

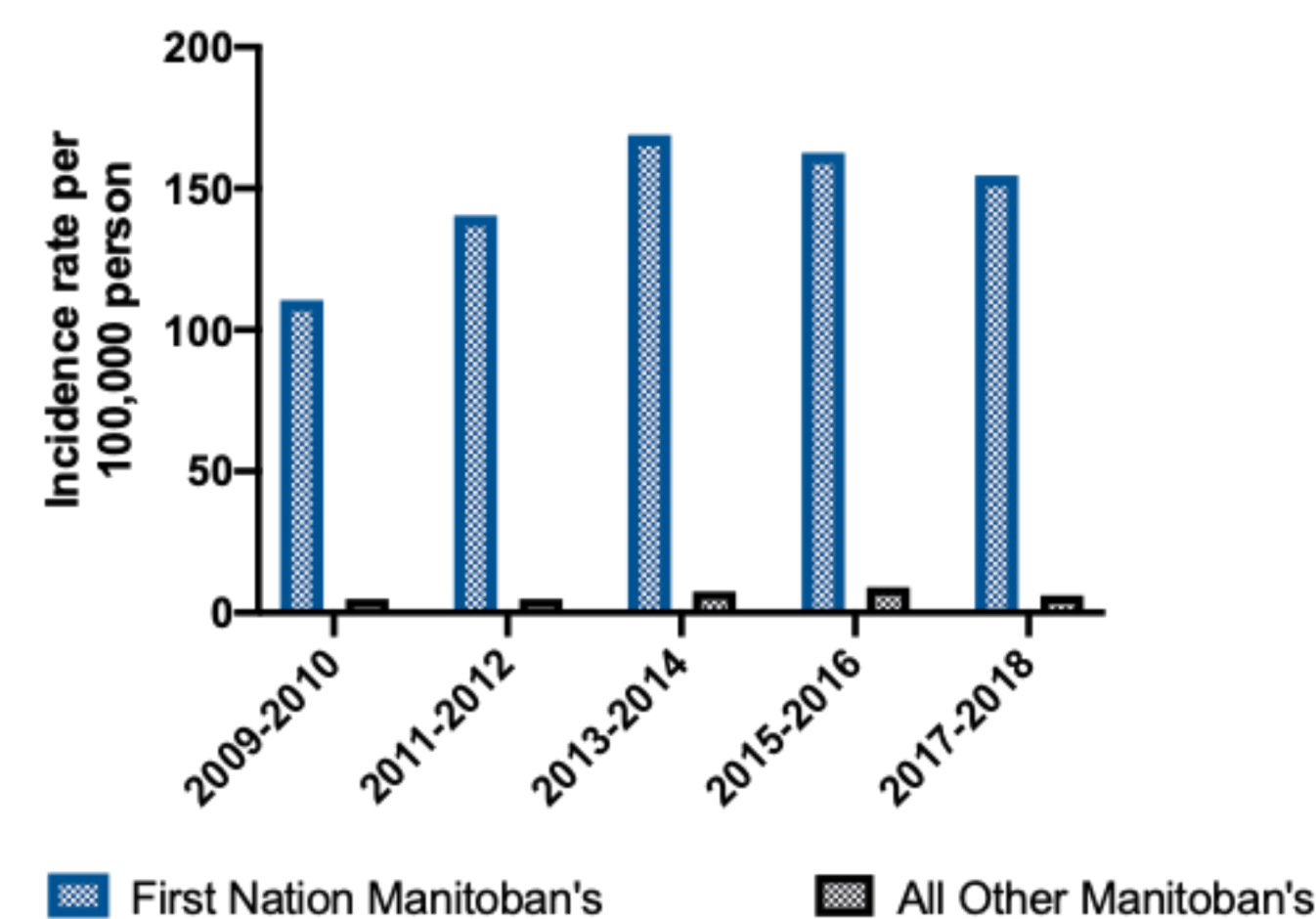
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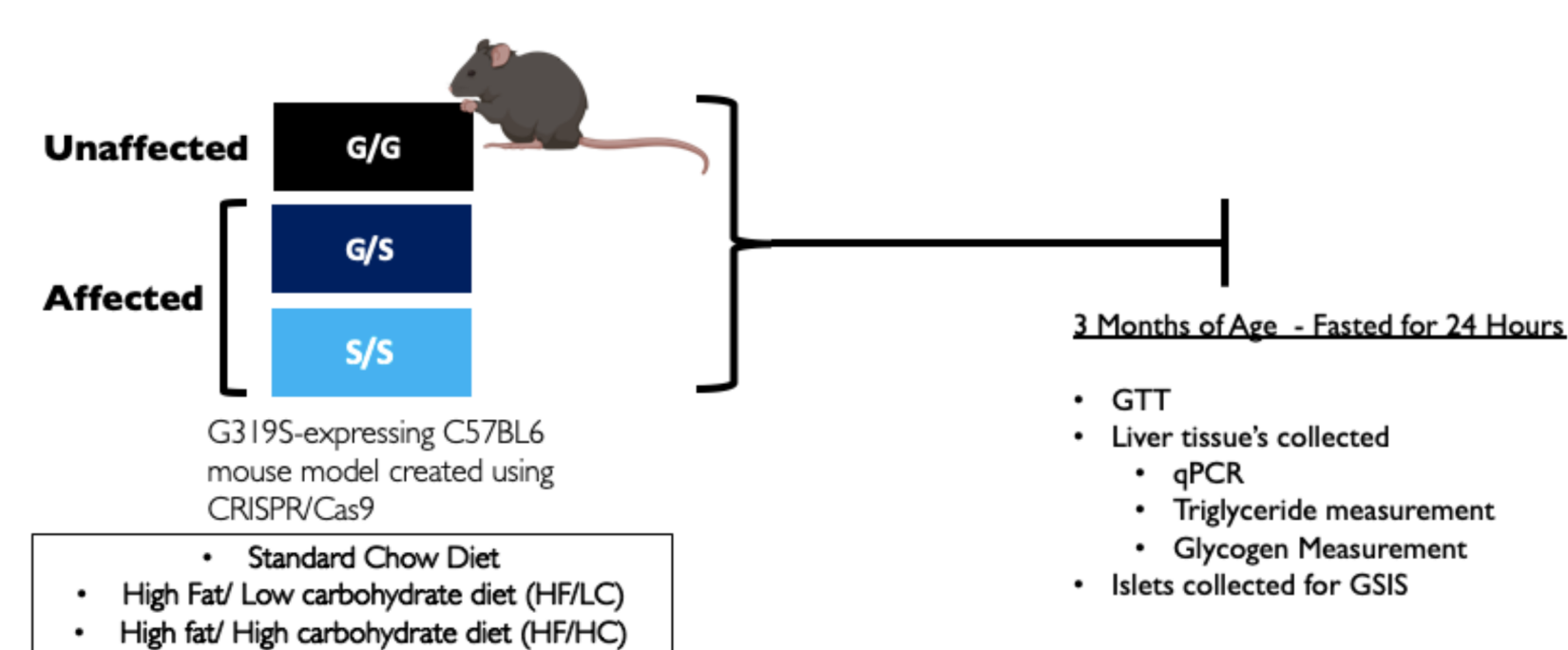
INTRODUCTION

