

Supplementary Table 2: Aspects of pregnancy understudied in placental transcriptomics

| Understudied themes | Key conditions | Rationale |
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| Common pathologies of pregnancy | Preterm labour | <ul style="list-style-type: none"> • Increased understanding of pathogenesis • Development of novel predictive biomarkers and interventions for prevention of preterm birth |
| | Intrauterine growth restriction | <ul style="list-style-type: none"> • Discovery of molecules to more accurately discriminate between babies who fail to reach their genetic growth potential <i>in utero</i> and those who are healthy and constitutionally small • To identify growth restricted babies that might benefit from expectant management and earlier delivery if required |
| | Gestational diabetes mellitus | <ul style="list-style-type: none"> • Growing problem worldwide • Transcript profiling may highlight the mechanisms that lead to maternal hyperglycaemia and fetal macrosomia • Potential new methods to prevent or treat gestational diabetes mellitus and improve health outcomes for mothers and babies |
| | Stillbirth | <ul style="list-style-type: none"> • Heterogenous condition affecting >2 million pregnancies annually • Investigating the placenta transcriptome may yield useful insights into fetal death, particularly in unexplained cases • Development of biomarkers to screen for those at high risk of stillbirth |
| | Abnormal placental development (placenta praevia, placenta accreta and molar pregnancies) | <ul style="list-style-type: none"> • Identifying the potential causative factors underlying abnormal development by transcript profiling • Potential new methods of prevention and treatment for affected women |
| | Infections during pregnancy (e.g. malaria, influenza, Ebola) | <ul style="list-style-type: none"> • Women at heightened risk of infection during pregnancy • Increased understanding through placental transcriptomics of how maternal infections affect the placenta • Highlight mechanisms to target to reduce transmission of harm to the growing fetus |
| Maternal nutritional, mental and emotional states | Malnutrition (obesity or undernutrition) | <ul style="list-style-type: none"> • Rapidly rising rates of maternal obesity globally, as well as high rates of maternal undernutrition in developing countries • Improve understanding of the impact maternal nutrition has on fetoplacental health • Mitigate the greater risk of adverse pregnancy and long-term offspring health outcomes associated with malnutrition |
| | Mental health (e.g. depression, anxiety) | <ul style="list-style-type: none"> • Growing evidence highlights the importance of maternal mental |

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| | | <p>health on neurodevelopmental offspring outcomes</p> <ul style="list-style-type: none"> Identifying the potential placental programming mechanisms involved by transcript profiling Develop novel therapies to prevent adverse effects of offspring health by poor maternal mental health |
| Pre-existing maternal conditions | Non-reproductive conditions including thrombophilia, asthma, abnormal thyroid function and autoimmune diseases (e.g. systemic lupus erythematosus, anti-phospholipid syndrome) | <ul style="list-style-type: none"> Strongly associated with an aberrant hormonal, metabolic and inflammatory milieu that is detrimental to placentation Placental transcript profiling could reveal how such conditions heighten a woman's susceptibility to obstetric complications Potential new treatments to prevent defective placental function and improve pregnancy outcomes in affected women |
| | Reproductive disorders (e.g. endometriosis and polycystic ovary syndrome) | |
| Environmental and chemical exposures in pregnancy | Tobacco smoking, alcohol and cannabis | <ul style="list-style-type: none"> Frequently consumed in pregnancy Improved understanding of the placental transcriptional response to a chemical exposure are critical in contributing to the development of new strategies to mitigate harms to the growing fetus |
| Pregnancy-specific factors | Advanced maternal age and use of assisted reproductive techniques | <ul style="list-style-type: none"> Given major societal changes, mothers are becoming older and increasing numbers of pregnancies are conceived by assisted reproductive techniques Placental profiling may reveal whether higher rates of obstetric complications observed are due to underlying infertility or the technologies, and appropriate strategies can be undertaken to mitigate harms |
| | Multiple pregnancies | <ul style="list-style-type: none"> Commonly an exclusion factor for transcriptome studies Further placental transcriptomic characterisation of multiple pregnancies may demonstrate the mechanisms through which the risk of obstetric complications are enhanced Comparative twin studies of discordant intrauterine growth may also elucidate novel placental regulatory mechanisms of fetal growth that could be targeted to improve growth <i>in utero</i> |