

# **The tenth RCCN workshop**

## **Nutrition and Aging Biology**

**San Francisco, CA, June 25-26, 2024**

# **Metabolic adaptations in adult baboons exposed to maternal nutrient reduction during development**

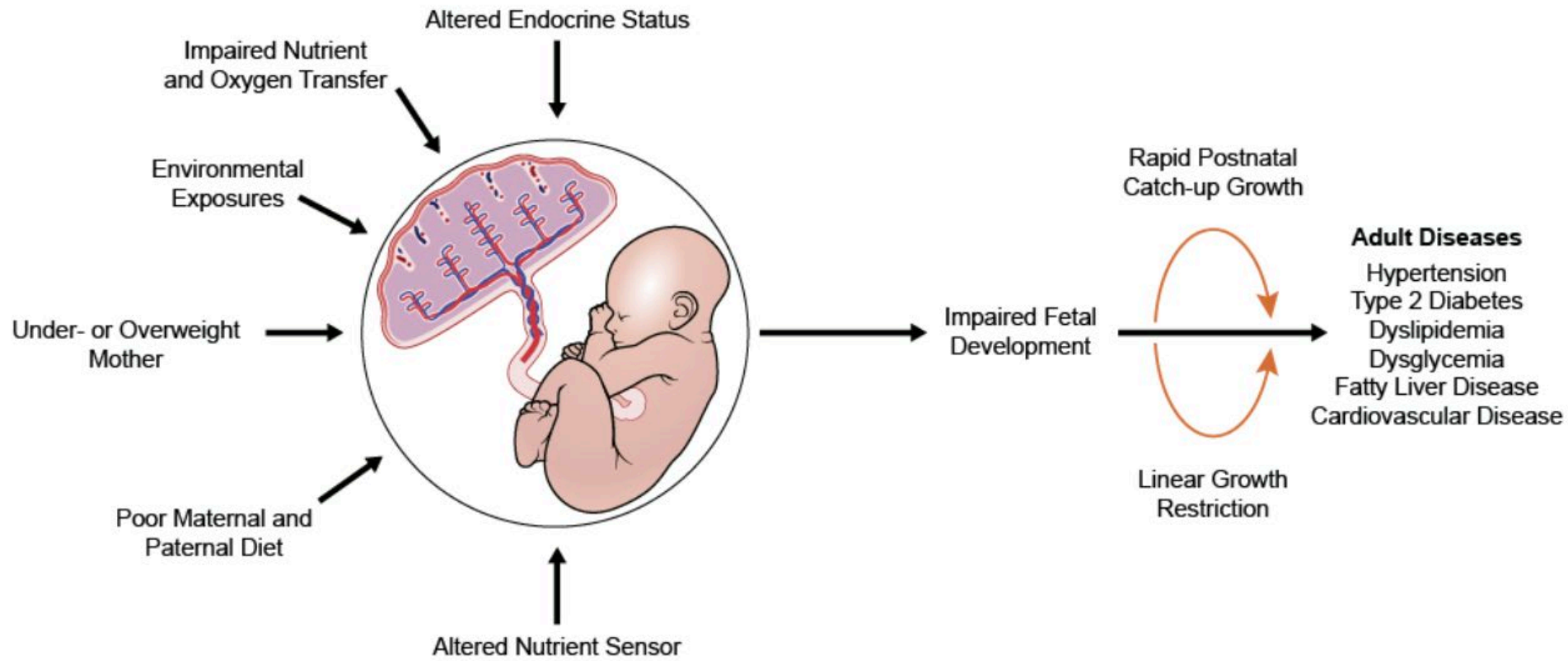
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Postdoctoral Research Fellow

# Developmental origins of health and diseases theory

## (Developmental programming)

Environmental exposures during early life (particularly the in-utero period) can permanently influence health and vulnerability to disease in later life.

