

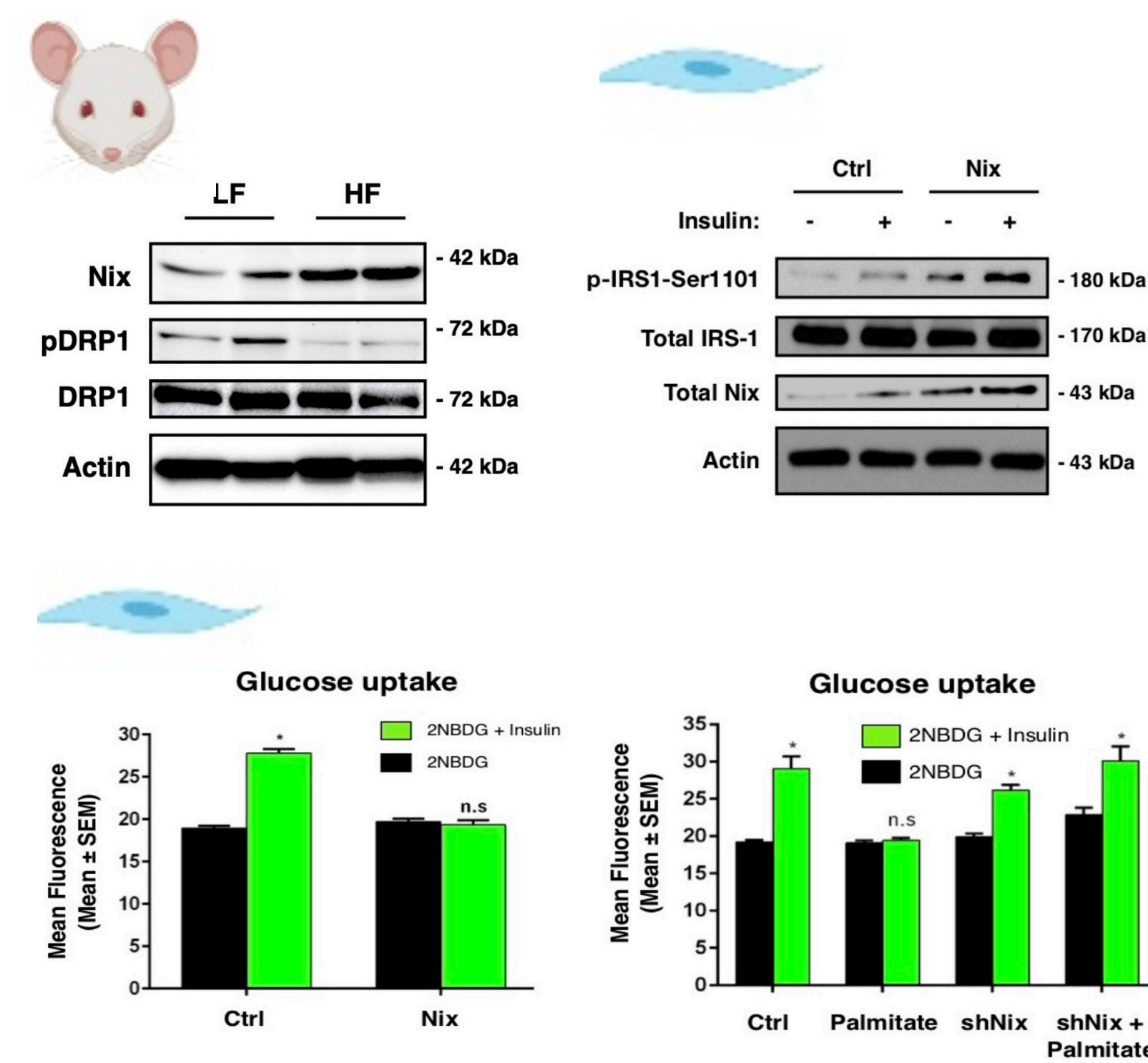
# Tuning Muscle Energy Homeostasis: The Role of Nix in Muscle Metabolism

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## INTRODUCTION

- Dysregulation of muscle metabolism is an early event in the natural history of **type 2 diabetes** and metabolic disease.
- Maintenance of high-quality mitochondria is essential for muscle metabolism.
- Nix is a protein of the BCL-2 family, and regulates mitochondrial turnover (mitophagy).**



## AIM

**Central Research Question: What aspects of skeletal muscle metabolism does Nix affect?**

- Hypothesis 1:** Deletion of Nix results in dysfunctional mitochondrial turnover leading to impaired muscle metabolic capacity.
- Hypothesis 2:** Deletion of Nix disrupts insulin signalling and glucose handling through dysfunctional mitochondrial turnover.

