

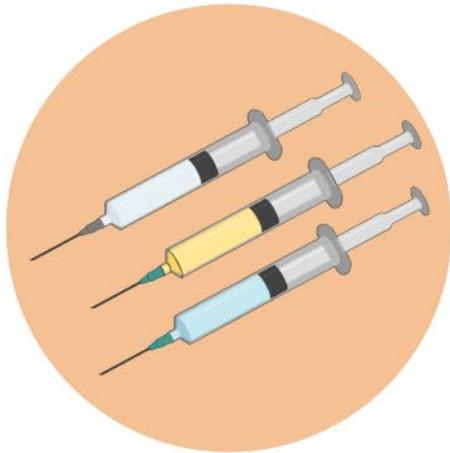


# Optimizing embryo culture media to prevent adverse outcomes induced by Assisted Reproductive Technologies

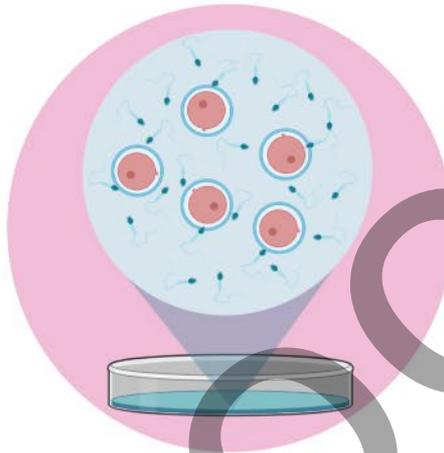
Lisa Vrooman, PhD | August 9, 2023

# Assisted Reproductive Technologies (ART)

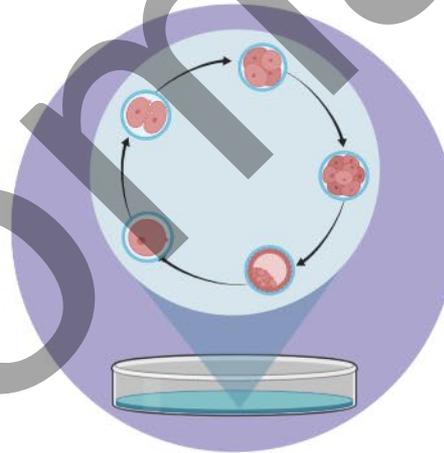
## BASIC ART PROCEDURE



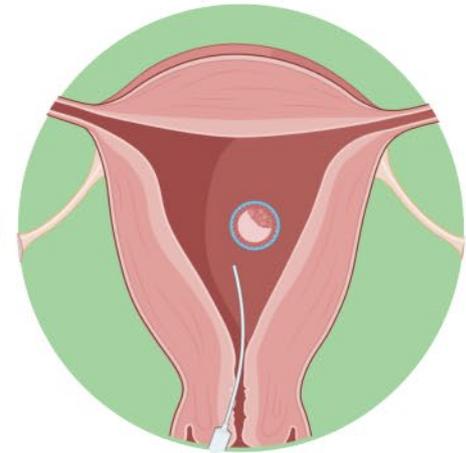
Hormone Stimulation  
(increase eggs)



IVF or ICSI  
(fertilization)



Embryo Culture  
(‘grow’ embryos)



Embryo Transfer  
(back to uterus)

# Current ART usage

Over 9 million ART children born worldwide (ESHRE, 2020)

ART use has more than doubled in the last decade (CDC, 2023)

According to the CDC, in the US:

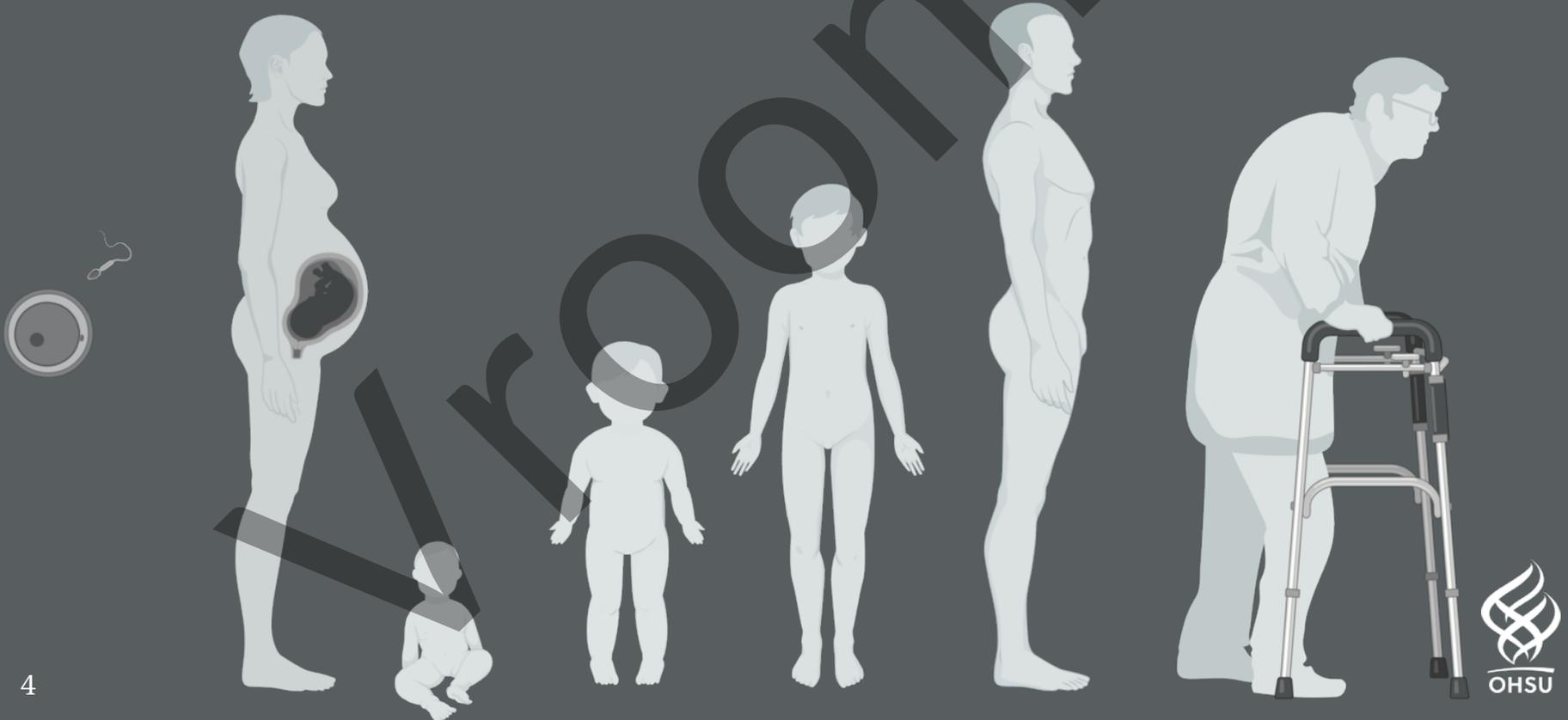
- ~ 450 ART clinics
- ~414,000 ART cycles/year (2021)
- ~167,000 were egg or embryo banking cycles
- ~97,000 ART children born/year
- 2.3% of all infants born are via ART



[www.freepik.com](http://www.freepik.com)

# Developmental origin of health and disease (DOHaD)

- Research demonstrating the link between maternal, perinatal, and early childhood factors and risk on non-communicable diseases
- Are ARTs a critical window of 'exposure'?



