

Diet composition influences intestinal mucositis in mice

Hannelouise Kissow, Rasmus Hytting-Andreasen, Bolette Hartmann, Jens Juul Holst

Department of Biomedical Sciences and NNF Center of Basic and Metabolic Research, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

Background

GI mucositis is an inflammatory-like condition in the GI tract induced by chemotherapy treatment. The symptoms are dehydration, abdominal pain, bleeding and risk of severe infections. No treatment is available and reduction in chemotherapy dose can be a consequence. Glucagon-like peptide-2 (GLP-2) is secreted from intestinal L-cells in response to nutrients, with protein and sugars as the main stimulators. Endogenous GLP-2 is important for intestinal protection and healing, and treatment with GLP-2 can ameliorate mucositis. We have recently shown that mice fed a high fat diet (HFD), which is low in protein and fiber, have decreased small intestinal weights and decreased GLP-2 secretion (unpublished).

We hypothesized that mice fed a HFD would be more susceptible to GI mucositis.

Method

Mice were allocated into two control groups (saline + HFD and saline + chow) and two groups in which mucositis was induced with 5-Fluorouracil (5-FU; 400 mg/kg) at day 0 (5-FU + HFD and 5-FU + chow). HFD was started at day -2. Body weight (BW) was measured daily from day 0. Mice were sacrificed at day 3 and 5 (n=8). Intestinal weight was measured upon sacrifice and tissue samples were collected from the proximal and distal part of the small intestine (SI). Histological analyses were performed and content of tissue myeloperoxidase (MPO) was analyzed.

Statistics

* Indicates $p < 0.05$, compared to saline + chow (ANOVA with Dunets post hoc)
a Indicates $p < 0.05$ compared to 5-FU + chow (ANOVA with Bonferroni post hoc or Man Whitney test)

