

# The Positive Effects of Tauroursodeoxycholic Acid on High-Fat Diet-Induced Cardiomyocyte Dysfunction and Endoplasmic Reticulum Stress

Speaker: Kacy Richmond

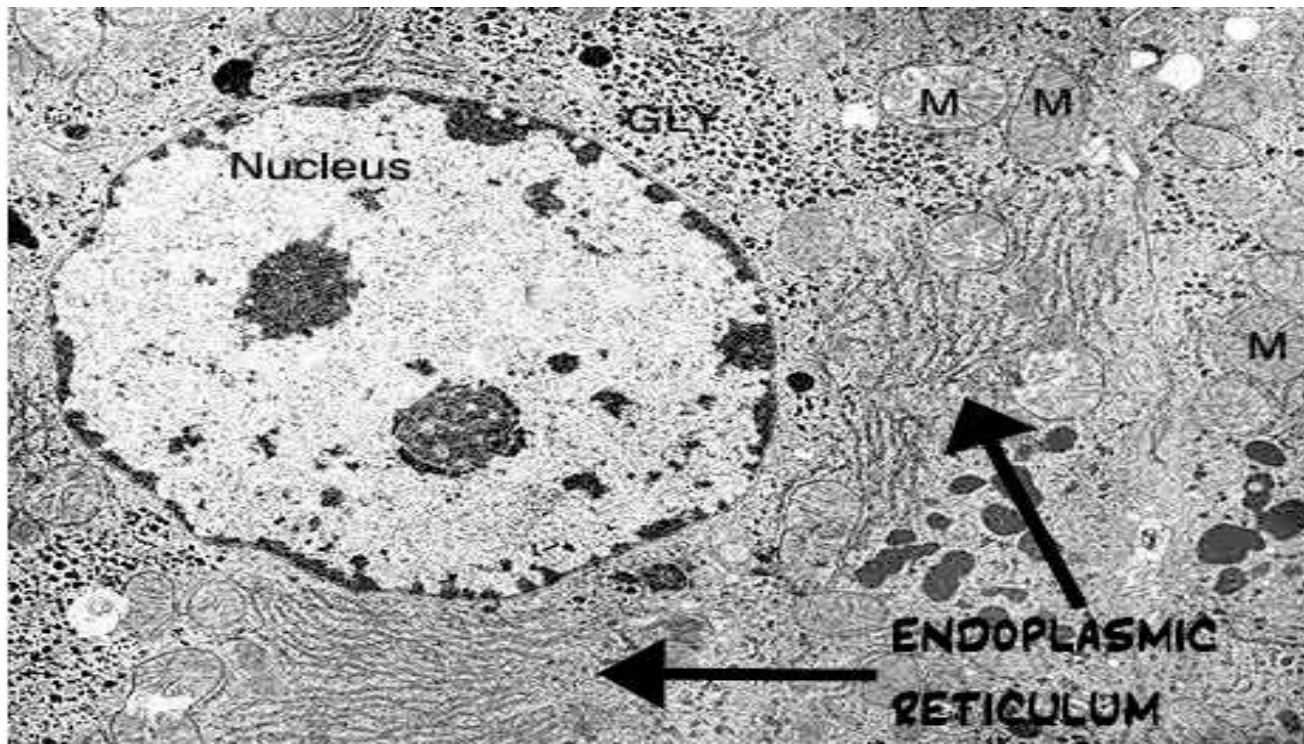
Advisor: Dr. Jun Ren (School of Pharmacy)

## Obesity and Endoplasmic Reticulum (ER) Stress

- Obesity (induced by high-fat diet) is closely associated with the activation of **cellular stress signaling** and inflammatory pathways.
- The ER plays a crucial role in the cellular stress response.

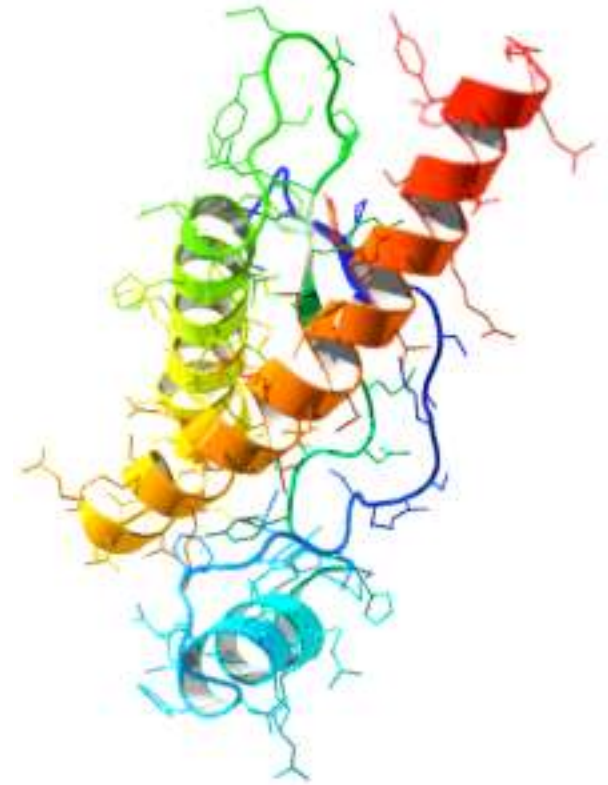
# Endoplasmic Reticulum (ER)

- The ER is a membranous network that functions in the synthesis and processing of secretory and membrane proteins.