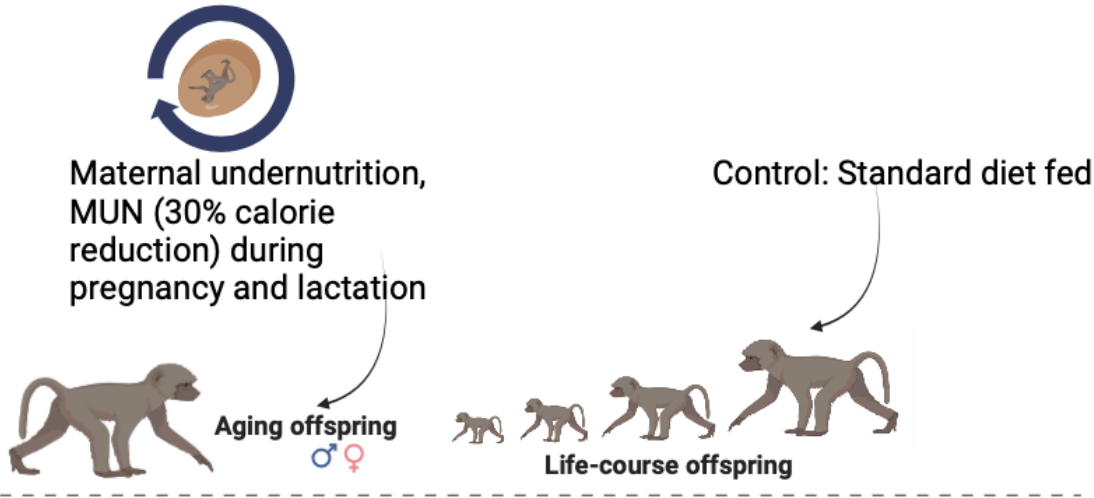


# Developmental programming alters aging trajectory

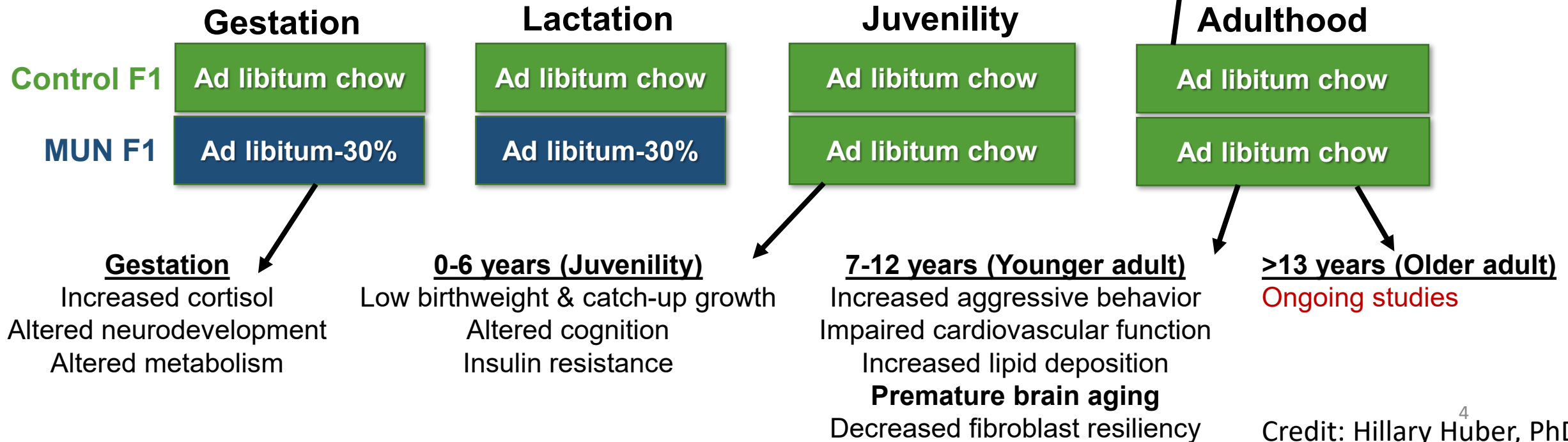


The metaphor of an automobile with suboptimal components

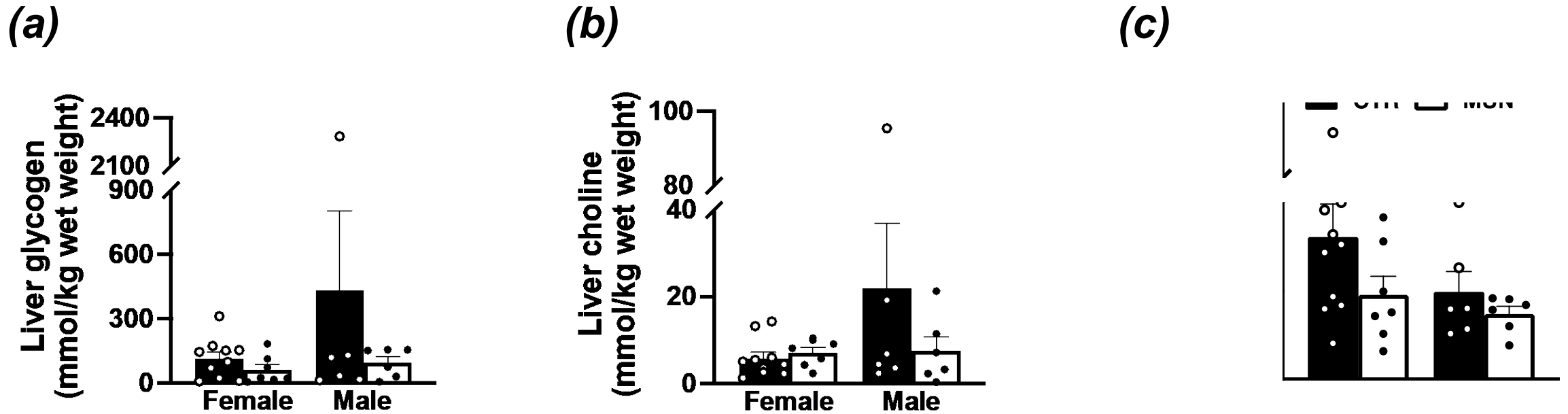
# Developmental programming model in Baboons



