

# **Chronic high fat diet increases vaginal sphincter laxity but not pelvic floor muscle function in mice**

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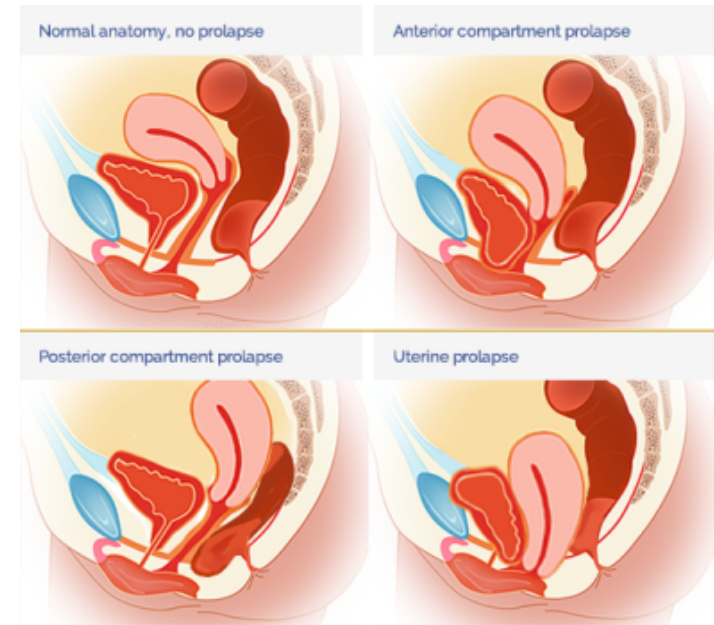


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## BRODY SCHOOL OF MEDICINE

# Pelvic Organ Prolapse (POP)

- POP affects 41% of women
- POP can negatively impact women's body image, daily activities, and quality of life
- Risk factors include parity, age, hysterectomy, and **obesity**
- In their lifetime, women in the US have a 13% risk of undergoing surgery to correct POP



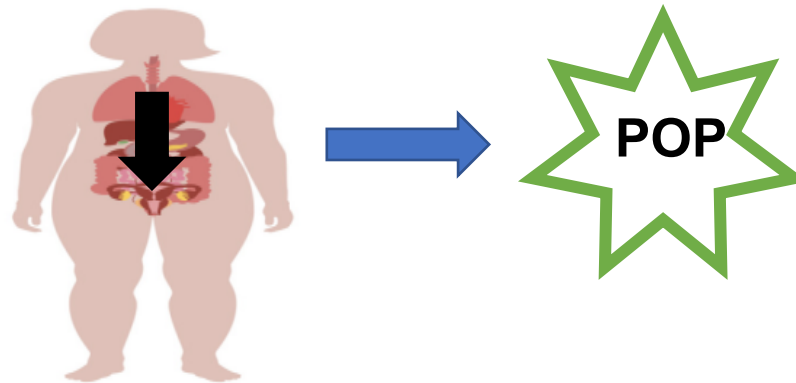
[www.starclinic.com](http://www.starclinic.com)

# Female Sexual Dysfunction (FSD)

- FSD symptoms include lack of desire, impaired arousal, inability to achieve orgasm, or dyspareunia
- Women with POP have reported incidence of FSD at 50-83%
- Conflicting data are available on the impact of POP surgical interventions and sexual function

# High Fat Diet (HFD) and POP

- Obesity increases intrabdominal pressure and directly weakens pelvic skeletal muscle and fascia



- HFD-induced obesity can cause skeletal muscle atrophy and decreased contractility in mice
  - Via impaired lipid metabolism → skeletal muscle remodeling

# Animal Models of Pelvic Floor Disorders

- Mice are a quadruped species with a horizontally oriented pelvic floor
- This eliminates mechanical stress of obesity on their pelvic floor muscles

The impact of obesity on both vaginal smooth muscle and pelvic floor skeletal muscle has not been investigated in an obese animal model.

