

# The pathophysiology of visceral hypersensitivity and food-induced abdominal pain: novel opportunities for treatment

Presencial Biomedical Seminar, Thursday, March, 3, 2022 at 16:00h

## Abstract:

**Background:** Food ingestion is a major trigger of abdominal pain in patient with irritable bowel syndrome (IBS), however, the underlying mechanism remains poorly characterised.

**Methods:** Balb/C mice were infected with *Citrobacter rodentium* while orally exposed to ovalbumin (OVA) or saline. After recovery of the infection, mice were re-exposed to OVA by oral gavage and visceral sensitivity was assessed measuring the visceromotor response upon colorectal distention. Colonic mucosal permeability and inflammation were evaluated by using chambers and by histology and qPCR, respectively. The roles of B cells, plasma cells, mast cells, IgE and histamine-1-receptor (H1R) were evaluated using pharmacological approaches and/or using transgenic mice. In humans, solutions of soy, wheat, gluten and milk were injected in the rectal mucosa of IBS patients and healthy volunteers (HV). Mucosal edema-diameter was measured, and biopsies were collected for molecular analyses.

**Results:** Wild type Balb/C mice developed visceral hypersensitivity (VHS) and increased colonic permeability upon re-exposure to OVA in the absence of overt inflammation, only if OVA was present during the infection. In contrast, mast-cell-deficient, B- and plasma-cell-depleted, H1R-deficient mice failed to develop VHS upon OVA re-exposure. VHS-mice showed increased OVA-specific IgE levels in the colon, but not in the small intestine, despite undetectable levels were found in serum. Treatment with a monoclonal antibody to IgE normalised abnormal visceromotor response in VHS mice, results that were confirmed in IgE-deficient mice. In humans, all IBS patients showed mucosal reactions to at least one of the food antigens tested in the absence of systemic allergy to these foods. Furthermore, increased IgE levels were detected in mast cells in a subset of IBS patients, which correlated with abdominal pain severity. IgE<sup>+</sup>-mast cells were found in closer proximity to nerves in IBS patients compared to HV.

**Conclusion:** Our results indicate that local IgE-mediated activation of mast cells leads to increased abdominal sensitivity induced after food ingestion. Our study unravels a novel peripheral mechanism underlying food-induced abdominal pain and suggests that targeting mast cell activation may represent an effective therapeutic strategy to treat VHS in IBS and other food-mediated functional disorders.

## Speaker :

Javier Aguilera-Lizarraga, PhD, KU Leuven

## Affiliation and CV Summary:

Javier Aguilera-Lizarraga was born in Logroño, Spain, on March 8th, 1989. He obtained his Bachelor's degree (BSc) in Biotechnology in 2011 and his Master's degree (MSc) in Biotechnology in Health Sciences in 2012. Thereafter, he worked in 2012 – 2013 as Graduate Research Assistant at the Centre for Biomedical Research of La Rioja (CIBIR), in Logroño, Spain, under supervision of Prof. José Antonio Oteo Revuelta and Dr. Patricia Pérez-Matute, thanks to a one-year Fellowship for University Graduates funded by the ADER and the University of La Rioja. Later, he moved to Belgium in September 2013 to perform his doctoral studies at the Translational Research Centre for Gastrointestinal Disorders, at the KU Leuven, under supervision of Prof. Guy E. Boeckxstaens and Dr. Mira M. Wouters. In October 2015, Javier received a PhD fundamental research Fellowship funded by Research Foundation — Flanders (Fonds Wetenschappelijk Onderzoek — Vlaanderen, FWO). After completing his PhD in Biomedical Sciences in 2019, Javier obtained a Junior Postdoctoral Fellowship in October 2019, funded by Research Foundation — Flanders (FWO), and continued his research under supervision of Prof. Boeckxstaens.

Javier's scientific work has contributed to a number of peer-reviewed publications — including journals such as *Gut*, *Cell* and *Nature*, amongst others. Furthermore, in 2015, 2016, 2017 and 2018, Javier received a Certificate of Recognition for the Scientific Accomplishment as an Early-Stage Investigator awarded by the American Gastroenterological Association (AGA) Institute for his abstracts presented at the Digestive Disease Week (DDW). In 2015 and 2016, he was also awarded with the AGA Student Abstract Prize by the AGA Research Foundation. Next, Javier was recognised with the Best Abstract of Basic Science at the NeuroGASTRO meeting in 2019, organised by the European Society of Neurogastroenterology and Motility. In 2020, he was selected as one of the 30 exceptional young investigators in Neurogastroenterology and Motility research and invited to attend the XVth Little Brain Big Brain meeting (LBBB) 2020 — finally held in 2021 due to the COVID 19 pandemic —, where he was later awarded with the LBBB2020 award and the Most interactive researcher during live discussions. Finally, Javier recently received the Early-Career Author Prize awarded by the American Journal of Physiology—Gastrointestinal and Liver Physiology journal in 2022 and was invited to submit a mini-review in this journal.

## Organizers:

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## Registration form:

<https://forms.gle/ME8kbec2V6TR1N2F8>



Place: Salón de Actos Lorente de Nó, Edificio CIBA. Avda. San Juan Bosco, 13. 50009. Zaragoza.



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