PREVIOUS EXERCISE PROMOTES ANTITUMORAL MECHANISMS IN THE EARLY STAGES OF COLON CARCINOGENESIS IN MICE

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Introduction and Aims

Rodent studies had observed that previous aerobic exercise enhanced antitumor efficiency, whereas the mechanisms behind this beneficial effect remain unclear, especially in the early carcinogenic stages [1].

This study investigated the effects of previous aerobic exercise on DNA repair mechanisms and the involvement of epigenetic factors in this regulation in colon of mice exposure to the carcinogen azoxymethane (AOM).

Methodology

Forty male C57/BL6 mice (8 weeks old) were randomized into four groups, n=10 (Figure 1A). Exercise protocol integrated a progressive endurance training (swimming), 5 times/week, for 20 to 60 min. The intensity was progressive and added 1% to 2% of body weight in mice tails. After six weeks of exercise protocol or not, the animals were euthanized eight or twenty four hours after the application of the single dose of AOM in treated groups. CEUA/INCA – 001/16

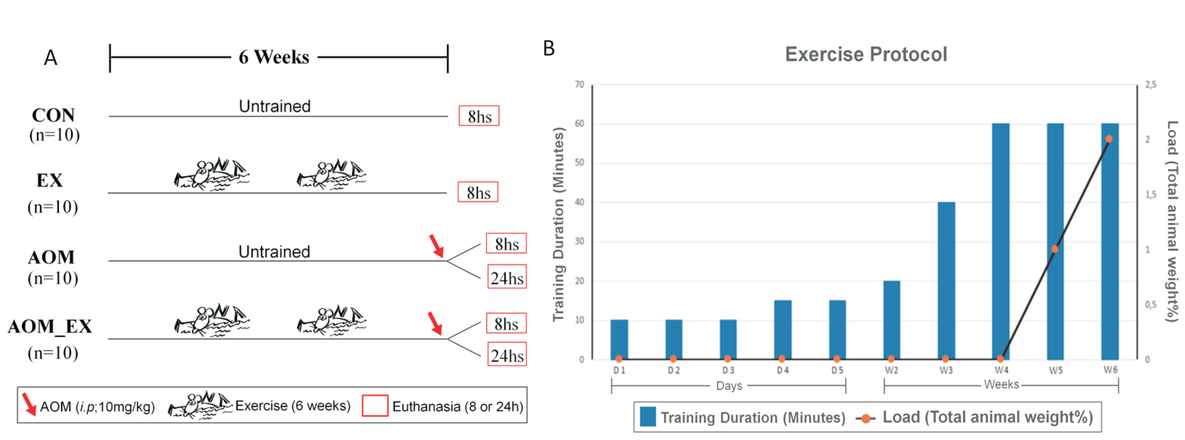


Figure 1. (A) Experimental Groups: Non-exercise control (CON); Exercise control (EX); Non-exercise, treaded with azoxymethane (AOM); Exercise and treaded with azoxymethane (AOM_EX). The euthanasia in AOM groups were subdivided in 8hs or 24hs after carcinogen injection; (B) Swimming protocol with progressive intensity. Blue column (X axis): Training duration (minutes); Orange circle (Z axis): Load (Total animal weight %); Y axis: Protocol elapsed time (D= days; W= weeks).

Results

Table 1. Effect of treatments on heart, epididymal fat and total body weight.

Groups	Body weight change (g)	Heart Weight (%/final weight)	Epididymal Fat (%/final weight)
C	3.11±2.76	0.54±0.52	1.55±0.18
EX	2.09±0.80	0.70±0.05*	1.41±0.25
AOM	2.57±1.39	0.51±0.59	1.51±0.31
AOM_Ex	1.99±2.48	0.56±0.54	1.34±0.17

Body weight change (g) represents the weight gain between day one and the last day of experiment; Heart and epididymal fat weight (% of final total weight) were adjusted by the last body weight before euthanasia; Mean + SD; *p < 0.05.