# Objectives

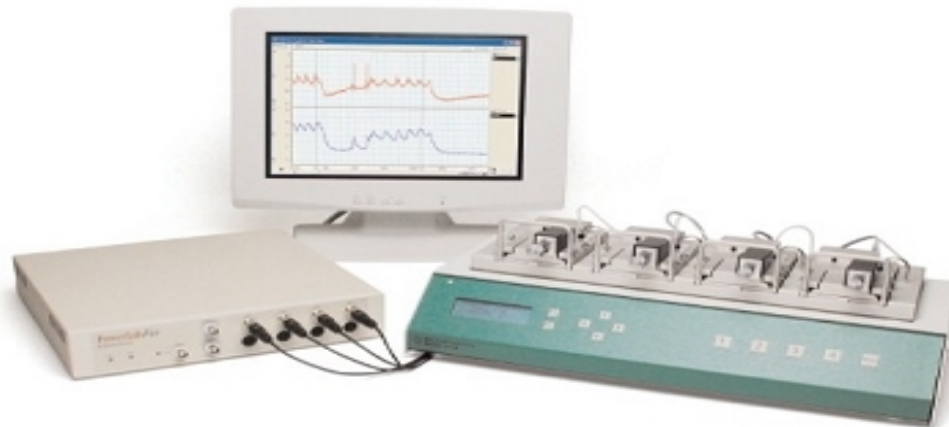
1. To investigate the effects of HFD-induced obesity on vaginal smooth and pelvic skeletal muscle function.
2. To evaluate structural changes in content of both pelvic floor skeletal muscle and vaginal smooth muscle.

# Hypotheses

1. HFD-induced obesity will decrease vaginal contractility, increase fibrosis, and increase tissue viscoelasticity.
2. HFD-induced obesity will lower skeletal muscle contractility, increase passive stiffness and decrease muscle fiber cross section area.

