



# IMMUNOLOGY OPPORTUNITY AT INSERM

BD & L :

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# OX1R AGONISTS FOR THE TREATMENT OF IBD (BIO14095)

## Product factsheet

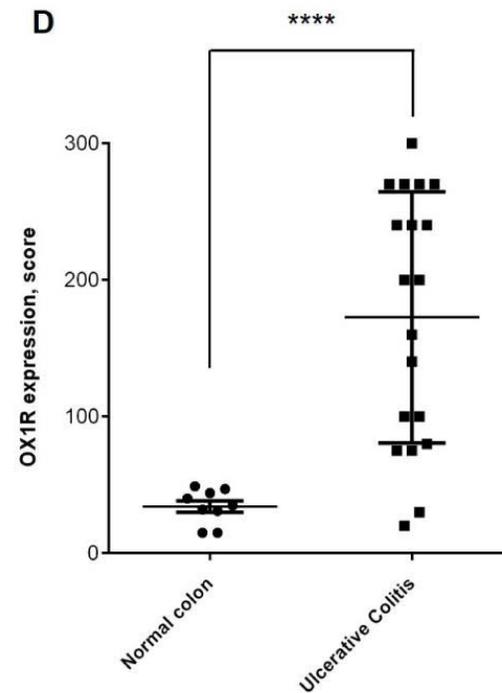
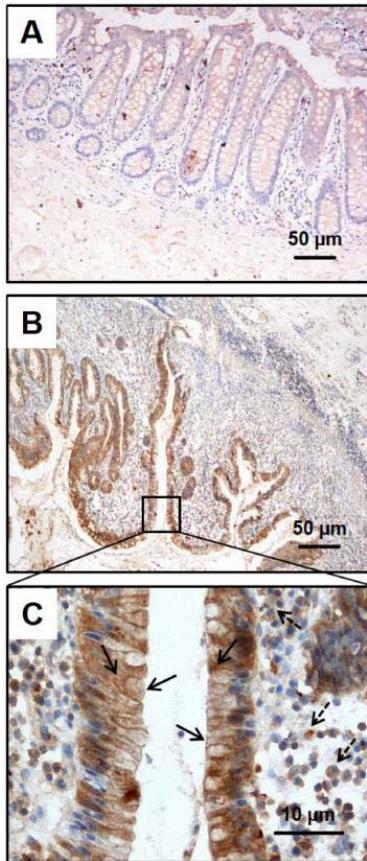
*In vivo POC*  
Biomarker in human

- ▶ **Target:**
  - ◆ 7TM Orexin Receptor (OX1R) ; Orexin A&B neuropeptides / OX1R known to be involved in the control of sleep and food intake (CNS) – no peripheral expression in normal tissues
  - ◆ Tumor associated antigen in pancreatic, prostate and colon cancer (all stages including cancers resistant to chemotherapy)
  - ◆ Orexins promotes apoptosis of cancer cells in vitro through an OX1R mediated novel signaling pathway
- ▶ **Product candidates:** OX1R agonist hmAb, Orexin A/B derived agonist peptides and small molecules (second use) and Orexin based fusion protein
- ▶ **POC:**
  - ◆ Orexin A ameliorates the Disease Activity Index (DAI) and the histological aspect of colon epithelium of DSS-treated mice
  - ◆ Orexin A reduces the secretion of pro-inflammatory cytokines in colon extracts of DSS-induced colitis mice
- ▶ **Publications :** Aberrant expression of OX1R for orexins in colon cancers and liver metastasis: an openable gate to apoptosis, Voisin T et al, Cancer Res. 2011 May 1;71(9):3341-51.
  - ◆ Impact of Orexin-A Treatment on Food Intake, Energy Metabolism and Body Weight in Mice. Blais A et al, PLoS One. 2017
  - ◆ Crucial role of the orexin-B C-terminus in the induction of OX1 receptor-mediated apoptosis: analysis by alanine scanning, molecular modelling and site-directed mutagenesis. Nicole P et al, Br J Pharmacol. 2015
- ▶ **Patent applications:** cover the target, orexin peptides and orexin based fusion protein, anti-orexin proprietary human mAb candidates, second use of known small molecules

# Ox1R AGONISTS FOR THE TREATMENT OF IBD (BIO14095)

## Proof of concept

- Orexin Receptor is ectopically expressed in inflammatory mucosa from patients with IBD



