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Jean-Vianney Haure-Mirande, Pierre de Coppet, Christian Bonnet, Arnaud Boureille, Gwenola Le Drean, Jean-Pierre Segain

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INTRAUTERINE GROWTH RETARDATION ALTERS THE COLONIC EPITHELIAL BARRIER AND INCREASES THE RISK OF COLONIC DISEASES IN ADULT RATS

V. Haure-Mirande [1,*], P. de Coppet [1], C. Bonnet [1], A. Bourreille [2], G. Le Dréan [1], J.-P. Segain [1]
[1]IMAD-INRA / Nantes University, [2]IMAD-CHU, Nantes, France

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INTRODUCTION: Infants born with intrauterine growth retardation (IUGR) are at increased risk for developing metabolic diseases in adulthood such as type 2 diabetes (1). It has been proposed that an adverse intrauterine environment could induce stable epigenetic modulation of gene expression, which in turn, alters the function of metabolic organs later in life (2). Epigenetic and metabolic modifications are also involved in the pathogenesis of inflammatory bowel disease and colorectal cancer but their origins are not completely understood (3).
AIMS&METHODS: The objective of this study was to determine the impact of IUGR upon colonic epithelial barrier and colonic diseases.The rat model of IUGR was obtained by restricting protein intake in pregnant rats. Birth weights of IUGR pups are 15-20% lower than controls. By the age of 5-8 months, colons were collected and colonocytes isolated. Permeability was assessed by mounting colonic tissues in Ussing chambers. Expression of key genes and epigenetic modifications were analysed by immunohistology, western-blot, qPCR and ChIP assays. Susceptibility to colitis was assessed by dextran sodium sulfate (DSS) treatment and colitis induced-carcinogenesis by azoxymethane (AOM) injection. Histological scores and neoplastic lesions were measured.
RESULTS: Proliferation of epithelial cells was decreased in colonic crypts from IUGR rats without modification of apoptosis, suggesting a lower self-renewal of colonic epithelium. IUGR increased intestinal permeability and this effect was associated with disorganisation of tight-junction proteins. Expressions of the transporter (MCT1) and ß-oxidation enzyme (scACAD) of butyrate were down-regulated in IUGR colonocytes suggesting impairment of butyrate utilisation, the main energy source for colonocytes (5). Among the posttraductional modifications of H3 and H4 histones, IUGR induced a drastic loss of H4K16 acetylation, an epigenetic mark of colorectal cancer (5). The severity of DSS-induced colitis was higher in IUGR rats than in controls. Moreover, the number of AOM-induced preneoplastic lesions (MDF) was higher in IUGR rats.
CONCLUSION: Our study suggests that IUGR induces epigenetic and metabolic modifications in colonic epithelium, which could affect the intestinal barrier and predispose to gastrointestinal diseases.
REFERENCES: 1) Barker, D.J. 1999. Ann Intern Med 130,322–324
2) Gluckman, P.D. et al. 2008. N Engl J Med 359,61-73
3) Grady, W.M. & Carethers, J.M. 2008.Gastroenterology 135,1079–1099
4) Thibault, R et al. 2010. Inflamm Bowel Dis 16,684-695
5) Fraga, M. et al. 2005. Nat Genet. 37,391-400
Contact E-mail Address: gwenola.ledrean@univ-nantes.fr

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