

**Abstracts**

In both segments, O-glycosylation of mucins was strongly affected, with the appearance of elongated poly-lactosaminic-chain containing O-glycan structures, associated with flattening and loss of the mucus layer cohesive properties specifically in the ileum. *L. farciminis* bound to intestinal Muc2 and prevented WAS-induced functional alterations and changes in mucin O-glycosylation and mucus physical properties.

**Conclusion:** WAS-induced functional changes were associated with mucus alterations resulting from a shift in O-glycosylation rather than from changes in mucin expression. *L. farciminis* treatment prevented these alterations, conferring epithelial and mucus barrier strengthening.

**Keywords:** gut permeability, mucus layer, water avoidance stress.

30

### Oxidative stress balance between pro- and anti-inflammatory factors in human intestinal epithelial cells

Eva Latorre<sup>1</sup>, Elena Layunta<sup>1</sup>, Aurora Gimeno<sup>1</sup>, Laura Grasa<sup>1</sup>, Marta Castro<sup>1</sup>, Santiago García<sup>2</sup>, Belen Gros<sup>2</sup>, M Pilar Arruebo<sup>1</sup>, Anna Isabel Alcalde<sup>1</sup>, José Emilio Mesonero<sup>1</sup>

<sup>1</sup>Department of Pharmacology and Physiology, University of Zaragoza, Spain; <sup>2</sup>Miguel Servet University Hospital, SALUD, Zaragoza, Spain

**Background:** Oxidative stress plays a key role in the development of intestinal inflammatory diseases. Several pro-inflammatory mediators may generate oxidation products that exacerbate the inflammatory damage. Gastrointestinal molecules, like serotonin (5-HT), adenosine and melatonin, which are involved in intestinal physiology, have also been described as intestinal pro-inflammatory factors; whereas IL-10, a known anti-inflammatory cytokine, has also been implicated in intestinal pathophysiology.

**Aim:** The aim of this study was to analyze the contribution of pro-inflammatory and anti-inflammatory molecules to oxidative stress balance, as well as to assess their effect on cellular antioxidant enzymes activity, in intestinal epithelial cells.

**Methods:** Caco-2 cells were treated with the different molecules, and the oxidative stress was determined by measuring lipid peroxidation (MDA+4HDA) and protein carbonyl levels. The activity of the anti-oxidant enzymes (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GPx) was also analyzed in treated cells.

**Results:** Pro-inflammatory factors (5-HT, adenosine, melatonin and TNF $\alpha$ ) increased oxidative damage in both lipids and proteins. These molecules, except melatonin, also inhibited the activity of antioxidant enzymes. With regard to IL-10, this cytokine was not shown to alter cellular oxidative damage, but was able to reduce the oxidative damage by pro-inflammatory

factors, and to restore their effects on anti-oxidant enzymes activities. Unexpectedly, IL-10, together with melatonin, was found to increase the antioxidant activity above the control.

**Conclusions:** The anti-oxidant effect of IL-10 emphasizes the role of this cytokine as a potential therapy for the treatment of intestinal inflammation induced by pro-inflammatory molecules.

This work was funded by grants from the Spanish Ministry of Science and Innovation and ERDF/FEDER (BFU2009-08149; BFU2010-18971), the Aragon Regional Government and ESF (B61) and the Foundation for the Study of IBD in Aragón (ARAINF 012/2008). E. Latorre and E. Layunta are fellowship recipients from Aragon Regional Government (B105/11; B022/13).

[The name of the third author was corrected 13 July 2015, following initial online publication].

31

### All-trans-retinoic acid (ATRA): a novel potential therapeutic agent for inflammatory diarrhea

Shubha Priyamvada<sup>1</sup>, Arivasaru N Anbazhagan<sup>1</sup>, Anoop Kumar<sup>1</sup>, Tarunmeet Gujral<sup>1</sup>, Alip Borthakur<sup>1</sup>, Seema Saxena<sup>1</sup>, Ravinder K Gill<sup>1</sup>, Waddah A Alrefai<sup>2</sup>, Pradeep K Dudeja<sup>2</sup>

<sup>1</sup>University of Illinois at Chicago, Chicago, IL, USA; <sup>2</sup>Jesse Brown VA Medical Center, Chicago, IL, USA

**Background:** DRA (Down Regulated in Adenoma) or SLC26A3 is the major apical anion exchanger mediating Cl<sup>-</sup> absorption in intestinal epithelial cells (IECs). Reduction in DRA function and expression has been implicated in diarrhea associated with inflammatory bowel diseases (IBD). Upregulation of DRA, therefore, appears to be a novel approach to treat IBD associated diarrhea. In this regard, ATRA, a key metabolite of vitamin A is known to have anti-inflammatory and immunomodulatory properties. We earlier showed that ATRA, increased DRA function, expression and promoter activity through RAR- $\beta$  via the involvement of transcription factor HNF-1 $\beta$ . Whether, ATRA could modulate DRA function and expression under inflammatory conditions is not known.

**Aims:** The aims were to evaluate the efficacy of ATRA in attenuating the inhibitory effects of IFN- $\gamma$  on DRA utilizing Caco-2 cells as an *in vitro* model and Dextran sodium sulfate (DSS)-induced colitis as an *in vivo* mouse model.

**Methods:** Caco-2 cells grown on filter inserts were co-treated with IFN- $\gamma$  (30 ng/mL) and ATRA for 24 hr or DSS colitis (3% DSS in drinking water for 7 days) mice were co-treated with ATRA (1 mg/kg body wt., i.p. for 7 days).

**Results:** Data demonstrated that ATRA abrogated IFN- $\gamma$  induced decrease in DRA function as measured by DIDS-sensitive <sup>125</sup>I uptake. Parallel to this, IFN- $\gamma$ -