Evidence of epigenetics in inflammatory bowel diseases

Inflammatory bowel diseases (IBDs) including Crohn's disease (CD) and ulcerative colitis (UC) are characterised by a persistent relapsing-remitting inflammation in the gut. These are some of the most complex diseases that afflict the digestive tract, involving multiple factors, including genetics, environment, and gut microbiota. These diseases seem to be on the rise worldwide and can affect the quality of life of patients drastically. They may predispose to colorectal cancer, and treatment can be very costly. The etiology of these diseases is not well understood. Genetic factors, environmental factors, including diet, the gut microbiota, and epigenetic factors have been implicated with these diseases.

We edited a series on "Evidence of Epigenetics in Inflammatory Bowel Diseases", combining four review articles and one original research article. The main purposes of this series are (I) to shed light onto potential links between epigenetic mechanisms and IBDs and to highlight new findings in this respect; (II) to explore progress in this field in pre-clinical models and in patients; and (III) to examine the role of environment in its broadest sense in IBD.

In the article by Rodrigues and collaborators titled: "The exposome-diet-epigenome axis in inflammatory bowel diseases—a narrative review" (1), the authors highlight the multifactorial nature of IBD. They point out that genetics does not explain the disease in its entire pathophysiology, emphasizing the need to investigate other pathways and factors, such as the epigenome, microbiome, diet, and exposome, to better understand IBD. They performed a thorough literature review to interpret the evidence on the association of environmental factors and endogenous factors in individuals with IBD and create a connection between these factors. They review known facts about genetic factors and IBD but mostly focus on the potential roles of environmental factors, summarised with the term 'exposome'. This includes diet, gut microbiome, and diet effects on microbiome, including food additives. They write, "*...epigenetic factors could mediate gene-environment interactions involved in resistant output and disease susceptibility*, *which makes epigenetics a key mechanism in IBD pathogenesis and other chronic and immune-mediated diseases*". They conclude their review by briefly outlining links between epigenetic mechanisms (DNA methylation, histone modifications) and IBD and focus on the role of noncoding RNA and microRNAs (miRNA) in this respect.

The topic of environmental influences is elaborated further by Zaltman and colleagues, who review what is published regarding the link between air pollution and IBD "Ambient air pollution and inflammatory bowel disease—a narrative review" (2). The authors conclude: "*Besides conflicting and inconsistent results from previous studies and notable knowledge gaps*, *there is a plausible chance that the development of IBD can be affected by air pollution*. *Future prospective studies are required to gain comprehensive insight into this correlation*."

The review by Pereira and Varga-Weisz 'Role of epigenetic mechanisms in inflammatory bowel disease' (3) highlights the role of epigenetic mechanisms in IBD, focusing on recent work on epigenetic factors that have been identified by genetic means, SP140 and SETD2.

The theme of epigenetic mechanisms is expanded by the piece of Fernandes and Vinolo reviewing 'Histone acylations as a mechanism for regulation of intestinal epithelial cells' (4).

The review articles are complemented by a report from Dao and colleagues that introduces "A promising DNA methylation analysis pipeline for epigenetic studies and clinical implementation in inflammatory bowel disease" (5).

Therefore, this series deals with the main possible factors involved with the occurrence of IBD, which has been investigated in the last two decades. This knowledge may help to better understand the disease pathways and pursue background for further new treatments and control of intestinal inflammation in the future.

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Footnote

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Raquel Franco Leal

Patrick Varga-Weisz

Raquel Franco Leal[1]^, MD, PhD
(*Email: rafranco@unicamp.br*)
Patrick Varga-Weisz[2,3]^, PhD
(*Email: Patrick.varga-weisz@essex.ac.uk*)
[1]Inflammatory Bowel Disease Research Laboratory, Colorectal Surgery Unit, Department of Surgery, School of Medical Sciences, University of Campinas, Campinas, SP, Brazil; [2]International Laboratory for Microbiome Host Epigenetics, Department of Genetics, Evolution, Microbiology, and Immunology, Institute of Biology, University of Campinas, Campinas, SP, Brazil; [3]School of Life Sciences, University of Essex, Colchester, UK

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^ ORCID: Raquel Franco Leal, 0000-0003-4285-4402; Patrick Varga-Weisz, 0000-0001-7409-8686.