

Oleic Acid Promotes Lipogenesis and Improves Mitochondrial Function in Bovine Adipocytes: The Role of PPAR α Signaling

Ursula Abou-Rjeileh, Adam L. Lock, and G. Andres Contreras

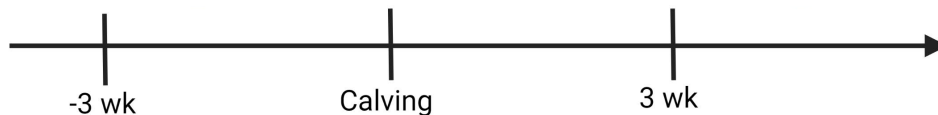
Michigan State University
East Lansing MI, USA

EAAP Annual Meeting
September 4, 2024

Transition Period in Dairy Cows

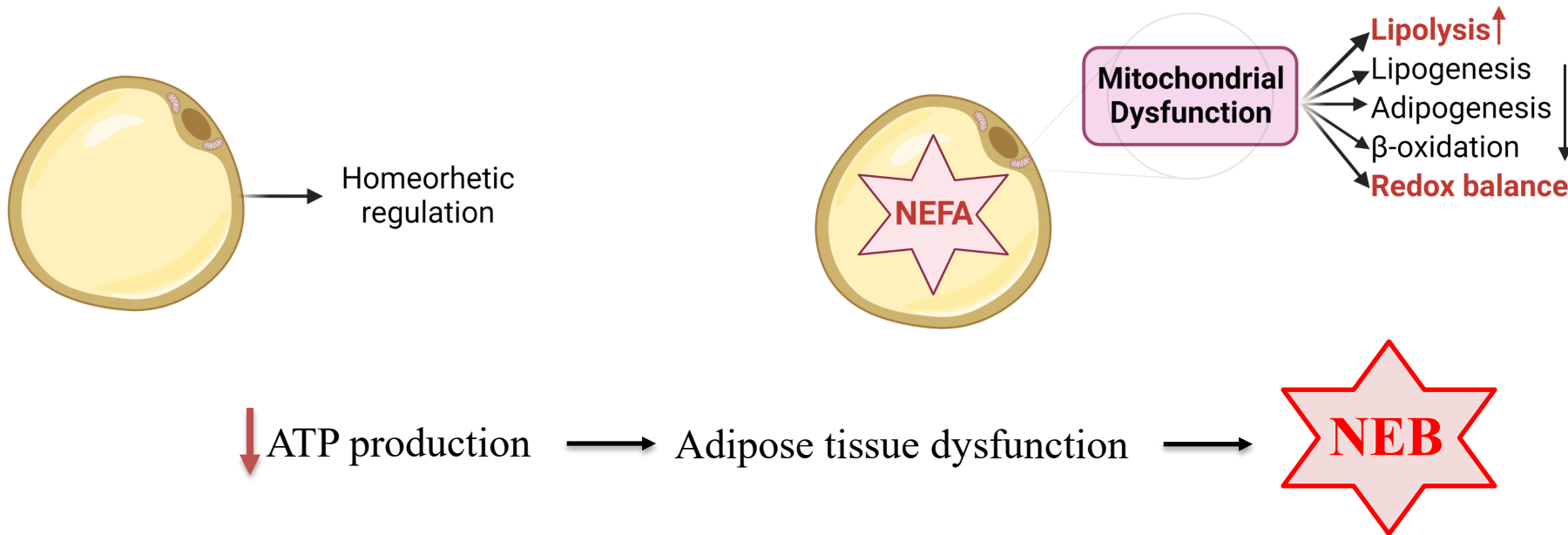


Lipolysis dysregulation → Diseases



Lipolysis: Fat breakdown
Lipogenesis: Fat synthesis

Mitochondrial Dysfunction in Adipose Tissue



↓ ATP production

→ Adipose tissue dysfunction



Lipolysis: Fat breakdown

Lipogenesis: Fat synthesis

Adipogenesis: Preadipocytes → Adipocytes

β -oxidation: Breakdown of FA in mitochondria to produce energy

Redox balance: Antioxidants = Pro-oxidants



antioxidants

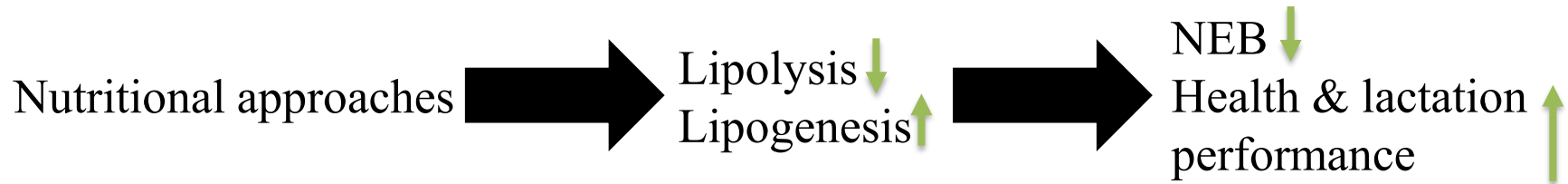


Review

Redox Regulation of Lipid Mobilization in Adipose Tissues

Ursula Abou-Rjeileh and G. Andres Contreras *

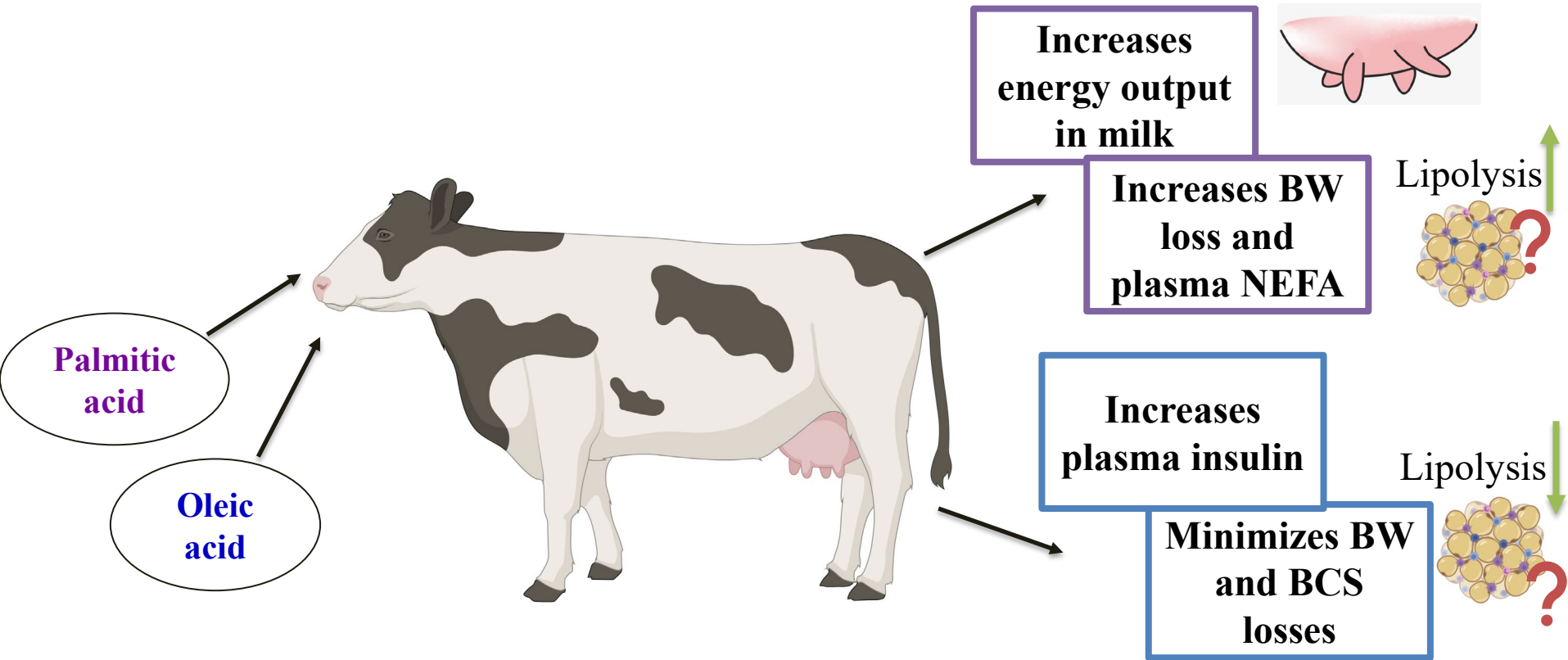
Solution?