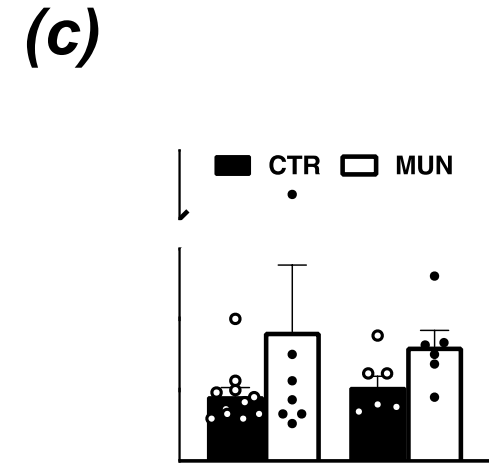
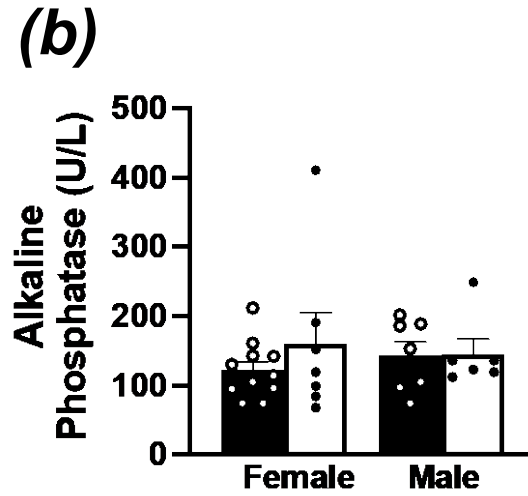
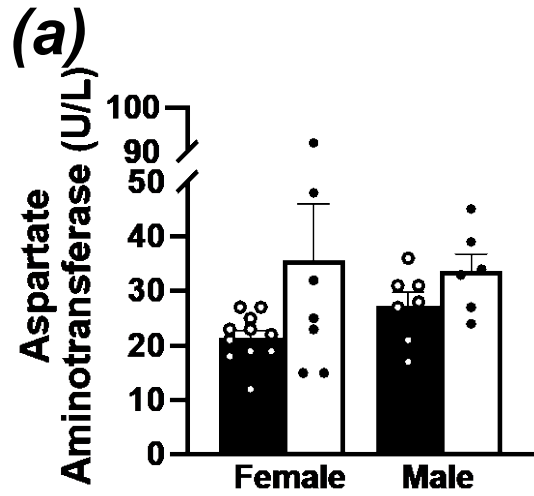
**>13 years (Older adult)**  
 Changes in steroid production in the hypothalamo-pituitary-adrenal axis  
 Changes to mitochondrial bioenergetics and cellular resilience  
 Molecular changes to liver and brain  
 Decline in walking speed



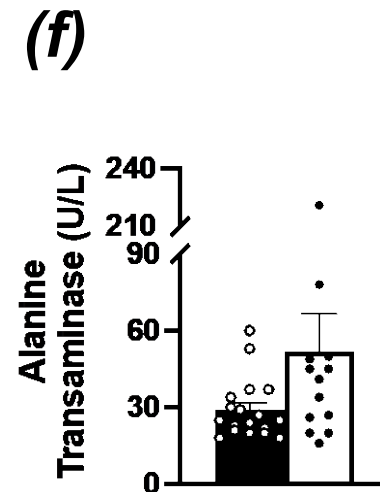
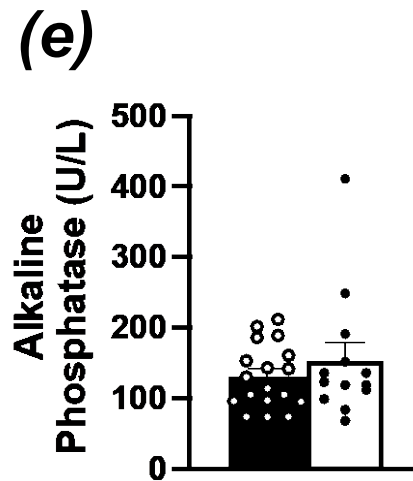
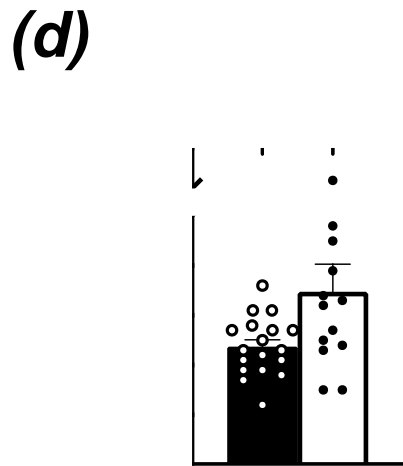
# Maternal undernutrition did not affect liver metabolites in adult baboons