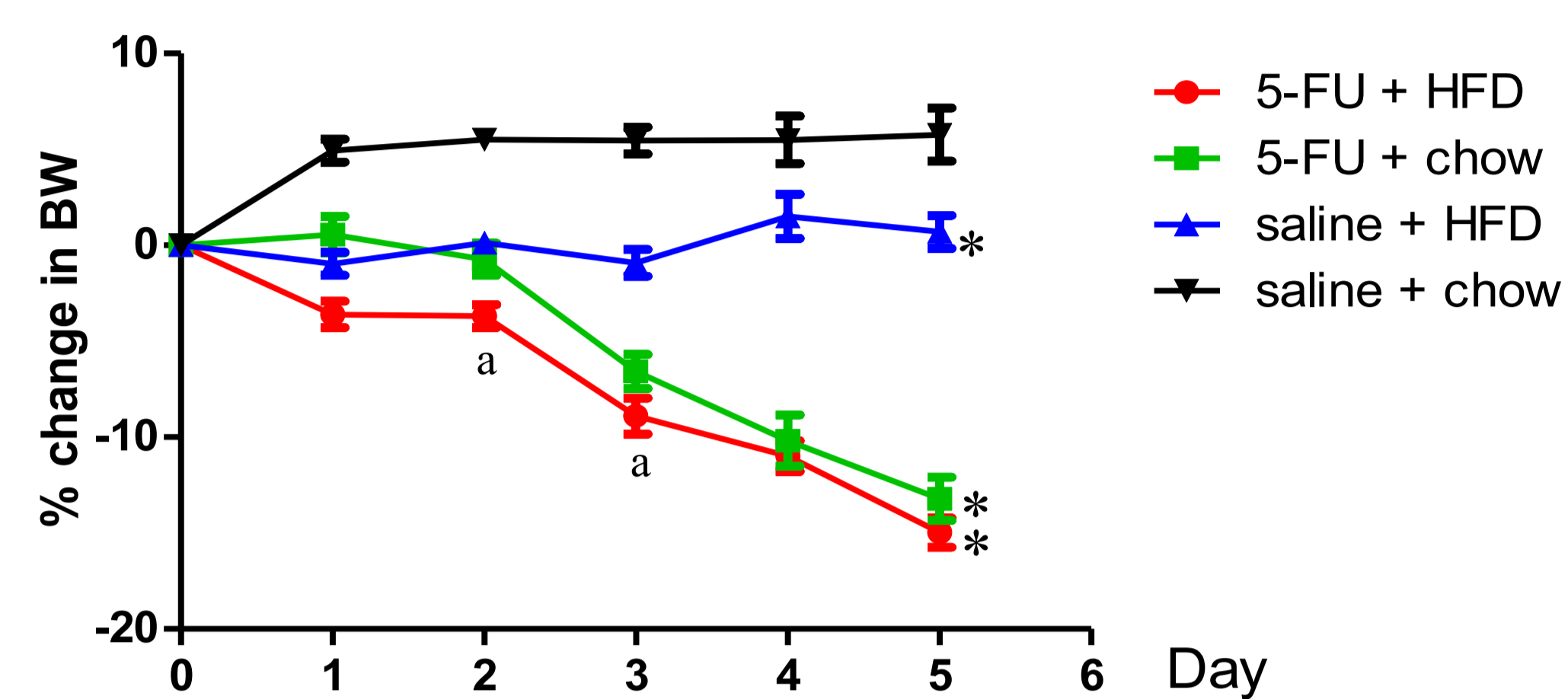
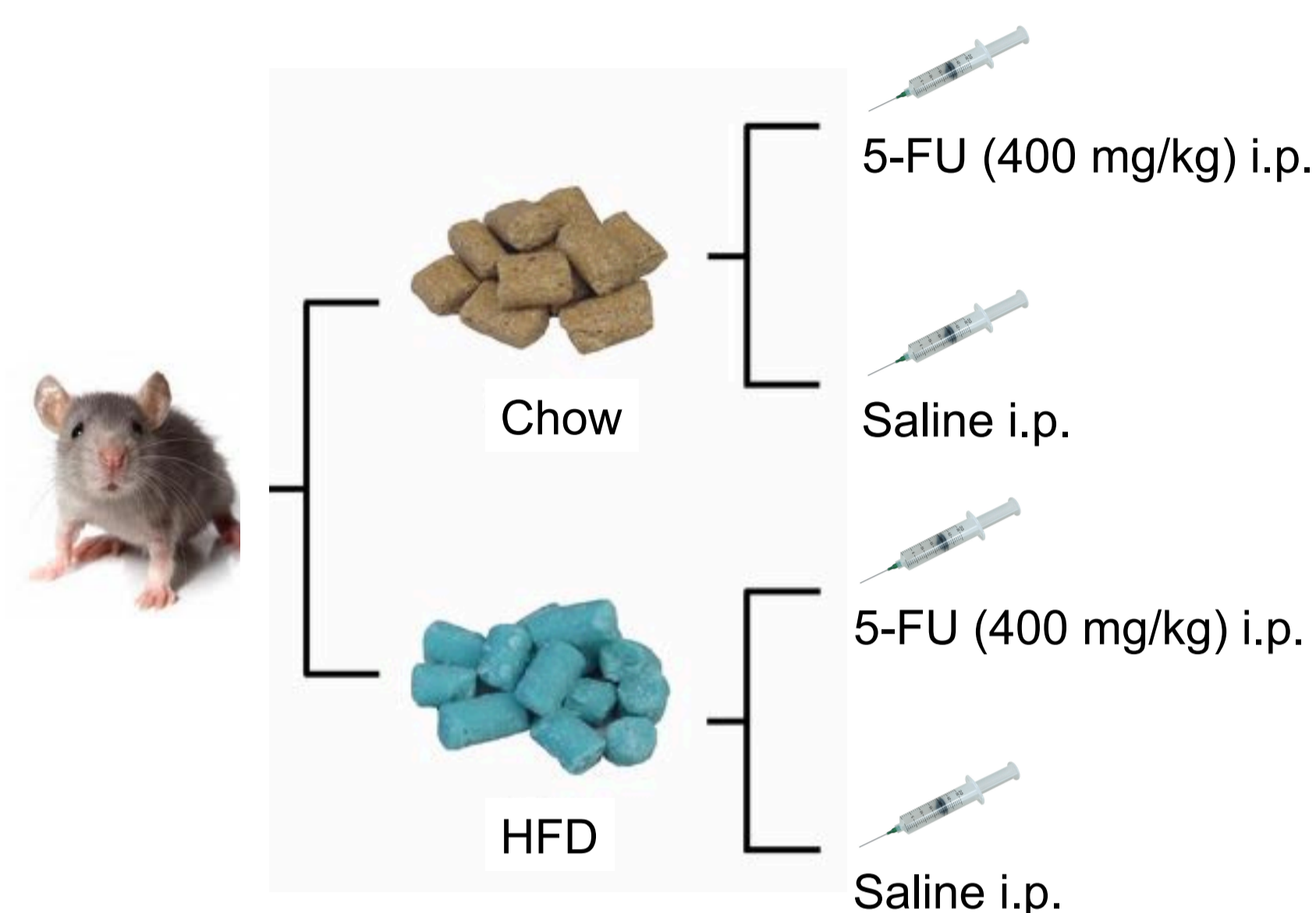
Conclusion