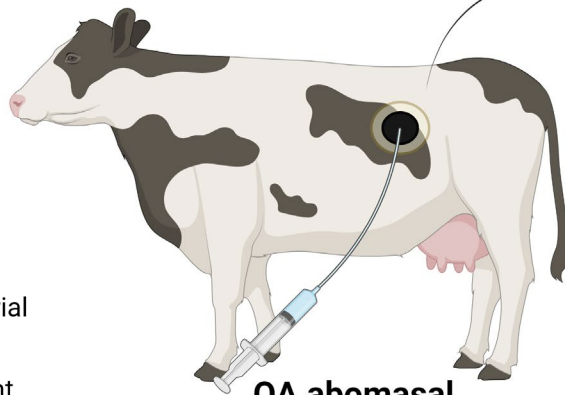
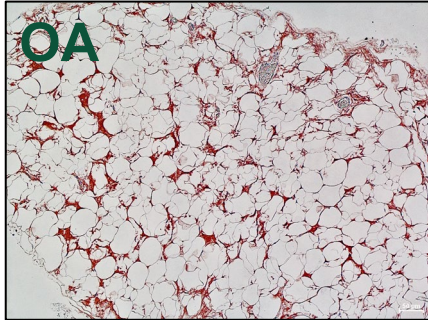
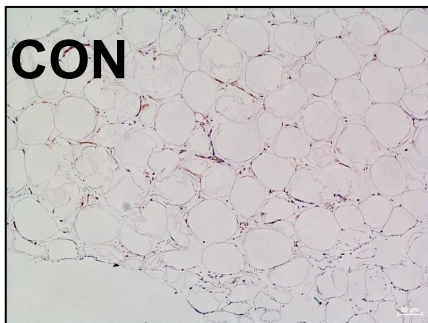
Lipolysis: Fat breakdown

Lipogenesis: Fat synthesis

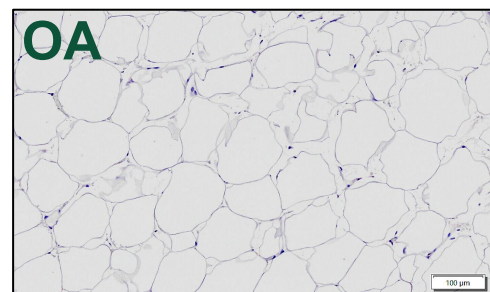
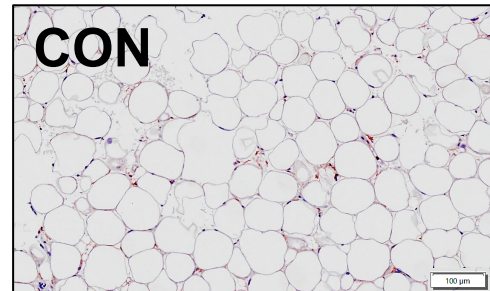
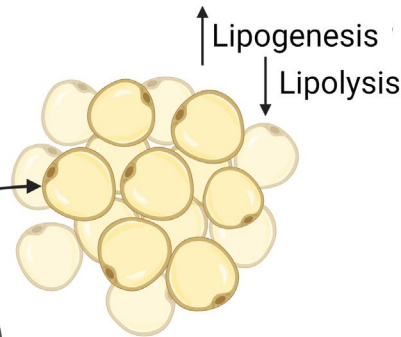
Fatty Acid Supplementation in Dairy Cows



OA Limits Lipolysis and Enhances Mitochondrial Function



**OA abomasal
infusions**



J. Dairy Sci. 106:4306–4323
<https://doi.org/10.3168/jds.2022-22402>

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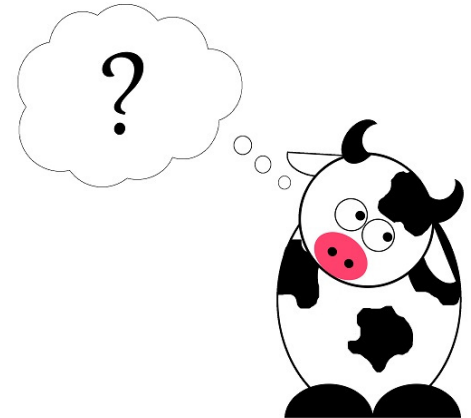
Oleic acid abomasal infusion limits lipolysis and improves insulin sensitivity in adipose tissue from periparturient dairy cows

Ursula Abou-Rjeileh,¹ José M. dos Santos Neto,² Miguel Chirivi,¹ Nial O'Boyle,³ David Salcedo,¹ Crystal Prom,² Juliana Laguna,¹ Jair Perales-Giron,² Adam L. Lock,^{2*} and G. Andres Contreras^{1*}

Gap in Knowledge



The mechanisms behind OA modulating lipid metabolism and mitochondrial function



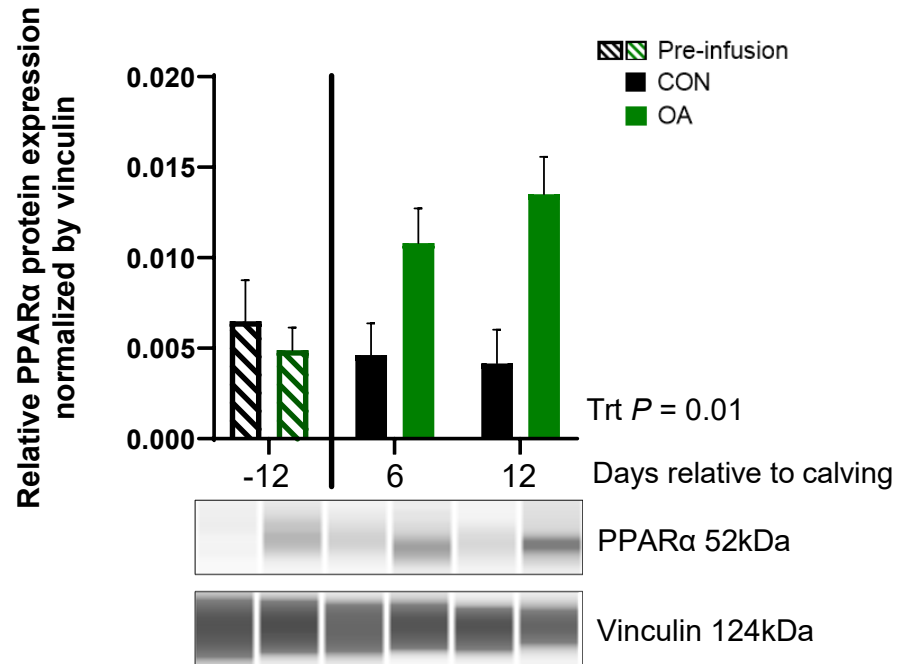
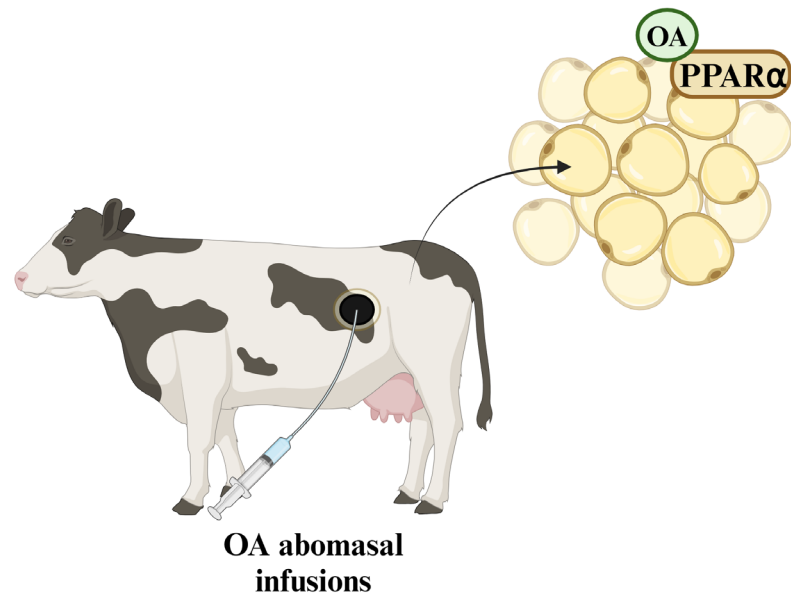
OA Increases PPAR α Protein Expression in Adipose Tissue