## ACKNOWLEDGEMENTS

Connect with us:  
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Supported by:

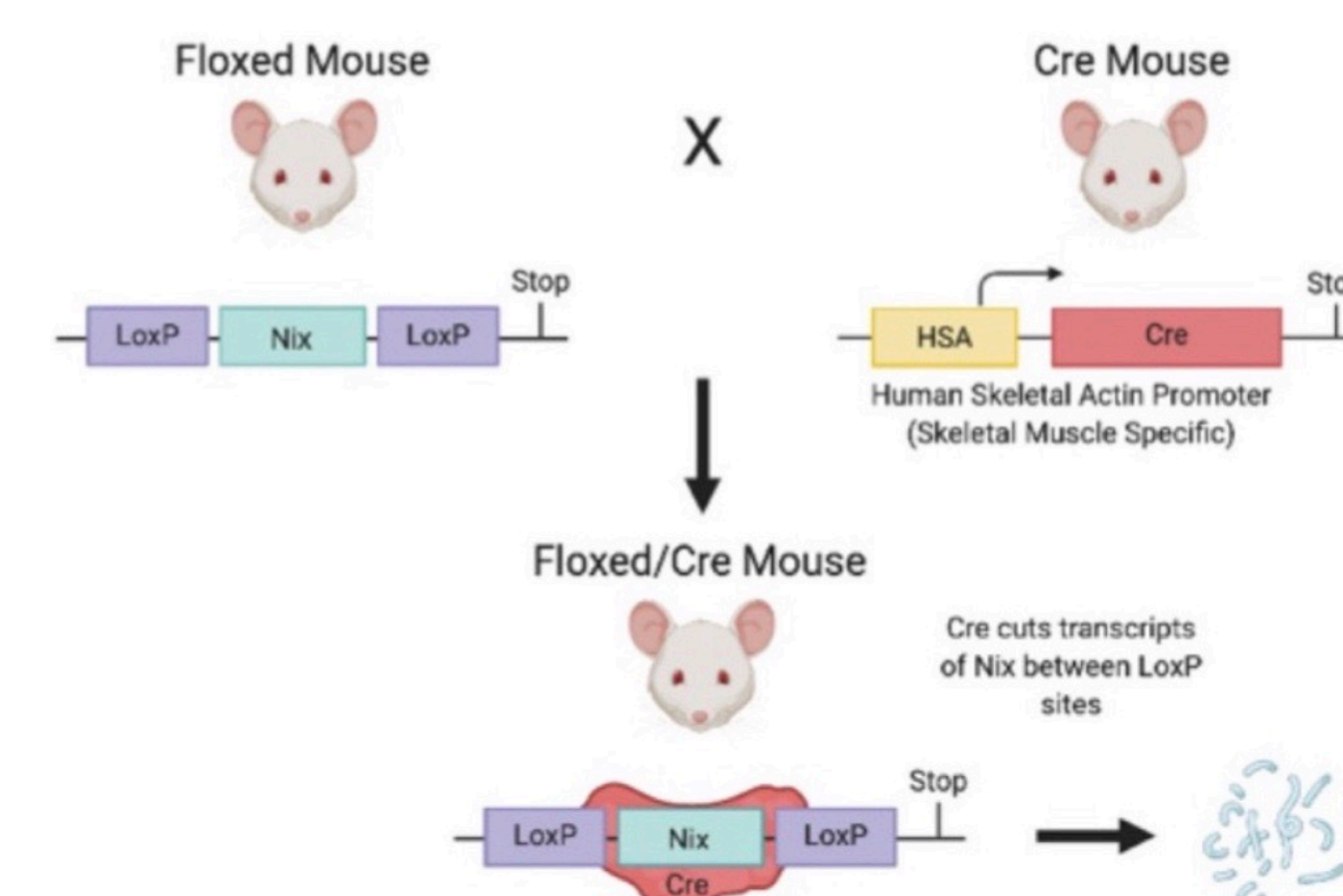