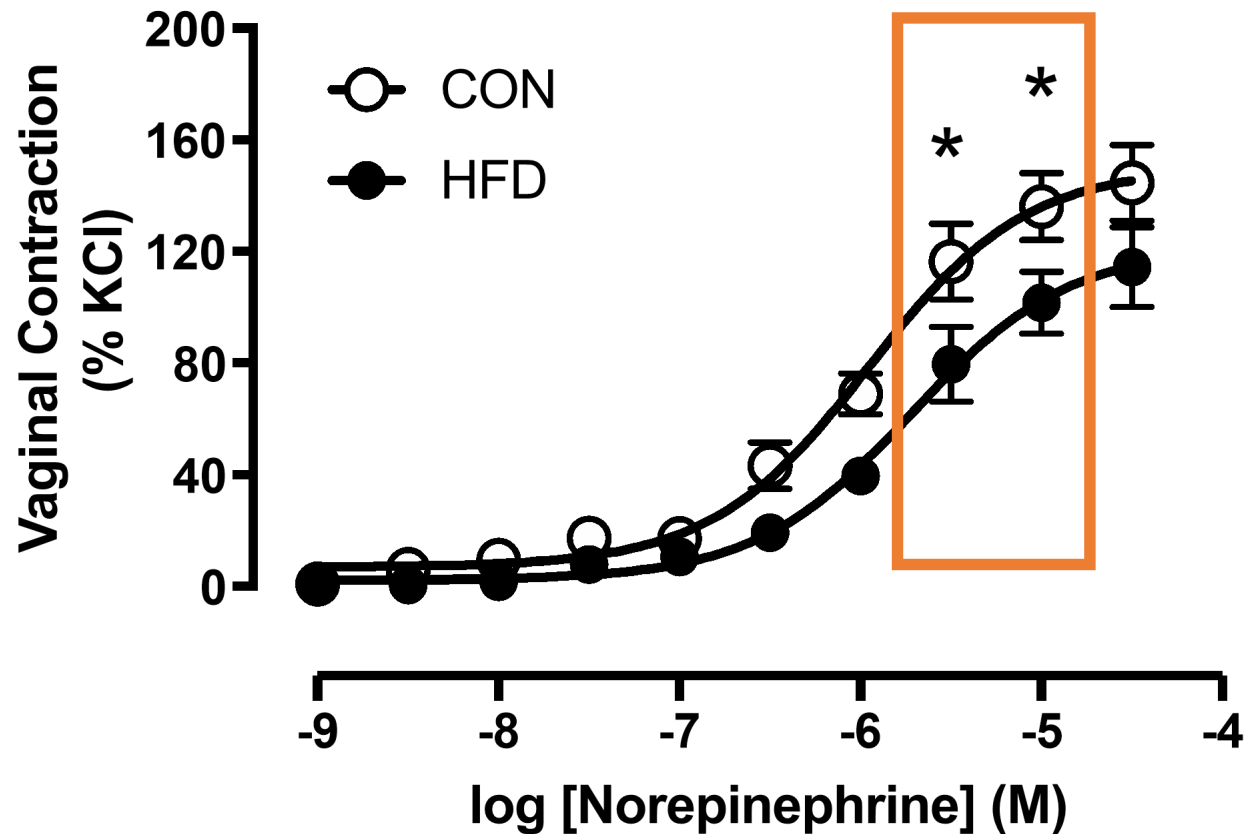
# Methods

- Adult female C57/Blk6N mice (n=16)
- Control (10% kcal fat) or HFD (45% kcal fat) for 24 weeks
- Tissue bath studies assess vaginal smooth muscle function *in vitro*
  - Contraction - Norepinephrine
  - Relaxation - DEA-NONOate, Electric field stimulation (EFS)



