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Modeling the impact of inflammatory bowel disease on prostate cancer in mice

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Introduction and objectives

- Recent epidemiological data has implicated inflammatory bowel disease (IBD) as a risk factor for clinically significant prostate cancer (PC).

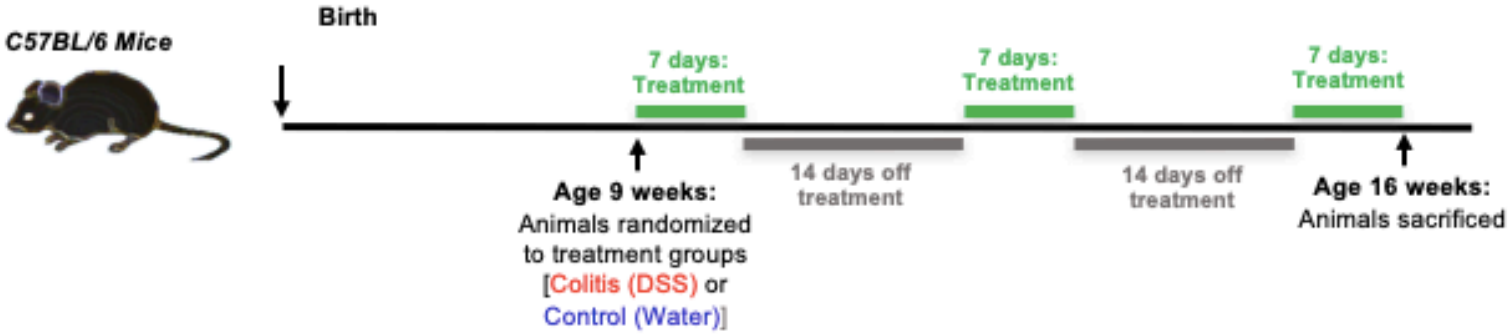
- A key driver of malignant transformation may include chronic inflammation, however, the effects of gut inflammation on the prostate are unknown.

- Objective: To determine whether gut inflammation leads to changes in the inflammatory milieu and pro-oncogenic signaling in the prostate of wild-type mice.

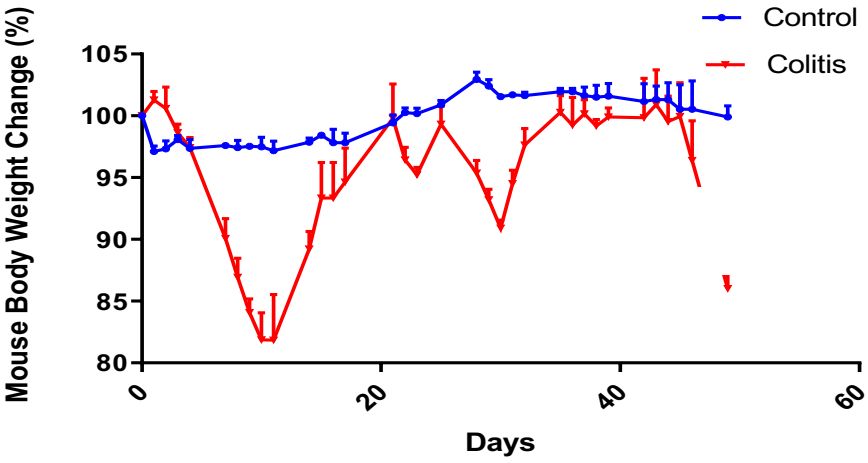
Methods

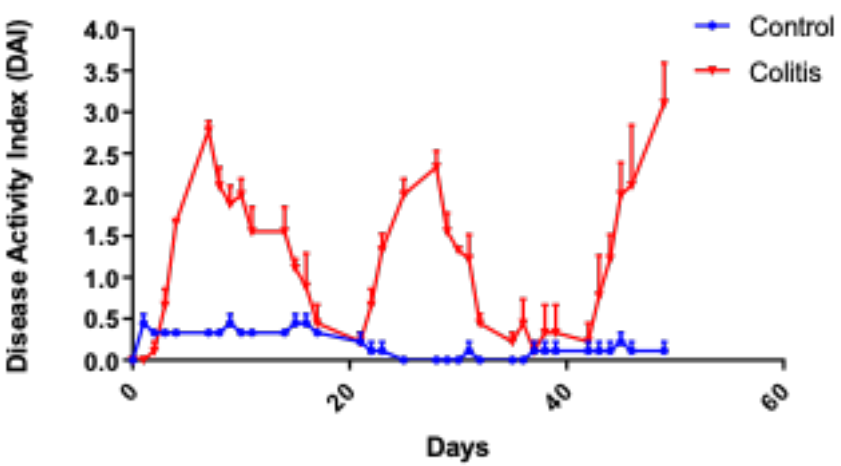
- We induced chronic colitis in post-pubertal C57BL/6 (wild-type) mice by administering 3 cycles of Dextran Sodium Sulfate (DSS)-treated water

