OC17 & P07 - **The food additive maltodextrin promotes endoplasmic reticulum stress-driven mucus depletion and exacerbates intestinal inflammation**

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Background: Food additives, such as emulsifiers, stabilizers or bulking agents, are present in the western diet and their consumption is increasing. However, little is known about their potential effects on intestinal homeostasis.

Objective: In this study we examined the effect of some of these food additives on gut inflammation.

Methodology: Mice were given drinking water containing maltodextrin (MDX), propylene glycol (PG) or animal gelatin (GEL) and then challenged with dextran sulfate sodium or indomethacin. In parallel, mice fed MDX-enriched diet were given the endoplasmic reticulum (ER) stress inhibitor Tauroursodeoxycholic acid (TUDCA). Transcriptomic analysis, real-time PCR, mucin-2 expression, phosphorylated p38 mitogen-activated protein (MAP) kinase quantification and hematoxylin and eosin staining were performed on colonic tissues. Mucosa-associated microbiota composition was characterized by 16S rRNA sequencing. For the in vitro experiments, murine intestinal crypts and the human mucus-secreting HT29MTX cell line were stimulated with MDX in the presence or absence of TUDCA or a p38 MAP kinase inhibitor.

Results: Diets enriched of MDX, but not PG or GEL, exacerbated intestinal inflammation in experimental models of colitis and ileitis. Analysis of the mechanisms underlying the detrimental effect of MDX revealed up-regulation of inositol requiring protein 1β (IRE1β), a sensor of ER stress, in goblet cells and reduction of mucin-2 expression with no significant change in mucosa-associated microbiota. Stimulation of murine intestinal crypts and HT29MTX cells with MDX induced IRE1β via a p38 MAP kinase-dependent mechanism. Treatment of mice with TUDCA prevented mucin-2 depletion and attenuated colitis in MDX-fed mice.

Conclusions / Implications for practice: In conclusion, this study shows, for the first time, that MDX-enriched diet triggers ER stress in goblet cells with consequent reduction of the intestinal content of mucin-2, thus making the host more sensitive to colitogenic stimuli. Our data supports the hypothesis that western diet rich in the food additive MDX can contribute to gut disease susceptibility.