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Oleic acid abomasal infusion limits lipolysis and improves insulin sensitivity in adipose tissue from periparturient dairy cows

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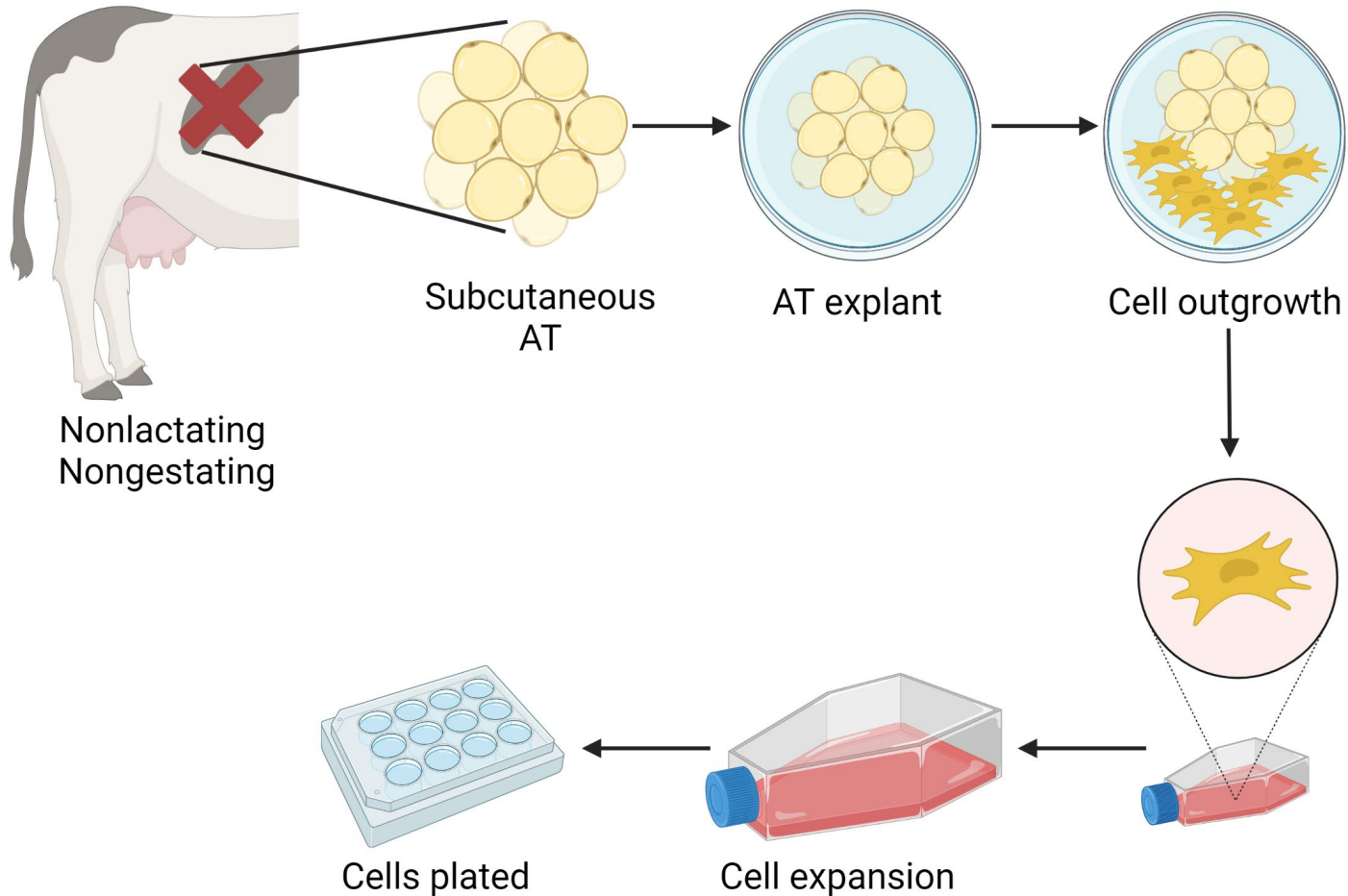
Objective

Evaluate the effect of OA on lipid metabolism and mitochondrial bioenergetics in bovine adipocytes

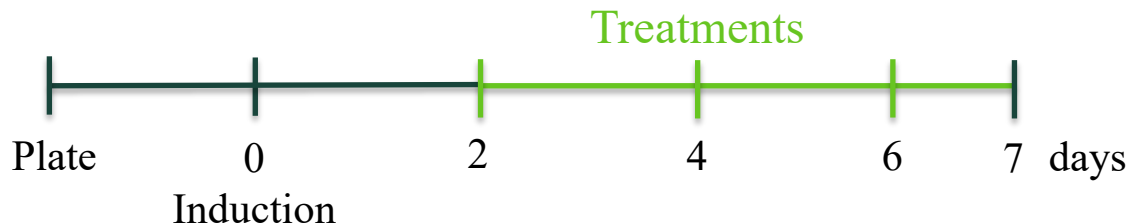
Hypothesis

- OA, alone or in combination with PA, promotes lipid accumulation in a PPAR α -dependent mechanism
- OA improves mitochondrial function

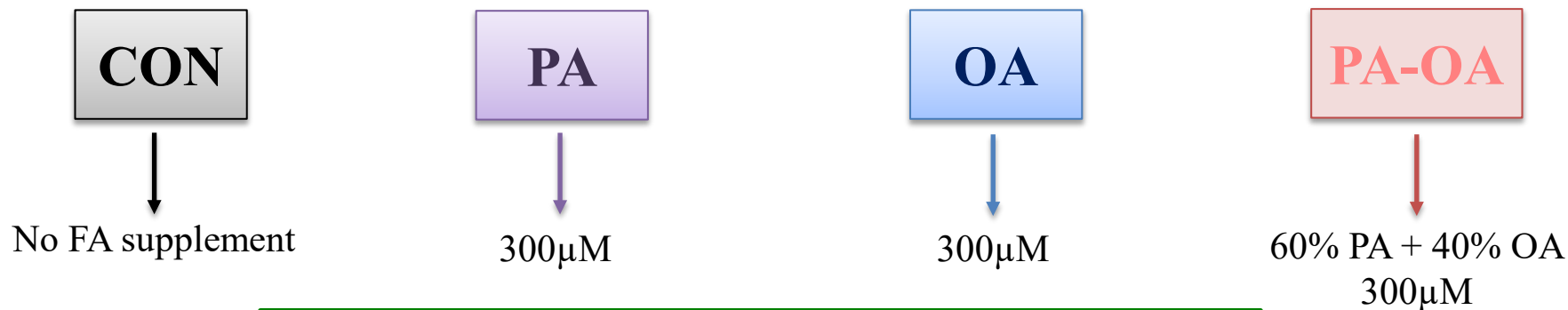
Harvesting and Growing Preadipocytes



Experimental Timeline

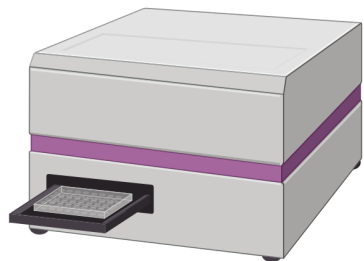
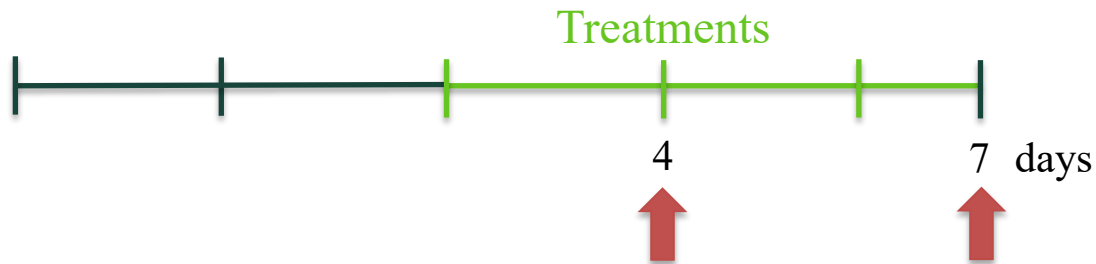