- Immediately following induction, mice were sacrificed and prostate tissues were harvested for immunophenotyping



Colitis mice developed weight loss, hematochezia, and histologic findings consistent with colitis

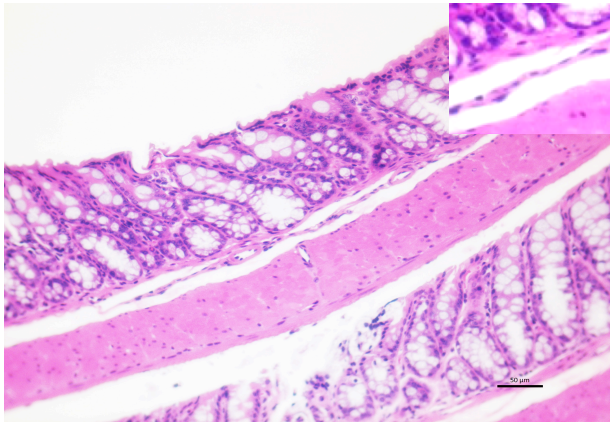


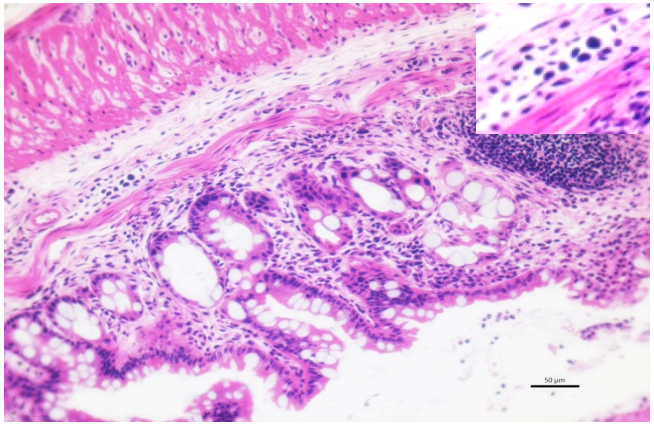


