Mitochondrial DNA variants in individuals born after ART compared to spontaneously conceived peers

Children born after ART

- Lower birth weight
- Congenital abnormalities
- Cardiometabolic disorders
Mitochondrial DNA mutations

- Lower birth weight
- Cancer
- β-cell failure
- Epilepsy
- Neurilemmal neoplasms
- Atherogenesis
- Increase in cholesterol synthesis
- Ataxia
- Ischemia
- Ophtalmoplegia
- Myopathy
- Neuropathy
- Type 2 Diabetes
- Rapid ageing
- Pancytopenia
- Infertility
Controlled ovarian stimulation during oogenesis

**Cellular stress**
- Replication stress $\uparrow$
- mtDNA mutation rate $\uparrow$

**Recruitment of multiple follicles**
- Prevents dominant follicle
- Includes recruitment of ‘less fit’ oocytes with mtDNA mutations?

Shoubridge et Wai, 2007
CHILDREN BORN AFTER ART CARRY MORE VARIANTS IN THEIR MITOCHONDRIAL DNA AND AT A HIGHER LOAD
Material & Methods

**Blood**
- 116 ICSI
- 65 Control

**Placenta**
- 28 ICSI
- 27 Control

**Saliva**
- 107 IVF
- 6 Control

**Buccal swab**
- 63 Control
Homoplasmy versus Heteroplasmy

Homoplasmic variant
- 100%

Heteroplasmic variants
- 60%
- 40%
- 20%
Subhaplogroup U4 is over-represented in the ART group

* p=0.006
More unique variants in the ART group

* $p=0.0004$
Homoplasmy versus Heteroplasmy

- **Homoplasmy**
  - Homoplasmic variant: 100%

- **Heteroplasmy**
  - Heteroplasmic variants:
    - 60%
    - 40%
    - 20%

  = Cumulative load
Increased cumulative heteroplasmic load in the coding region in ART

Cumulative coding heteroplasmic load (%)

Combined heteroplasmic load in coding regions

p=0.0294
Increased cumulative heteroplasmic load in the coding region in ART
Increased cumulative loads seem to correlate with a lower birth weight
Maternal age doesn’t seem to correlate with a higher cumulative load.
Conclusion

• Subhaplogroup U4 is over-represented in the ART group: a link to maternal infertility?

• Increase in non-described homoplasmies:
  → mostly synonymous: origin?

• Increased cumulative coding heteroplastic variant load

• Higher cumulative load appears to correlate with lower birth weight

• Maternal age doesn’t seem to influence mtDNA variant load
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