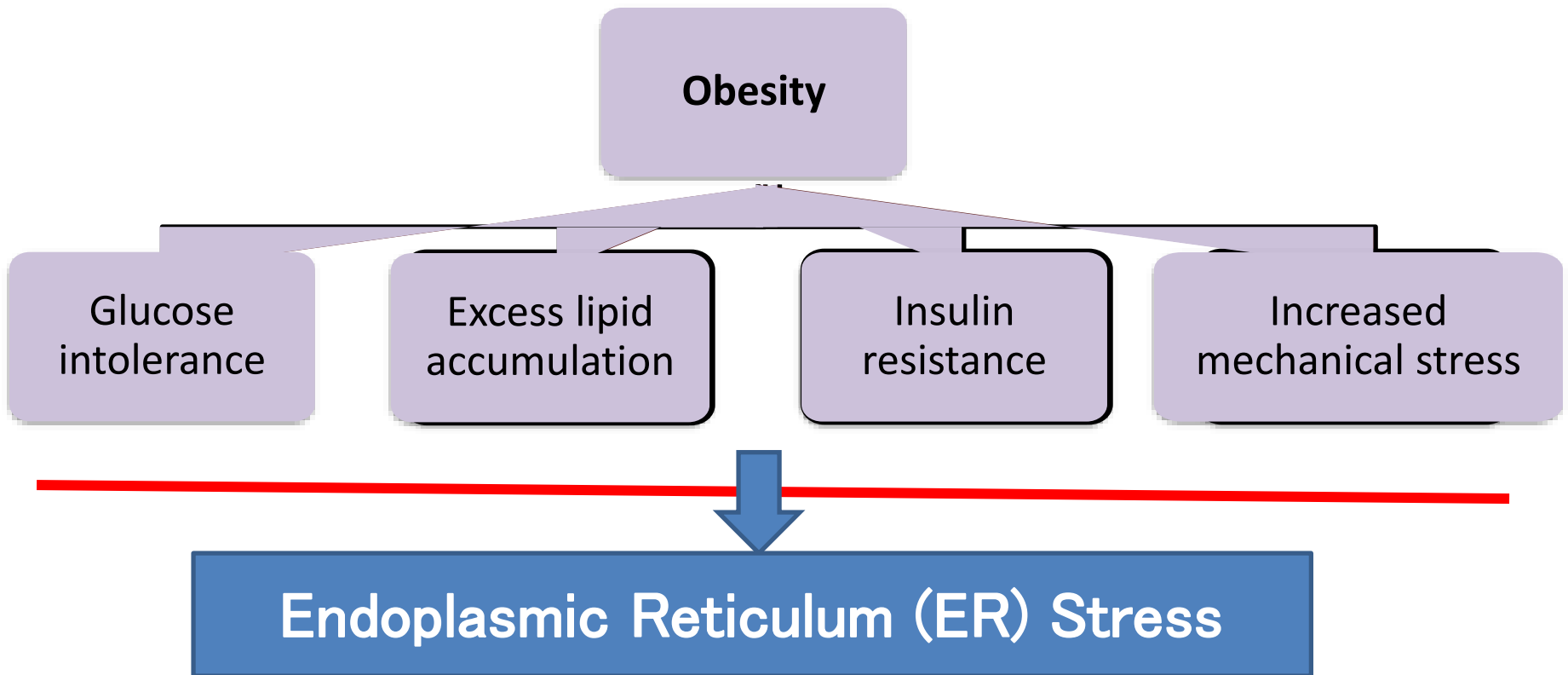


# Obesity and Endoplasmic Reticulum (ER) Stress

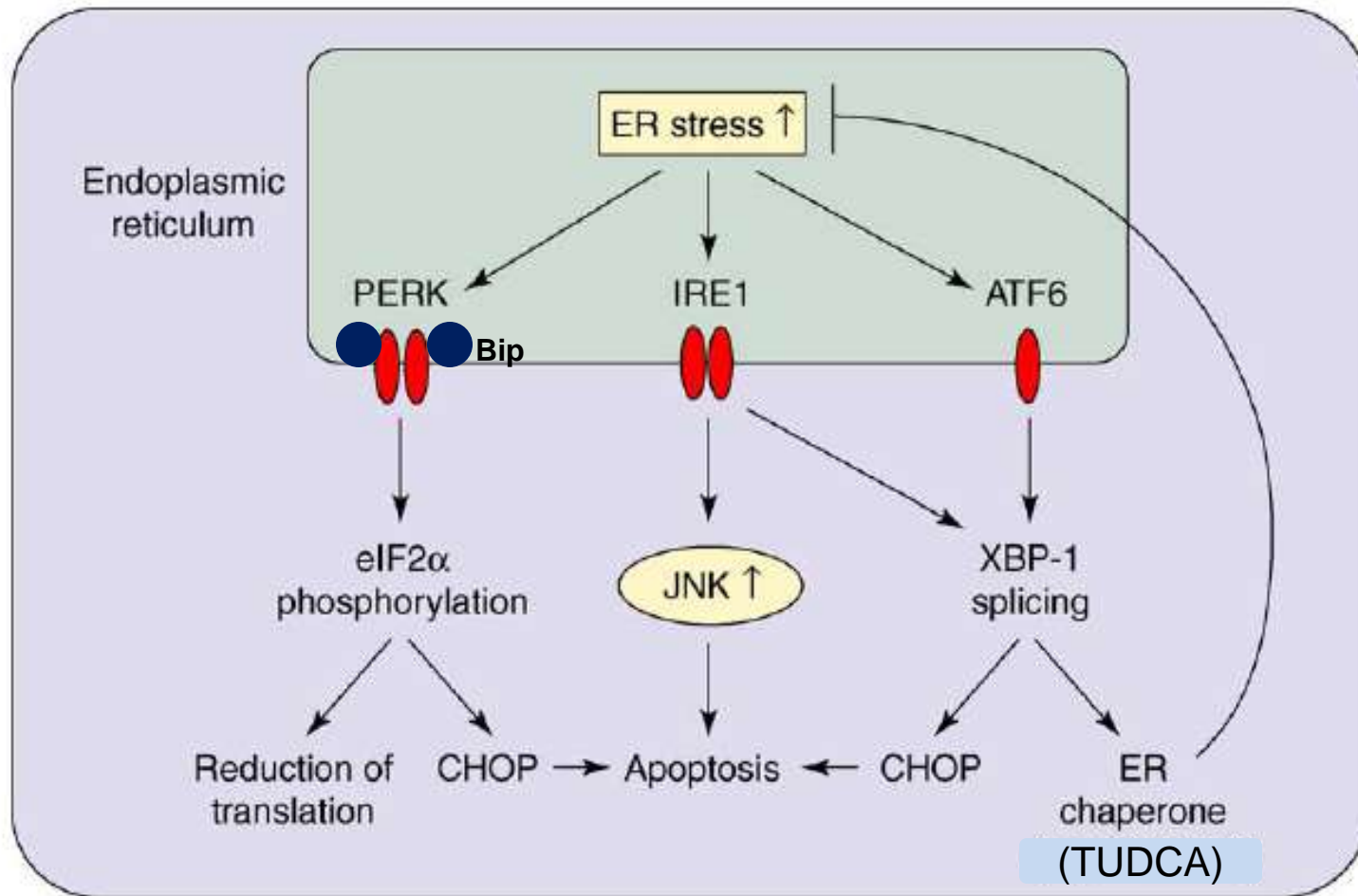
- Numerous conditions, including aging and obesity, can lead to the disruption of ER homeostasis and result in **the accumulation of unfolded or misfolded proteins** in the ER lumen. This often leads to cell death.