## METHODS

### Skeletal Muscle-Specific Nix Deletion

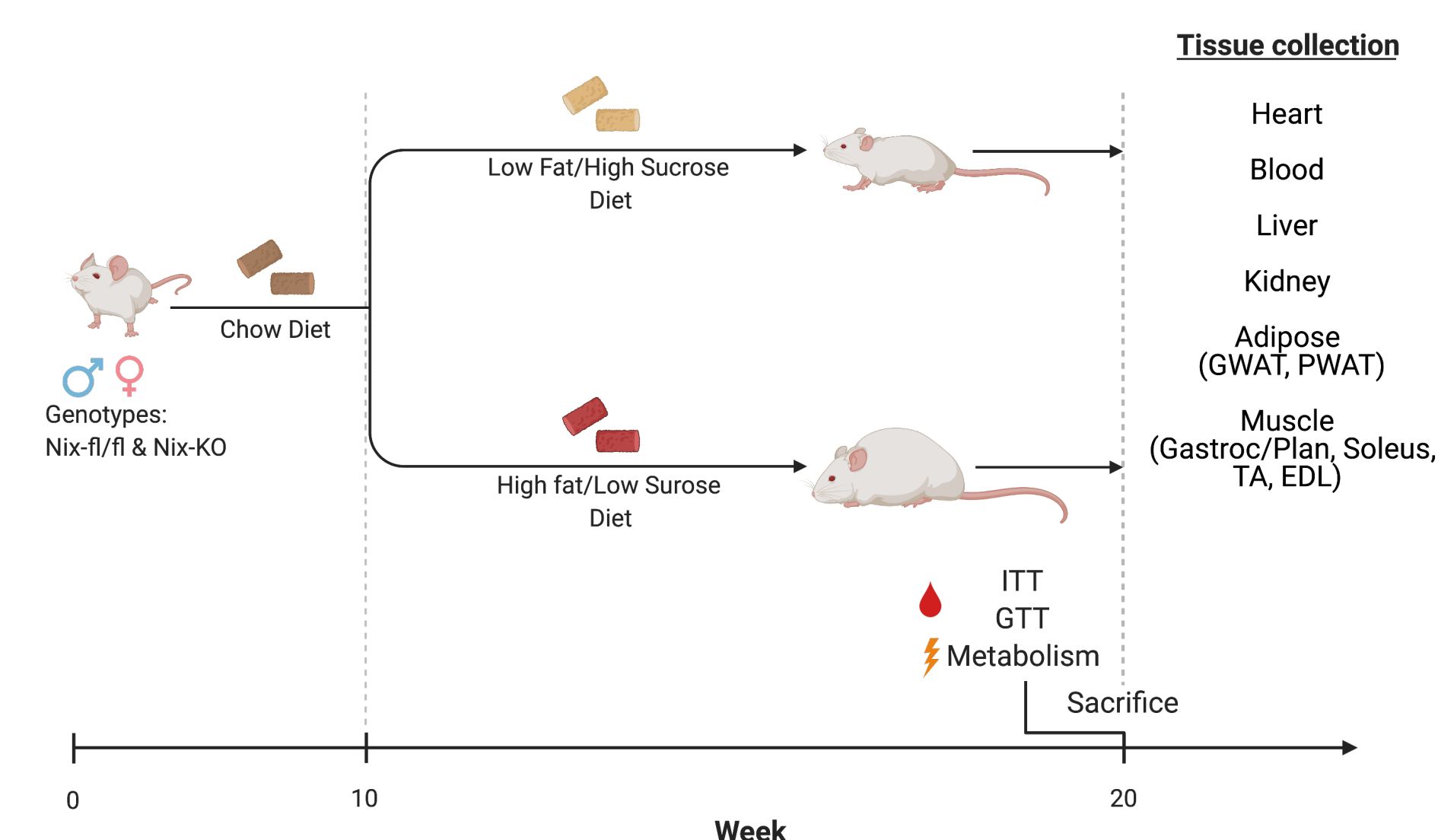
In vivo physiological Endpoints: Whole-body metabolism, Insulin/Glucose tolerance tests.