# Plasma liver enzymes were largely unaffected by maternal undernutrition in adulthood



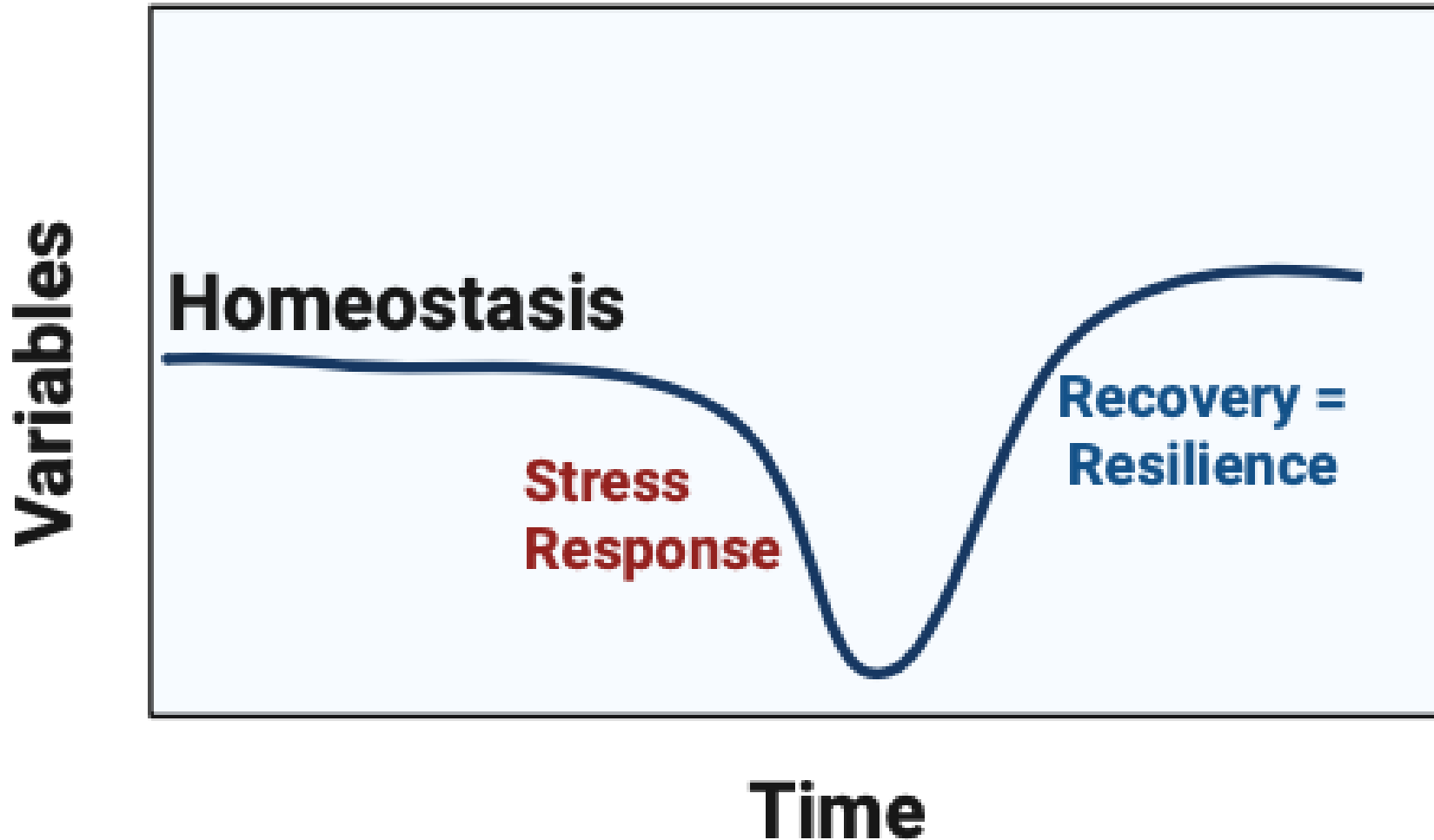
Male and Female combined



Average age 15 years, human equivalent 60 years

# Is developmental programming coupled to resilience?

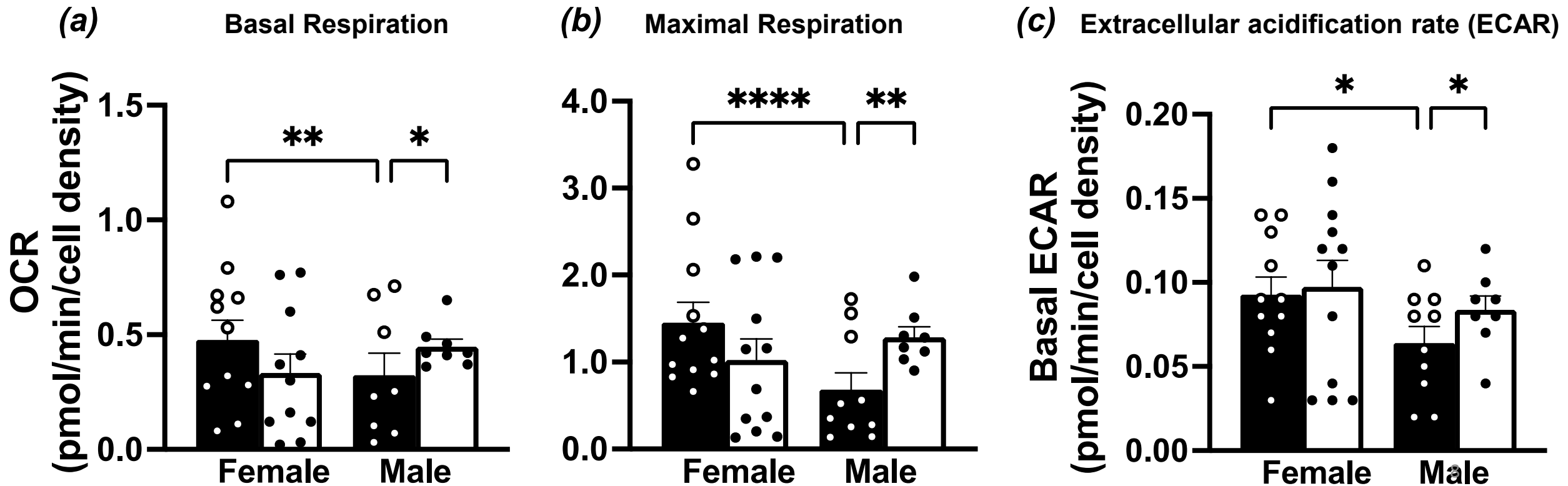
(Fetal adaptation for survival)