Treatments



With or without PPAR α antagonist (GW6471) at 10 μ M

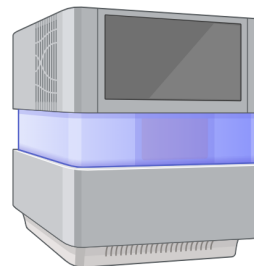
Collection and Analysis



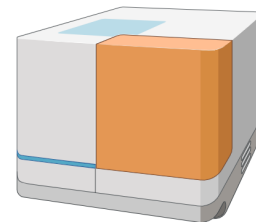
Triglyceride Accumulation
TAG levels



Lipid droplet Accumulation
LD stain intensity



Gene Expression
Bulk RNA-seq



Protein Expression
Wes Simple

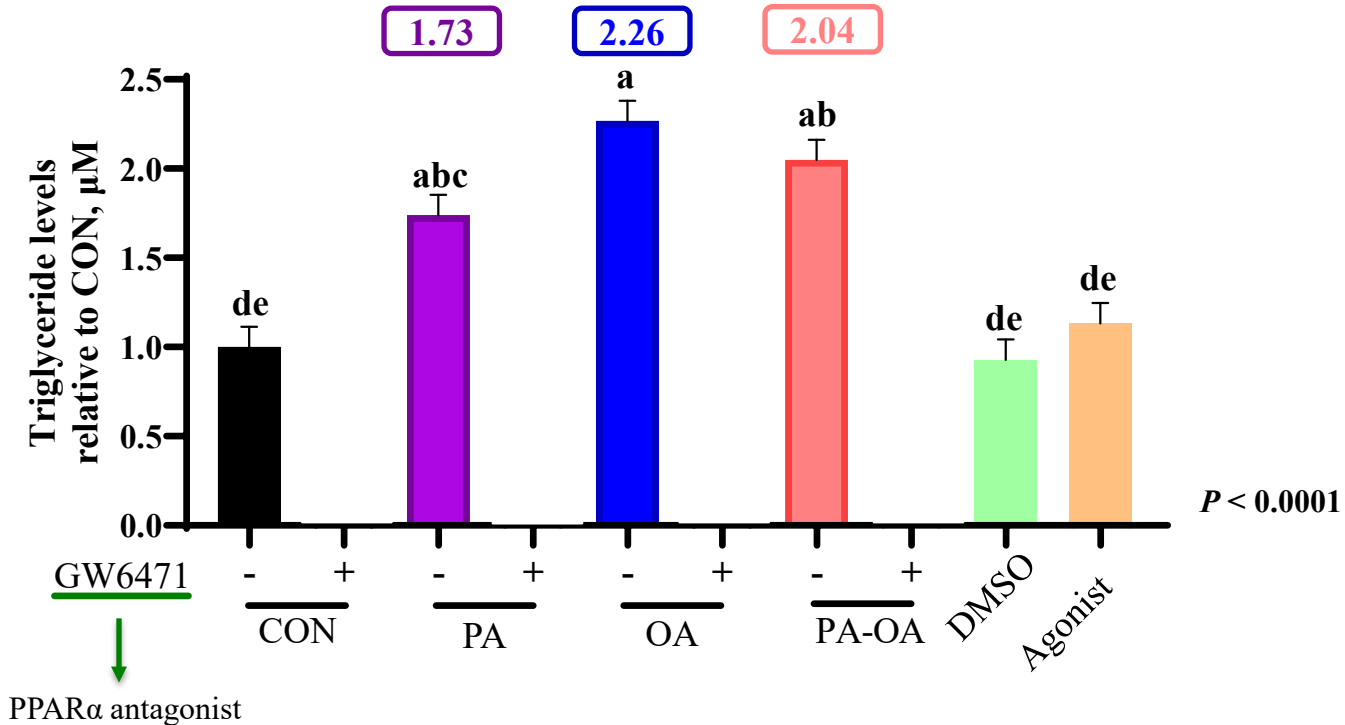


Did someone say
Oleic Acid?



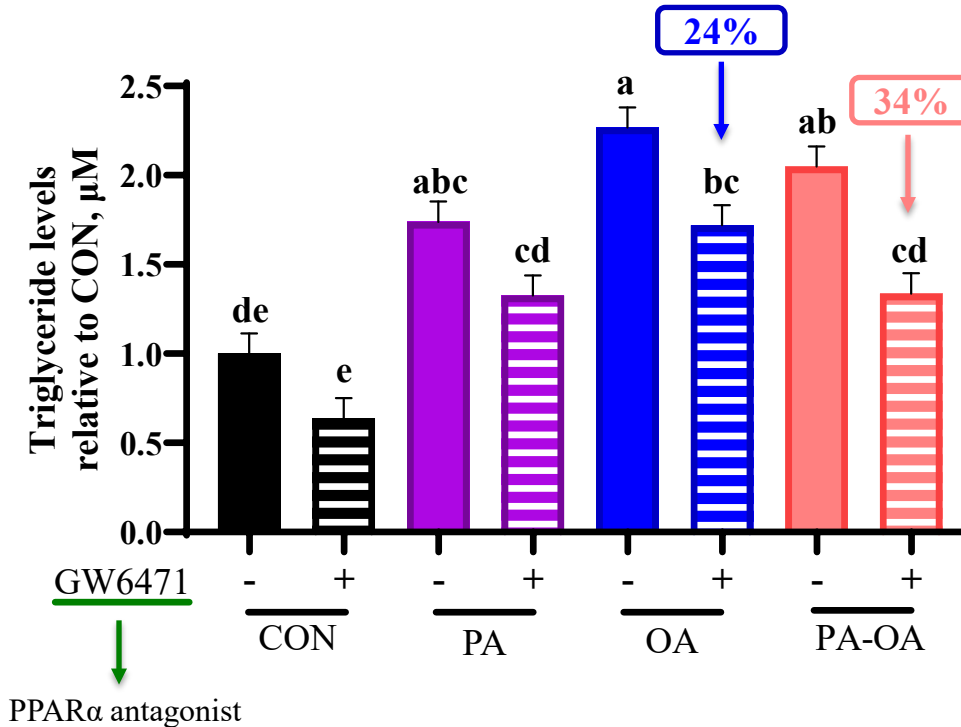
Results

OA's Lipogenic Effect is PPAR α Dependent



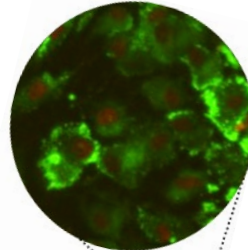
d 7
n = 6
Mean $\pm$ SEM

OA's Lipogenic Effect is PPAR α Dependent



$P < 0.0001$

d 7
n = 6
Mean $\pm$ SEM



Lipid Droplet (Bodipy, 10 μ M)

