



# Low protein diet improves metabolic health but not lifespan in aged mice

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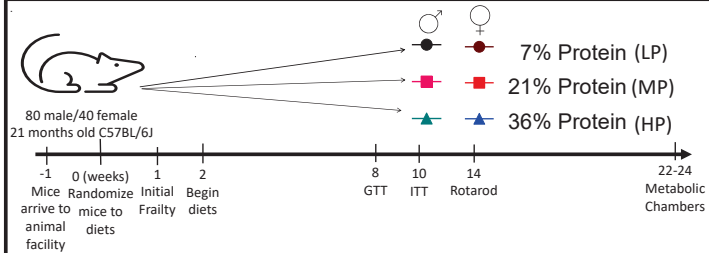
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## Introduction

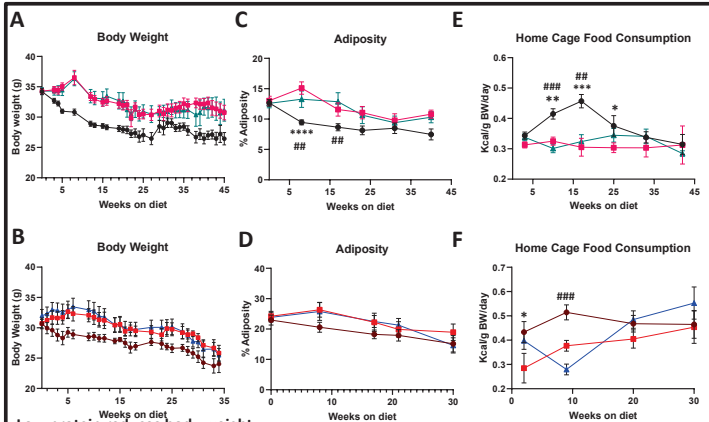
- Low protein (LP) dietary intervention has been shown to improve metabolic health, decrease frailty, and improve lifespan when used as a lifelong dietary pattern.
- High protein (HP) diets are often recommended to aging individuals to combat age-related muscle loss (sarcopenia) and retain adequate muscular function.
- Typical dietary protein content lies around 21% of calories from protein (MP).
- The effects of late-life dietary protein restriction or supplementation on lifespan remain unclear.

## Methods



- Male and female C57BL/6J mice were obtained from the NIA aging colony and separated into weight-matched diet groups at 21 months of age.
- Body weights were tracked weekly while frailty, MRI, and food consumption measurements were obtained approximately every 8 weeks.