Control

Colitis

Mouse Colon





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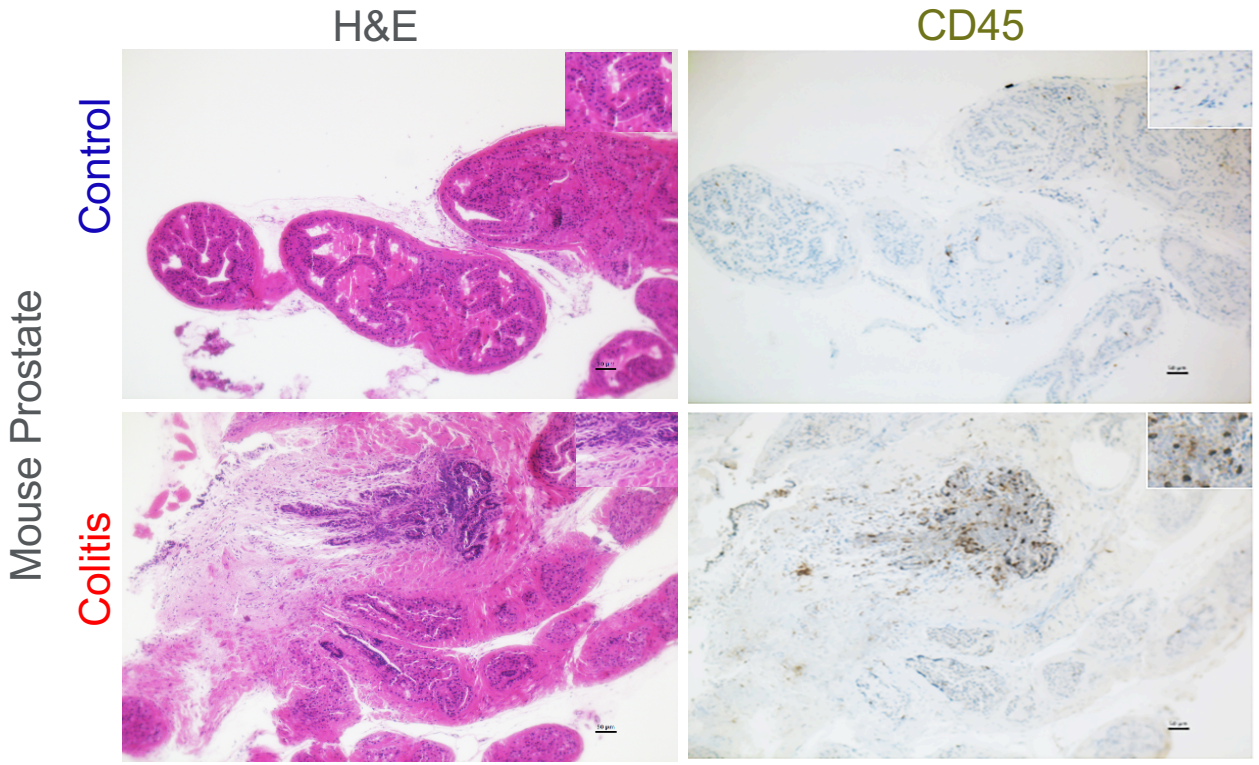
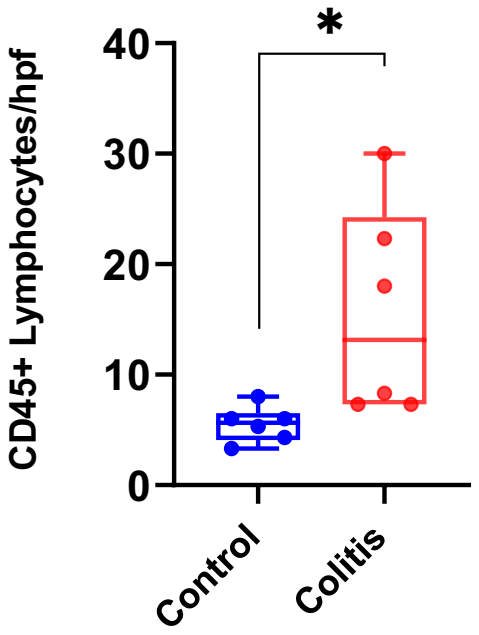
Colitis is associated with greater inflammatory infiltrate in the prostate in wild-type mice: CD45+ leukocytes