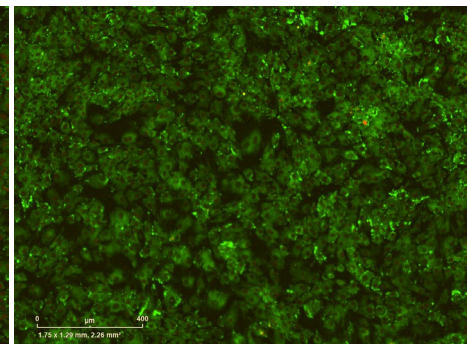
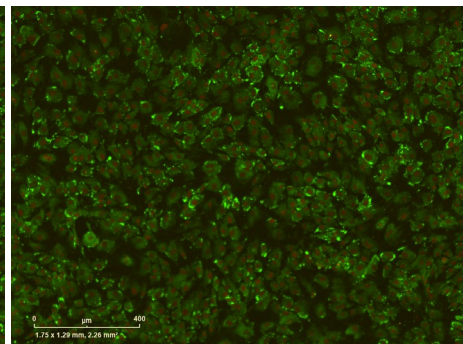
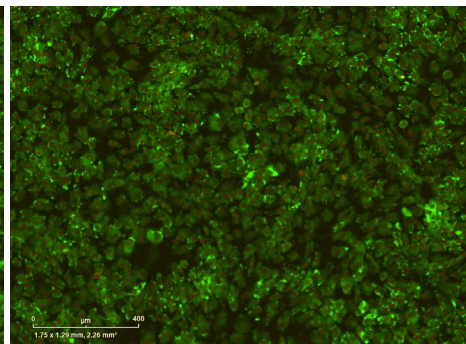
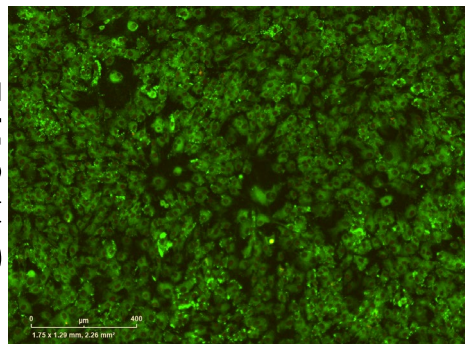
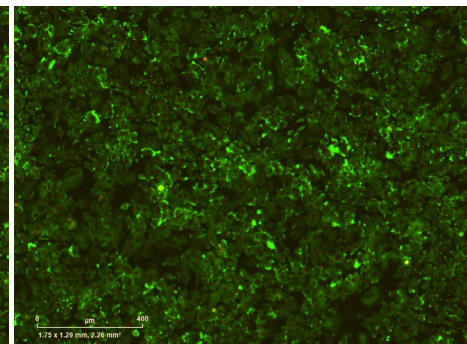
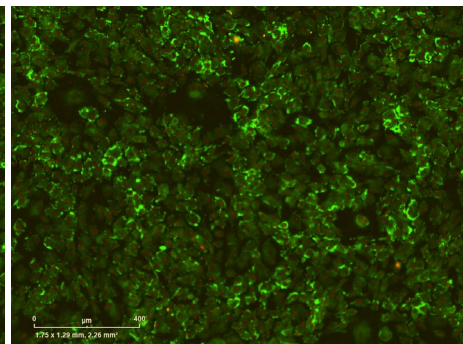
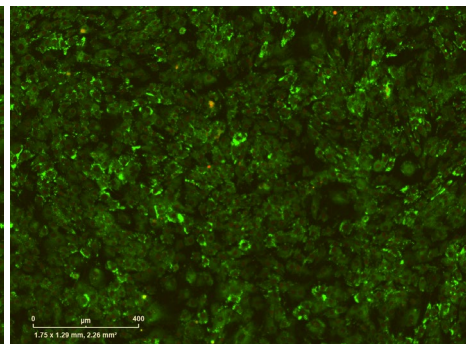
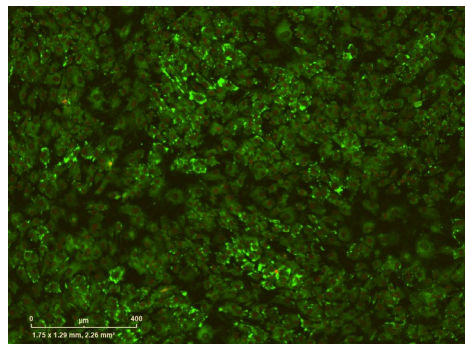
Nucleus (NucSpot, 2 μ L/ml)

CON

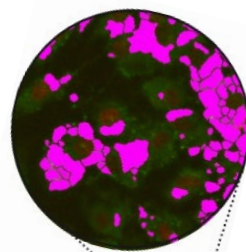
PA

OA

PA-OA



GW6471



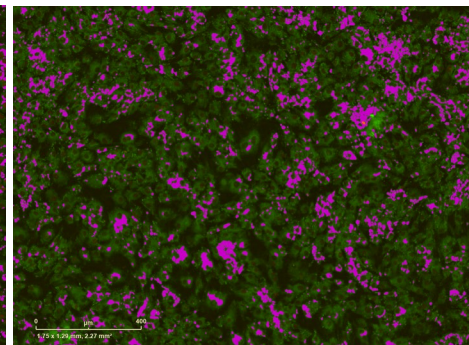
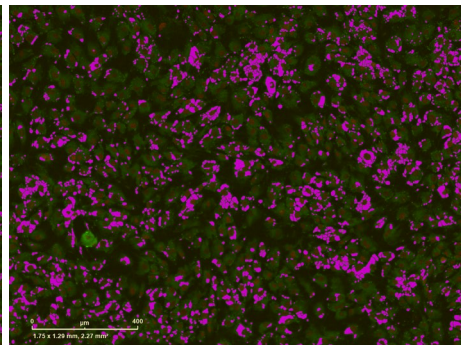
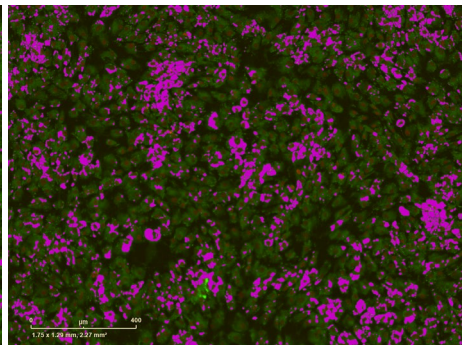
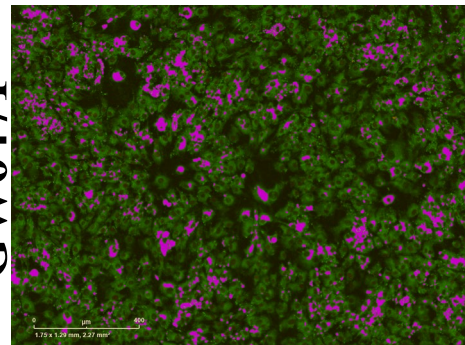
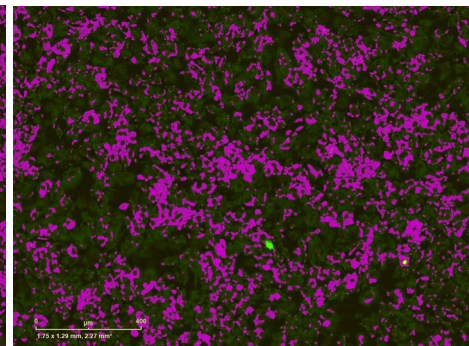
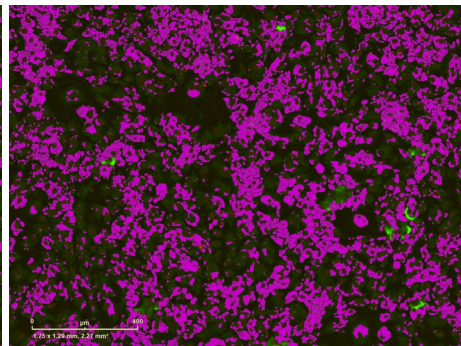
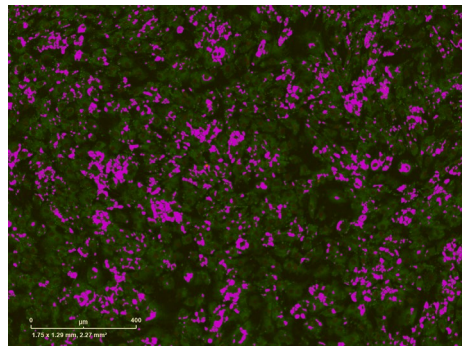
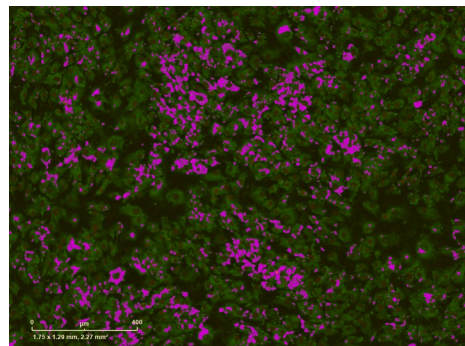
Lipid Droplet
Nucleus