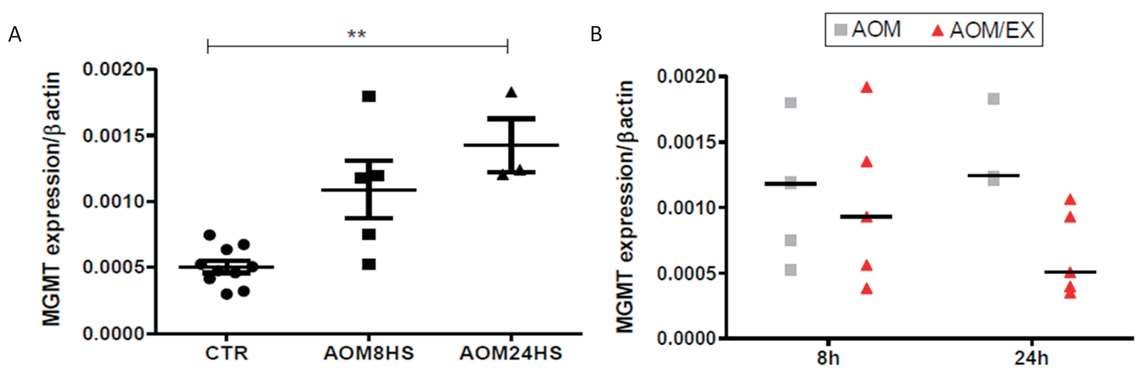
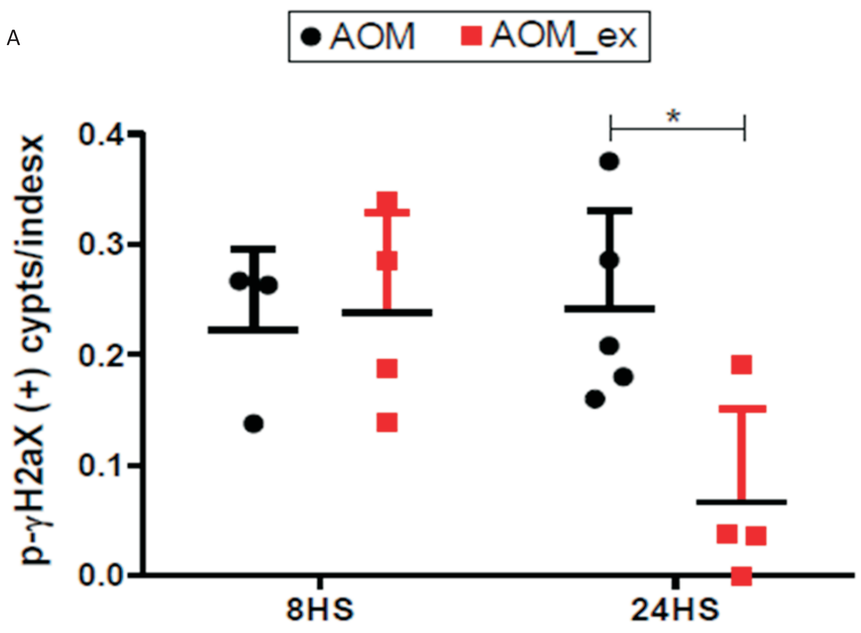
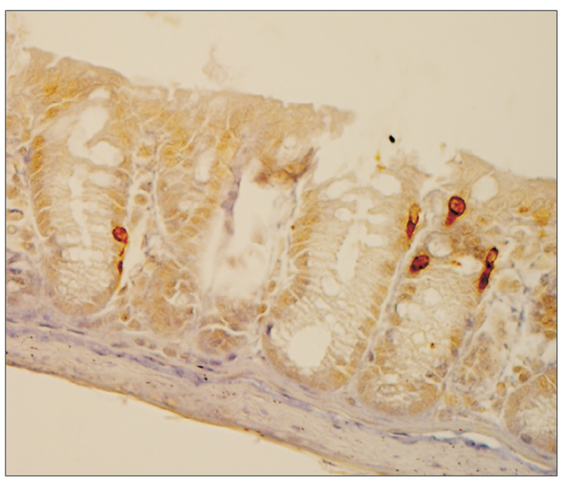


Figure 2. qPCR-RT analysis of methyl-guanine methyl-transferase MGMT response to acute AOM exposure (A) in control and AOM groups. **p < 0.01, Kruskal-Wallis test, followed by Dunn's post-hoc test. (B) in AOM and AOM_EX groups B. Two-way ANOVA, followed by Bonferroni post-hoc test.





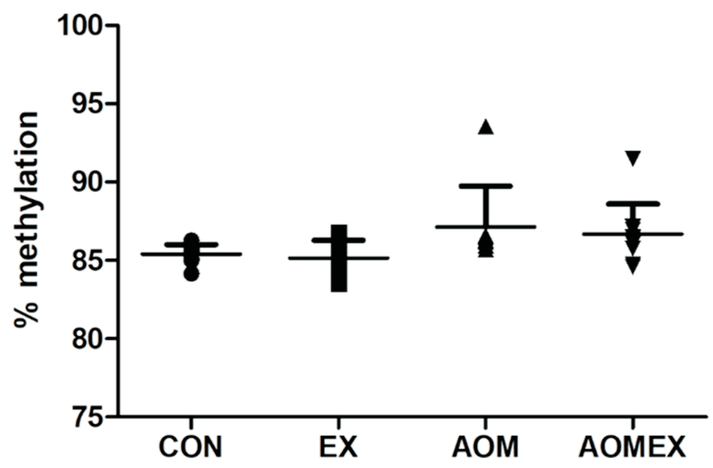


Figure 3. (A) Crypts with positive focus of p-γH2aX (immunohistochemistry), adjusted by total crypts; (B) IHC representative staining. Data are mean ±SD. n = 4±1 *P<0.05, ANOVA followed by Bonferroni post-hoc test.

Figure 4. Methylation percentage of LINE-1 in colonic tissue among experimental groups. Median + Interquartile range. Kruskal-Wallis test, followed by Dunn's post-hoc test.

Conclusion

Previous regular exercise enhanced a most effective DNA repair mechanisms in response to a carcinogenic genotoxic insult ,preventing double-strand breaks formation in colon tissue possibly due to DNA-repair machinery regulation. *LINE-1* methylation status shown no variation between groups and next we shall analyze the epigenetic machinery and the methylation status of *MGMT* and *MLH1*.

References

1. ASHCRAFT, K.A. et al. Efficacy and mechanisms of aerobic exercise on cancer initiation, progression, and metastasis: a critical systematic review of in vivo preclinical data. Cancer research, 2016.

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