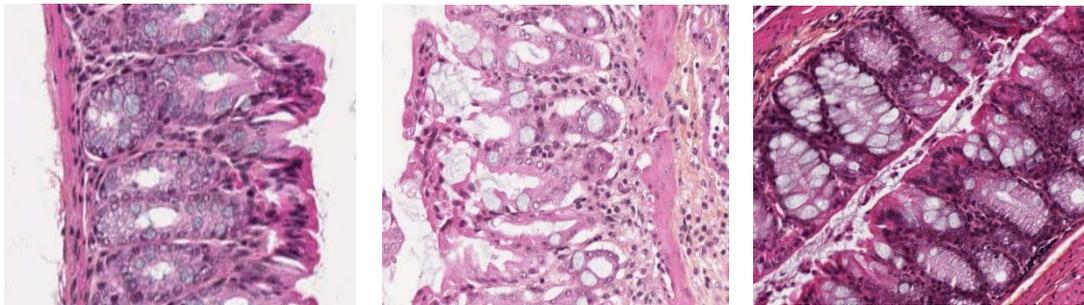
Representative OX1R immunostaining of human normal colonic mucosa from healthy controls (A); patients with UC(B); magnification (C). Black arrows indicate OX1R immunostaining in the plasma membrane and cytoplasm, and dashed arrows in immune cells. Representation of OX1R expression in human normal colonic mucosa from 9 patients and UC colonic mucosa from 19 patients. (D)

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## Proof of concept

- OXA ameliorates the Disease Activity Index (DAI) of DSS-induced colitis

### Histologic aspect of colon epithelia

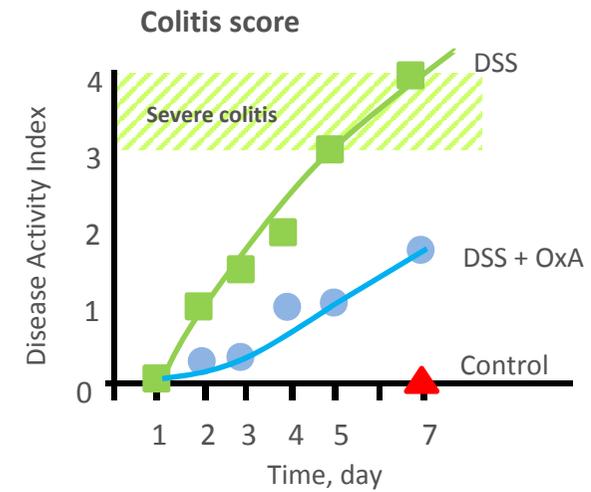
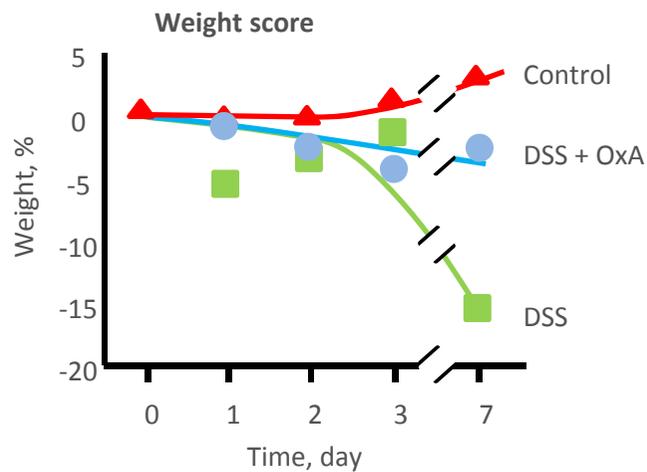


