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Microbiota dysbiosis induced by defect of paneth cells triggers visceral hypersensitivity in mice

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Abstract Title (171)

MICROBIOTA DYSBIOSIS INDUCED BY DEFECT OF ENTERIC ANTIMICROBIAL ACTIVITY TRIGGERS VISCERAL HYPERSENSITIVITY IN YOUNG ADULT MICE

A short description of your research project (3000)

Our research project focuses on early and long course consequences of adverse events during perinatal period on intestinal barrier functions and immune system maturation and education. Indeed, perinatal period has been identified as a critical window for intestinal barrier and immune system establishment leading to an appropriate relationship between host and intestinal content i.e. homeostasis. Adverse events during this period might be responsible for disestablishment of host - microbiota relationship responsible for various diseases where an inappropriate host immune response toward luminal content has been identified. Luminal content is represented by food and microbial antigens. A rupture of tolerance toward microbiota has been observed in organic (inflammatory bowel diseases) and functional (irritable bowel syndrome) gastrointestinal disorders whereas during food intolerance, dietary factors are the target of the exacerbated immune response.
We address the consequences of adverse events during perinatal period on intestinal barrier functionality and immune response in different model challenged with stress, chemical or infections within the framework of collaborations.
We developed an expertise in the field of intestinal barrier, immune system and microbiota analysis in adult but also in young rodents. Concerning intestinal barrier, we develop experimental protocols to measure intestinal permeability in vivo and ex vivo, enteric antimicrobial peptides expression and antimicrobial assay toward commensal bacteria, visceral sensitivity in response to colorectal distension, immune response associated to intestinal epithelium. Regarding immune system, we perform not only immune cells characterization but also evaluation of their functionality.
Recently, a growing body of evidence highlighted the tight link between immune response and metabolism named immuno-metabolism. Metabolic disorders including type 2 diabetes and obesity are characterized by a low grade inflammation, intestinal hyper-permeability and microbiota dysbiosis. Within the framework of collaboration, we included the consequences of adverse events during perinatal period on metabolism at adulthood.

Abstract of the project you want to present

A. Riba[1], M. Olier[1], S. Lacroix-Lamandé[2], C. Lencina[1], V. Bacquié[1], C. Harkat[1], M. Gillet[1], M. Baron[1], C. Sommer[1], V. Mallet[1], C. Salvador-Cartier[1], F. Laurent[2], V. Théodorou[1], S. Ménard[1].

[1] INRA, ToxAlim (Research Centre in Food Toxicology), team Neuro-Gastroenterology and Nutrition, Toulouse, France

[2] Equipe Apicomplexes et Immunité Mucosale (AIM), UMR 1282 INRA/Université-Infectiologie et Santé Publique (ISP), Centre INRA Val de Loire, Nouzilly, FRANCE

Paneth cell-derived antimicrobial peptides like lysozyme provide antibacterial protection and maintain intestinal homeostasis. We aimed to analyze the consequences of altered Paneth cells function on fecal antimicrobial activity, intestinal homeostasis and visceral sensitivity at adulthood. In 50-days old Sox9$^{flox/flox}$-vil-Cre female mice, absence of Paneth increased fecal population of *Enterobacteriaceae* associated to visceral hypersensitivity. Daily gavage of conventional adult mice with commensal *E. coli*, induced visceral hypersensitivity. Occurrence of adverse events during neonatal period impairs intestinal homeostasis establishment. Maternal separation (MS) is a well described rodent model of psychological stress characterized by a decrease of intestinal secretory cells and visceral hypersensitivity mimicking what we observed in Sox9$^{flox/flox}$-vil-cre mice. We wondered if in this model we also observed a dysbiosis in favor of *Enterobacteriaceae.* Mice submitted to MS, presented a defect of fecal antimicrobial activity associated with a fecal overgrowth of *Enterobacteriaceae*. Furthermore, this antimicrobial defect and its consequences on visceral sensitivity were prevented by oral administration of lysozyme. Our results show that a defect of enteric antimicrobial functions leads to microbiota dysbiosis in favor of *Enterobacteriaceae* responsible for visceral hypersensitivity providing new mechanistic insights in maternal separation-induced visceral hypersensitivity.

Short tabular CV

Ambre RIBA

E-mail: ariba@ukaachen.de

Current Position

Post-Doctoral Position in intestinal physiology and infection, UNIKLINIK, Medizinische Mikrobiologie, Aachen, Deutschland, « Consequences of early infection on intestinal homeostasis at adulthood in mice», DFG Grant), team leader: Pr Mathias Hornef *(since April 2015)*

Education

- **2012-2015**: PhD in intestinal physiology, INRA Toxalim, Equipe NGN (NeuroGastroentérologie et Nutrition), Toulouse, France, «Consequences of early life stress on intestinal homeostasis and response toward microbiota at adulthood », Bourse DGER école d'ingénieur de Purpan grant, scientific directors: S. Ménard et V. Théodorou (defended in February 2015)
- **2010-2011**: Master's degree in food science and human nutrition (2011), ONIRIS – University of Nantes, Nantes, France.
- "Impact of antibiotic therapy in rat on intestinal barrier et visceral sensitivity at different ages of life", scientific director: Dr H. Eutamene, ToxAlim, INRA, Toulouse, France.
- **2010**: Master's degree in Nutrition & Health – Food Technology, ETH of Zurich, Switzerland. Physiology of eating, Dietary, Toxicology, Sensory science
- **2008-2011**: Engineer formation in food technology, ONIRIS, Nantes, France

Sciences and technology of industries and food science.

Own publications (500)