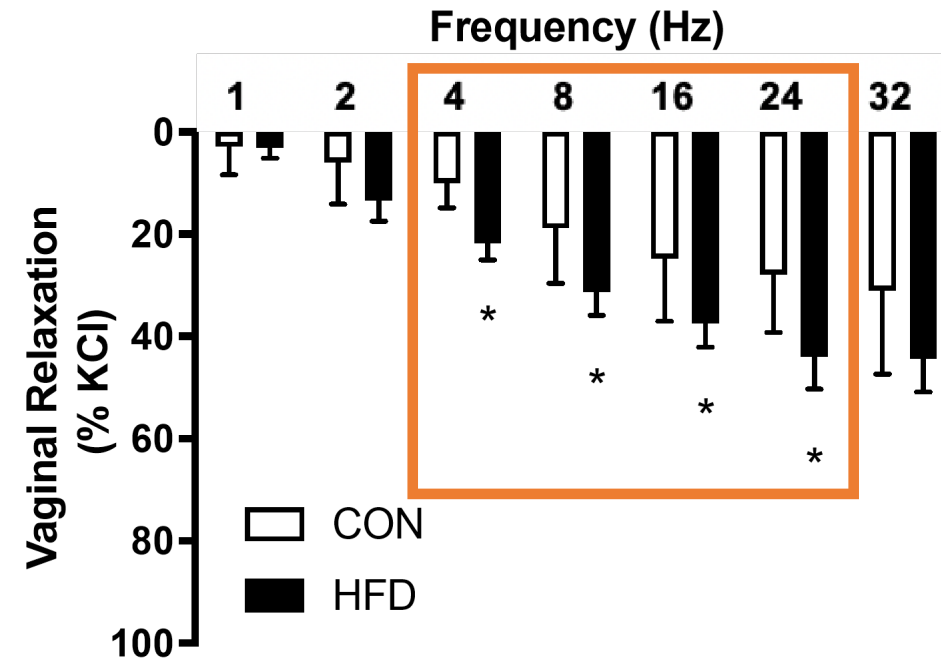


# Vaginal adrenergic contractions are decreased following chronic HFD



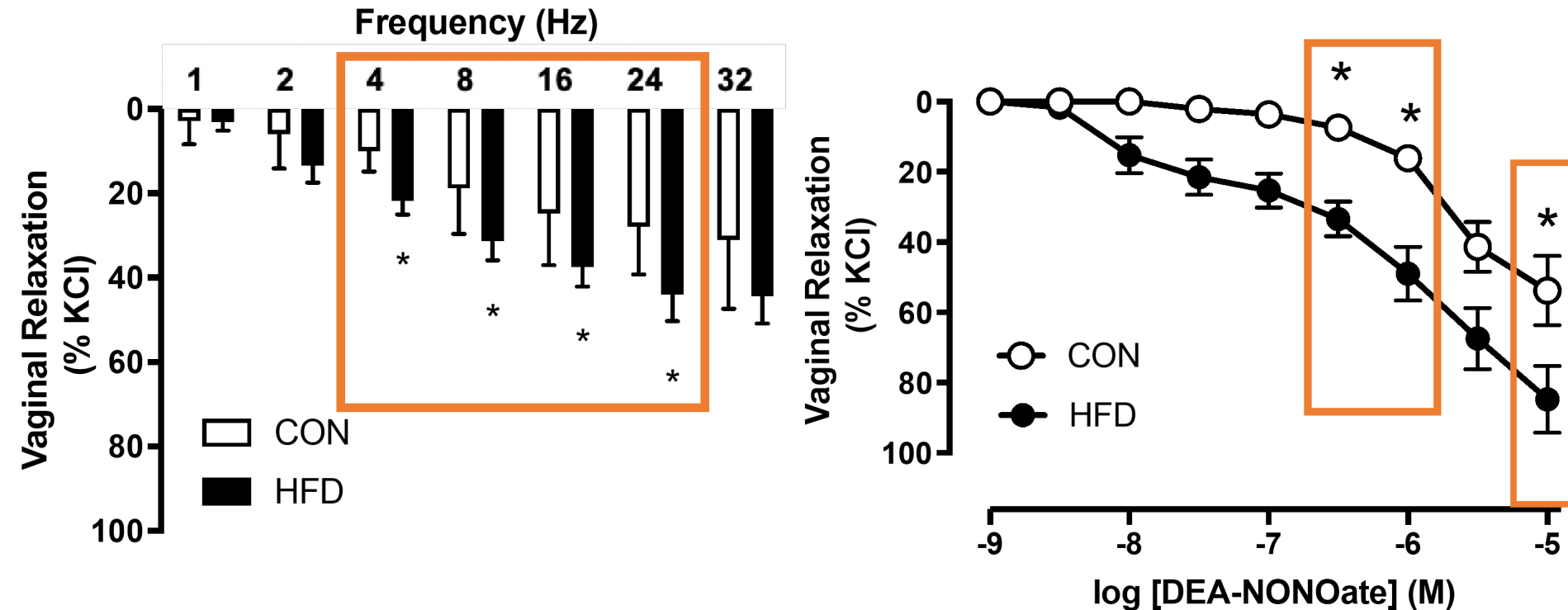
\*  $p < 0.05$  vs CON,  $n = 8/\text{group}$