CON

PA

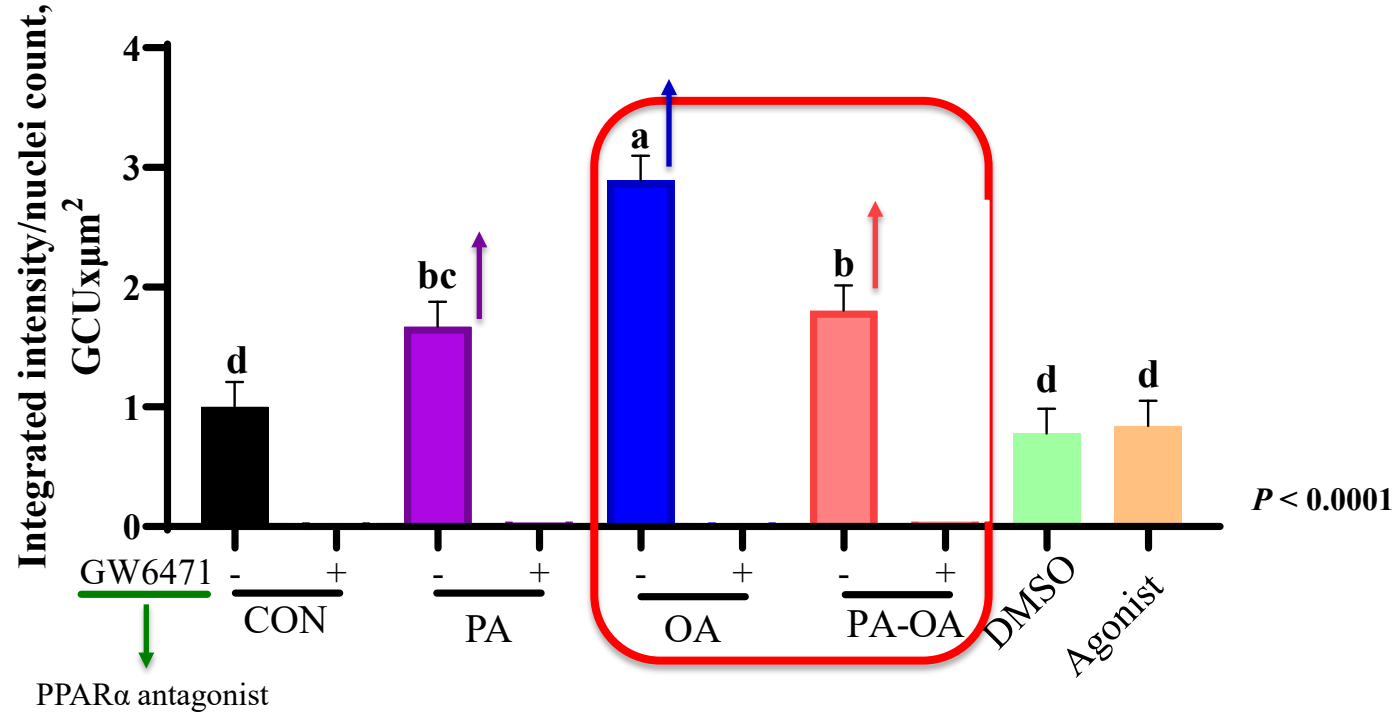
OA

PA-OA



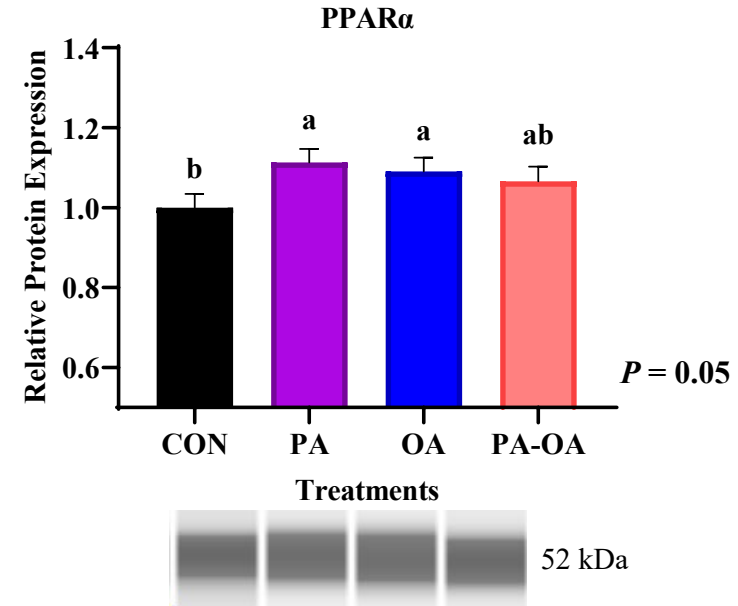
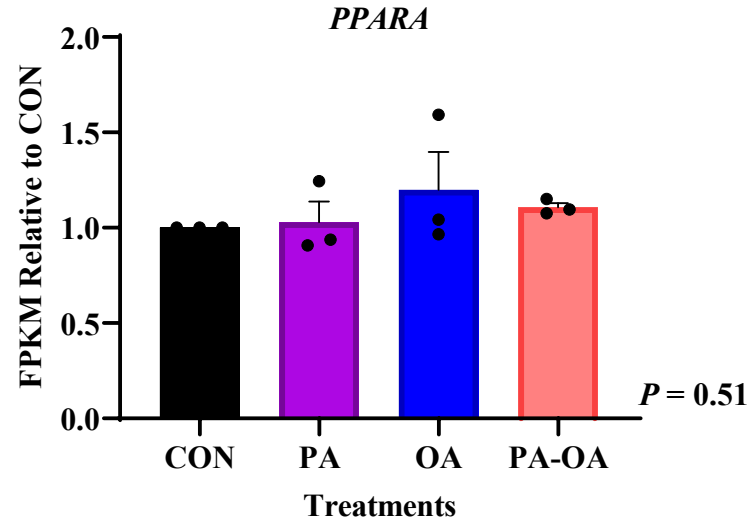
GW6471

OA's Lipogenic Effect is PPAR α Dependent



d 7
n = 5
Mean $\pm$ SEM

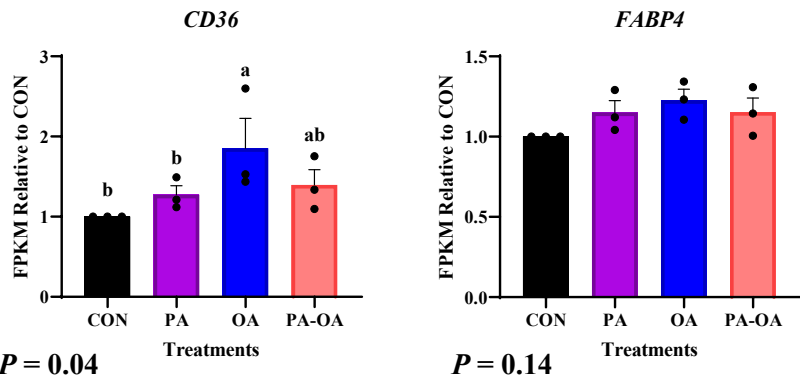
PA and OA Increase PPAR α Protein Expression



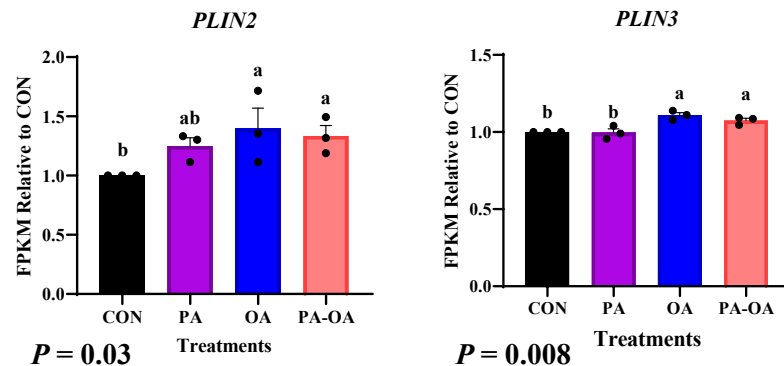
OA Enhances Expression of Lipogenic Gene Networks