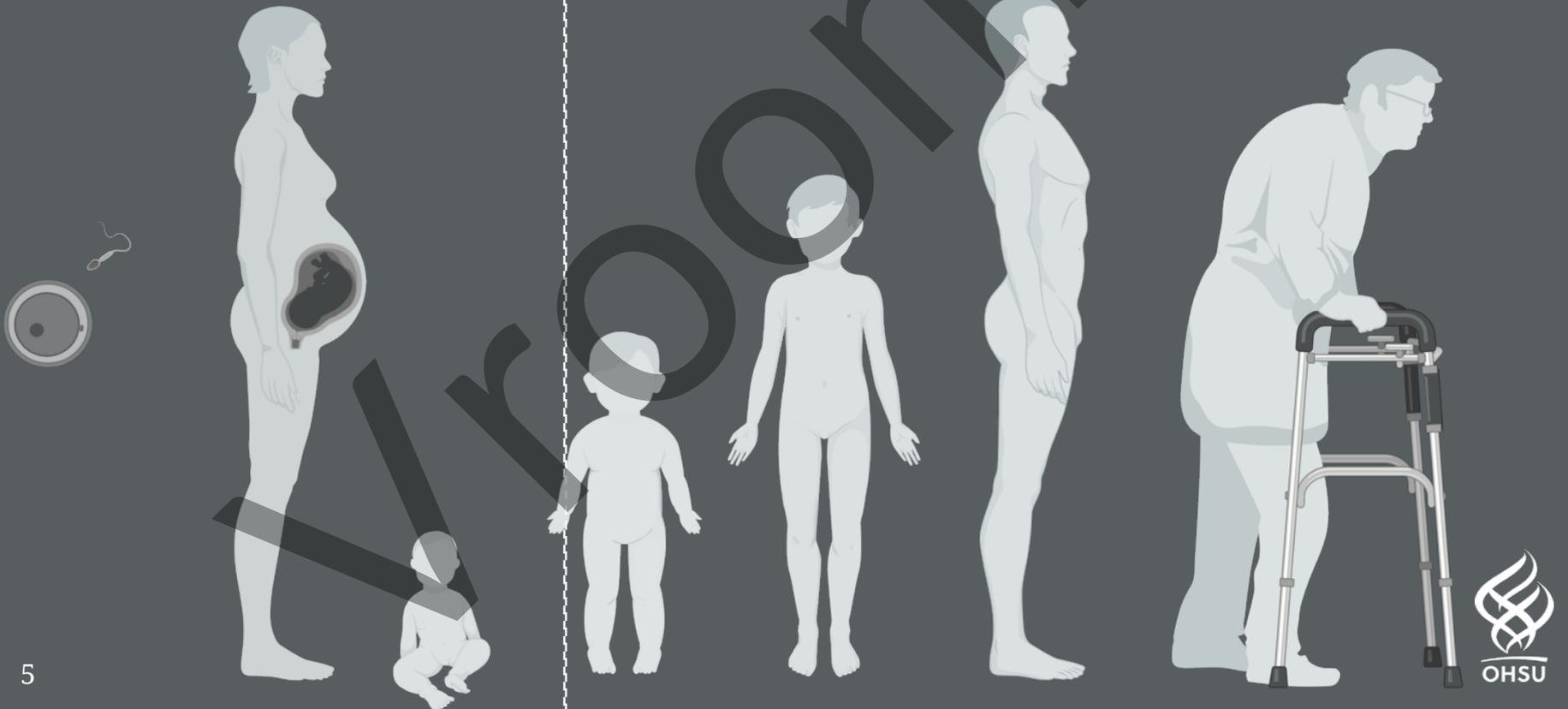
# Developmental origin of health and disease (DOHaD)

## SEVERE

- Infertility
- Pregnancy loss
- Congenital abnormalities

## MILD

- Relatively normal postnatal development
- Risk for chronic diseases later in life
- Directly affect fetus or indirectly affect fetus via placenta



# What are the problems associated with ART?

**Human ART pregnancies are associated with:**

- miscarriage/stillbirth
- perinatal mortality
- imprinting disorders
- low and high birth weight
- abnormal placentation
- preterm birth
- preeclampsia

**Animal Models of ART**

- ✓ embryonic loss
- ✓ imprinting disorders
- ✓ low and high birth weight
- ✓ abnormal placentation



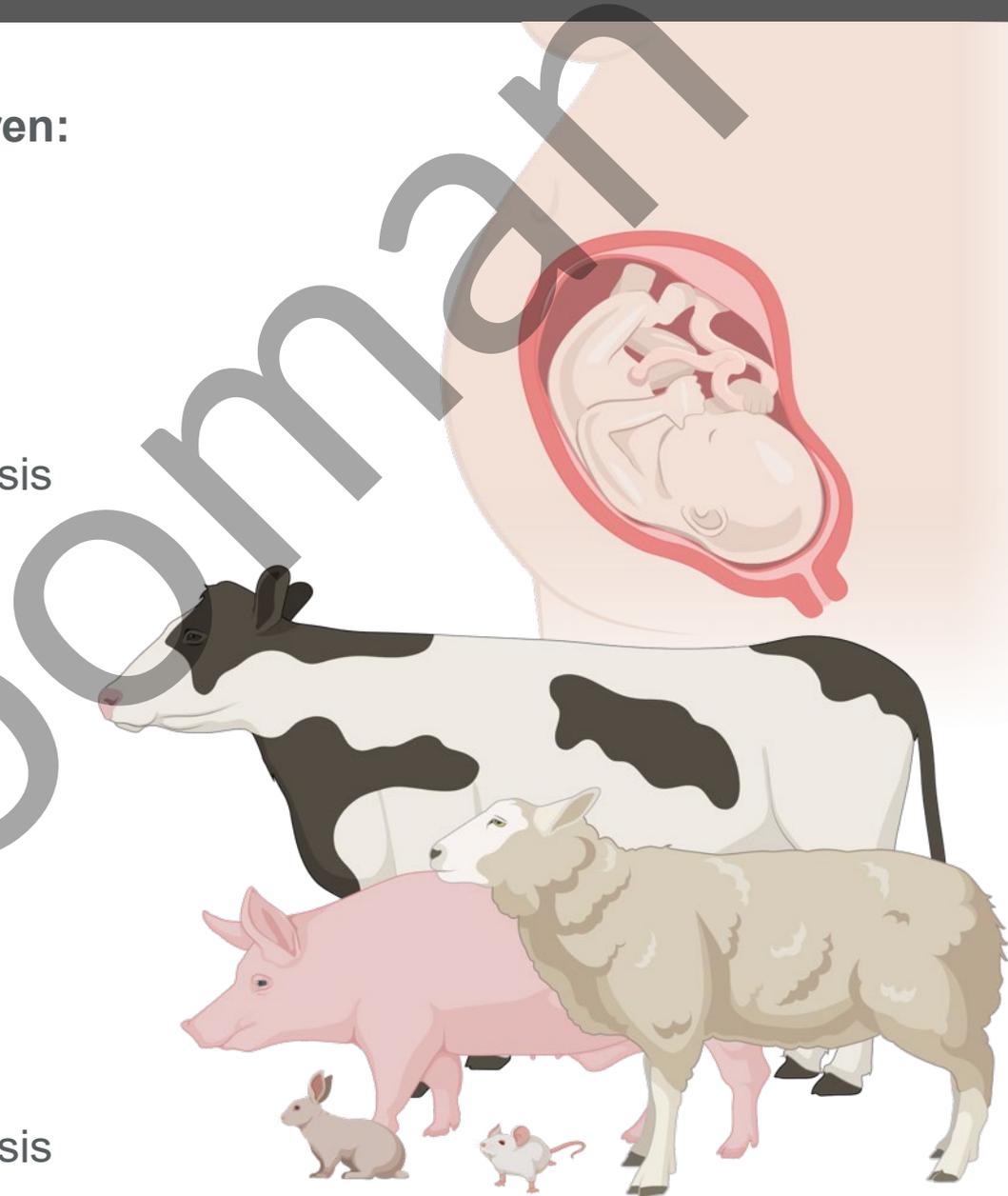
# What are the problems associated with ART?

