Placental tissue and cellular metabolism

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Tissue and cellular metabolism

Placental tissue and cell metabolism are crucial functions for study

- Placental metabolic functions are vital for the growth and development of the placental supply line.

- The placenta is metabolically active, consuming a significant fraction of the metabolic substrates it takes up, thus altering output to the fetus.

- The placenta also acts as a metabolic sensor. Under abnormal or stress conditions such as hypoxia, placental metabolism is modified resulting in alterations to the substrate profile presented to the fetus.
Pathophysiology:
Intrauterine growth restriction (IUGR), preeclampsia (PE) and diabetes in pregnancy

Pathophysiologic processes:
Those that alter the distribution and utilization of energy-generating substrates, primarily oxygen and glucose
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Oxygen:

- Reduced uteroplacental blood flow
- Hypoxia
  - Altered placental metabolism
  - Reactive oxygen species
  - Oxidative damage
- Intrauterine growth restriction
- Preeclampsia
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Glucose:
- Maternal glucose concentration
- Glucose transfer
- Glucose consumption

**DIABETES**

HYPOXIA

Glucose concentration

PLACENTA

Glucose transfer

IUGR/PE

Fetal glucose concentration

Macrosomia
HUMAN PLACENTA PROJECT

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Pathophysiologic processes
Those that alter the distribution and utilization of energy-generating substrates, primarily oxygen and glucose

What are the sort of questions we need to answer?

• When does placental hypoxia occur? Can we measure intervillous pO$_2$ and oxygenation in other placental blood spaces?

• What is placental glycemic status? How can we measure placental glucose transfer and consumption in vivo?

• What is the balance between glycolytic and oxidative energy metabolism in the placenta? Can we measure this in real time?

• When does flow reduction, hypoxia, reperfusion lead to generation of ROS? Can we devise ongoing measures of oxidative stress?
In what other in vivo conditions is assessment of these pathophysiologic processes important?

- Cardiac conditions such as ischemic heart disease
- Cerebral hypoxia/ischemia; hypoxia/reperfusion injury
- Solid tumor development/progression
- Obesity, type 1 and type 2 diabetes mellitus

What methodologies and techniques are used in these conditions?
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Oxygen:

**With access to tissue:**
- **Physical:** Oximetry, near(mid)-infrared spectroscopy, electrodes, other physical probes
- **Chemical:** 2-nitroimidazoles

**With access to blood:**
- **Physical:** Electrodes, other physical probes,
- **Chemical:** microRNA, metabolomics

**No access:**
- **Physical:** MRS/\(^1\)H-lactate, fMRI/BOLD
- **Chemical:** MRS/\(^{19}\)F-fluorocarbons
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Glucose:

With access to tissue:
- Physical: Near-infrared spectroscopy, electroenzymatic
- Chemical: Phenylboronic acid, Concanavalin-A sensors

With access to blood:
- Physical: Electrodes, other physical probes,
- Chemical: microRNA, metabolomics, PBA/Con-A sensors

No access:
- Physical: MRS/\textsuperscript{1}H-lactate, glucoCEST,
- Chemical: PET, SPECT
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Conclusions

• It is currently impractical to screen for events which lead to placental metabolic disturbances in the absence of other clues such as prior history.

• By the time a pathology such as IUGR is detected clinically, it is probable that significant, irreversible (feto)placental damage has occurred.

• It is necessary to devise new methods of in utero assessment which will enable therapeutic intervention prior to the establishment of disease.