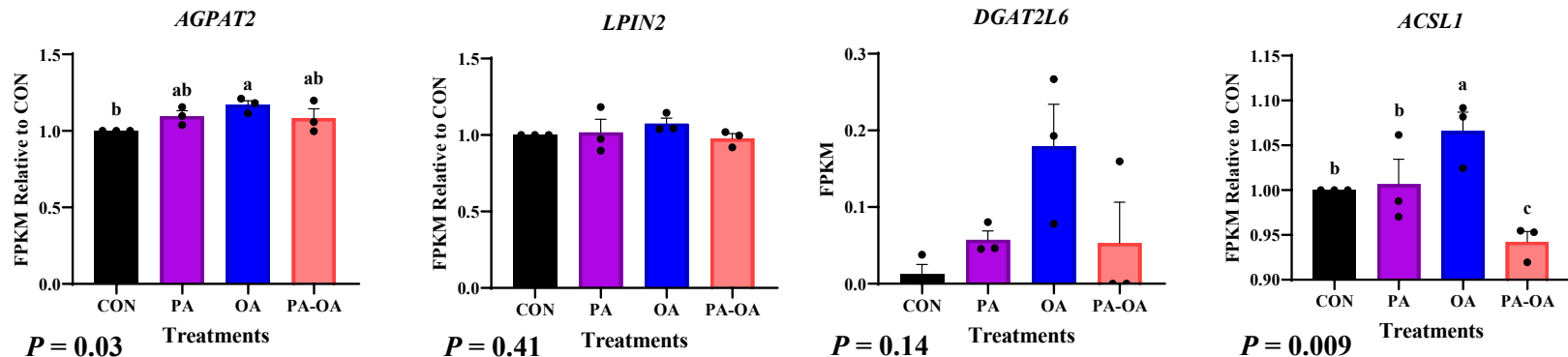
FA Transporters



LD Formation

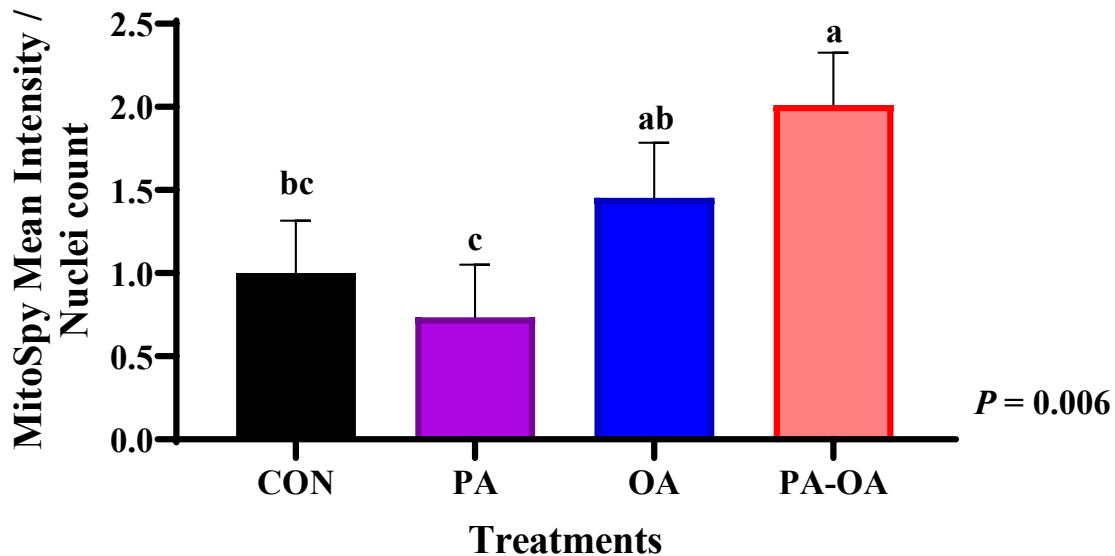
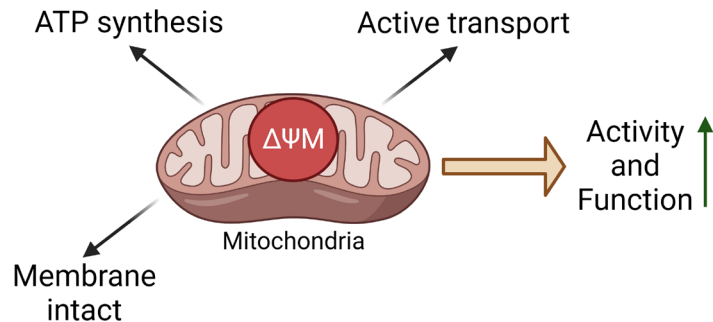


TAG Synthesis



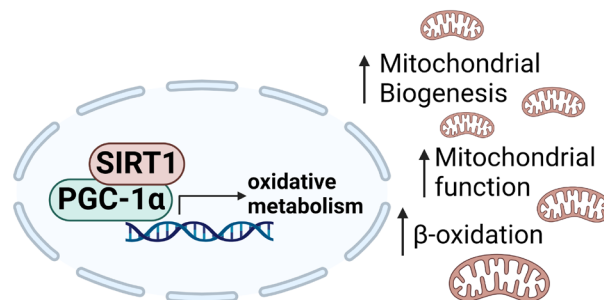
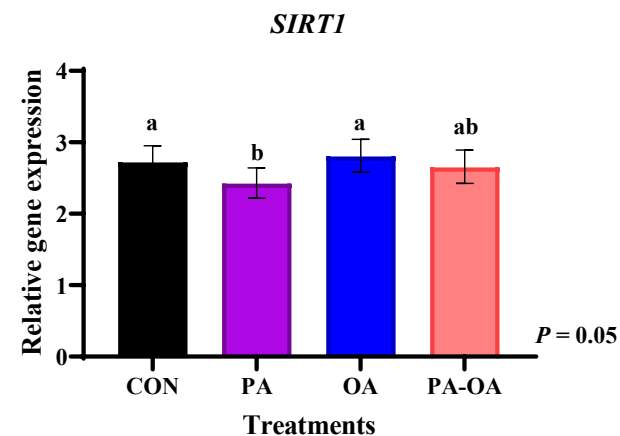
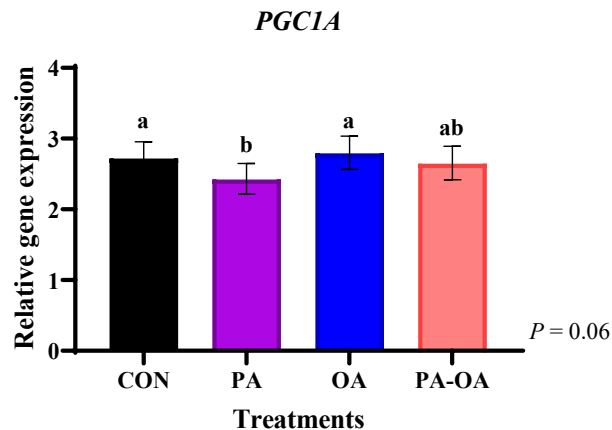
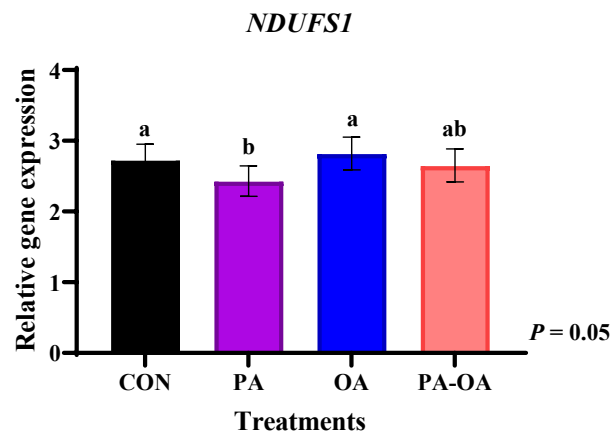
d 4
n = 3
Mean $\pm$ SEM