## Postnatal outcomes in ART children:

- increased blood pressure
- vascular differences
- increased adiposity
- hyperlipidemia
- impaired glucose homeostasis

## Animal Models of ART

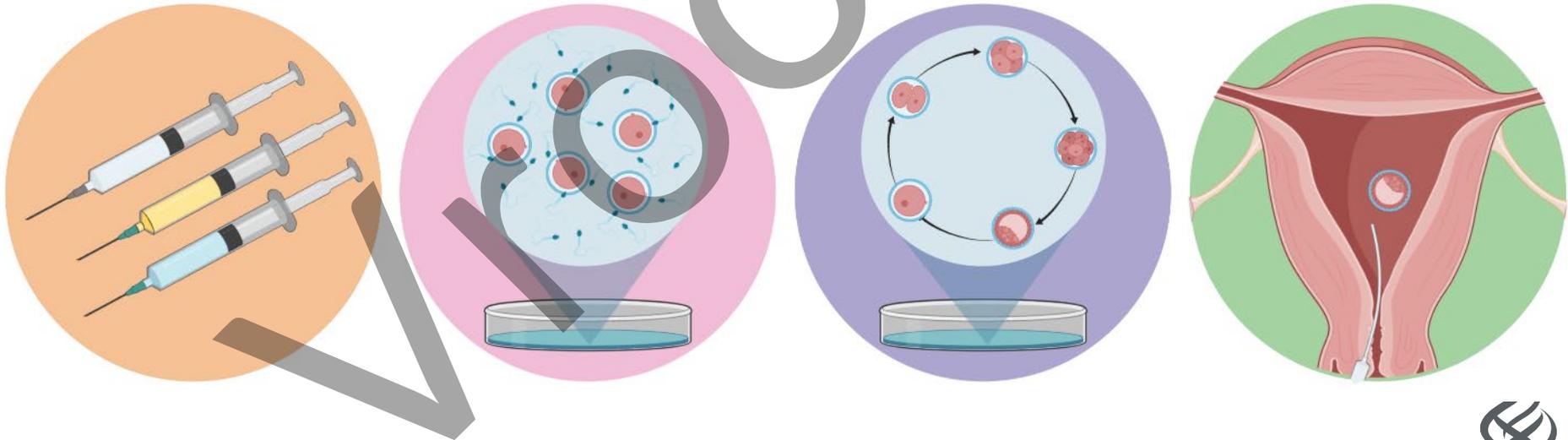
- ✓ increased blood pressure
- ✓ vascular differences
- ✓ increased adiposity
- ✓ hyperlipidemia
- ✓ impaired glucose homeostasis



# What could be causing adverse effects?

*In-vivo* vs *in-vitro* exposures:

- hormone exposure
- mechanical stress
- temperature
- oxygen levels
- culture media and conditions