# Mitochondrial bioenergetics as a measure of resilience

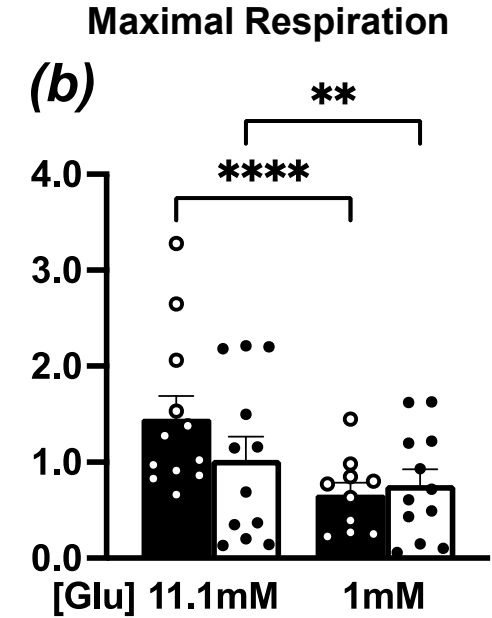
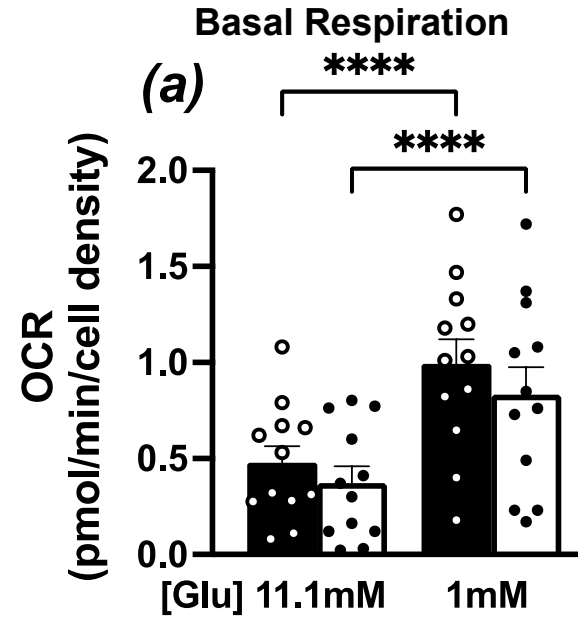


Seahorse Bioenergetics

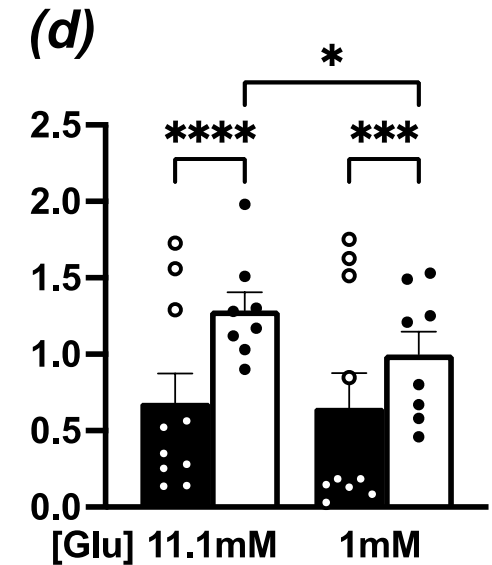
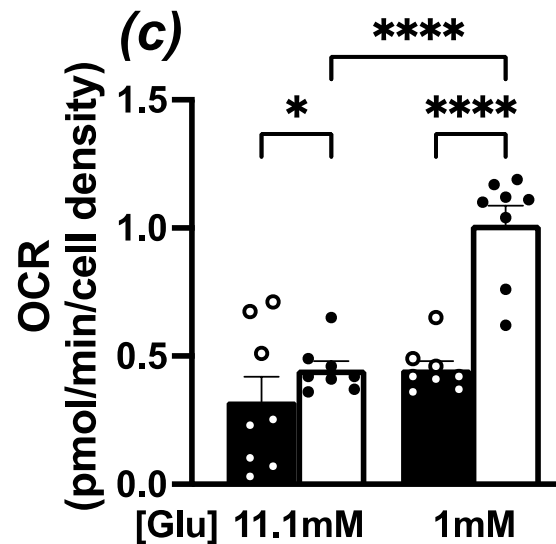


