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Antibiotics Reduce While Forced-Exercise Increases Inflammation in the Small Intestine

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Risk of metabolic and intestinal inflammatory disorder development increases significantly with age. In contrast, exercise has shown to reduce disease risk and promote longevity. Interestingly, adenylyl cyclase 5 knock out (AC5KO) mice demonstrate an enhanced exercise capacity and improved longevity. **PURPOSE:** We aimed to examine the inflammatory status along the gastrointestinal tract of AC5KO mice compared to Wild type (WT) mice. **METHODS:** 21 C57BL WT and AC5KO male mice were randomly assigned to one of 2 groups: (1) sedentary and (2) exercise for 12 weeks. Mice had *ad libitum* access to food and water. Exercised mice were trained for 4 weeks at 60-70% max speed for 1 hr each session, 5 d/wk. WT sedentary and exercised groups were given antibiotics via oral gavage during the last 7 days of the exercise protocol. At the end of 4 weeks, mice were sacrificed and intestinal tissues were fixed for histological analysis and immunohistochemistry for cyclooxygenase-2 (COX-2), a marker of inflammation. Group means of staining score were analyzed using a one-way ANOVA and LSD post hoc tests. A difference of mean with a *p* value of ≤ 0.05 was considered statistically significant. **RESULTS:** In the duodenum, COX-2 expression was isolated in the lamina propria and staining occurred predominately within macrophages. COX-2 expression in the duodenum was less in sedentary animals given antibiotics ($p \leq 0.015$). In the ileum, COX-2 expression was localized to both the crypts and lamina propria. Expression in ileal crypts was less in sedentary animals given antibiotics compared to WT exercised animals ($p = 0.02$) while expression in the ileal lamina propria was increased in WT exercised animals ($0.001 \leq p \leq 0.009$). **CONCLUSIONS:** Antibiotics reduce small intestinal inflammation. COX-2 expression localizes differently in the mucosa along the small intestine. Forced-exercise increases inflammation to a greater degree in the lamina propria of the distal small intestine.