# Reactive oxygen species

## Reactive molecules derived from molecular oxygen

- natural byproducts of cell respiration and enzyme reactions

## Too much, causes damage to:

- cellular lipids
- organelles
- DNA
- enzymes

ROS



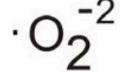
Oxygen



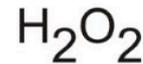
Superoxide anion



Peroxide



Hydrogen Peroxide



Hydroxyl radical

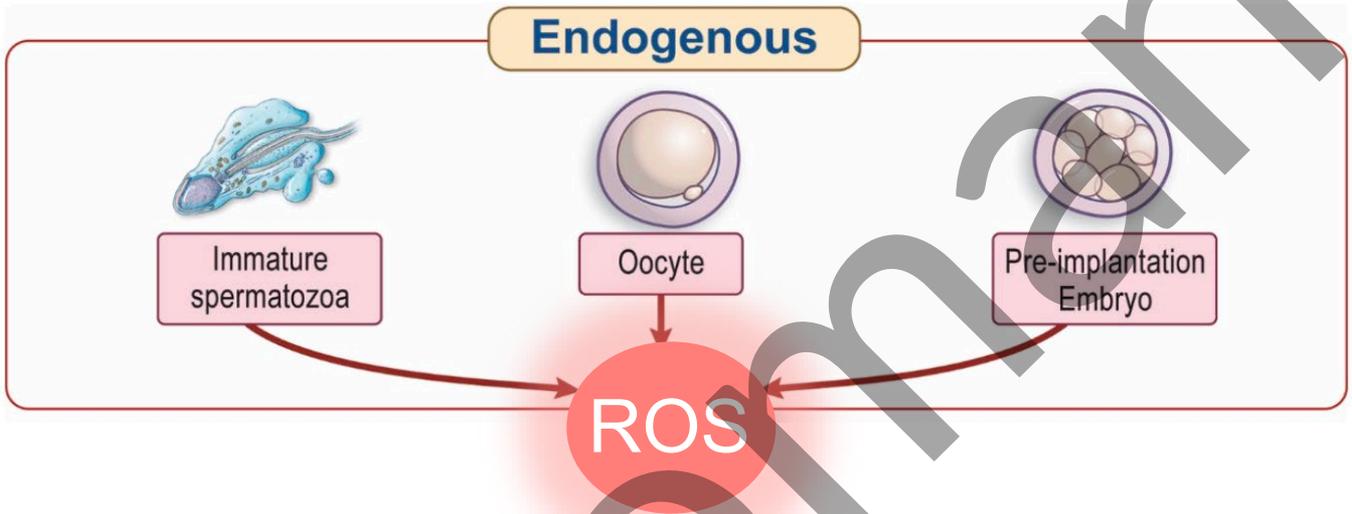


Hydroxyl ion



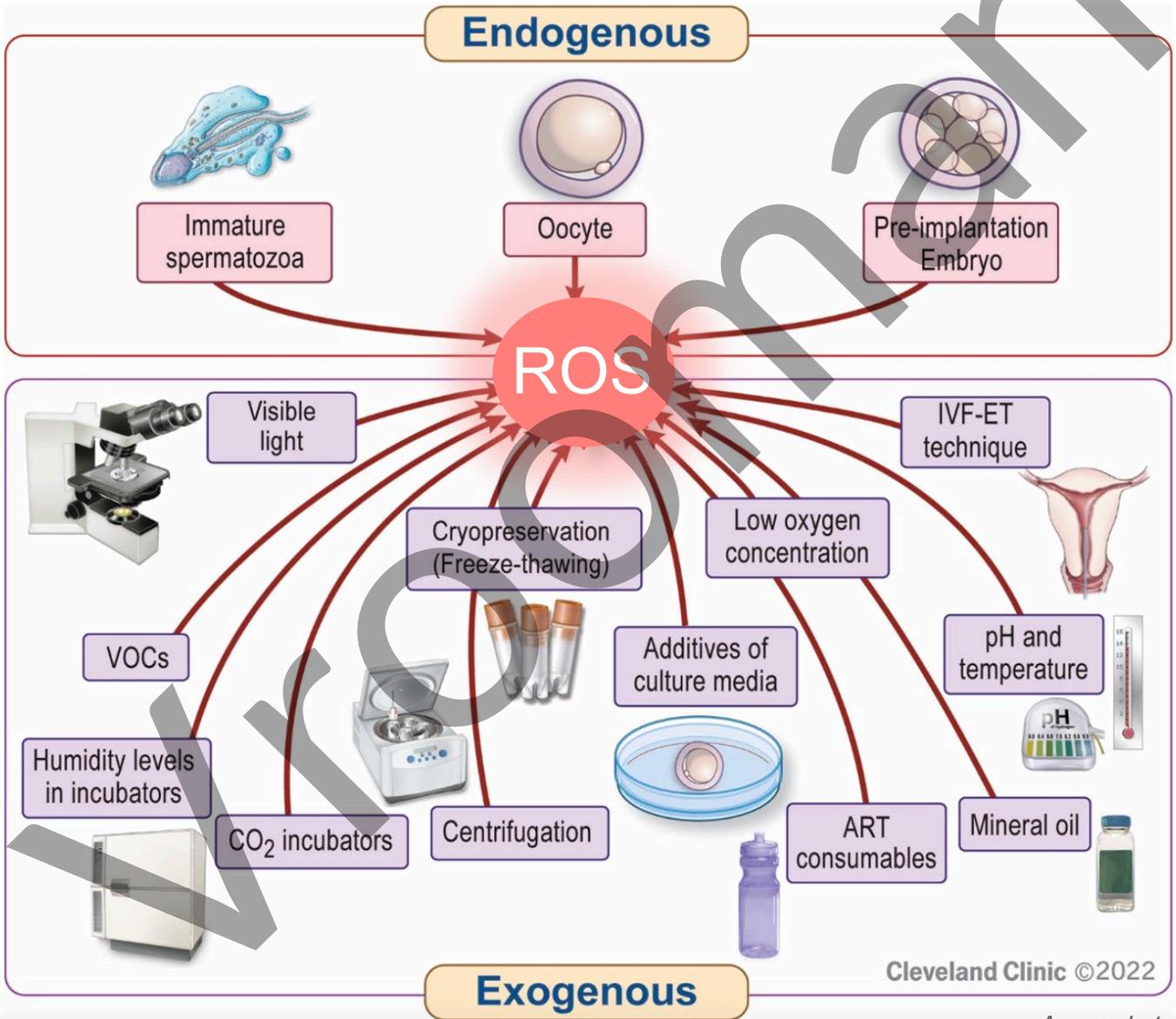
[www.agilent.com](http://www.agilent.com)

# Reactive oxygen species



Vroonman

# Reactive oxygen species



Cleveland Clinic ©2022



# Can effects be prevented with antioxidant treatment?

Cells in the body normally deal with ROS with:

- enzymes
- antioxidant molecules

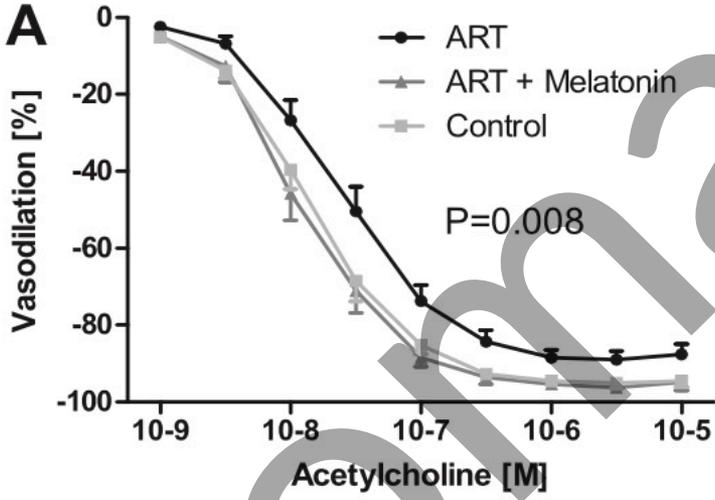
Several antioxidants have been tested for protective effects in embryo culture

- glutathione
  - vitamin C
  - acetyl-L-carnitine
  - N-acetyl-L-cysteine
  - alpha-lipoic acid
  - melatonin
- } 'A3'





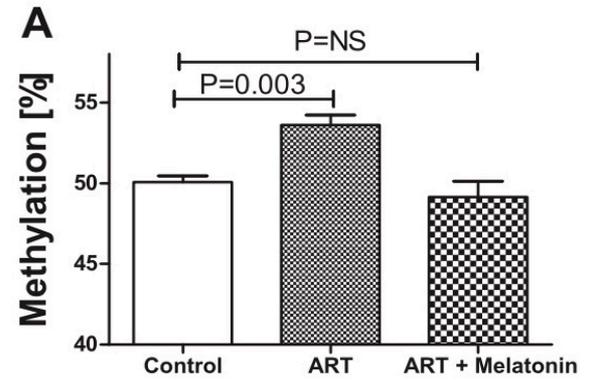
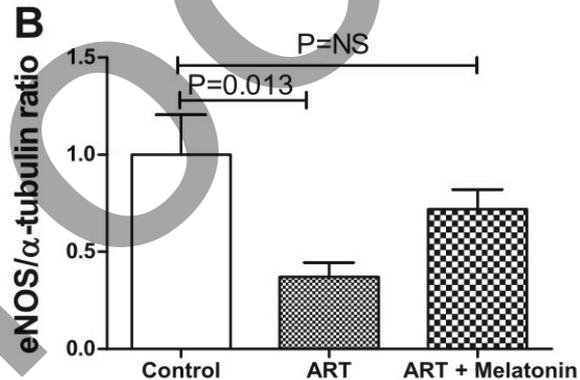
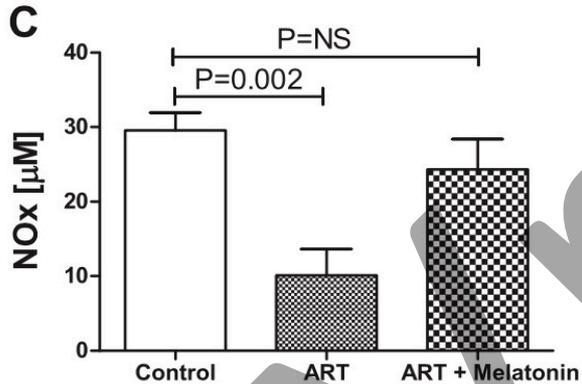
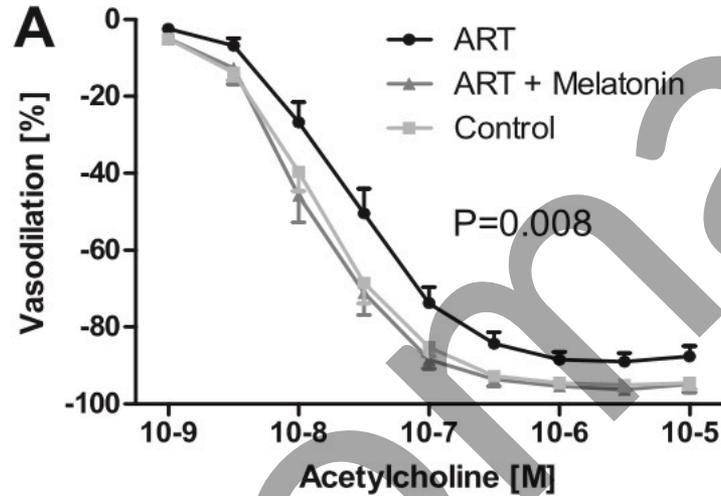
# Melatonin supplementation improves vascular outcomes