# Hepatocyte bioenergetics in response to low glucose challenge

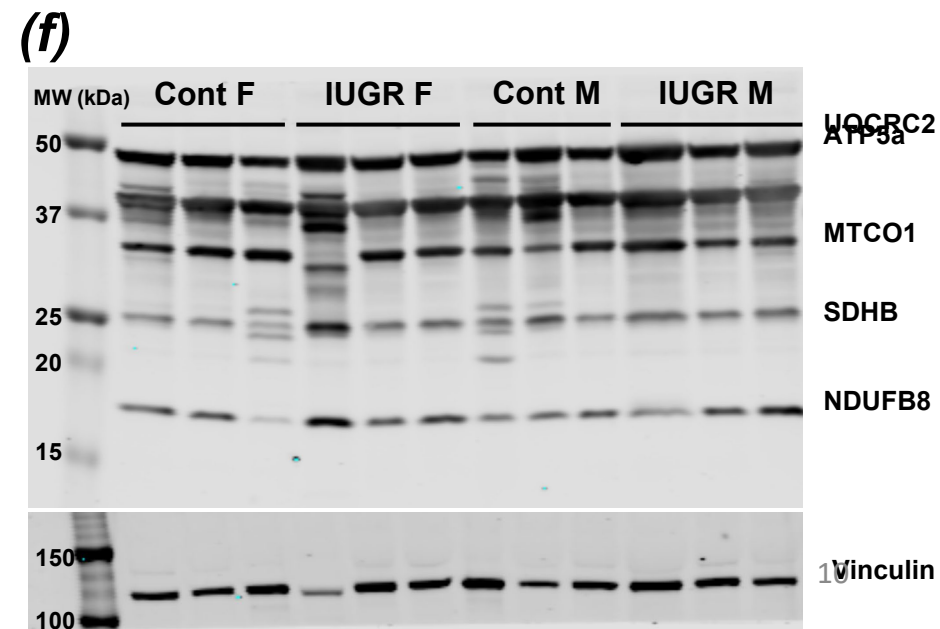
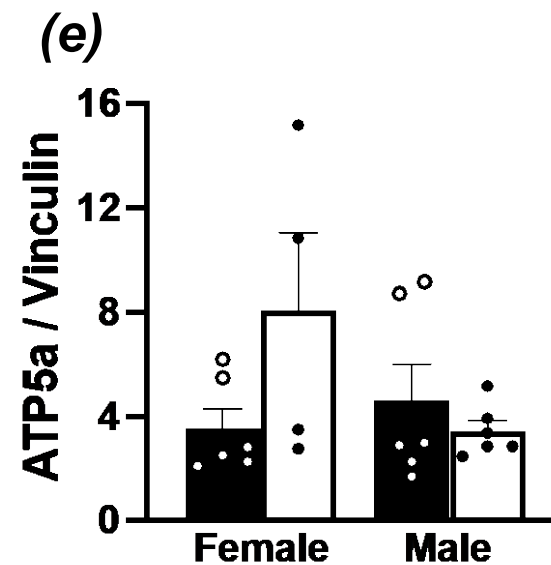
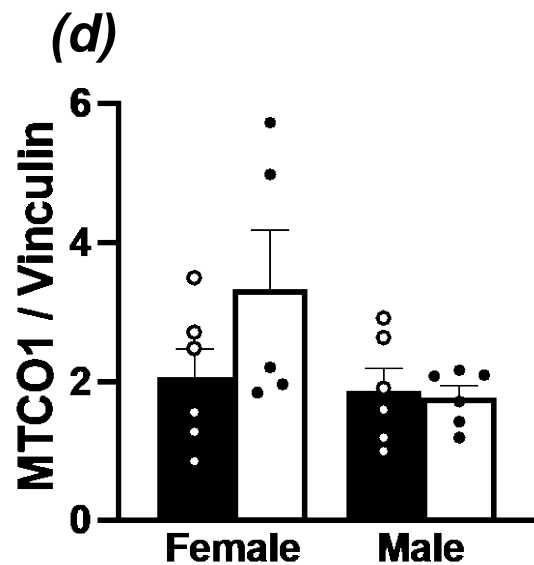
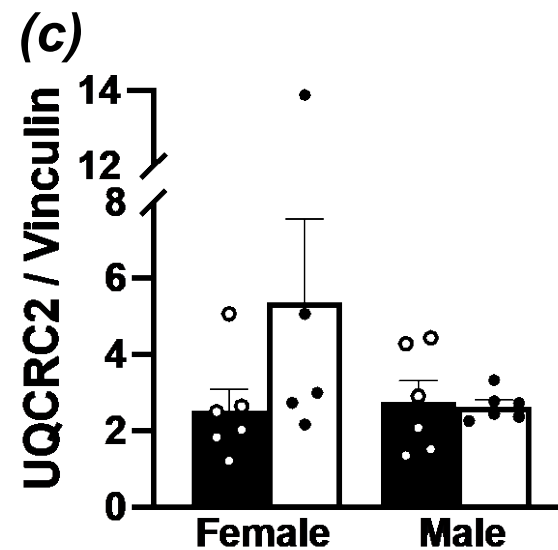
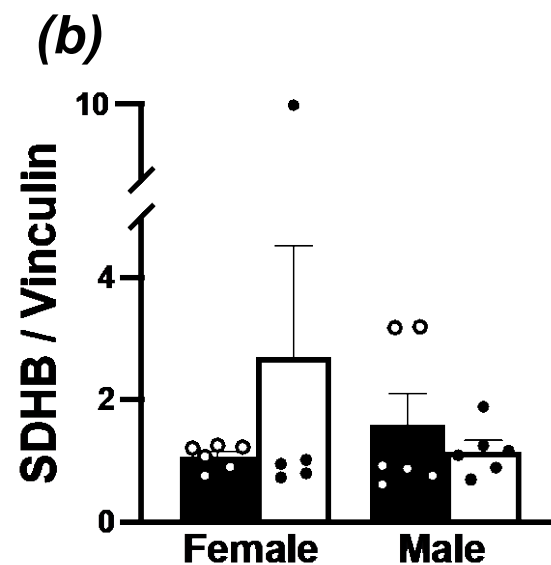
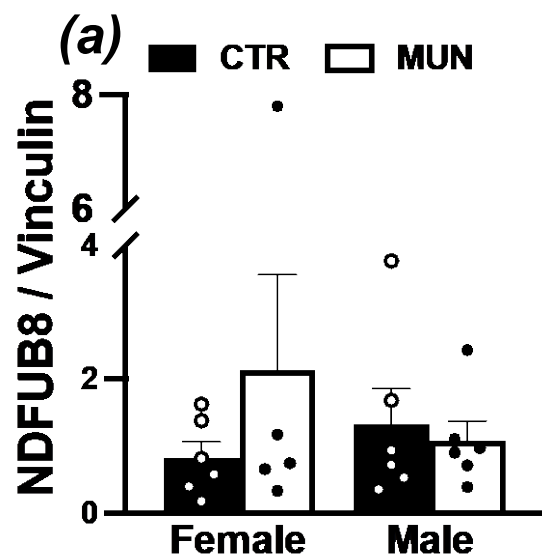
Female



