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## Discovered two markers related to the alteration of the epithelial permeability in the irritable bowel syndrome

- A study led by researchers of the Vall d'Hebron Institute of Research and the University Hospital Heidelberg (Germany) identifies two microRNAs that regulate the expression of proteins, located in the jejunum, altered in patients with irritable bowel.
- The discovery has the potential to validate these molecules as biomarkers of the alteration of the permeability and so, to the design of tests to make possible the diagnosis of irritable bowel and other systemic diseases.

**Barcelona, January 25th.** Researchers from the group of Physiology and Pathophysiology of the Digestive Tract of VHIR and the Department of Human Molecular Genetics at the University Hospital in Heidelberg, have discovered two molecular mechanisms that control the expression of some proteins indispensable for the maintaining of the integrity of the intestinal epithelium. This finding will allow the validation of these markers for the diagnosis of irritable bowel and other systemic diseases associated to the intestinal permeability, such as diabetes or cirrhosis. The study has just been published in *Gut* and was led by Dr. Javier Santos, Dr. María Vicario and Dr. Beate Niesler.

The research shows how the microRNAs 16 and 125b modulate the molecules Claudin 2 and Cingulin in a different way in the intestine of patients than in the intestine of healthy controls. The function of these proteins, which are molecules of intercellular unions, is to maintain an optimal barrier between the exterior and the interior, controlling thus the epithelial permeability and avoiding that harmful substances can access inside of the body. In the present study, VHIR researchers have focused on the mechanisms that trigger the alteration of the expression of these proteins, after detecting it in previous researches.

To perform the analysis, they compared the biopsies of the jejunum of 43 patients of Vall d'Hebron University Hospital with irritable bowel and diarrhoea predominance with the biopsies of 24 healthy people. For 10 days, all the

subjects completed a daily questionnaire where they indicated and measured aspects such as abdominal pain and frequency and number and consistence of the depositions.

**“We checked that the expression of these markers is altered in the small bowel of patients with irritable bowel and diarrhoea predominance, and not in healthy people”**, explains Dr. Vicario. After some experiments, the team proved that if the mechanisms that regulate Claudin 2 and Cingulin were inhibited, changes contrary to their expression and in the intestinal permeability were observed. For this reason, Dr. Santos adds that **“the markers may be useful to diagnose the disorders of intestinal permeability in the future, which we know is specially suffered by patients with serious disorders of irritable bowel”**.

Nowadays, there are not agreed biological markers for irritable bowel and the diagnosis is performed purely based on clinical criteria and after dismissing other diseases. This means the diagnosis is made late, normally after two years, and only between 20 and 40 per cent of the patients are correctly diagnosed, according to the estimations performed by the medical community.

After the publication of the study, the researchers started a second study to validate in a non-invasive way if the markers are specific of the irritable bowel or general markers of diseases in which a disorder of the permeability is observed such as diabetes, rheumatoid arthritis or cirrhosis. This research will be done with a cohort of 200 patients with irritable bowel with diarrhoea or constipation, celiac disease, inflammatory bowel disease and microscopic colitis, among other diseases.

### Collaborative study

This international and interdisciplinary study was carried out by researchers from VHIR and the Institute of Human Genetics in Heidelberg (Germany). Dr. Cristina Martínez, who was a visiting scientist in Heidelberg, supervised by Dr. Nielser, performed the genetic and molecular validation of the results. Moreover, the research is part of the European consortium GENIEUR, funded within the COST program of the European Commission, and endorsed by the European Society of Neurogastroenterology and Motility (ESNM), in order to identify genetic factors to explain the irritable bowel syndrome.

### Bibliographic reference

Martínez C, Rodiño-Janeiro BK, Lobo B, et al. Gut Published Online First: 12 January 2017 doi:10.1136/gutjnl-2016-311477

## Vall d'Hebron Barcelona Hospital Campus

The Vall d'Hebron Campus comprises the Vall d'Hebron University Hospital, the Vall d'Hebron Institute of Research (VHIR), the Vall d'Hebron Institute of Oncology (VHIO) and the Multiple Sclerosis Centre of Catalonia (Cemcat). The new project represents a new way of working, where the research, teaching and clinical practice go together, in the same direction in order to pull together to become more useful, productive and effective.

*Unidad de Comunicación e Imagen Vall d'Hebron Barcelona Campus Hospitalario*

*Fran Garcia: 672204546- fran.garcia@vhir.org*

*David Collantes: Tel. 934 894 440- 675782156- dcollantes@vhebron.net; comunicació@vhebron.net*

*Twitter: @VHIR\_ @hvhebron*

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