OA Restores Mitochondrial Membrane Potential



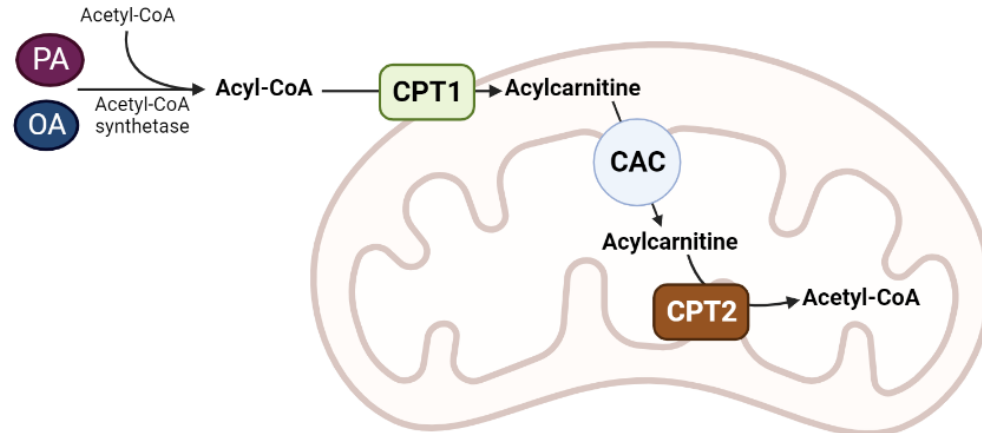
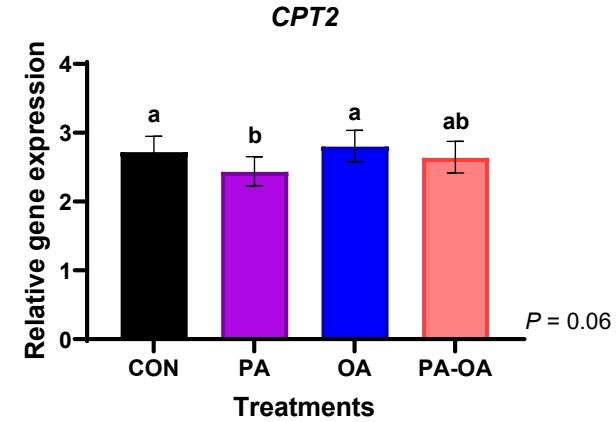
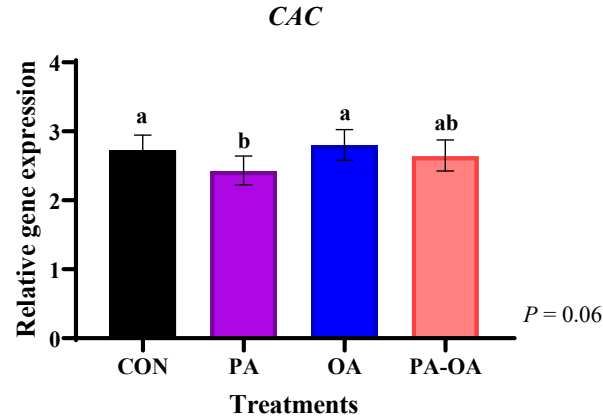
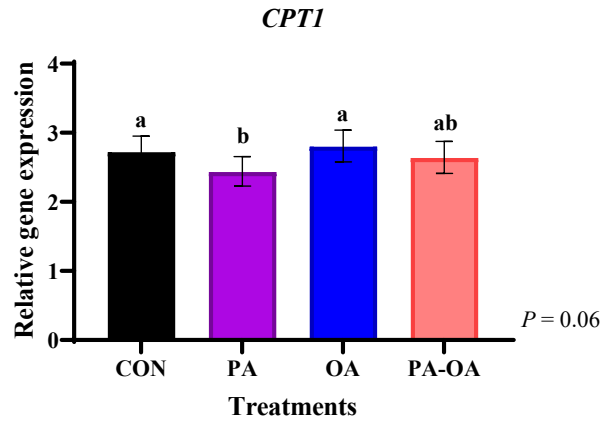
d 7
n = 7
Mean $\pm$ SEM

PA Reduces Mitochondrial Oxidation and Biogenesis



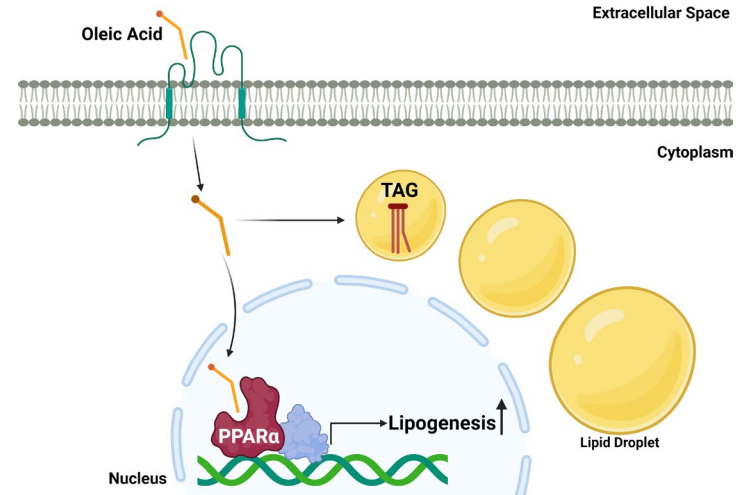
d 7
n = 6
Mean $\pm$ (LL,UL)

PA Reduces FA Transport into the Mitochondria



Summary

- **OA**, alone or in combination with **PA**, enhances lipid accumulation in a PPAR α -dependent manner and increases the expression of lipogenic gene networks
- **OA** enhances mitochondrial membrane potential compared with **PA**
- **PA** alone suppresses the expression of mitochondrial genes, however, when combined with **OA**, the effect is attenuated



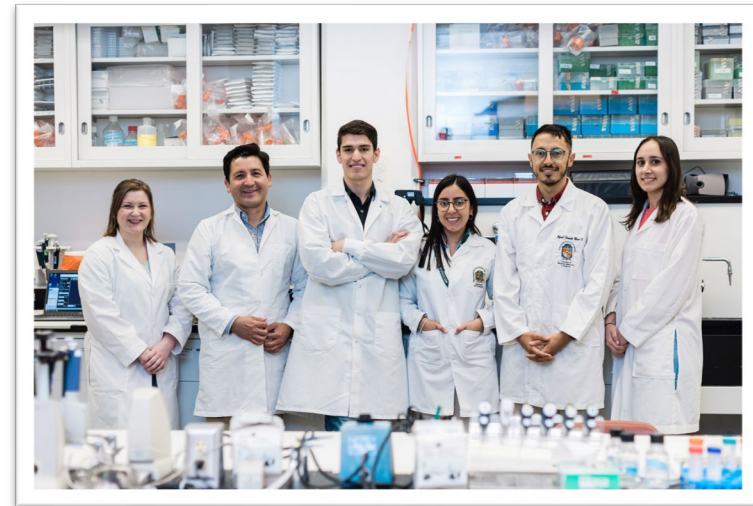
Implications



- Mechanistic evidence for the use of OA along with PA in postpartum dairy cow diets to
 - Enhance fat storage
 - Decrease lipid mobilization
 - Recover adipose tissue bioenergetics
 - Lowering their risk of health issues and maximizing production
- Future direction

Assess the effects of OA and PPAR α activation during lipolysis, inflammation, and oxidative stress

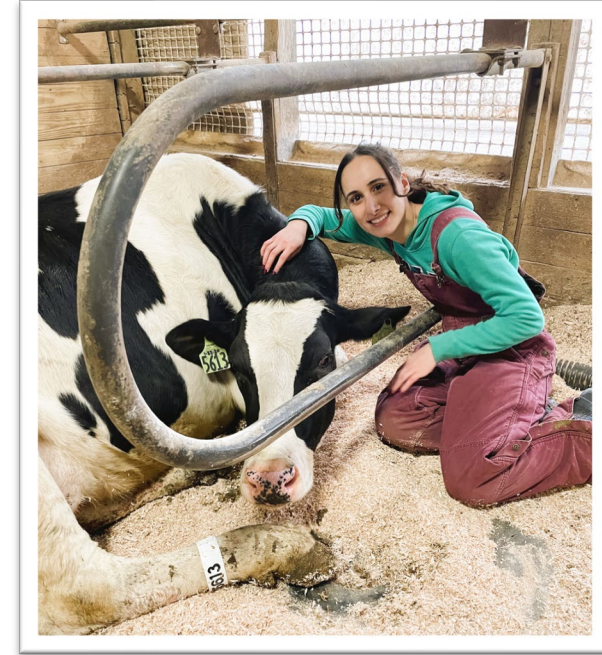
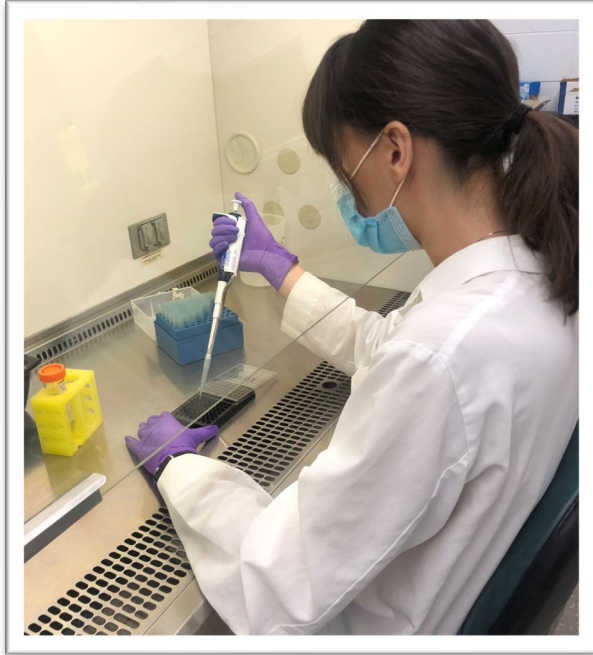
- Contreras lab group
- USDA grants (2019-67015-33386, 2021-67015-29443)
- AFRI-EWD Program Predoctoral Fellowship (2024-67011-42894)
- Novus International ADSA/EAAP PhD Student Travel Award



United States Department of Agriculture
National Institute of Food and Agriculture



Thank You!



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