Mice fed with HFD a few days before 5-FU were more susceptible to GI mucositis, indicated by a decreased crypt depth and increased content of MPO in the proximal part of the small intestine, both 3 and 5 days after mucositis was induced.

These results indicates that fibers and protein are important for intestinal healing and this could be by increased endogenous GLP-2 secretion.

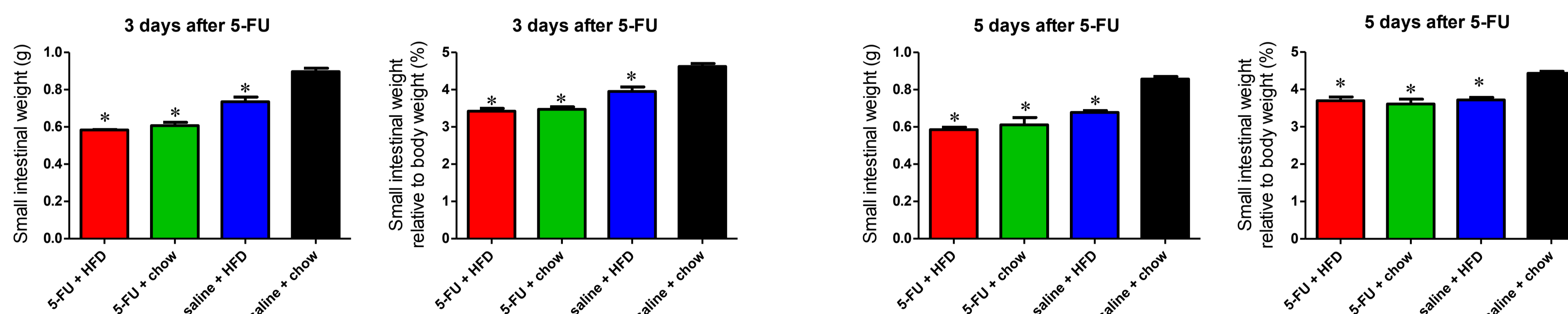
Further investigations are needed to clarify whether changes in diet composition could be a method to attenuate GI mucositis in cancer patients receiving chemotherapy.

Results



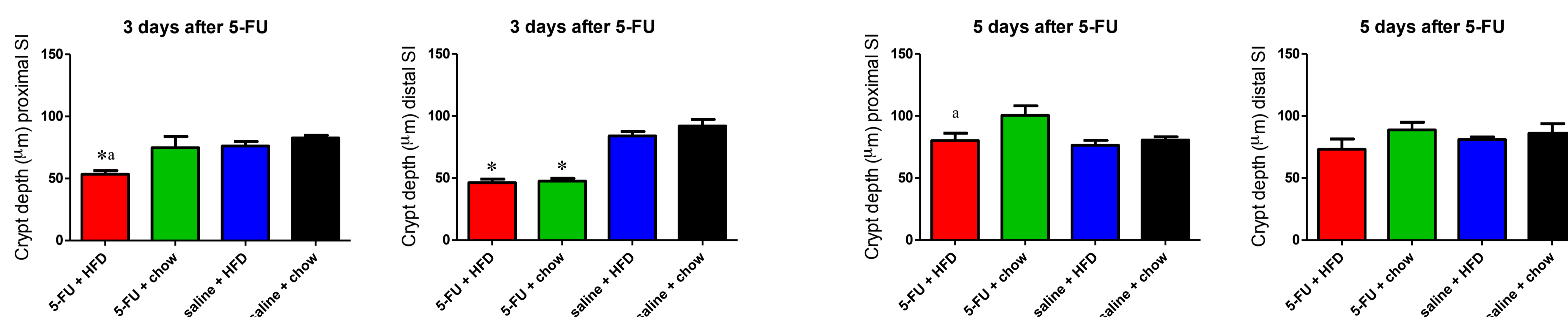
Body weight (BW)

One and two days after 5-FU mice fed a HFD had a significant BW loss compared to chow fed mice. However, this was also seen in the two control groups. From day 3 to 5 there was no difference between the HFD and the chow fed.