Control

DSS 5%

DSS + OxA

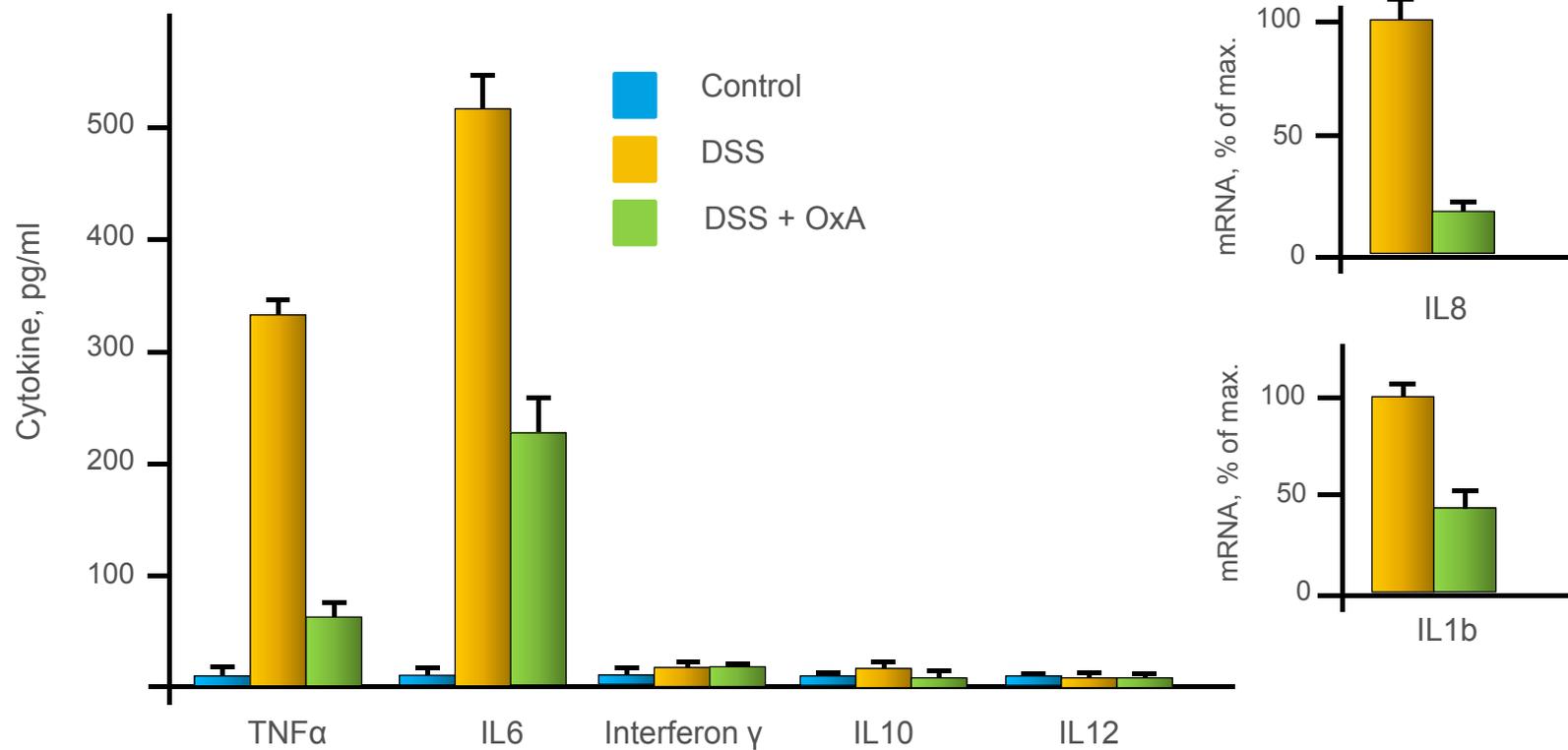
Mice were orally treated with 5% DSS for 7 days



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## Proof of concept

❖ OXA inhibits pro-inflammatory cytokine secretion in DSS-induced colitis

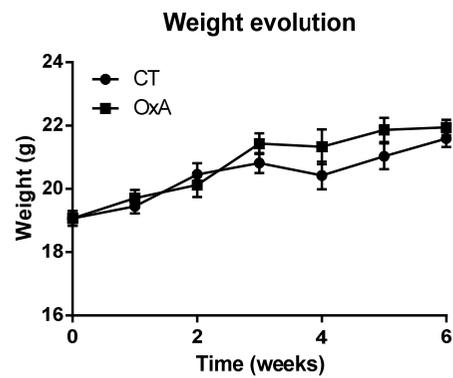


BALB/C mice were orally treated with 5% DSS for 7 days

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## Proof of concept

➤ Chronic OxA treatment has not a major impact on the physiology of mice



Mice were orally treated during 6 weeks