- Type 2 Diabetes (T2D) diagnoses in Anishinew linguistic group of Northeastern Manitoba and Northwestern Ontario are among the highest in the world
- 82.4% of youth with T2D diagnoses in Manitoba are registered as first nations
- Genetic variant known as HNF-1a G319S in this population has been associated with earlier development of T2D
- Historically, T2D was rare in this population when consuming a traditional diet and lifestyle consisting of fasting.
- G319S variant was present prior to rise of T2D. Therefore the interaction of diet, lifestyle, and genetics in rise of T2D remains poorly understood

Incidence Rate of T2D Among children aged 7-17 in Manitoba



METHODS



HYPOTHESIS

• The G319S variant increases hepatic fuel production after a long term fast, in a gene dose dependent manner

• In the pancreatic beta cells, mice with the G319S variant will show a greater depletion of insulin content (less insulin/ reduced number of mature granules) after a long term fast

RESULTS

Liver Triglyceride

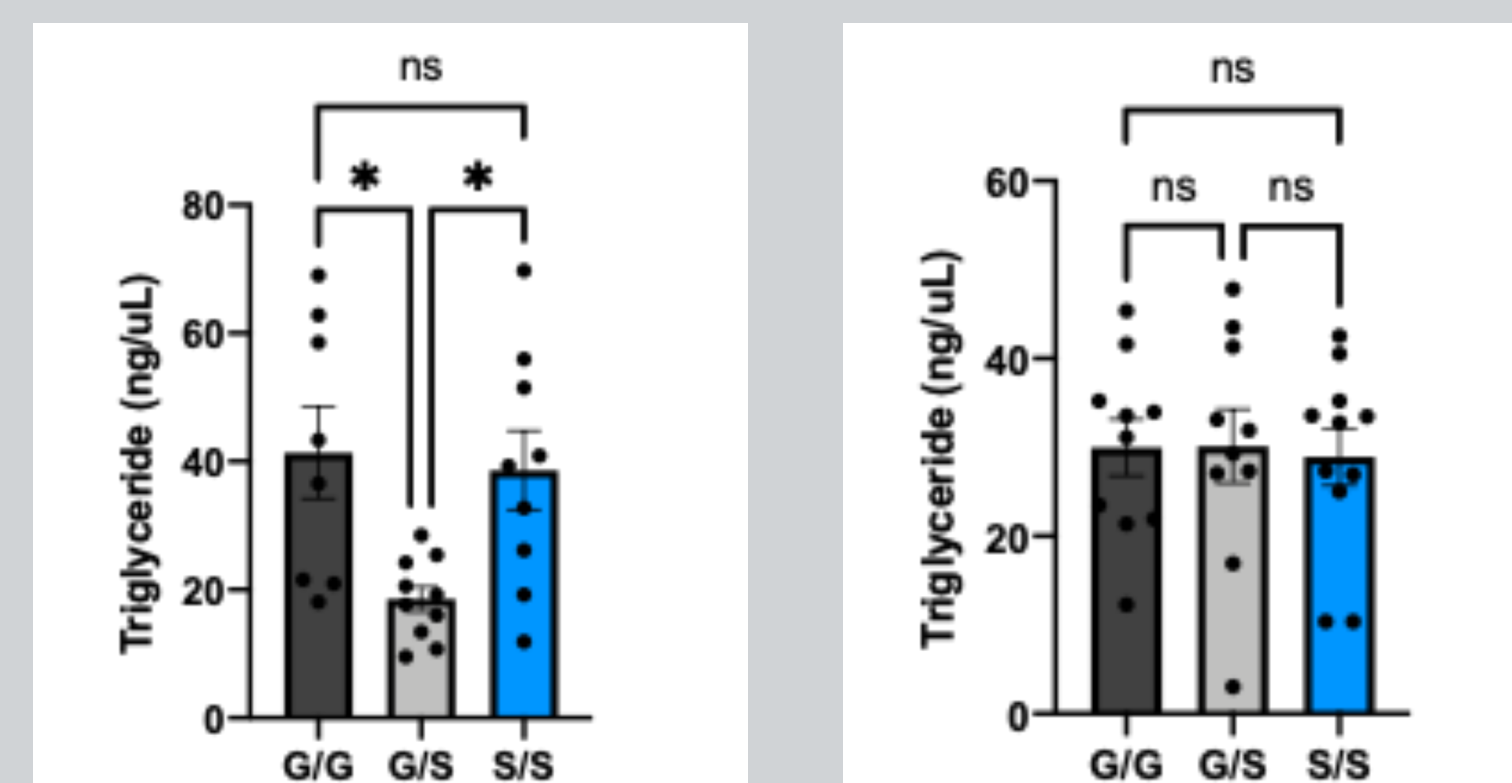


Figure 1: Liver triglyceride content of chow fed male mice (1A) and female mice (1B). Data represented as group mean ± SEM. N=10-12 *p <0.05, **p <0.01 determined by 1-way anova