# Obesity increases vaginal EFS neurogenic-mediated relaxations



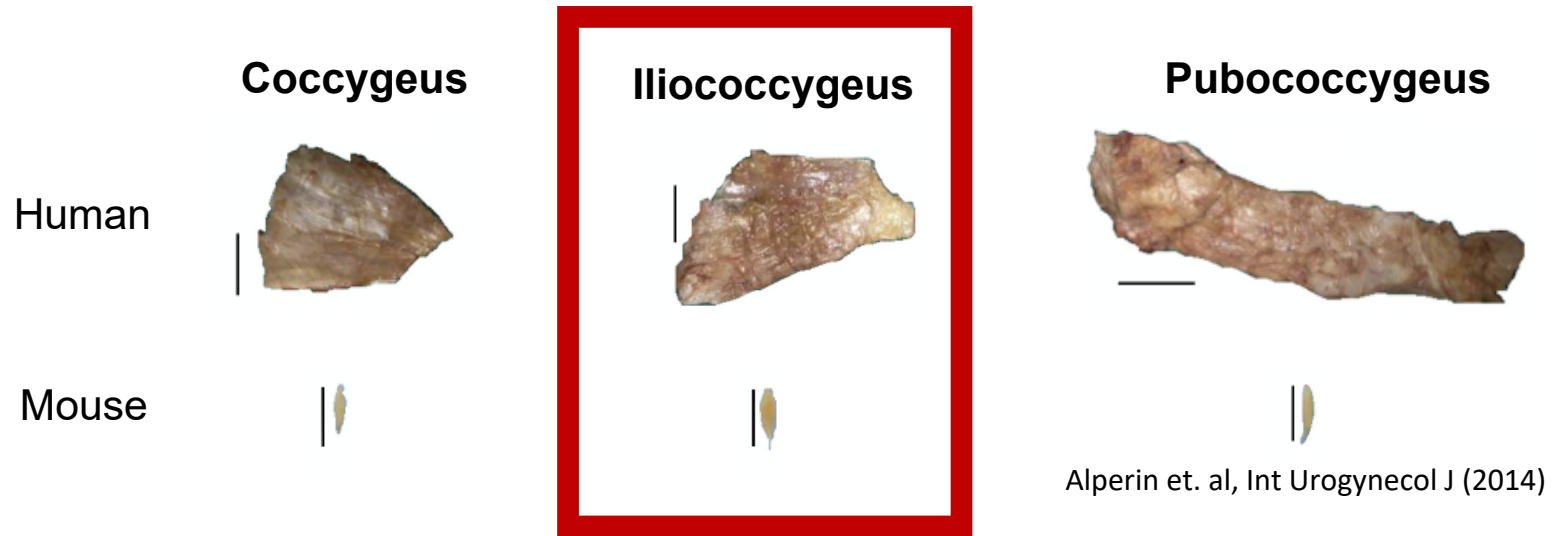
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# Obesity increases vaginal nitric oxide-mediated relaxations



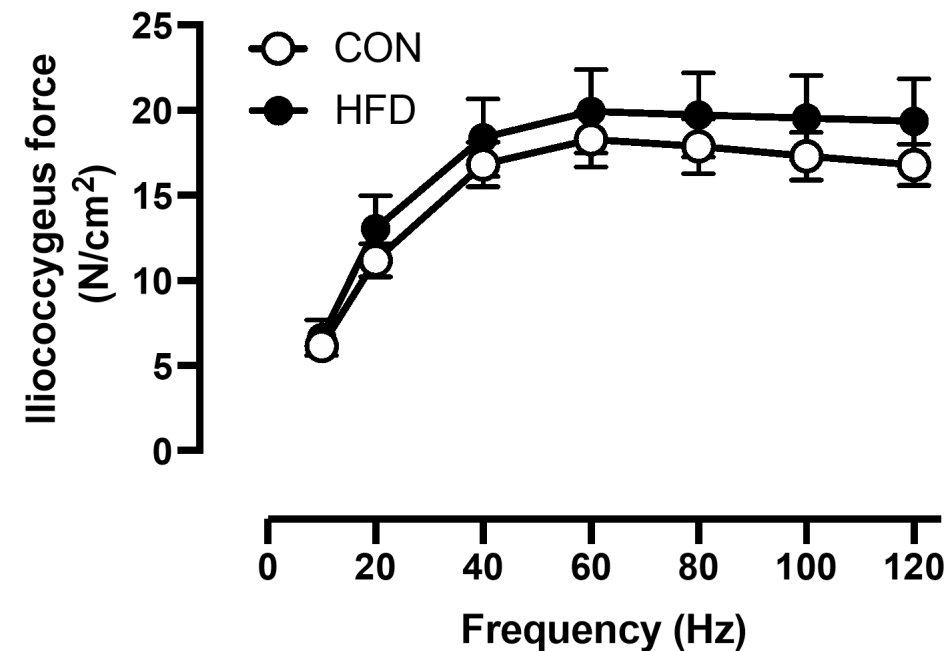
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# Methods