Histology (Gomori Trichrome & TEM). Kinase-omics (kinomics)



### Diet Study - Challenged with High Fat or High Sucrose Diets

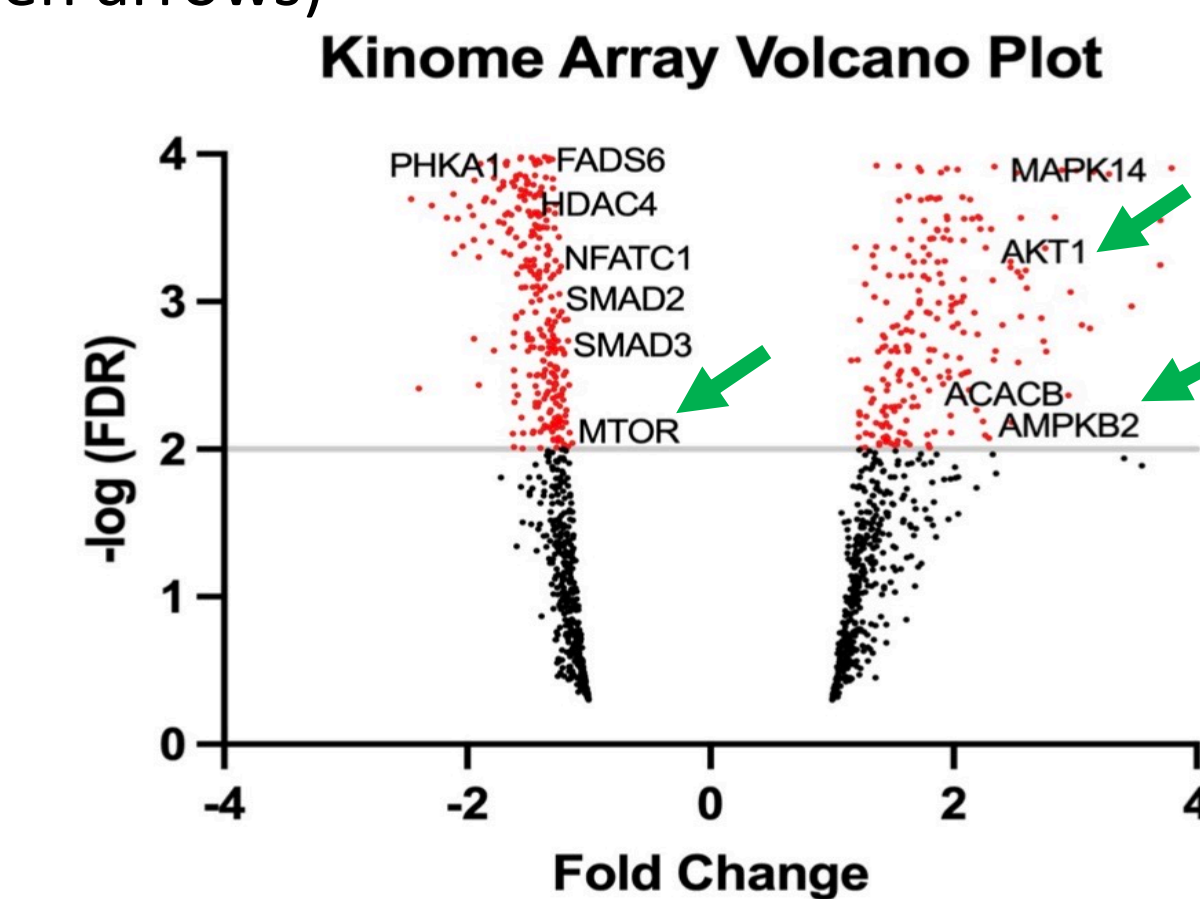
In vivo physiological Endpoints: Insulin/Glucose tolerance tests