# ER Stress induction

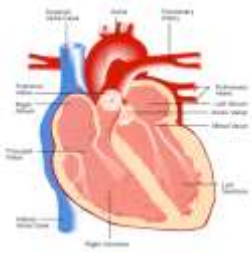


# ER stress signaling



# Tauroursodeoxycholic Acid (TUDCA)

- Taurine-conjugated derivative of ursodeoxycholic acid (TUDCA) is a potent chemical chaperone that inhibits ER stress.
- TUDCA administration to obese and diabetic mice normalized hyperglycemia; restored systemic insulin sensitivity; and enhanced insulin action in skeletal muscle.
- Nevertheless, whether or not TUDCA has an effect on obesity-induced cardiac contractile dysfunction is not clear.



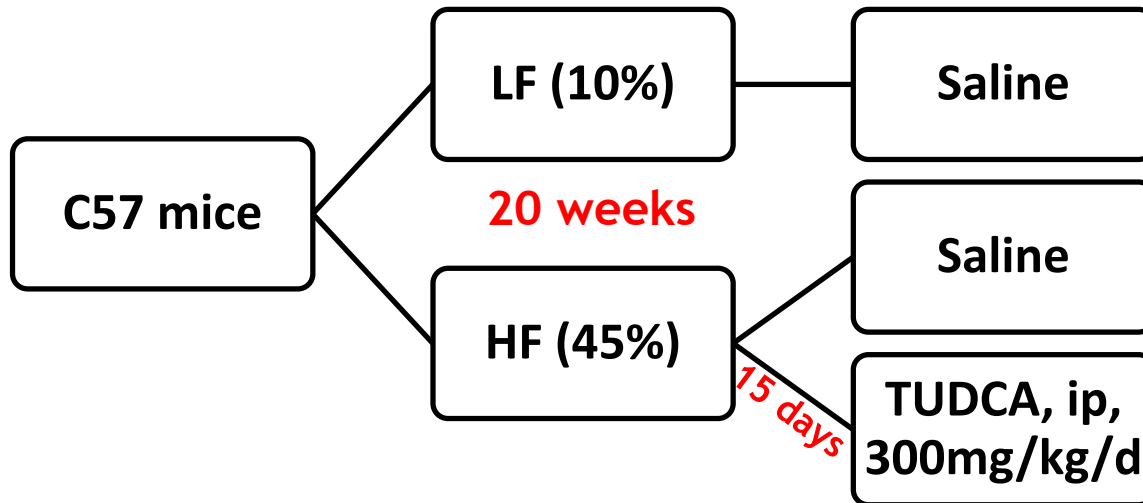
# Hypothesis

- ER stress chaperone — taurooursodeoxycholic acid (**TUDCA**) – can alleviate cardiac contractile dysfunction induced by high-fat diet (HFD).