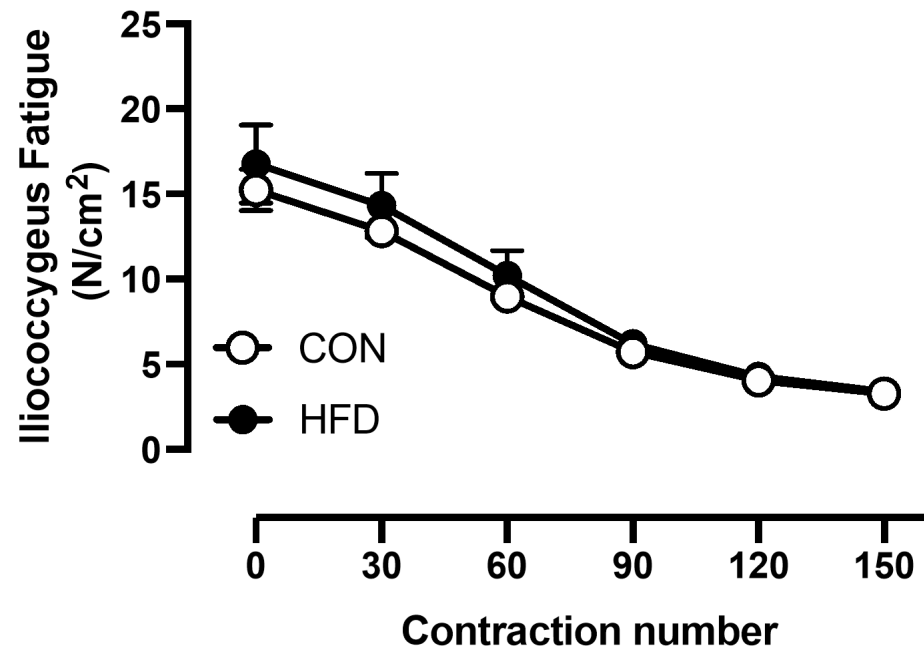
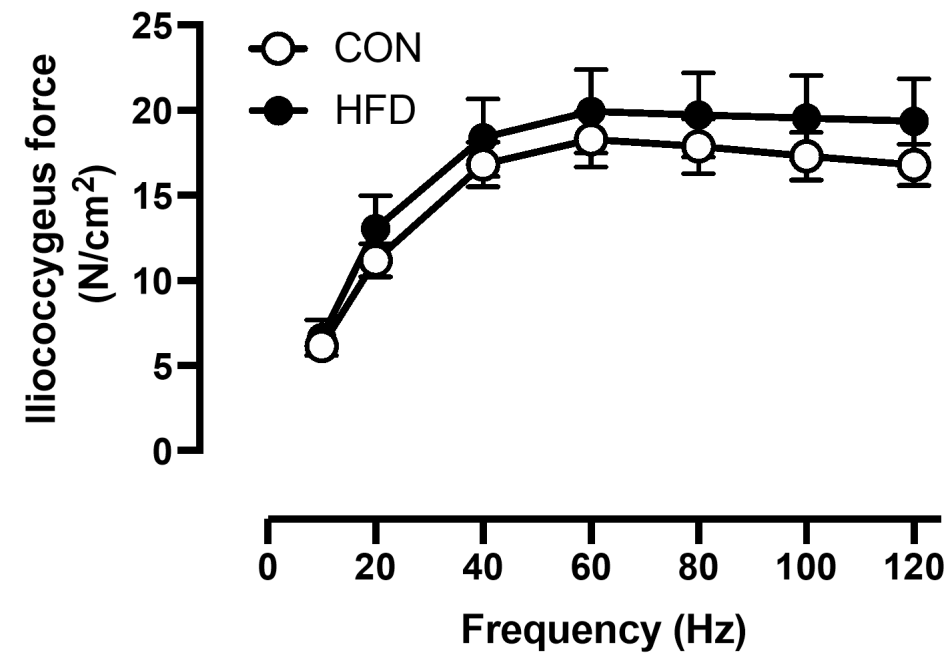
- *In vitro* isometric specific force production and fatigue of iliococcygeus muscle
- Histology
  - Iliococcygeus stained with anti-myosin antibodies to assess cross sectional area and fiber types