## RESULTS

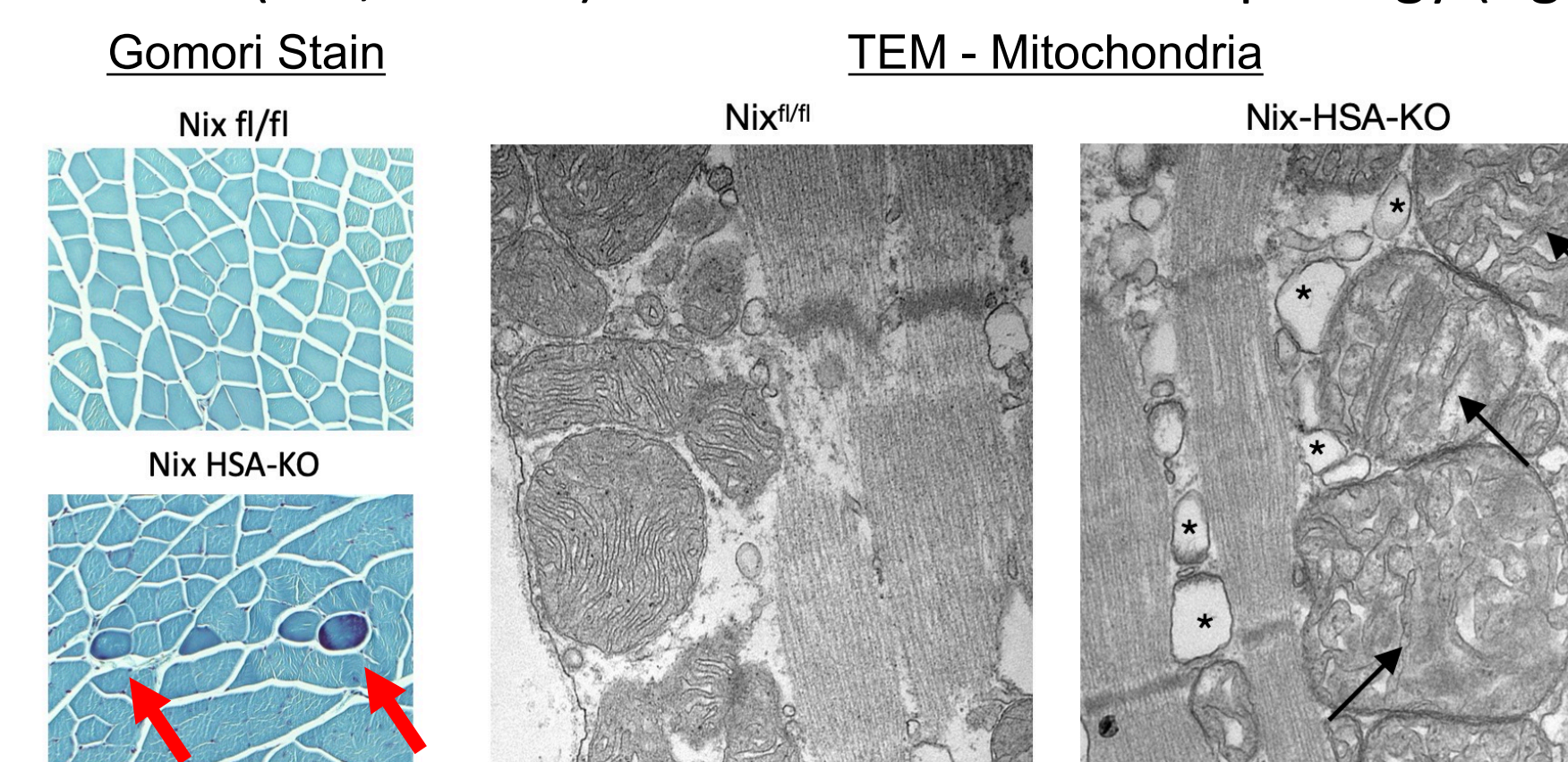
### Kinase-omics

Dysregulation of key metabolism and insulin signalling kinases (green arrows)