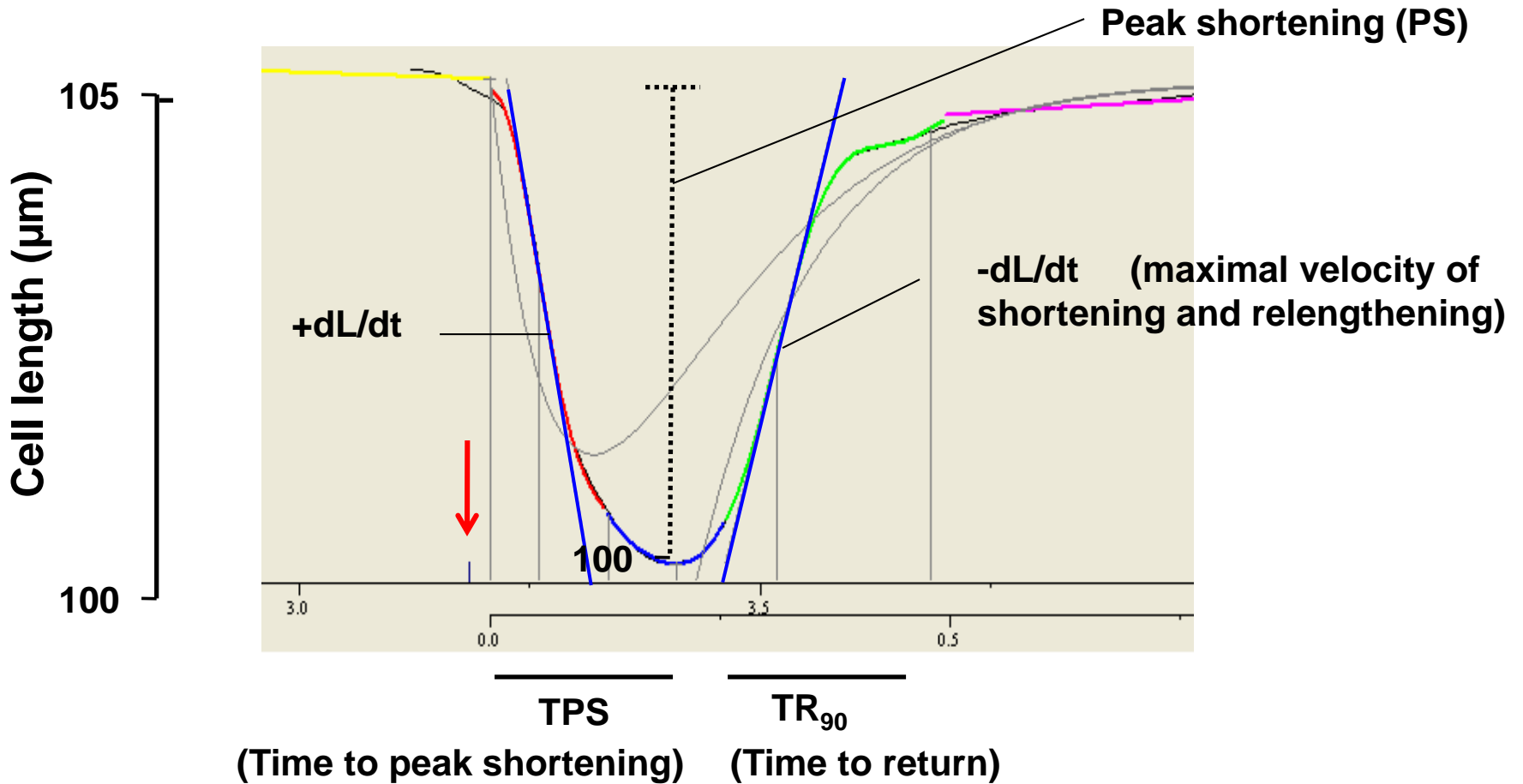
# Methods

- High-fat diet induced obesity model:



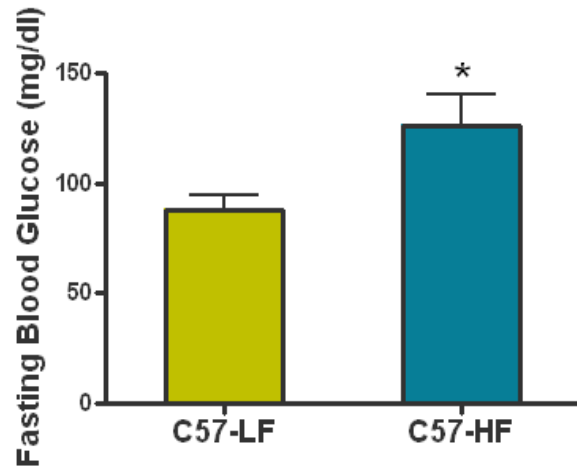
- [Isolated cardiomyocyte contractile functions;](#)
- Western blot analysis of ER stress proteins

# Isolated cardiomyocyte contractile function

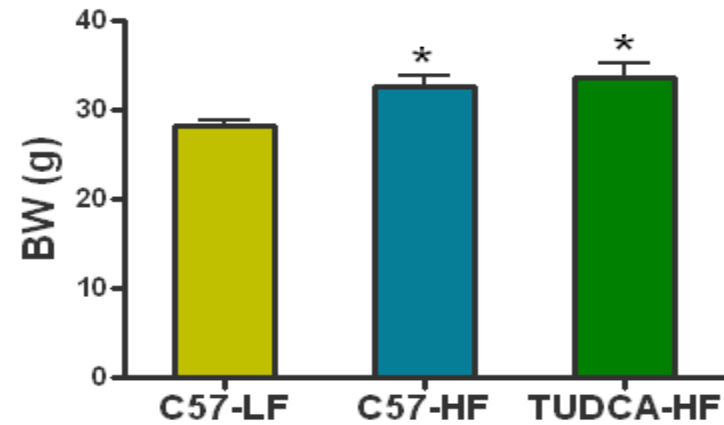


# General characteristics of the mice

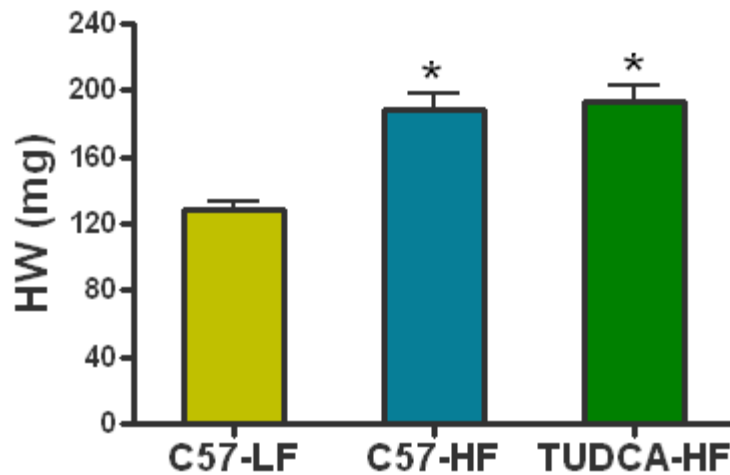
A.