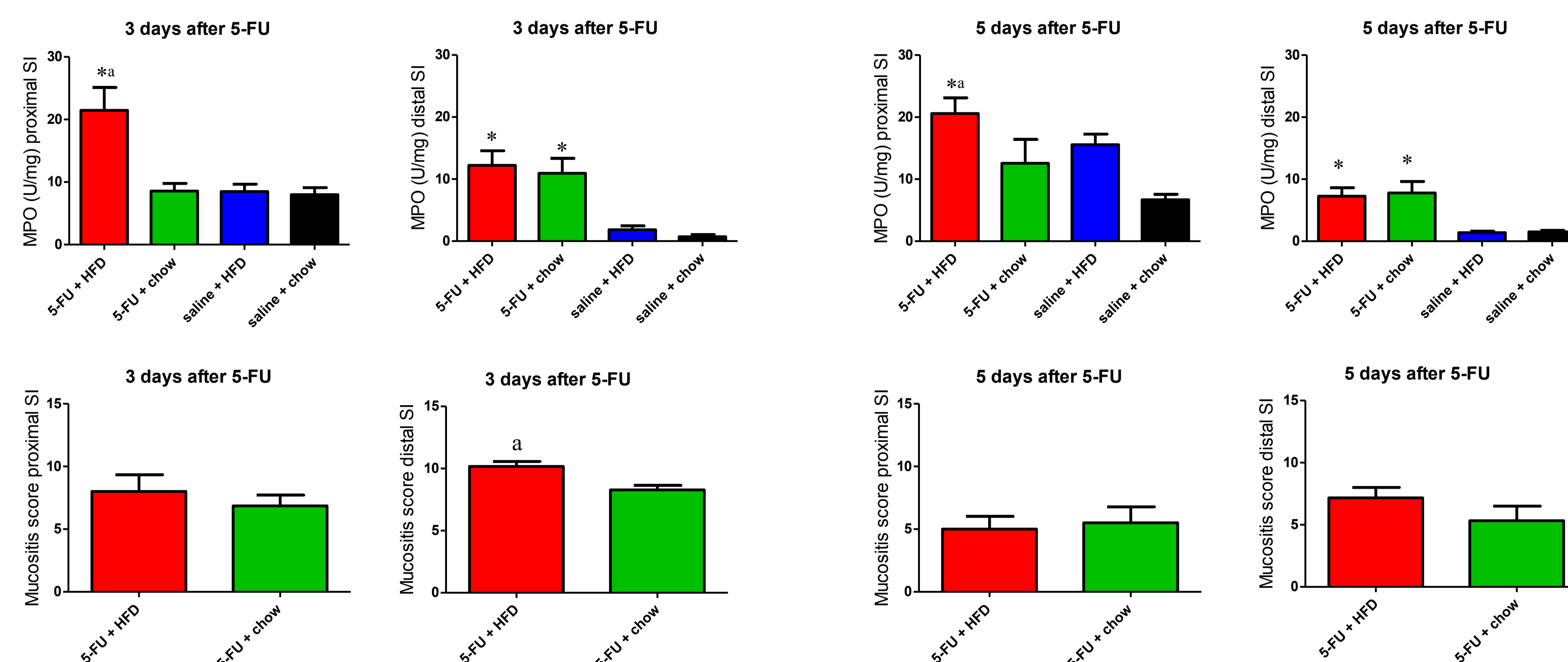
Small intestinal weight

In 5-FU injected mice there were no difference between HFD and chow fed, however there was a significant decrease in small intestinal weight in control mice fed with HFD



Crypt depth

Both 3 and 5 days after 5 FU there was a significant reduction in crypt depth in the proximal SI in mice fed a HFD compared to chow. Five days after 5-FU we found a small (ns) increase in crypt depth the distal SI in mice fed with chow (as a sign of compensatory hyperproliferation), this was not seen in the HFD fed.



MPO and mucositis score

Both 3 and 5 days after 5-FU there was a significant increase in MPO in the proximal SI in HFD compared to chow fed. We did find an increase in mucositis score in the distal part of the SI, however this was only significant at day 3.