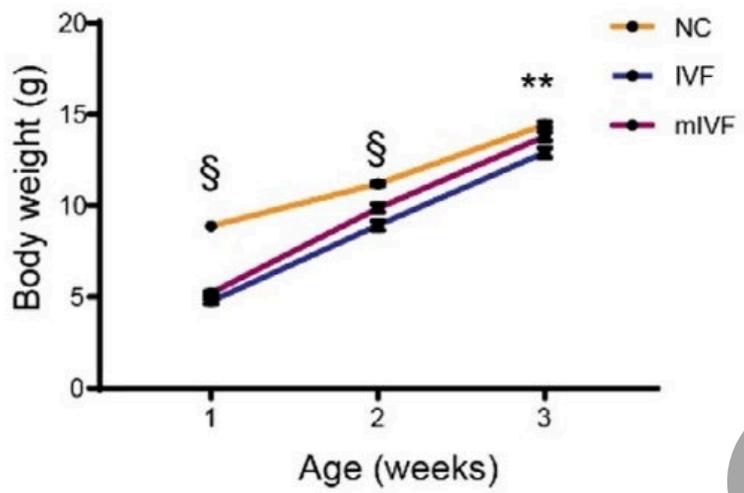
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# Melatonin supplementation improves vascular outcomes



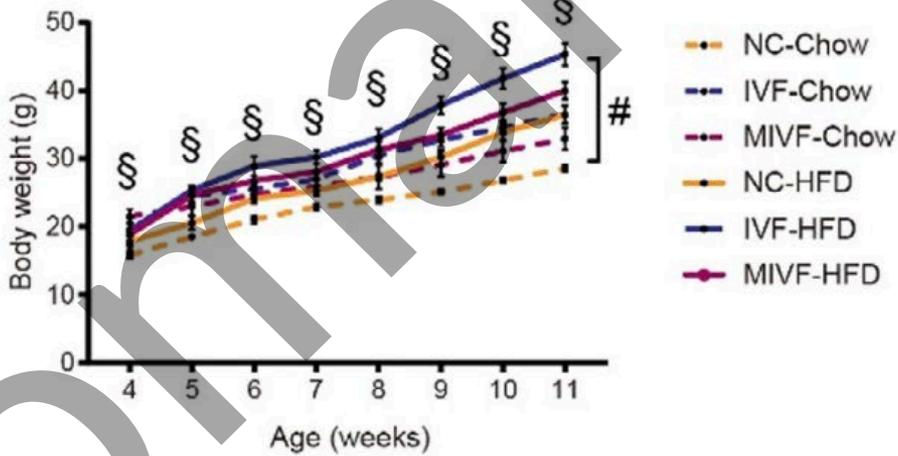
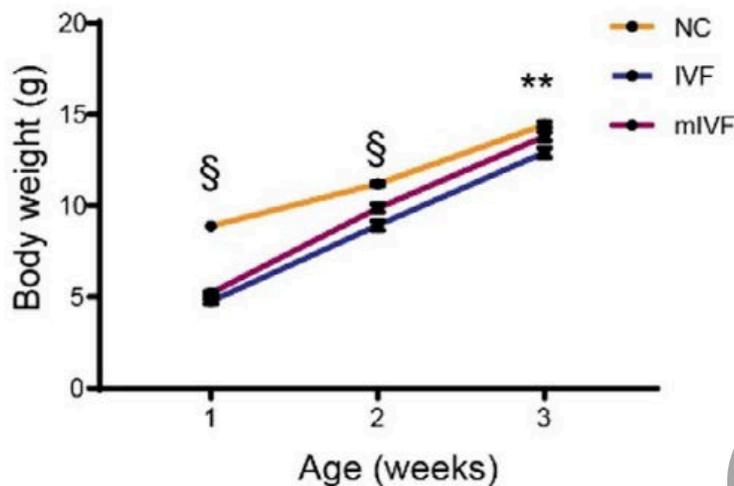
# Melatonin supplementation improves metabolic outcomes



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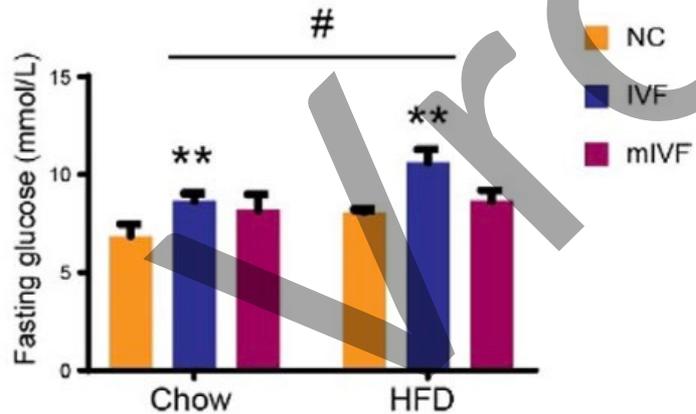
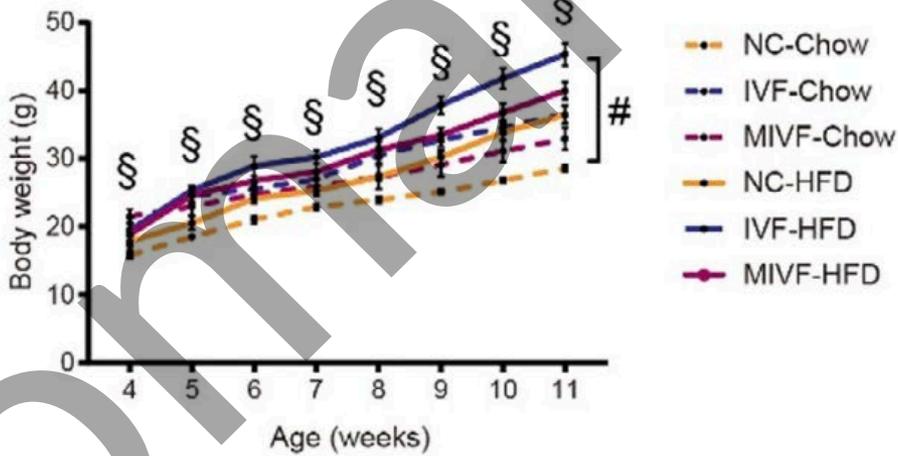
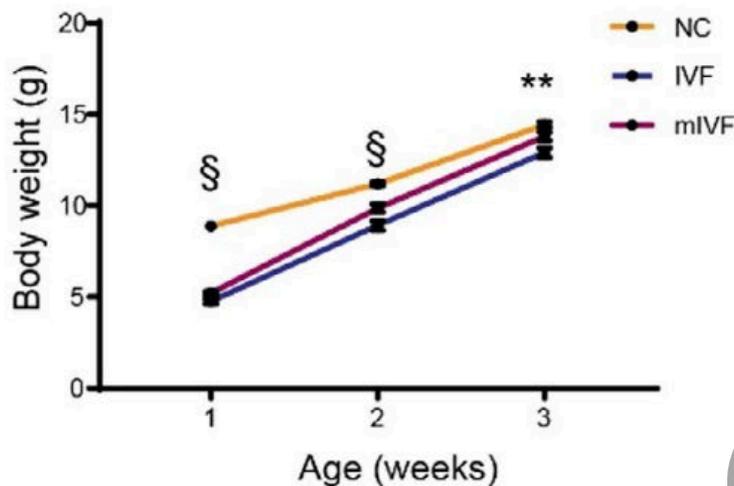


