



Enhanced B-cell Metabolism in Glycemic Improvement Following Sleeve Gastrectomy

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BACKGROUND

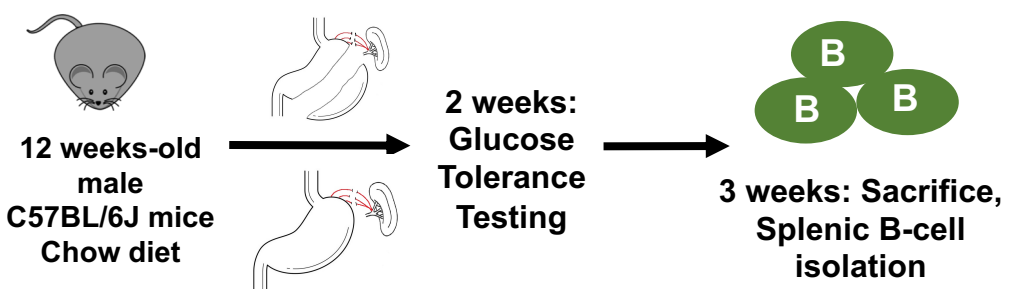
Sleeve gastrectomy (SG) can result in rapid and sustained diabetes remission (1), via uncertain mechanisms.

Improved immune function is a key potential mechanistic contributor. Enhanced B-lymphocyte metabolism appears particularly important (2).

Objective: to characterize SG's effect on B-cell metabolism and glucose homeostasis.

Hypothesis: post-SG glycemic improvement is associated with enhanced B-cell metabolism and increased anti-inflammatory function.

METHODS



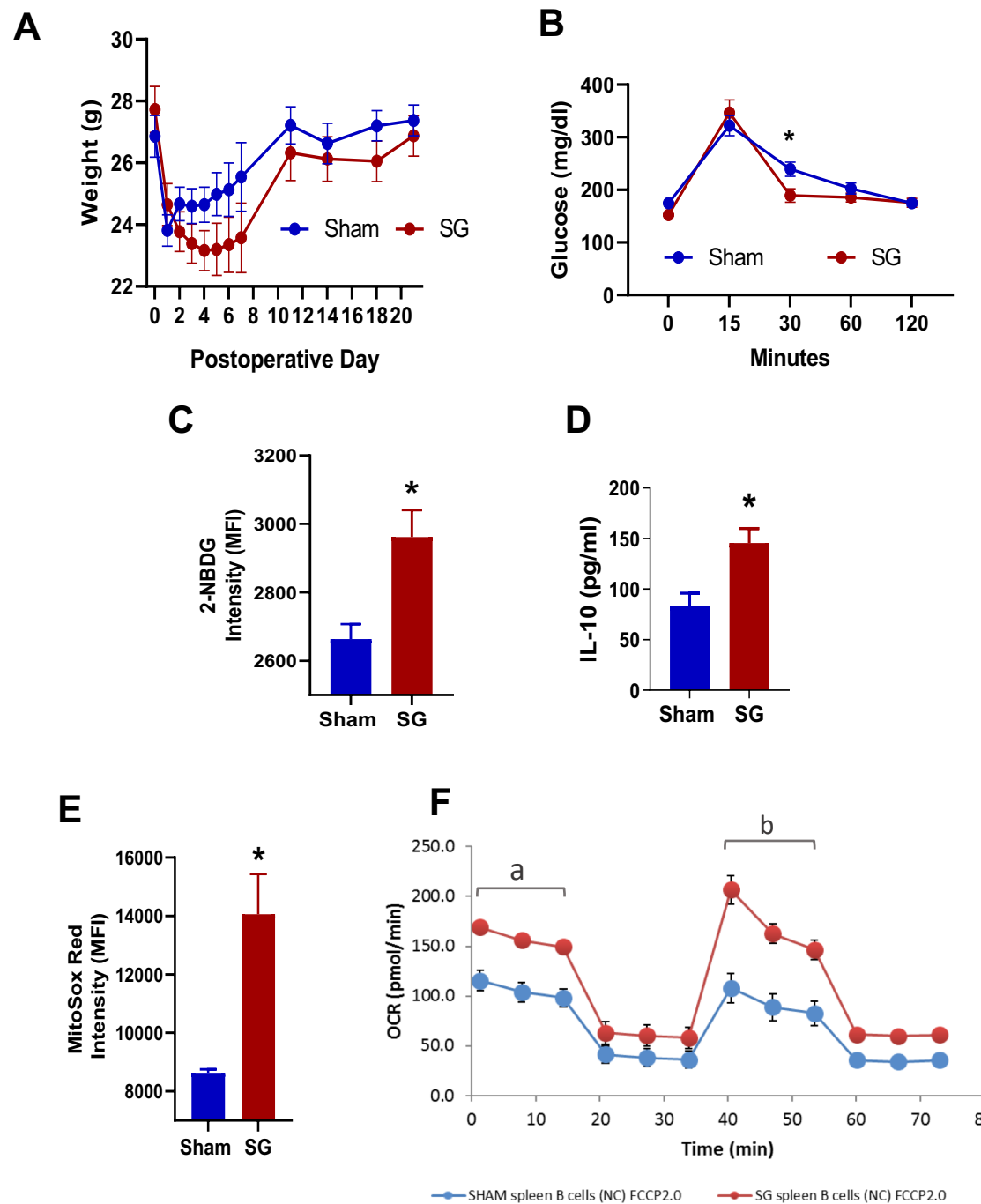
1. Fluorescent glucose (2-NBDG) uptake

2. MitoSOX™ Red staining for mitochondria superoxide activity

3. Seahorse™ Mito Stress test

RESULTS

- A. SG mice had greater weight loss shortly after surgery, followed by a gradual increase in weight. n=8 per group
- B. Oral glucose tolerance test (OGTT): SG improves glucose tolerance, *p=0.018
- C. SG increases B-cell glucose uptake, *p=0.016
- D. SG increases (1.7X) anti-inflammatory cytokine (IL-10) secretion in response to lipopolysaccharide (LPS) stimulation
- E. MitoSox™ Red Staining: SG B-cell mitochondria had higher superoxide production, p=0.005
- F. Seahorse™ Mito Stress: SG B-cell had higher basal respiration (a) and higher maximum respiratory capacity (b)



CONCLUSION

Post-SG glycemic improvement is associated with increases in splenic B-cell metabolism and anti-inflammatory function, revealing a tantalizing target for anti-diabetic therapy.

REFERENCES

1. Courcoulas, A. P. et al. Seven-year weight trajectories and health outcomes in the Longitudinal Assessment of Bariatric Surgery (LABS) study. *JAMA Surg.* 153, 427–434 (2018).
2. Harris, D. A., Subramaniam, R., Brenner, T., Tavakkoli, A. & Sheu, E. G. Weight and organ specific immune cell profiling of Sleeve Gastrectomy. *bioRxiv* 2020.06.28.176628 (2020) doi:10.1101/2020.06.28.176628.