# Iliococcygeus specific force is unchanged following HFD



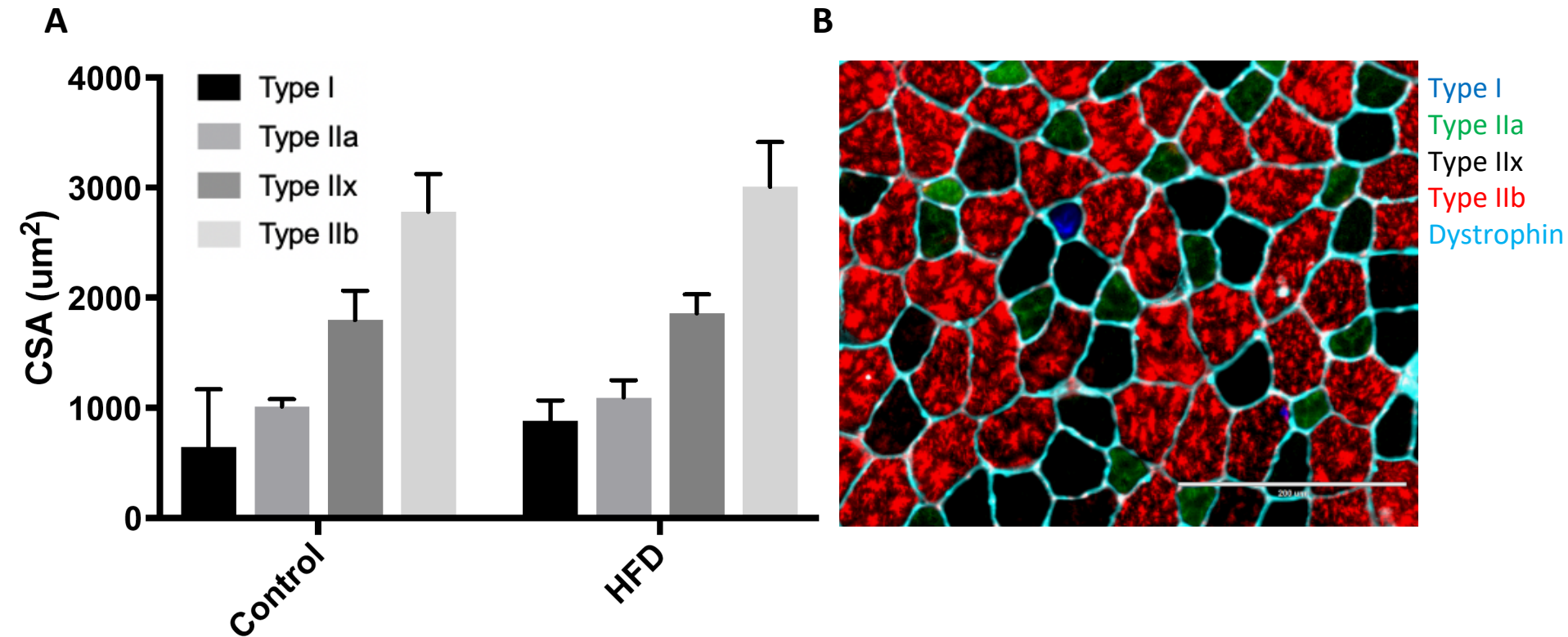
\*  $p < 0.05$  vs CON,  $n = 8/\text{group}$