Liver gene expression

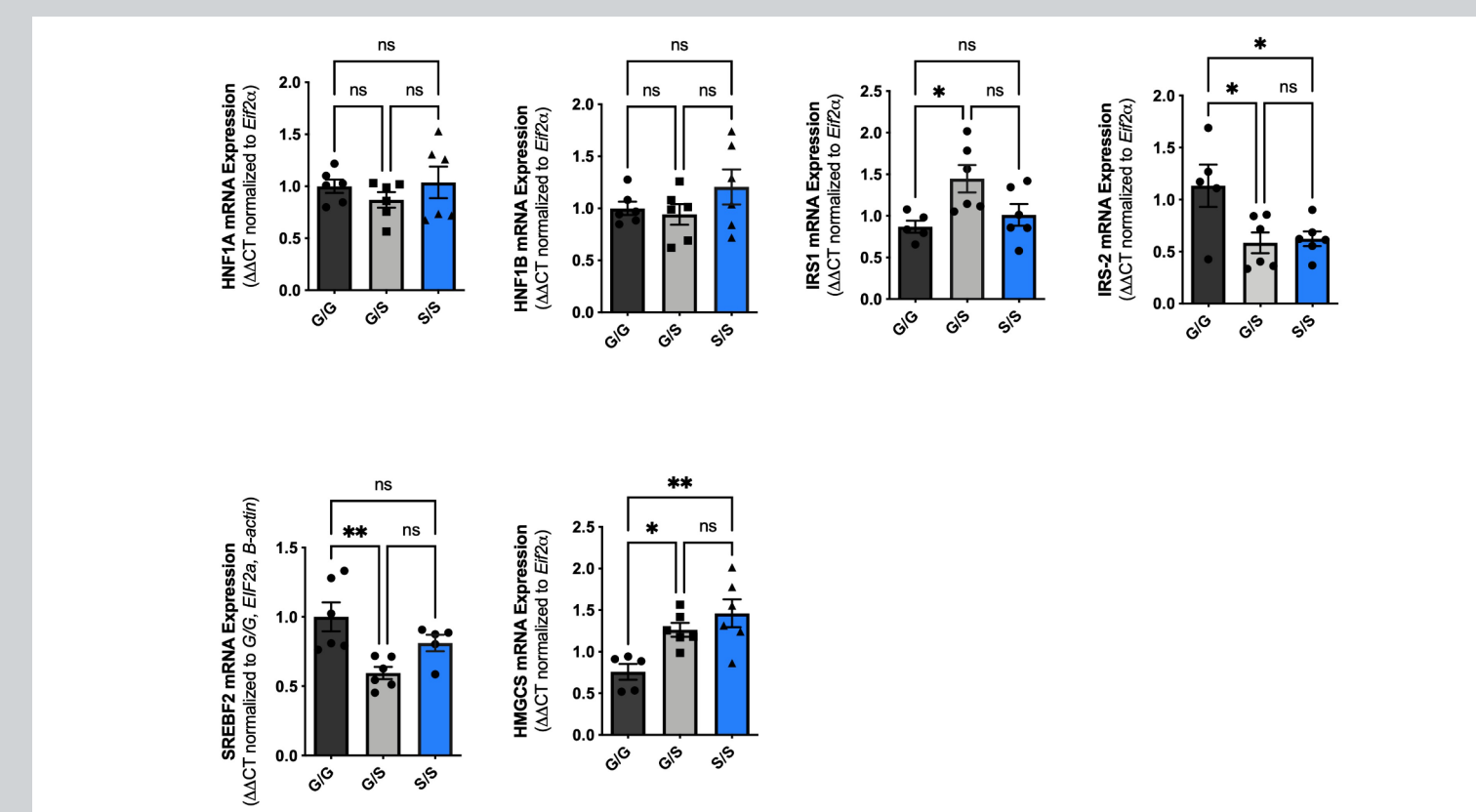


Figure 2: Liver triglyceride content of female mice fed chow diet, HF/LC, and HF/HQ. Data represented as group mean ± SEM. N=5-6 *p <0.05, **p <0.01, ***p <0.001, ****p <0.0001 determined by 2-way anova