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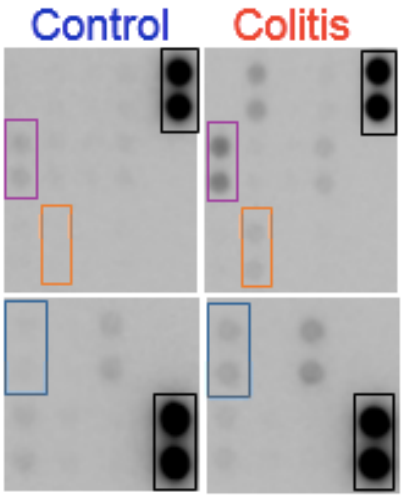
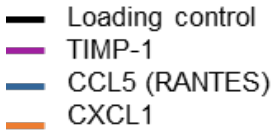
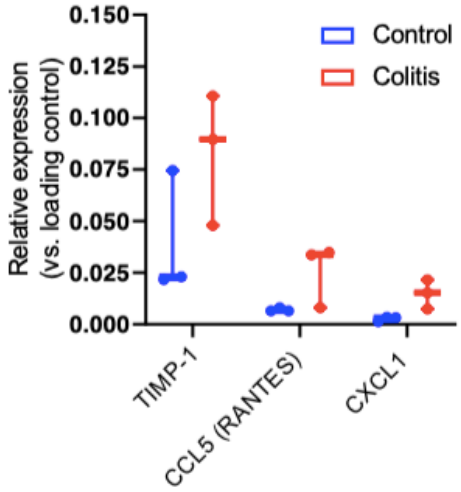
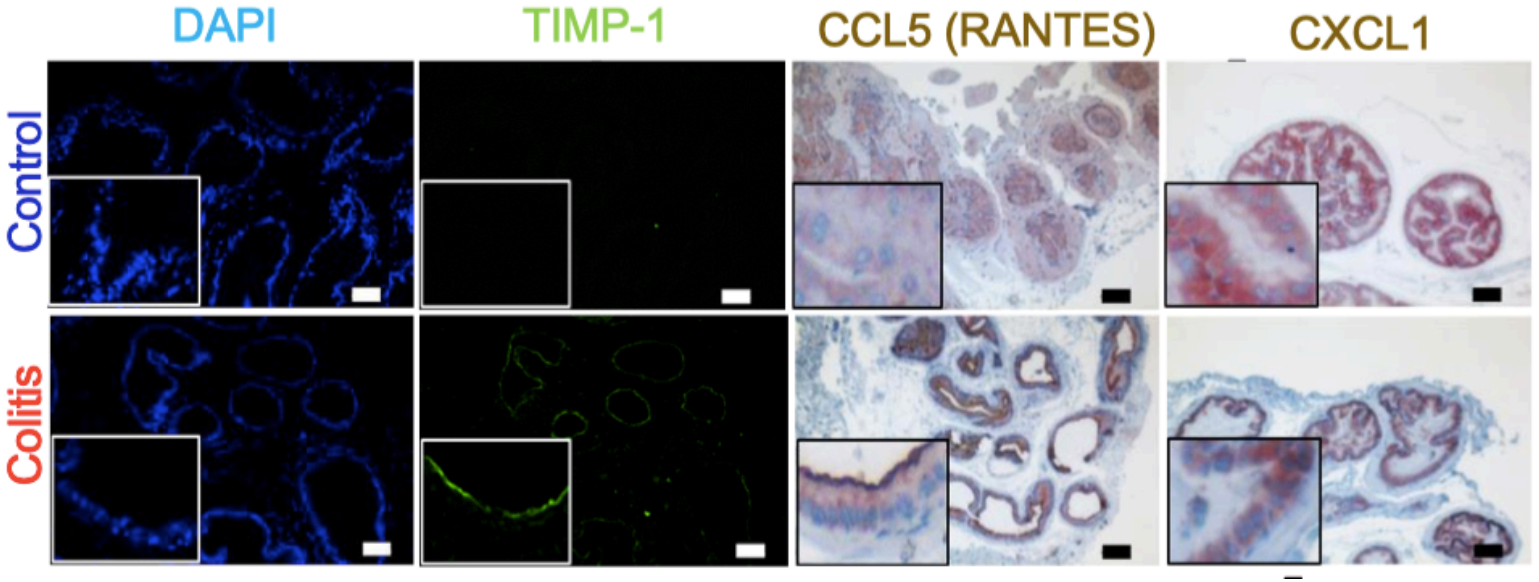
Prostatic levels of TIMP1, CCL5, CXCL1 expression were elevated in colitis mice