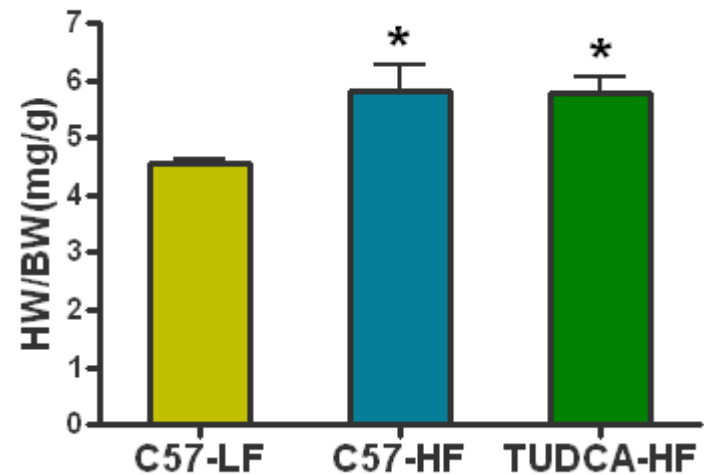
B.



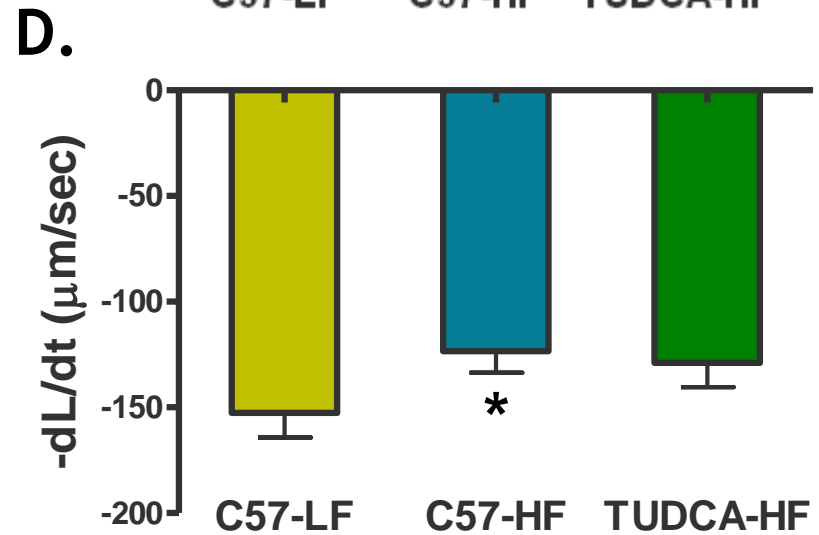
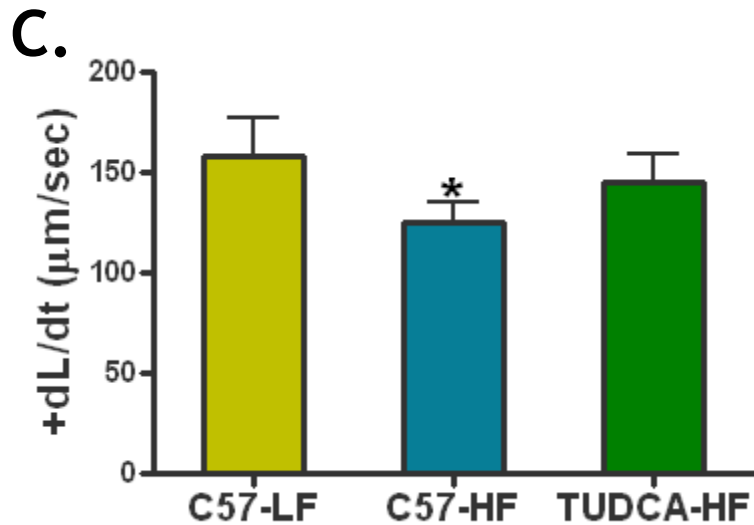
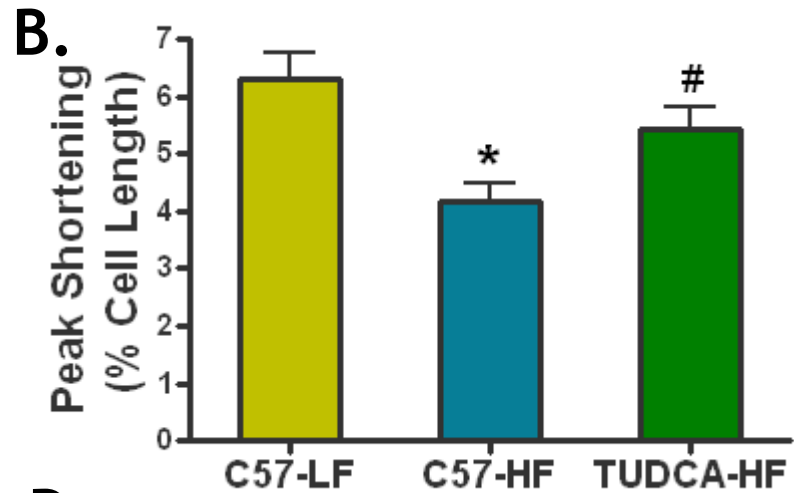
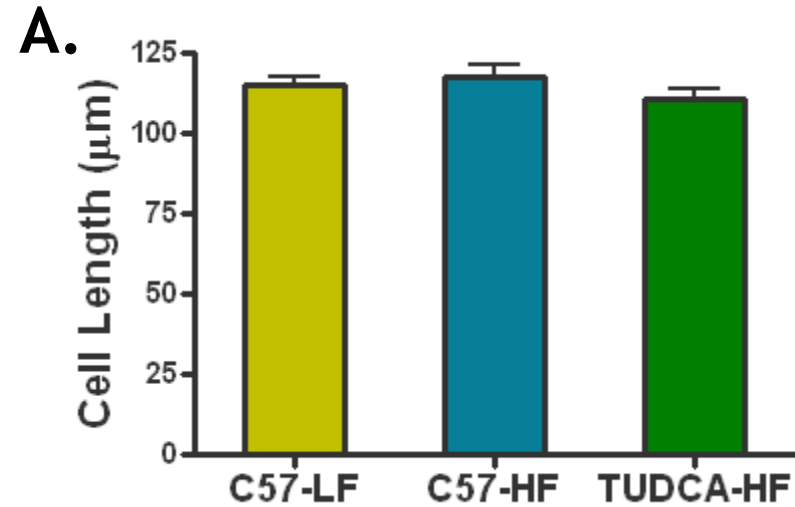
C.