24 hour fasted blood glucose and ketones

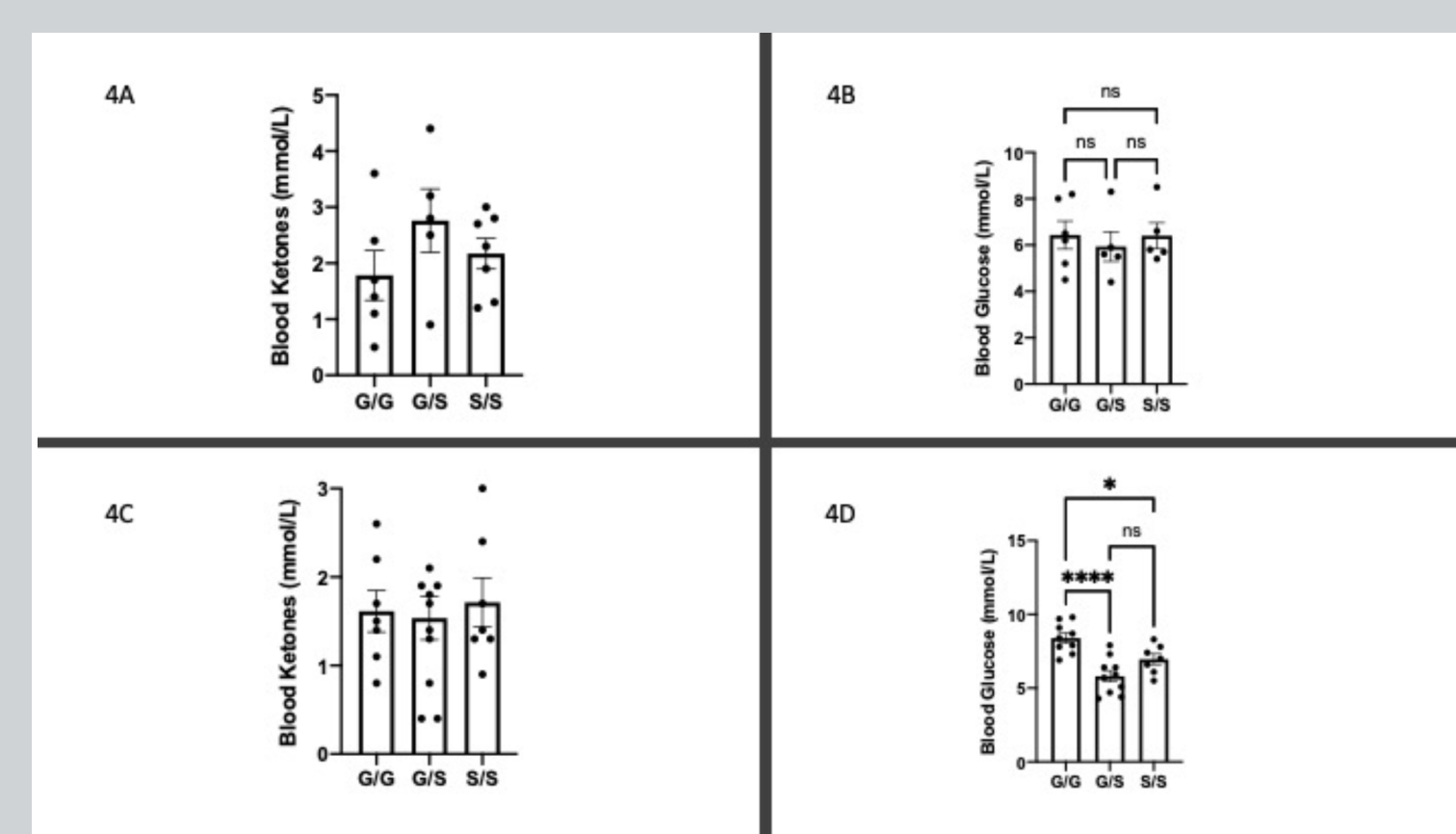


Figure 4: 3 Month male and female 24 hour fasted blood glucose and blood ketone levels. Data represented as group mean ± SEM. N=10-12 *p <0.05, **p <0.01 determined by 1-way anova