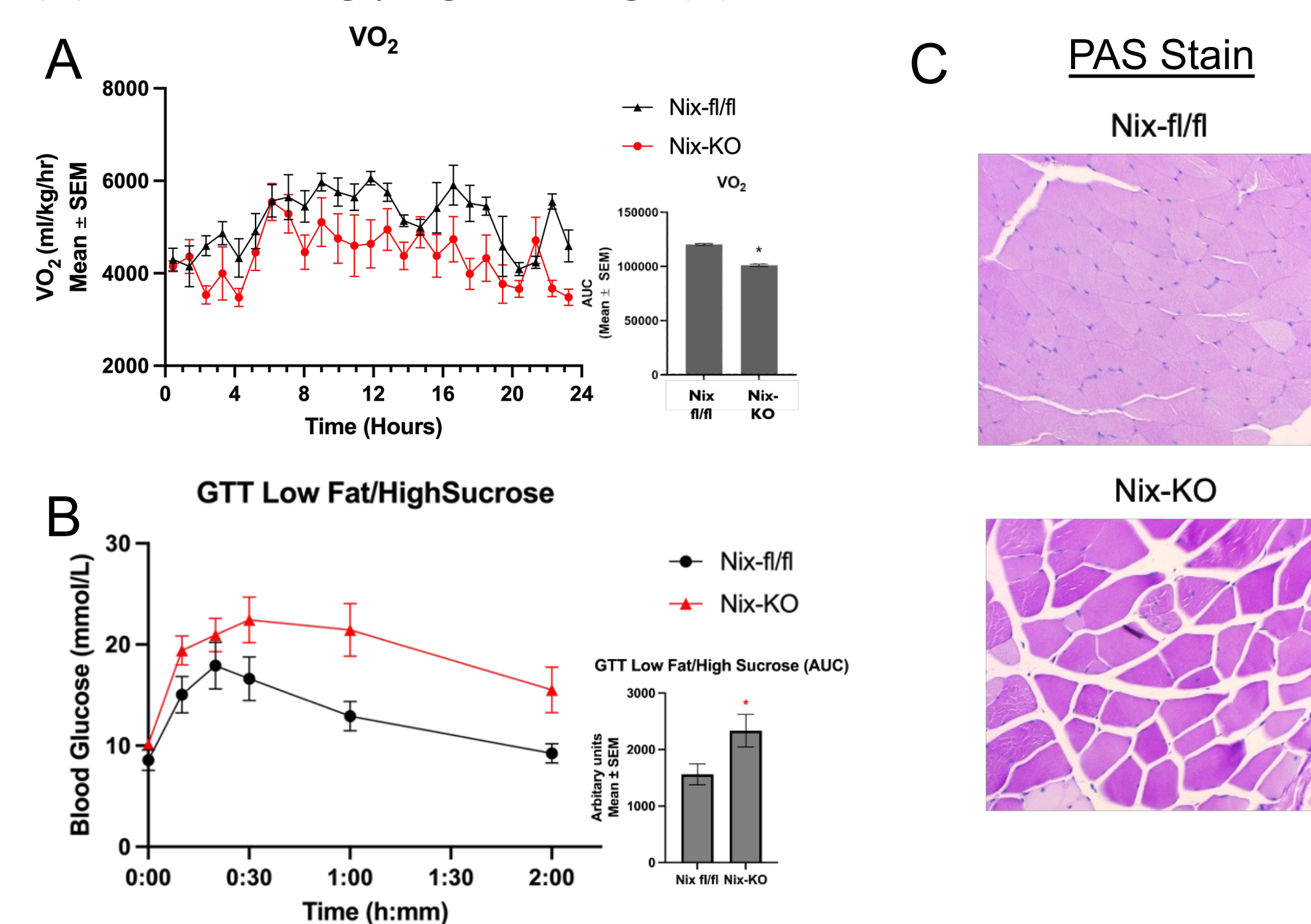
### Mitochondrial Disruption

Impaired removal of senescent mitochondria. Ragged red fibres (left, arrows) and mitochondrial morphology (right)