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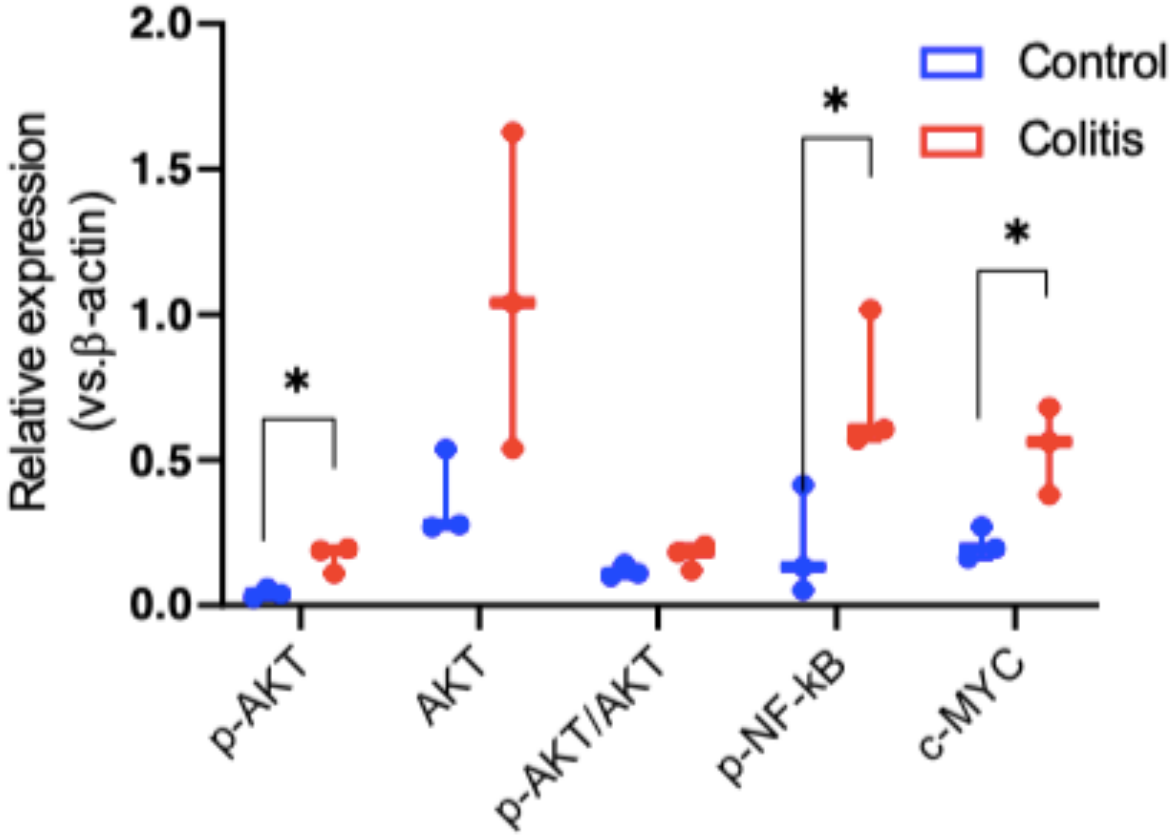
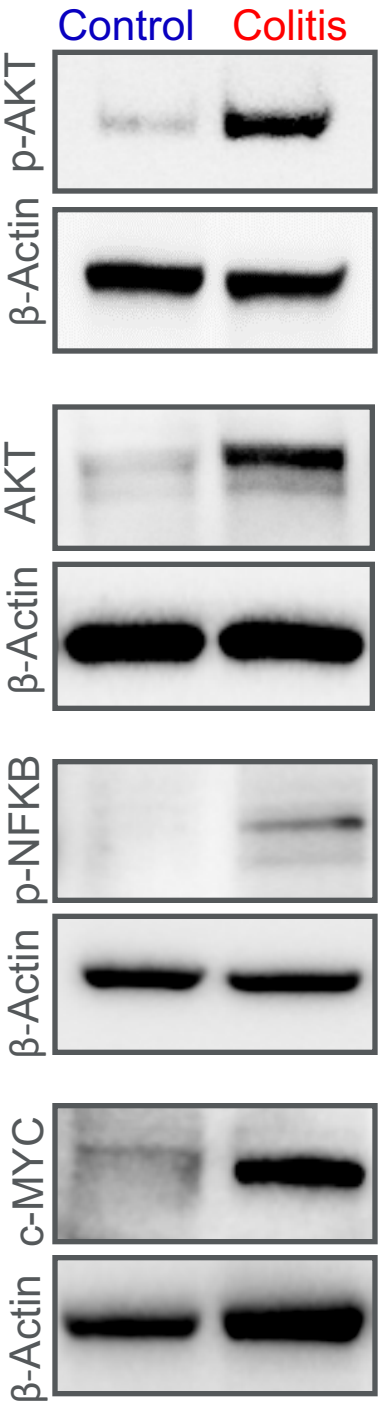
Colitis leads to upregulation of pro-oncogenic pathway signaling in the prostate