Glucose Stimulated Insulin Secretion of Islets

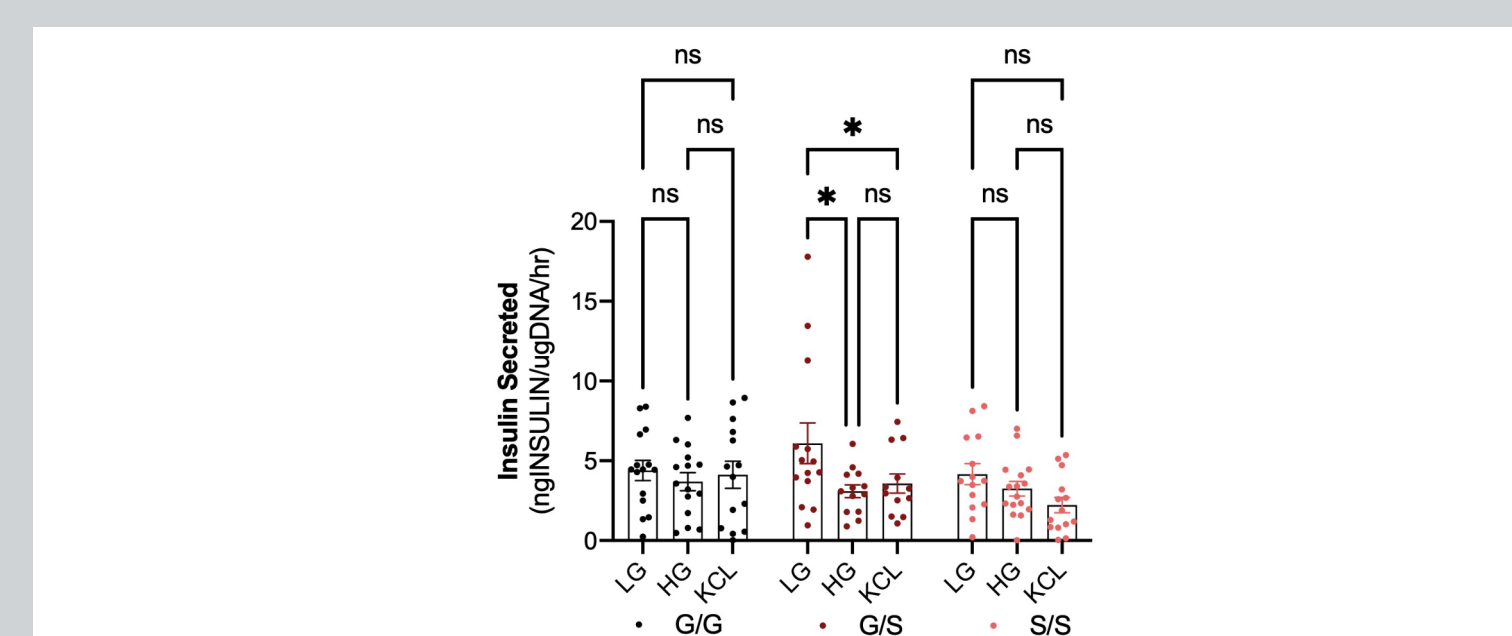


Figure 7: 3 Month male and female 24 hour fasted blood glucose and blood ketone levels. Data represented as group mean ± SEM. N=10-12 *p <0.05, **p <0.01 determined by 1-way anova