D.



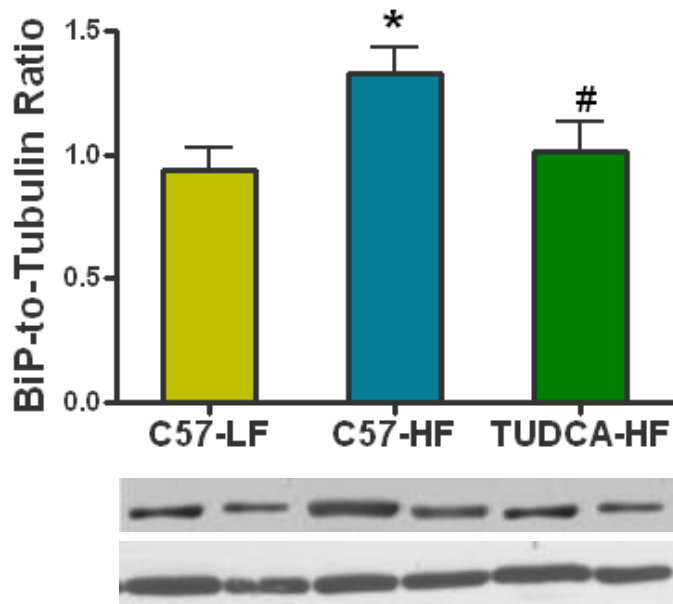
## 2. TUDCA partially restores cardiomyocyte function



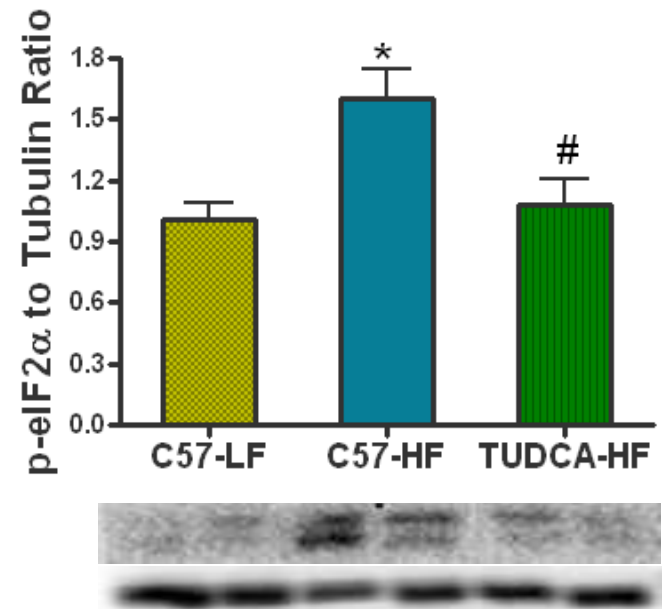
\* $p < 0.05$  vs C57-LF; # $p < 0.05$  vs C57-HF;