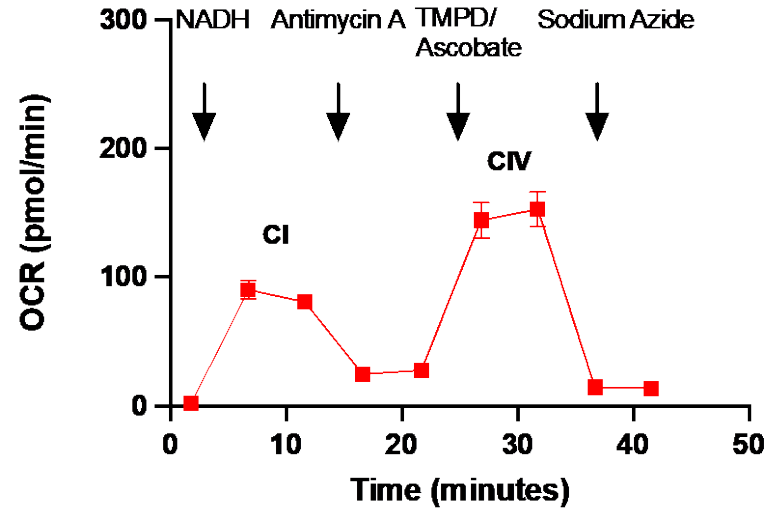
Male



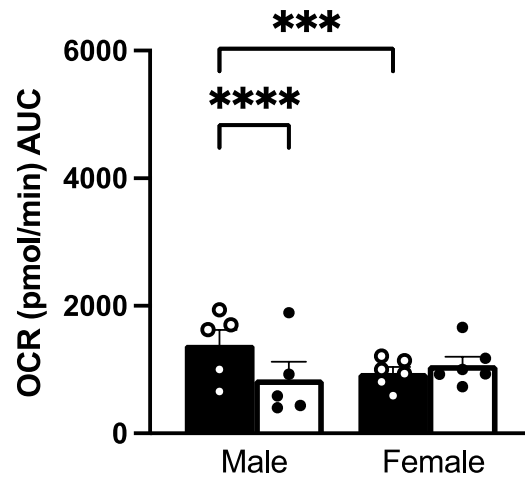
# Differences in mitochondrial bioenergetics are not due to mitochondrial content differences



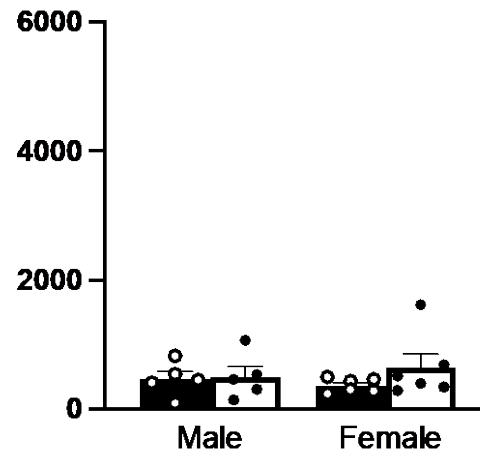
# Electron transport chain (ETC) complexes I- IV activity in control and IUGR baboon liver