Electron Microscopy Imaging of Pancreatic Islets

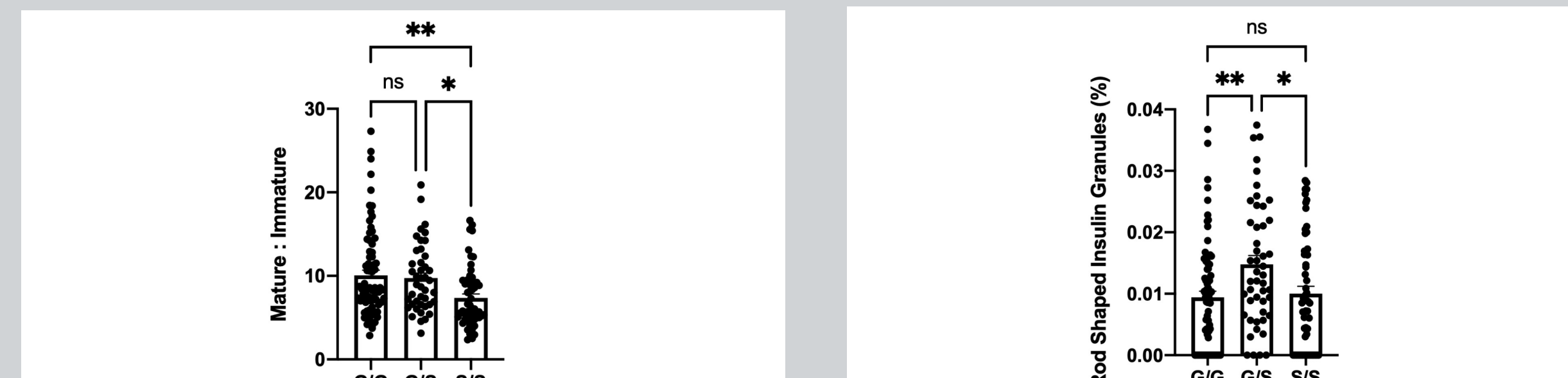
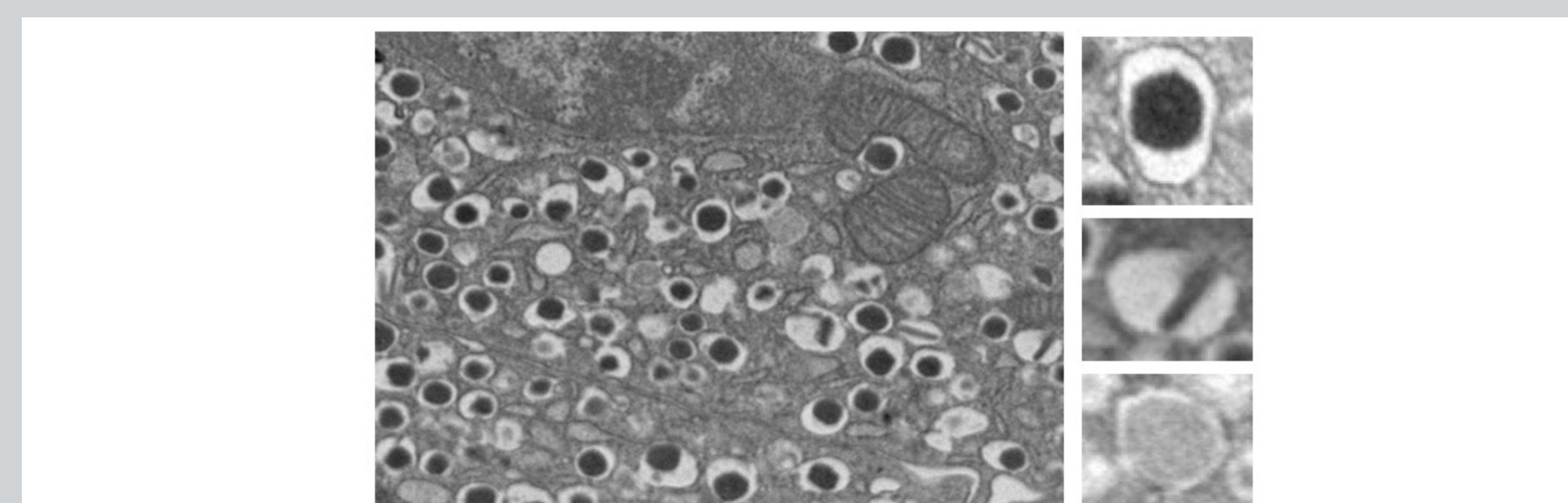


Figure 5: Electron Microscopy Imaging of pancreatic islets. Data represented as group mean ± SEM. *p <0.05, **p <0.01 determined by 1-way anova

24 Hour fasted Glucose Tolerance of 3 Month Mice

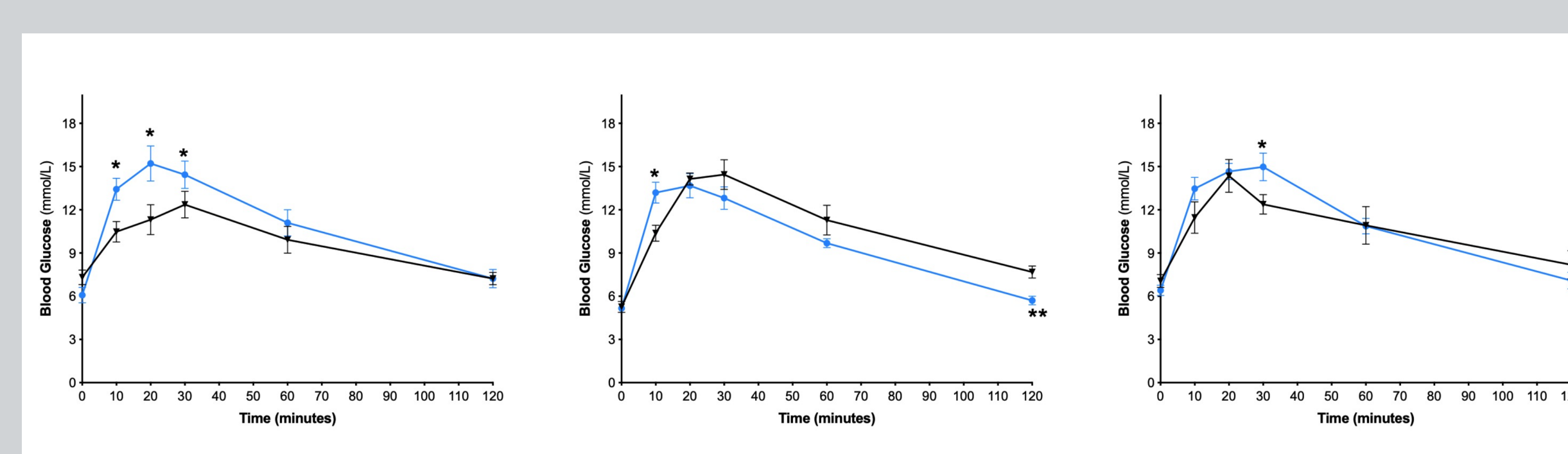


Figure 6: 3 Month male (24 Hour fasted - blue), and overnight fasted (black) Data represented as group mean ± SEM. N=10-12 *p <0.05, **p <0.01 determined by 1-way anova