# Melatonin supplementation improves metabolic outcomes

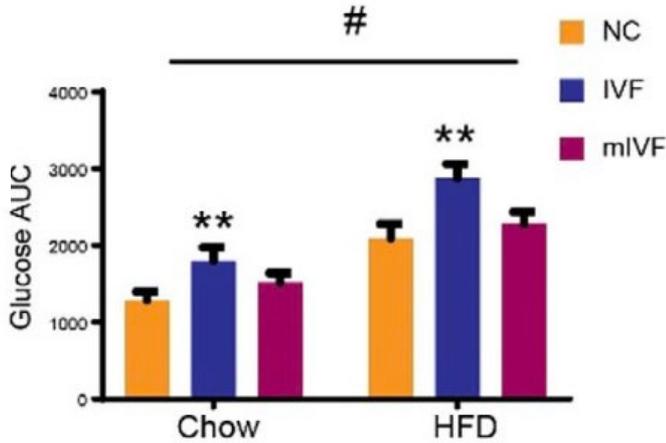
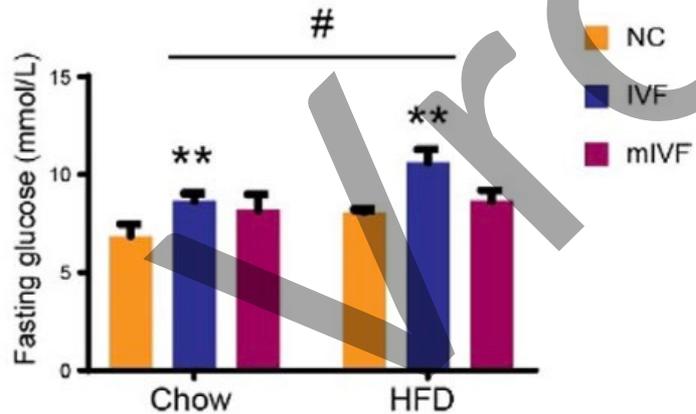
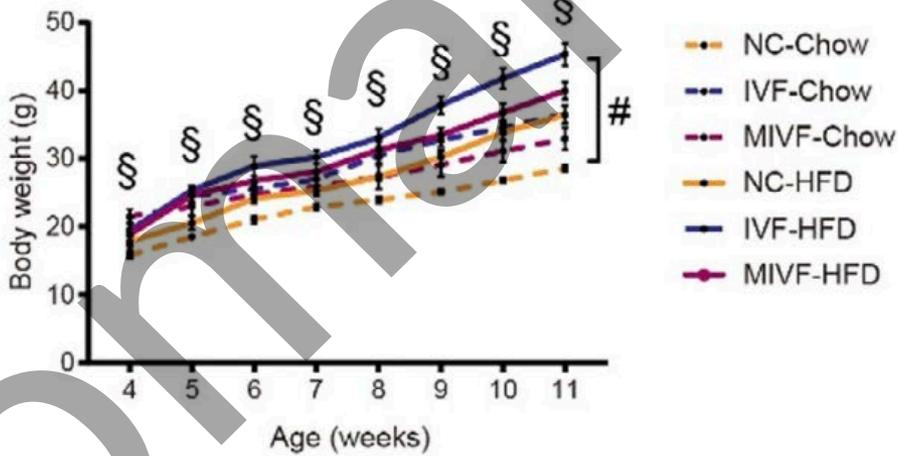
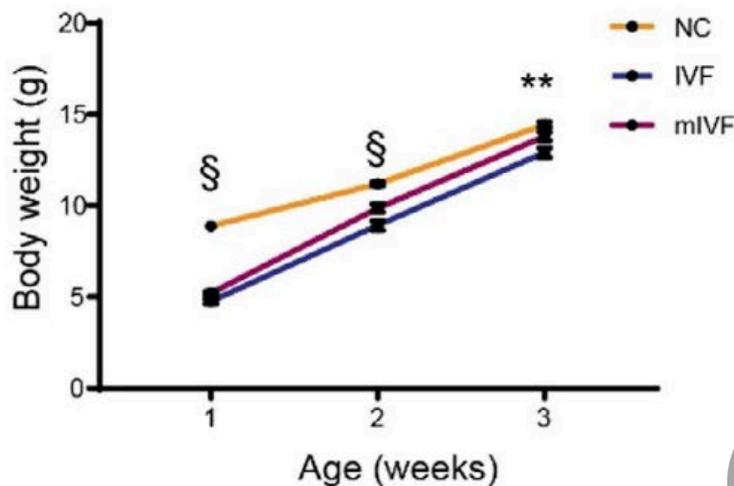


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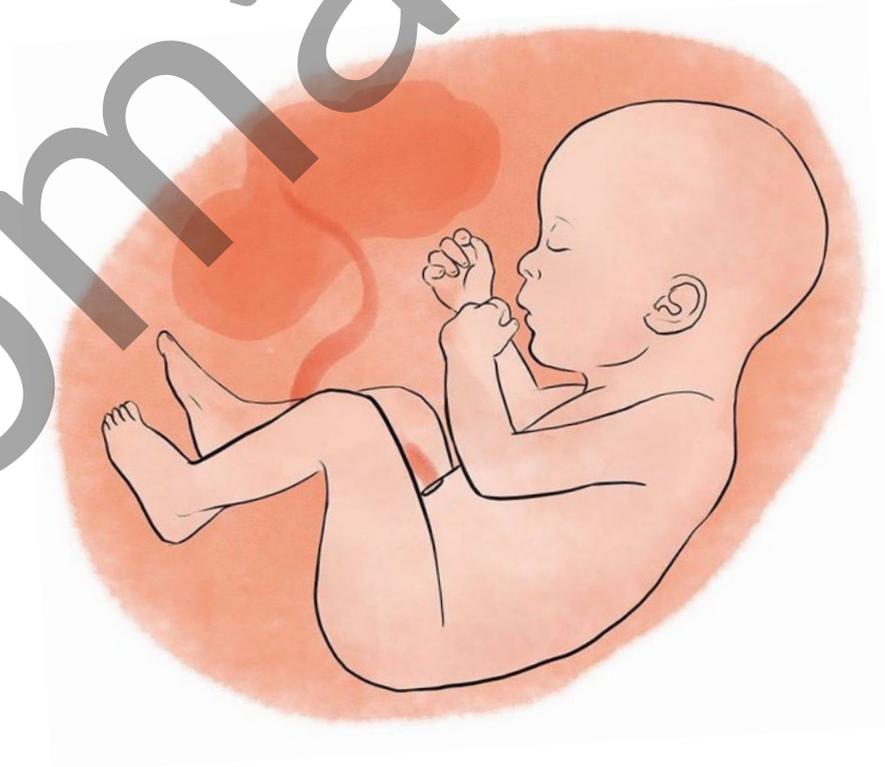


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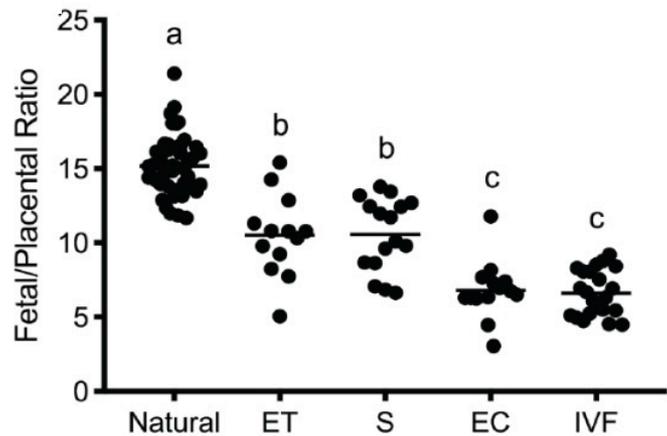