## TUDCA inhibits ER stress

**A.**

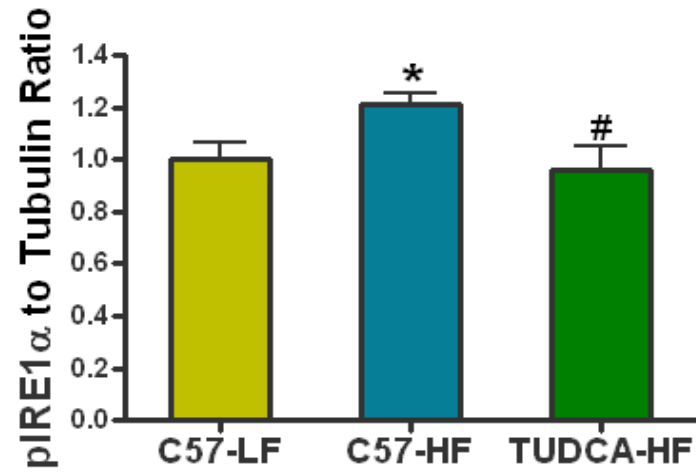


**B.**



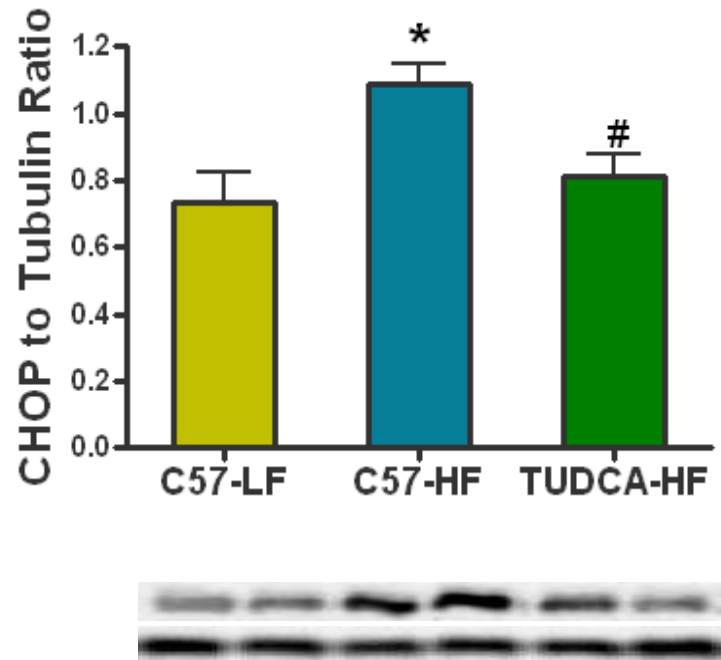
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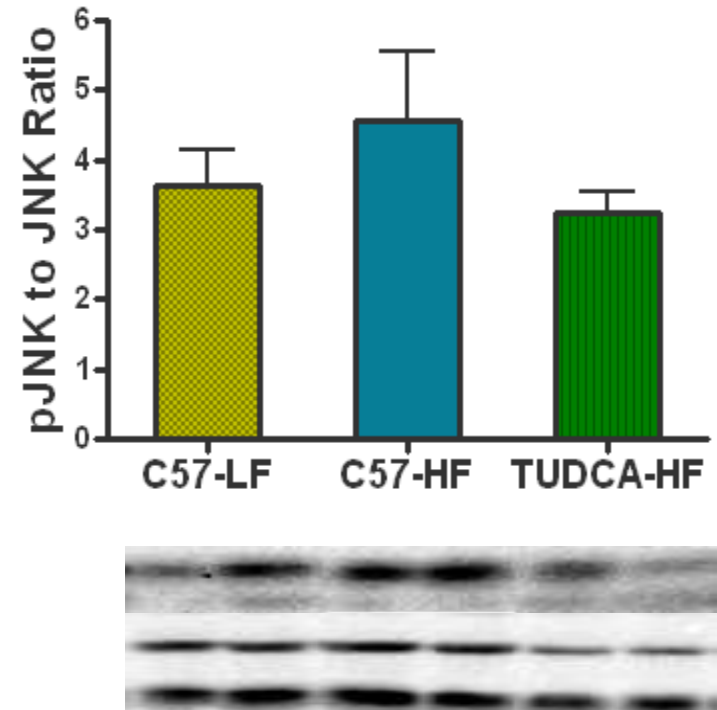