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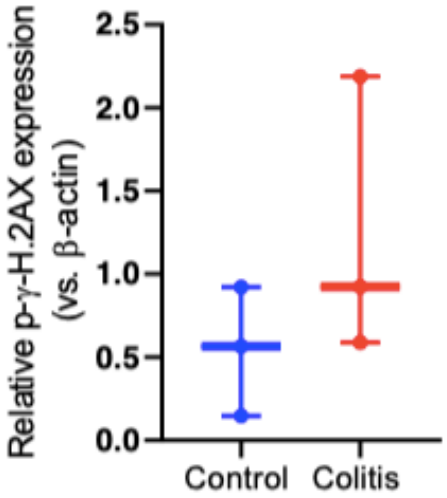
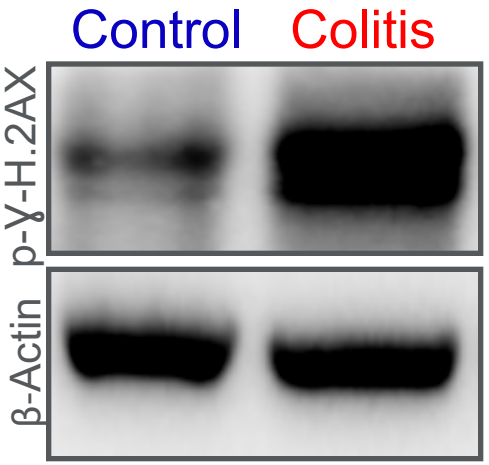
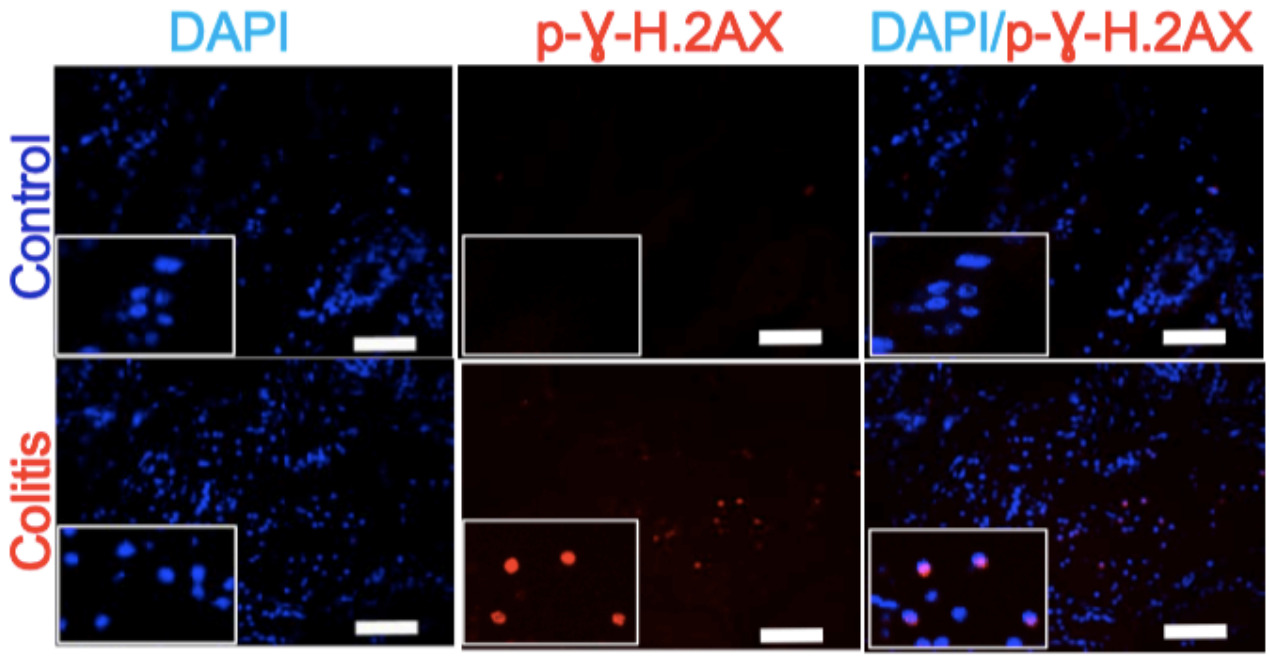
Colitis leads to prostatic DNA damage (p-ɣ-H.2AX)







Preliminary conclusions

- Chronic colitis leads to elevated prostatic inflammatory infiltrate

- Prostatic inflammation in the setting of colitis leads to downstream upregulation of AKT/NF-kB signaling and DNA damage, a characteristic pre-neoplastic phenotype in inflammation-mediated carcinogenesis