# The potential role of the placenta in ART effects

**Postnatal cardiometabolic effect may be due to impaired placental development and function**

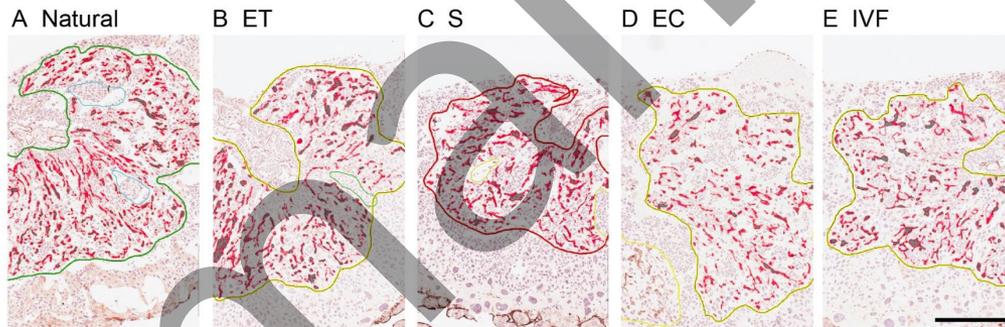
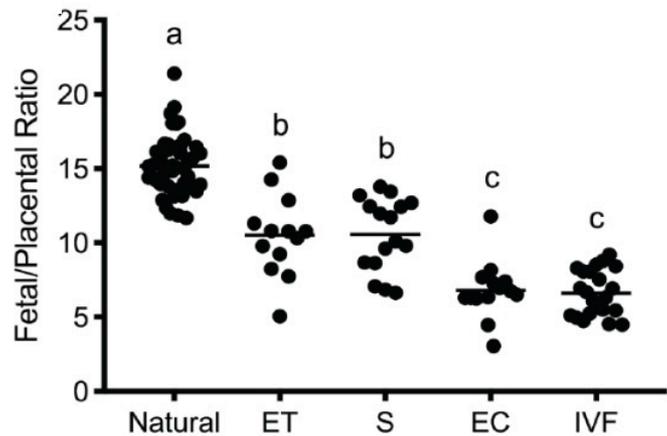


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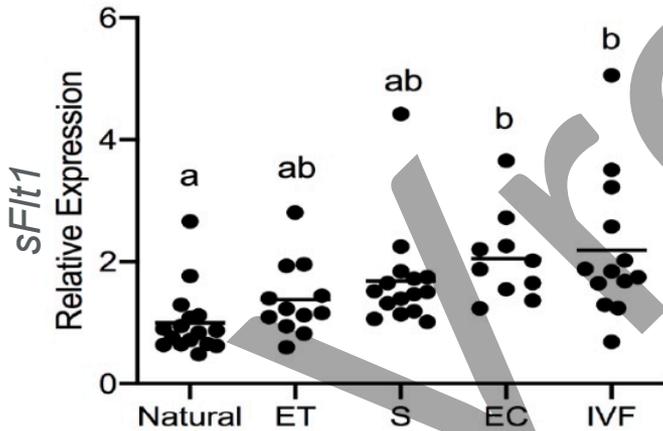
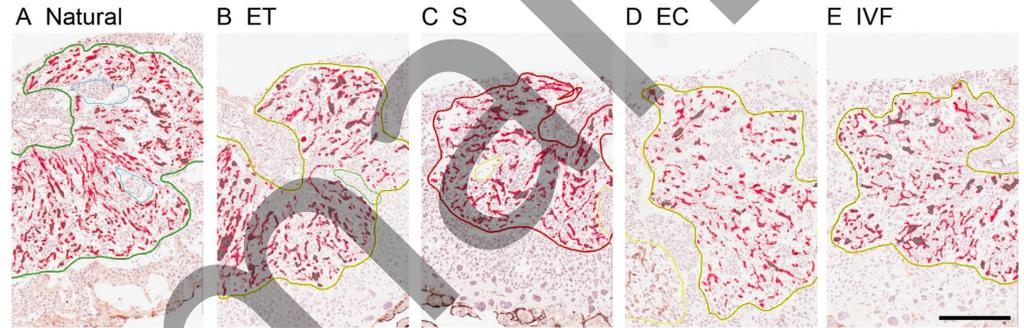
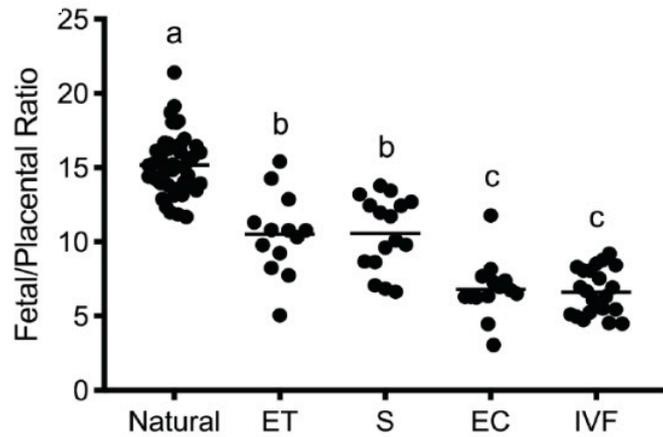
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# The potential role of the placenta in ART effects