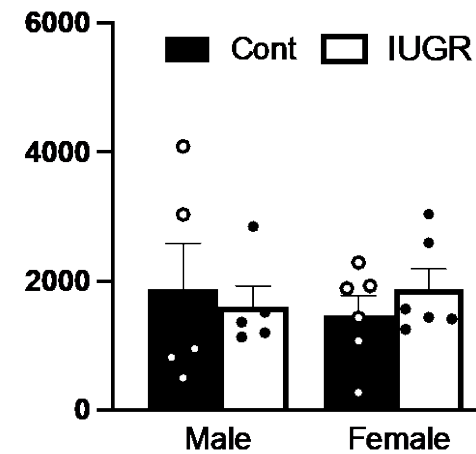
Complex I



Complex II

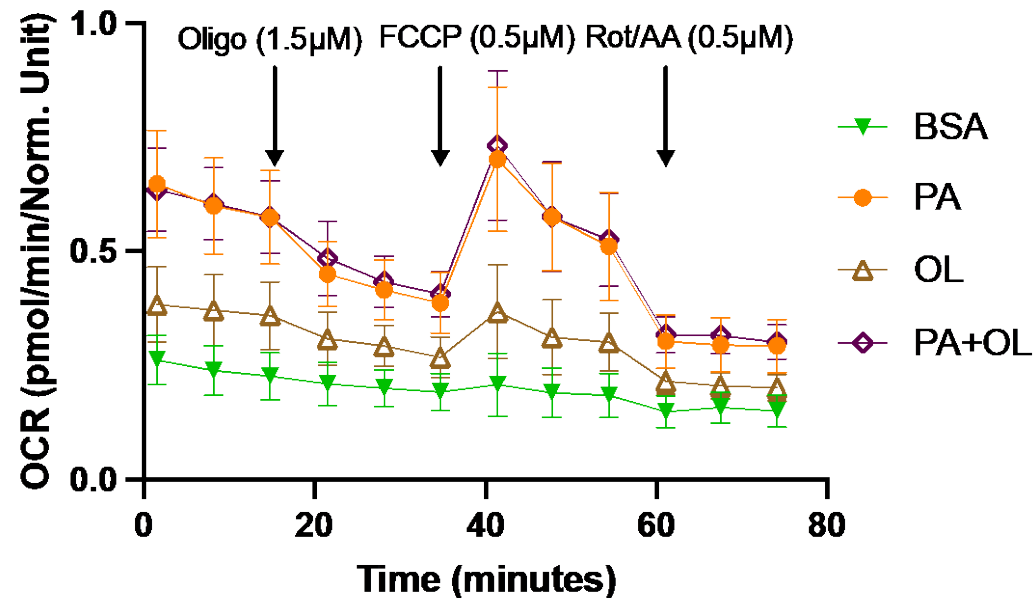


Complex IV



# Will fatty acid challenge reveal vulnerabilities in IUGR hepatocytes? **Ongoing studies**

- Hepatocyte response to saturated (palmitate) and unsaturated (Oleate) fatty acid



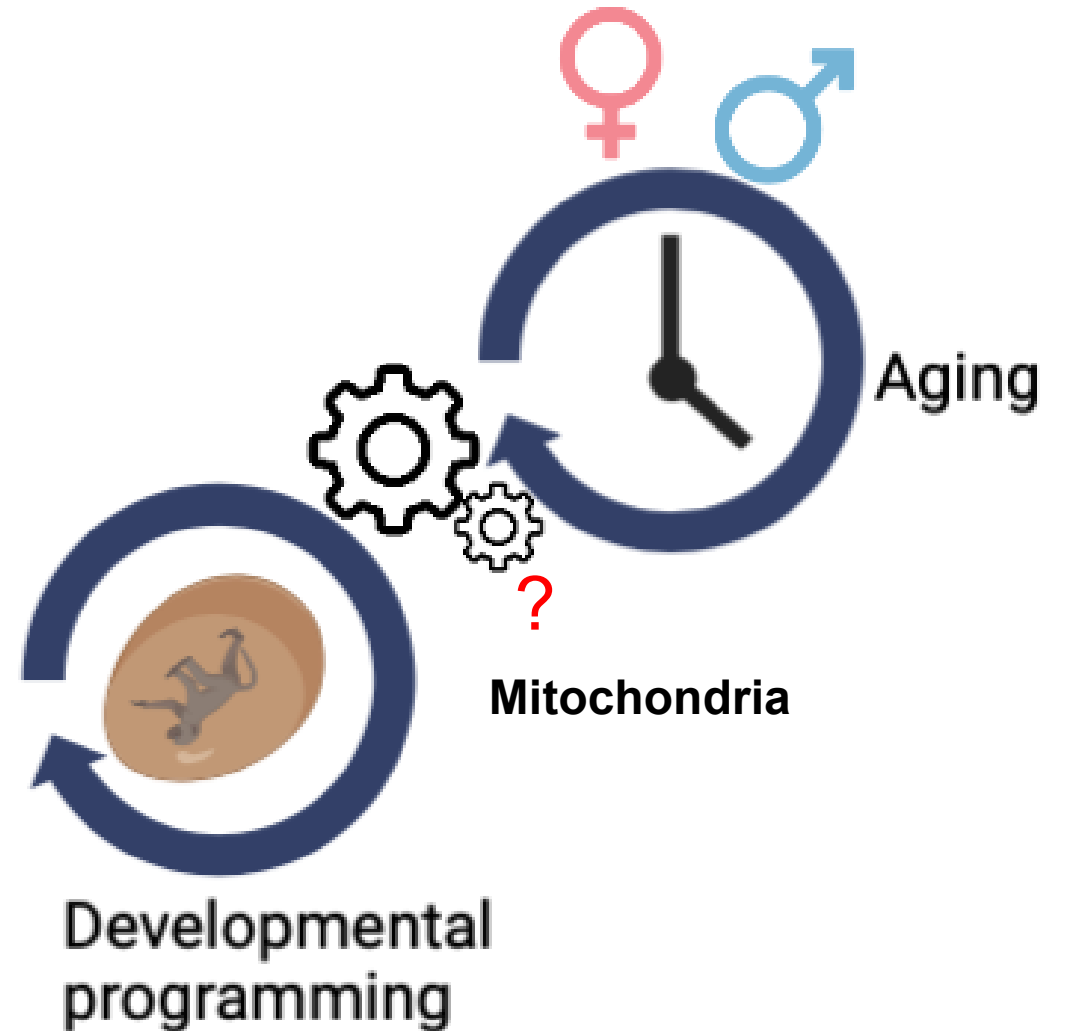
# Conclusion

Calorie restriction during development (not adulthood) negatively influences healthspan (impaired CV function, insulin resistance, altered cognition etc).

Clinical liver phenotypes in adulthood are largely unaffected by exposure to CR during development

In our baboon MUN model, aging male MUN offspring exhibit changes in mitochondrial bioenergetic parameters without concurrent systemic liver function alterations.

This supports the idea that hepatic mitochondrial dysfunction may precede detectable circulatory defects



# Open questions

- What are the mechanisms that support fetal adaptation to stressful environment?
- Do resilience mechanisms differ between fetal and adult life?
- Why is calorie restriction beneficial to longevity postnatally but alter the rate of aging if exposure is during fetal life?
- Need for methods to determine predisposition to adult diseases.
- Possible interventions for declines caused by programming?

# Acknowledgment



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*Thank you!*