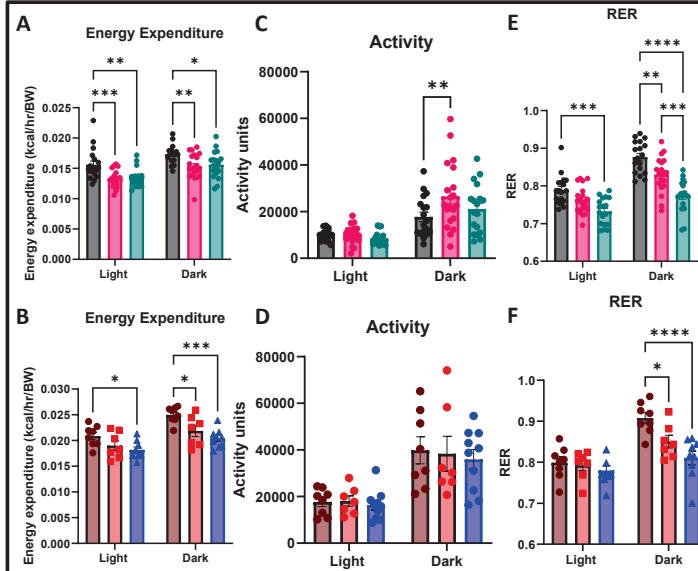
## Results



### Low protein reduces body weight

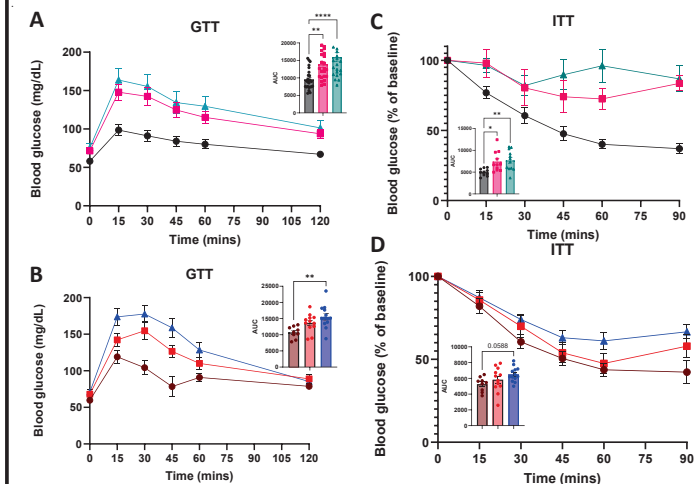
Longitudinal body composition data from aged mice in which LP fed mice display reduced body weight (A,B) and reduced adiposity in males (C,D), even though LP-fed mice consume more food (E,F). (Max n=13-28 animals per group). Data are represented as mean ± SEM. \* =LPvs.MP, \*\* =LPvs.HP(C,E,F). Two-way repeated measures ANOVA followed by Tukey's. \* =p<.05, \*\* =p<.01, \*\*\* =p<.001.

## Results (continued)



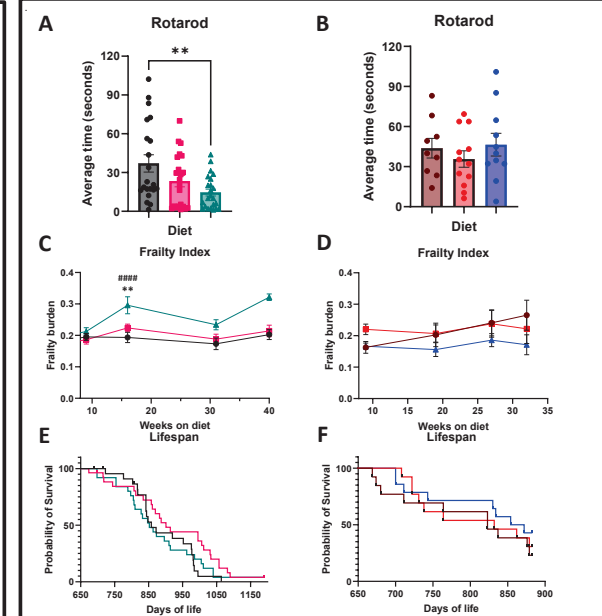
### LP fed mice have increased metabolic activity

Metabolic chamber data where LP fed mice display increased energy expenditure per body weight in both light and dark phases (A,B), a difference which is not attributable to differences in body weight by ANCOVA analysis (data not shown). Differences in energy expenditure are not due to higher activity levels (C,D). LP fed mice exhibit increased RER in the dark phase (E,F). Data are represented as mean ± SEM (n=8-18 animals/group). Two-way ANOVA followed by Tukey's. \* =p<.05, \*\* =p<.01, \*\*\* =p<.001, \*\*\*\* =p<.0001.



### LP fed mice have improved glucose tolerance and insulin sensitivity

LP fed mice display improved glucose tolerance by glucose tolerance test (1g/kg) after 6 weeks on diet (A,B). Insulin tolerance test (.75unit/kg) at 8 weeks on diet reveals only LP fed males show improvements in insulin sensitivity (C,D). Inlaid bar graphs represent area under curve (AUC)(A-D). (N=10–26 animals per group). One-way ANOVA followed by Tukey's. \* =p<.05, \*\* =p<.01, \*\*\*\* =p<.0001.



### LP fed males trend towards reduced lifespan

Average rotarod performance (A,B). Accumulated frailty burden over observed lifespan (C,D). Lifespan survival % after diet start at approximately 655 days of life (E,F). Data are represented as mean ± SEM. One-way ANOVA followed by Tukey, verified by ANCOVA (A, B). \* =LPvs.MP, \*\* =LPvs.HP(C). Repeated two-way ANOVA with Tukey's (C,D). Pairwise log-rank Mantel-Cox test (E,F). \* =p<.05, \*\* =p<.01, \*\*\*\* =p<.001.

## Conclusions

- Late life LP diet recapitulates effects of lifelong LP diet including reduced body weight and adiposity despite increased food consumption.
- LP significantly improves glucose and insulin sensitivity in males, with reduced effects in females.
- Late life LP diet results in elevated energy expenditure and RER across sex.
- Late life HP diet increases frailty burden in males, but has no impact on frailty in females.
- LP diets may reduce lifespan in males when introduced as late life dietary interventions.

## Acknowledgements

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