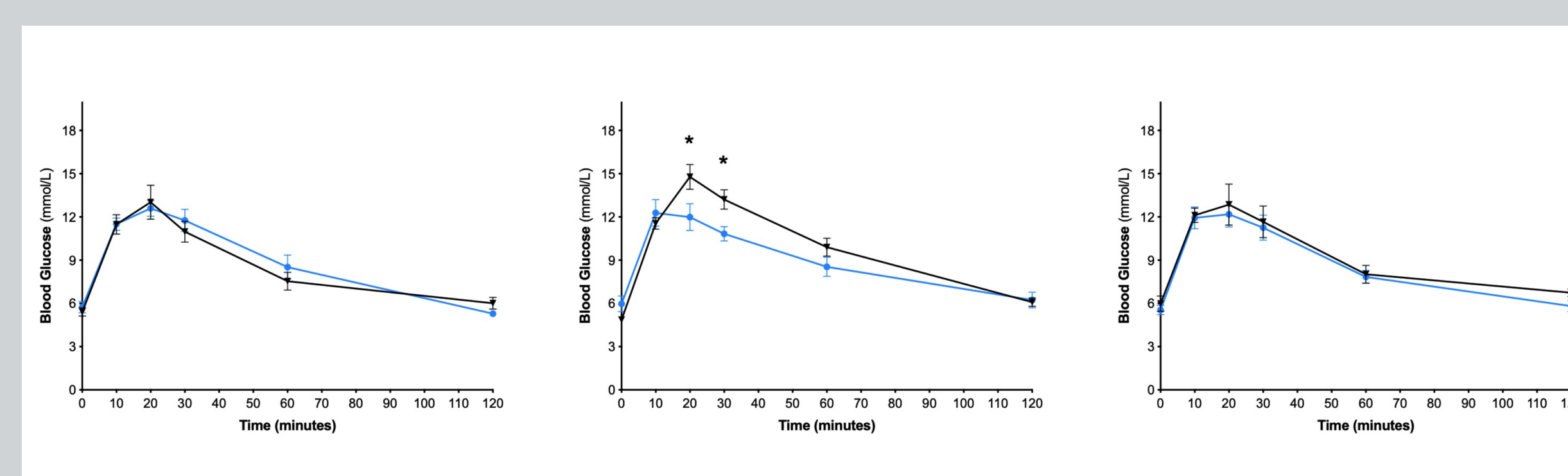


Figure 7: 3 Month female (24 Hour fasted - blue), and overnight fasted (black) Data represented as group mean ± SEM. N=10-12 *p <0.05, **p <0.01 determined by 1-way anova