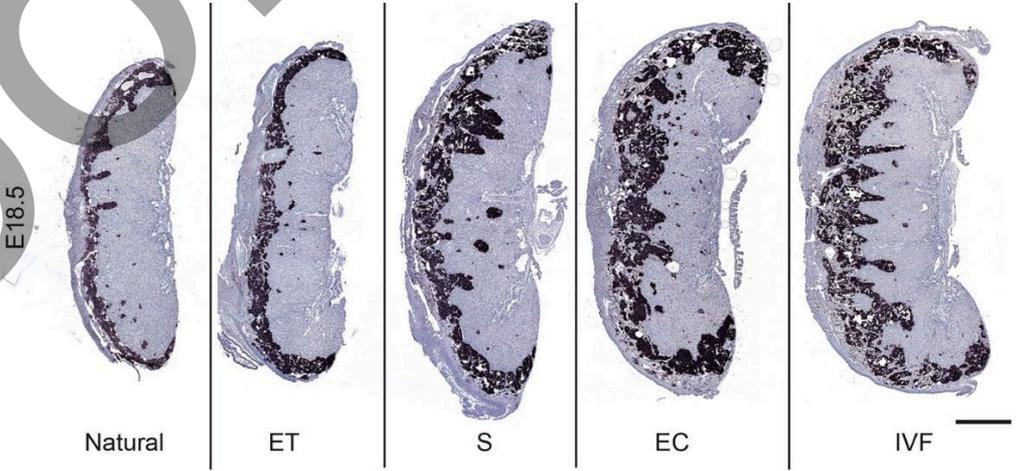
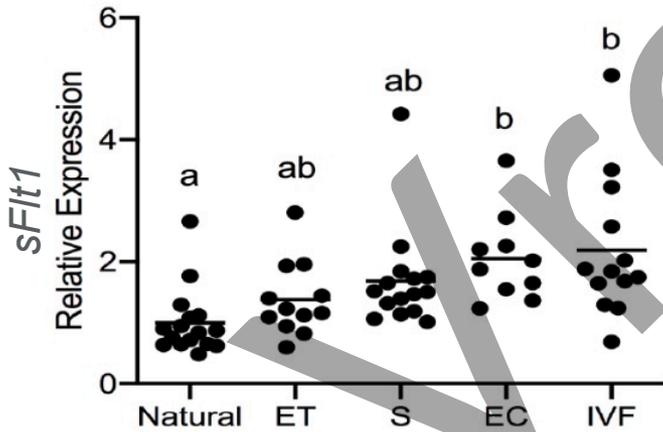
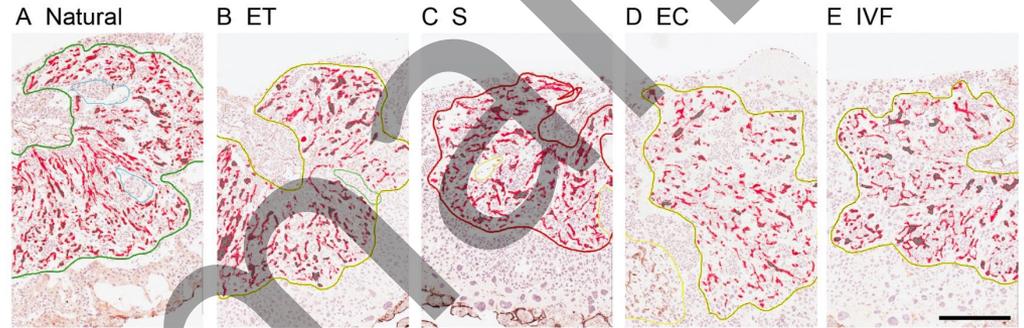
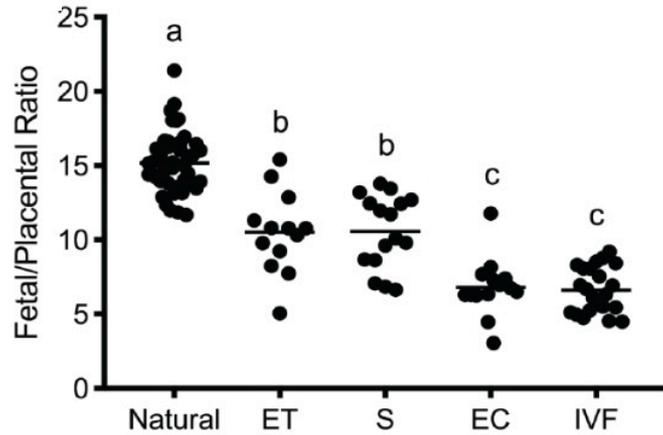


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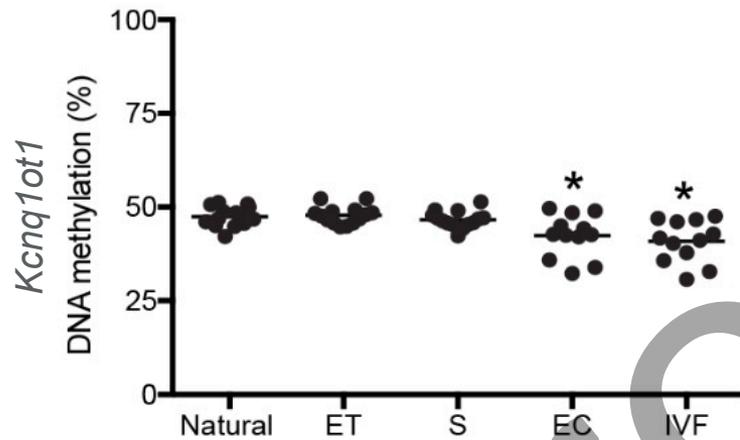
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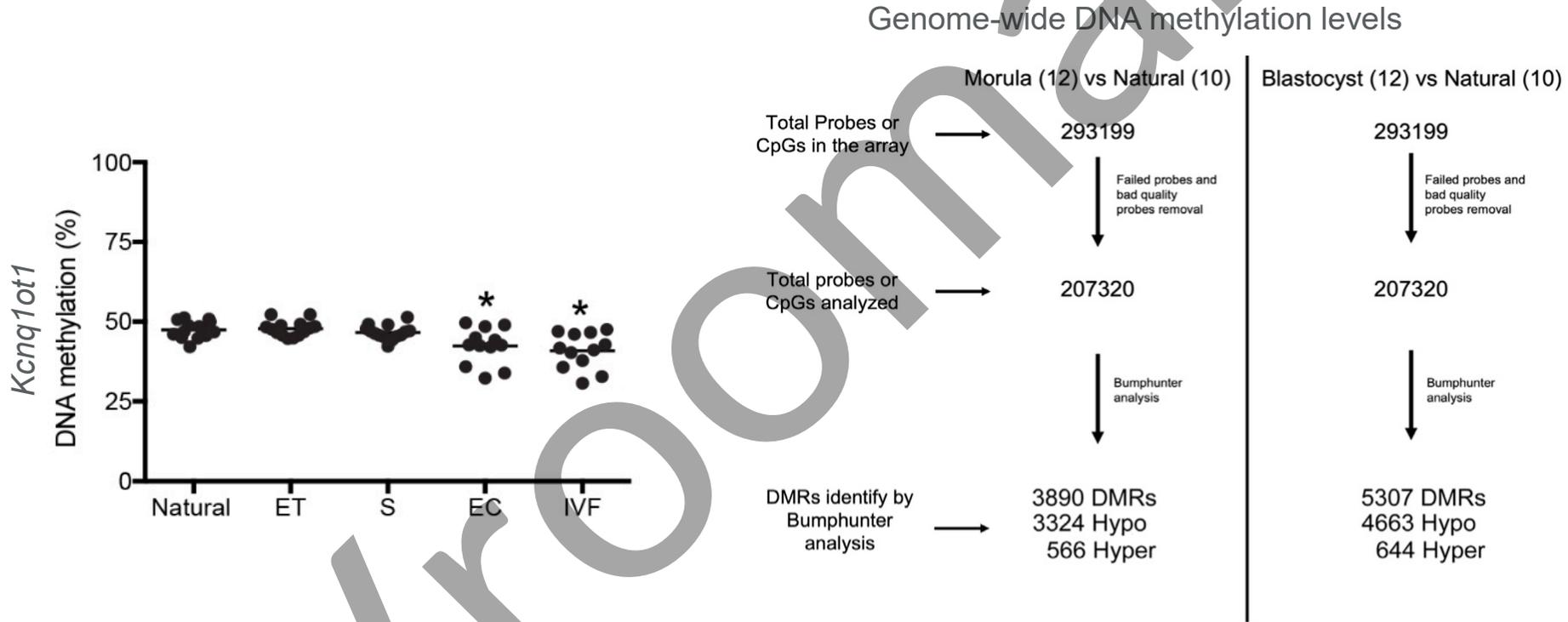
# The potential role of the placenta in ART effects



# The potential role of the placenta in ART effects



# The potential role of the placenta in ART effects



# The potential role of the placenta in ART effects

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# Summary

- ART is a widely used medical intervention that has the potential to cause pregnancy complications and adverse long-term health outcomes
- Reactive oxygen species impairing placentation might be a root cause of these adverse effects
- Culture media supplementation with antioxidants has shown potential benefits
- More research is needed to ensure culture additives are safe



Thank You