## TUDCA inhibits ER stress

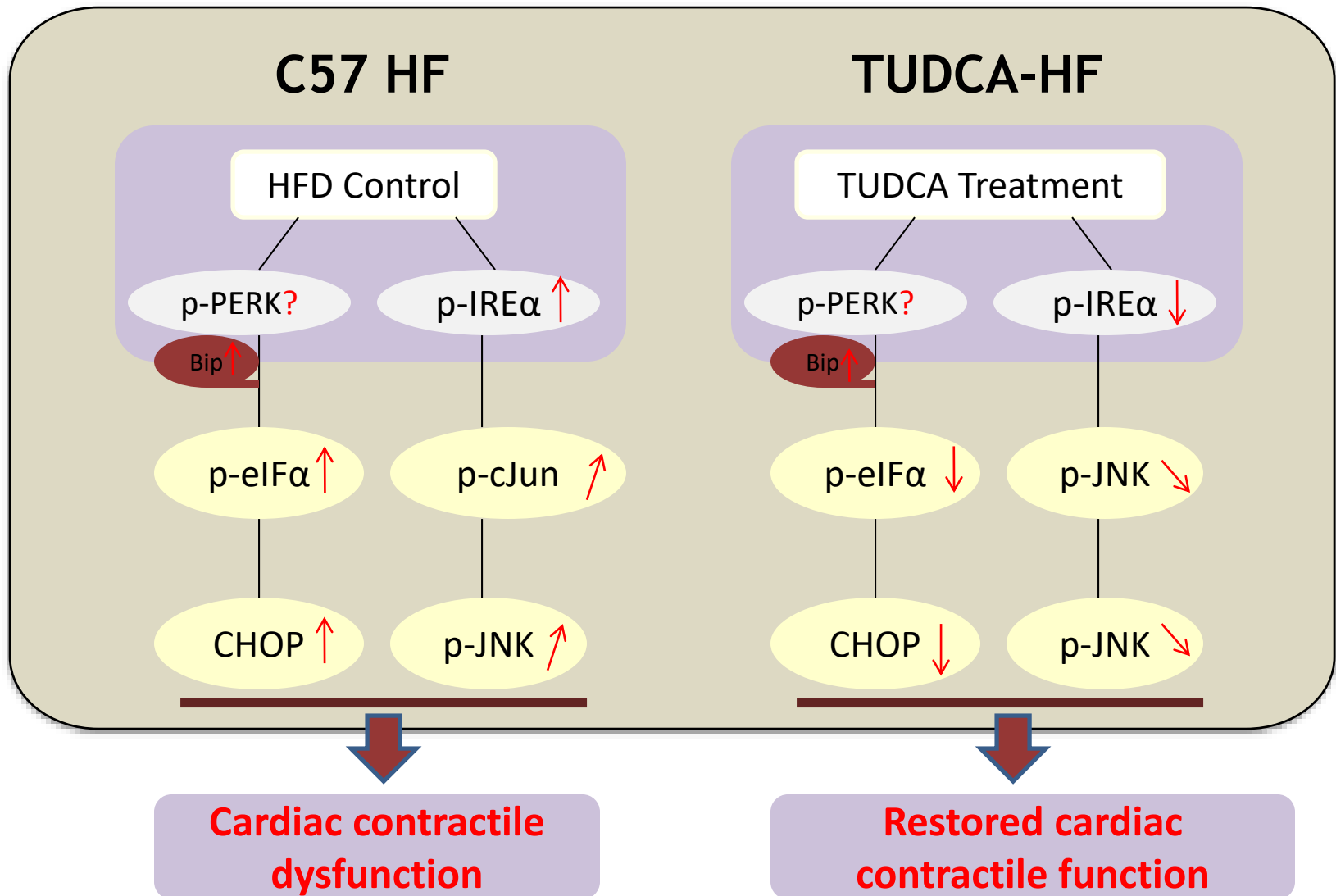
**A.**



**B.**

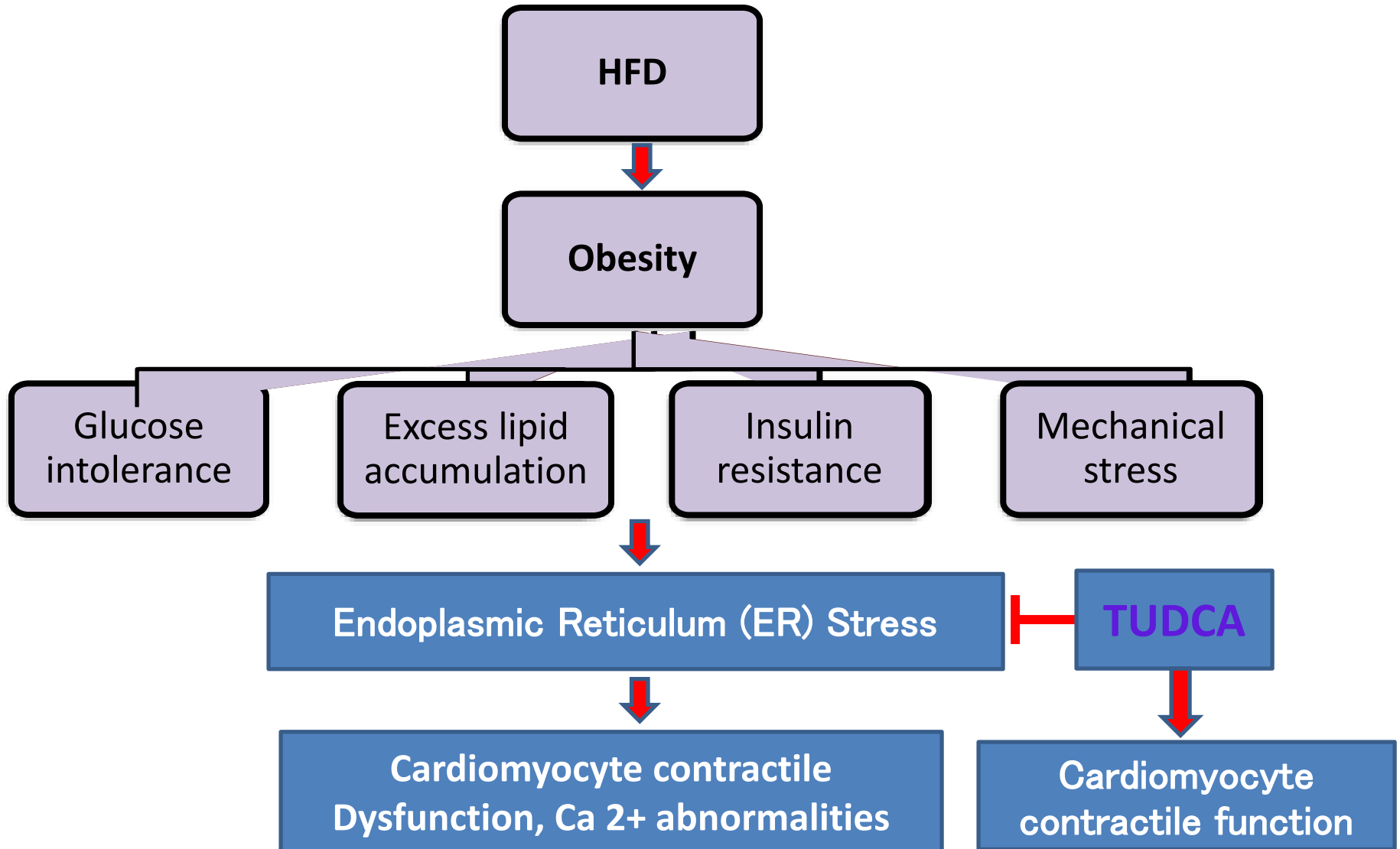


# ER Stress Signaling Pathway Summary





# Results, Summary and Conclusion



# Future directions

- Study the impact of TUDCA on cardiac insulin signaling
- Effects of TUDCA on cardiomyocyte function using tunicamycin-induced ER stress in vitro

# Acknowledgment

- Dr. Jun Ren
- Subat Turdi

**Thank you!**