### Metabolic Disruption

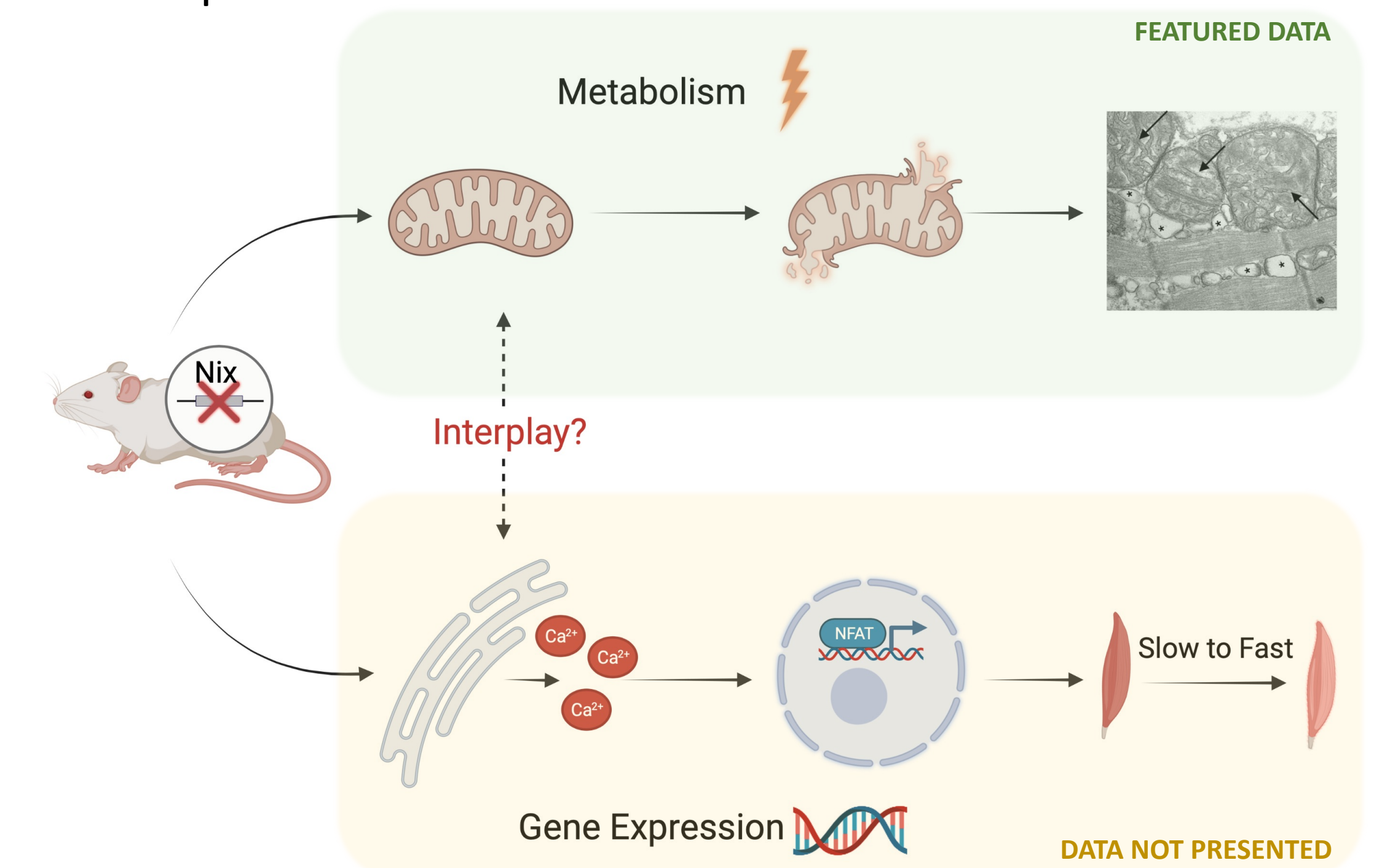
Impairment of whole-body metabolism (A), glucose tolerance (B) and altered glycogen storage (C)



## Summary

### Graphic summary of phenotypes of Nix-KO mouse

Metabolic disruption (top) featured here. Calcium-regulated changes in gene expression (bottom) not presented.



## CONCLUSION

**Nix appears to be a key regulator of muscle mitophagy, metabolism, & fiber type characteristics**

In Skeletal Muscle Nix Has a Role in:

- Mitochondrial Clearance
- Basal Metabolism & glucose metabolism