# Iliococcygeus muscle fatigue is unchanged following HFD



\*  $p < 0.05$  vs CON,  $n = 8$ /group

# Obesity did not change iliococcygeus cross sectional area or muscle fiber type



\*  $p < 0.05$  vs CON,  $n = 8/\text{group}$

# Summary

- HFD-induced obesity led to:

## **Vaginal Smooth Muscle**

1. Decreases in adrenergic-mediated contraction
2. Increases in neurogenic EFS relaxation
3. Increases in nitric-oxide mediated relaxation



# Summary

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## **Vaginal Smooth Muscle**

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## **Pelvic Skeletal Muscle**

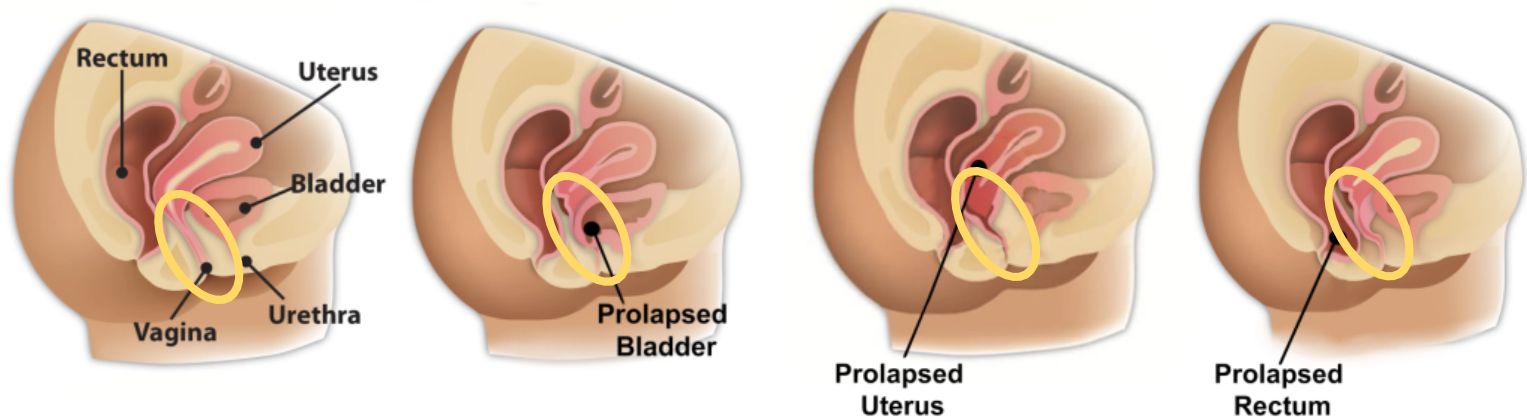
1. No change in specific force production
2. No change in muscle fatigue
3. No change in CSA or muscle fiber type

# Next Steps

- Measure the passive stiffness of vaginal smooth muscle and pelvic floor skeletal muscle by nanoindentation studies
- Vaginal smooth muscle histology to assess smooth muscle and collagen deposition
- Quantitative PCR and Western blots to evaluate the relative gene and protein expression of collagen and muscle content

# Conclusions

- Chronic HFD **does** impair *vaginal smooth muscle* contraction and relaxation
- Chronic HFD **does not** alter *skeletal pelvic floor muscle* composition or function



**Clinically, poor vaginal smooth muscle tonicity may contribute to obesity induced POP and FSD.**

# Acknowledgements

## East Carolina University

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