



Mid Atlantic Regional Chapter of the American College of Sports Medicine

Annual Scientific Meeting, November 4th- 5th, 2017
Conference Proceedings

International Journal of Exercise Science, Issue 9, Volume 6



Metabolic and Microbial Responses to Exercise in C57 Wild-type and Adenylyl Cyclase 5 KO Mice

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Healthy aging, including protection against diabetes, obesity, cardiovascular disease and enhanced exercise tolerance, have been observed in our longevity model of disruption adenylyl cyclase type 5 (AC5KO). This is a critical observation since the aging population would not enjoy extra years if they accompanied by chronic disease and exercise intolerance. It has been demonstrated that aging is associated with alterations in composition, diversity, and functionality of gut microbiota. The extent to which the microbiota contributes to the healthy aging phenotype is unknown. **PURPOSE:** The goal of this study was to confirm that gut microbiota can mediate the protection against diabetes and enhanced exercise tolerance in AC5KO mice compared to wild type (WT) mice. **METHODS:** 24 (n=6/group) 6-week old C57BL/6NTac male WT and AC5KO were randomly assigned to either exercise or sedentary control groups: (1) wild type-exercise (WT-EX), (2) wild type-sedentary (WT-CON), (3) AC5-exercise (AC5-EX) and (4) AC5-sedentary (AC5-CON). Mice were exercised via forced treadmill running at 60-70% max intensity for 60-minutes 5 days/week, for 5 weeks. Following exercise training, mice were given an oral cocktail of ampicillin and vancomycin for five days to eliminate gut microbiome. All measurements were taken at the following time points: prior to exercise, post training/pre-antibiotic and post antibiotic; and included max exercise test (i.e. distance), glucose tolerance test (GTT) (2 U/kg [body wt.]) and insulin tolerance test (ITT) (1 U/kg [body wt.]). **RESULTS:** AC5KO mice have a unique microbiota with *Helicobacter typhlonius* & *Bacteroides sartorii* spp. being dominant in AC5KO and not in WT mice. Furthermore, AC5-EX mice showed altered glucose tolerance and reduced exercise tolerance following antibiotic treatment (p=.05). Interestingly, post antibiotic AC5-EX mice showed severe insulin sensitivity following (1 U/kg [body wt.]) treatment. **CONCLUSION:** Our results show that AC5KO mice have a unique microbiota compared to WT mice and their insulin/glucose control phenotype appears to be dependent on the microbiota.

Statement of Disclosure: The authors have nothing to disclose.