RESULTS

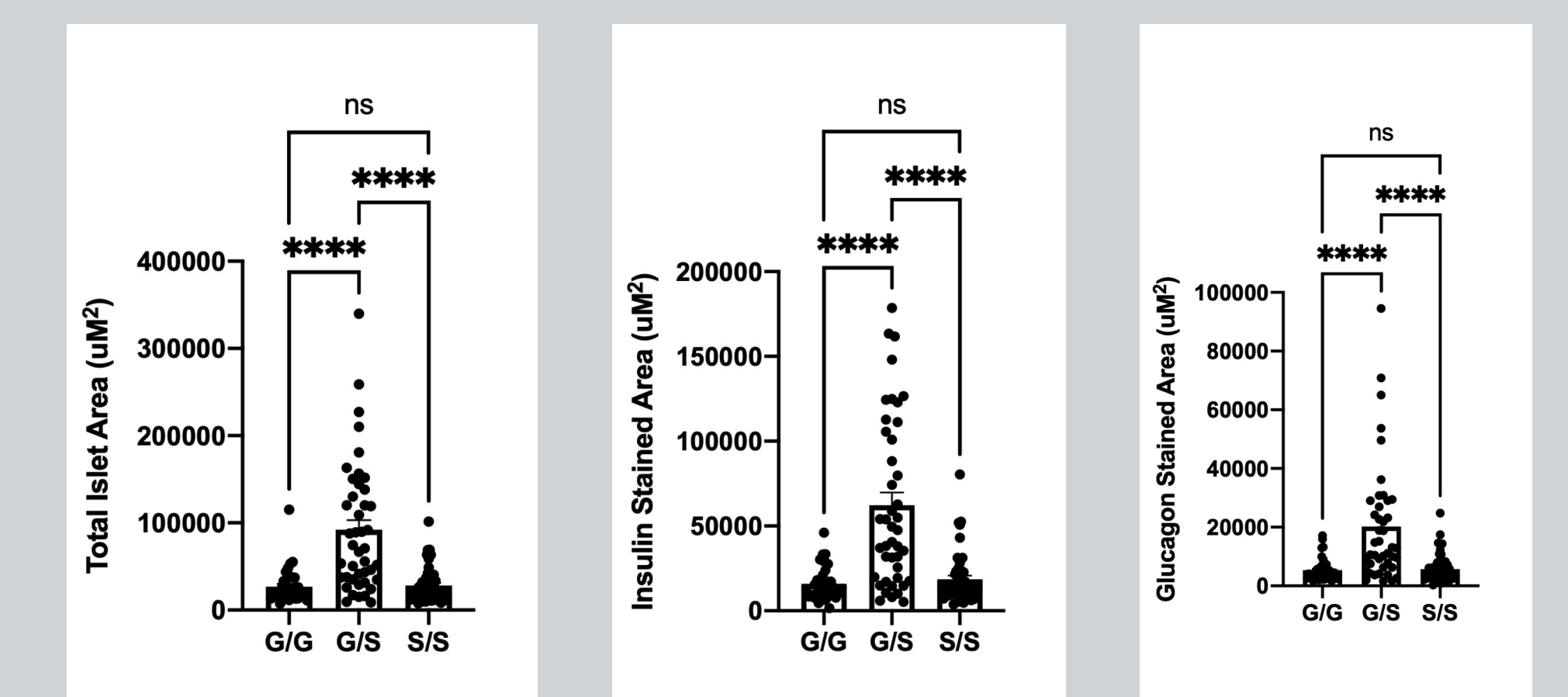
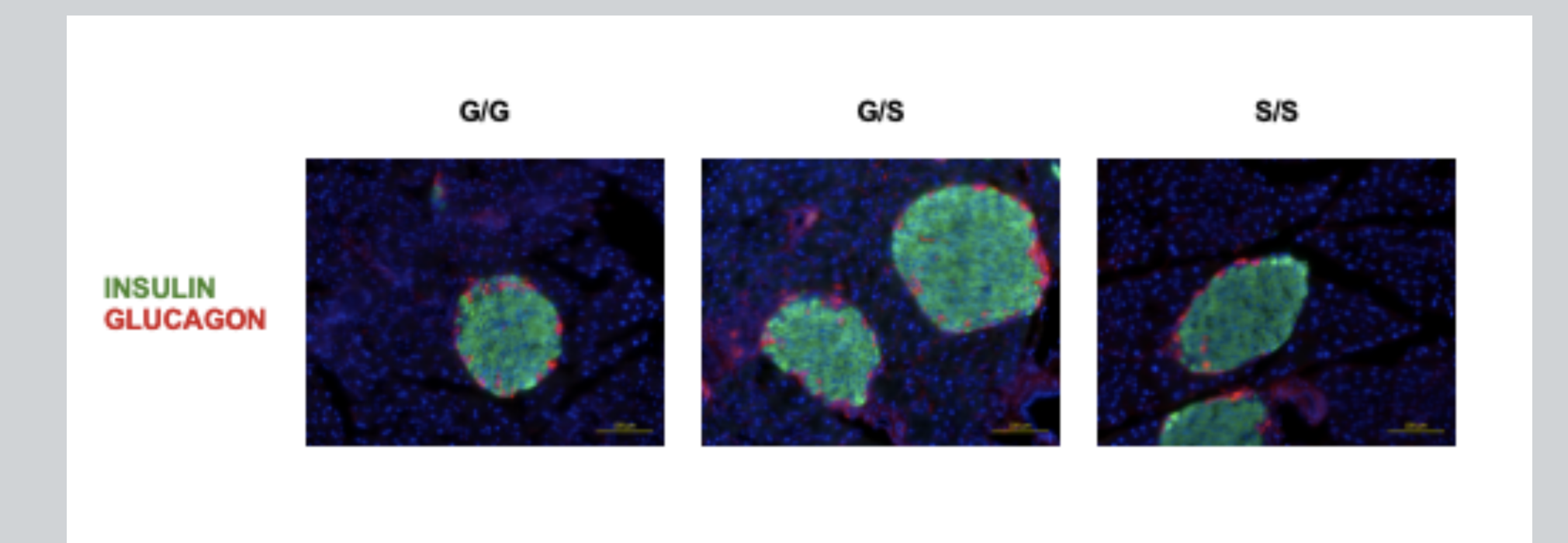


Figure 8: Immunofluorescence staining of pancreatic islets. Data represented as group mean ± SEM. N=10-12 *p <0.05, **p <0.01 determined by 1-way anova

CONCLUSION

- Fasting did not worsen glucose tolerance in mice with the variant S-allele
- Increase in immature insulin granules in S/S mice after prolonged fasting suggests less bioactive insulin available which may benefit fasting response
- Changes in expression of insulin responsive genes in G/S liver suggests decreased action of insulin on the liver, which may benefit responses to fasting
- Increased expression of ketogenic genes in livers and a trend towards increased ketones suggest a metabolic shift

ACKNOWLEDGEMENTS

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