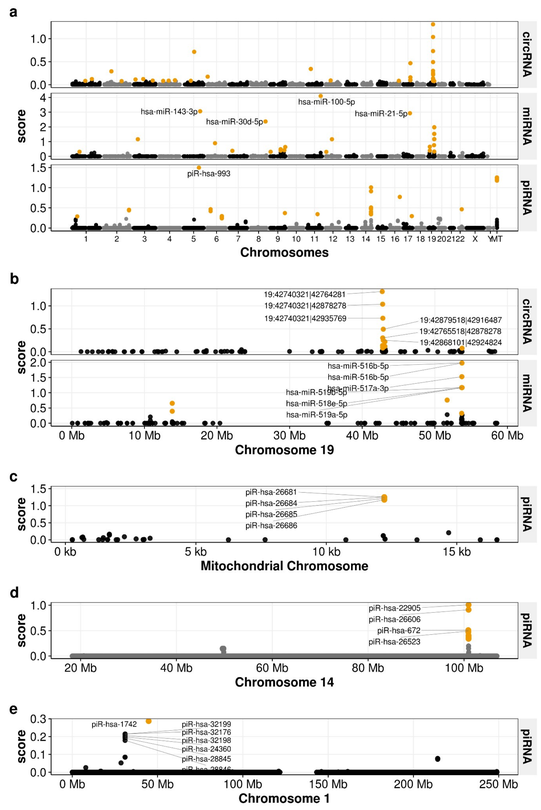

Figure 4: Manhattan plots showing relative abundance of short RNAs

4. A putative miRNA sponge

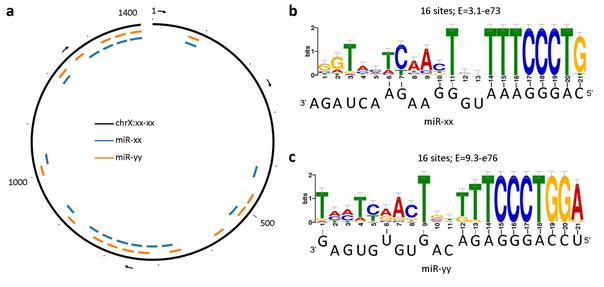

Figure 5: A putative miRNA sponge and its targets miRNAs (sorry, data at non-disclosure stage)

5. Size distribution of placental small RNAs

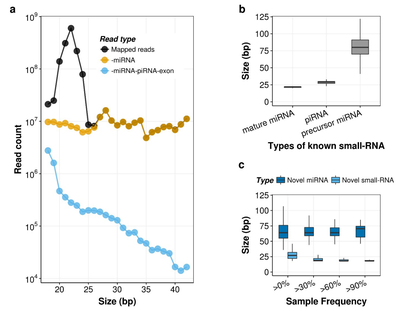

Figure 6: Size distribution of placental small RNAs. (‘Mapped reads’: mapped at least 10x, ‘-miRNA’: ‘Mapped reads’ minus miRNA, ‘-miRNA-piRNA-exon’: ‘Mapped reads’ minus miRNA, piRNAs and exon)

Conclusions

1. More than 300 well phenotyped placentas sequenced to high depth.
2. High quality data with strand-specific total-RNA (not poly-A+ selected).
3. Circular RNAs were characterised in the placenta.

Data availability

- Manuscript in submission
- https://sung.github.io/Placenta_Transcriptome_GI2019 (this poster)
- https://www.obgyn.cam.ac.uk/placentome (will be open to public soon)
- https://www.ebi.ac.uk/ega/studies/EGAS00001002205

References

Gaccioli, Francesca, Susanne Lager, Ulla Sovio, D. Stephen Charnock-Jones, and Gordon C. S. Smith. 2017. “The Pregnancy Outcome Prediction (Pop) Study: Investigating the Relationship Between Serial Prenatal Ultrasonography, Biomarkers, Placental Phenotype and Adverse Pregnancy Outcomes.” *Placenta* 59 (Suppl 1): S17—S25. https://doi.org/10.1016/j.placenta.2016.10.011.

Pasupathy, Dharmintra, Alison Dacey, Emma Cook, D Stephen Charnock-Jones, Ian R White, and Gordon C S Smith. 2008. “Study Protocol. A Prospective Cohort Study of Unselected Primiparous Women: The Pregnancy Outcome Prediction Study.” *BMC Pregnancy and Childbirth* 8: 51. https://doi.org/10.1186/1471-2393-8-51.

Sovio, Ulla, Ian R White, Alison Dacey, Dharmintra Pasupathy, and Gordon C S Smith. 2015. “Screening for Fetal Growth Restriction with Universal Third Trimester Ultrasonography in Nulliparous Women in the Pregnancy Outcome Prediction (Pop) Study: A Prospective Cohort Study.” *Lancet (London, England)* 386 (10008): 2089—2097. https://doi.org/10.1016/S0140-6736(15)00131-2.