Epithelial Response to Parasitic Infections

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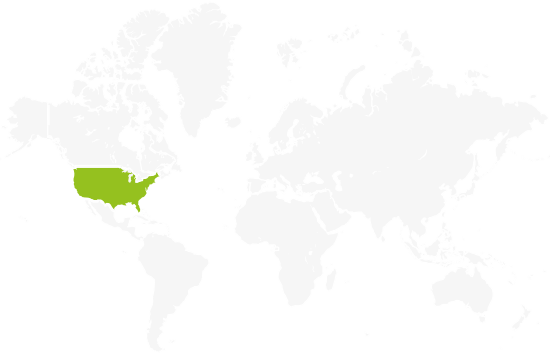

Epithelial response to enteric infections

I did my undergraduate program at the Pierre et Marie Curie University (Paris VI, France) from 1997 to 2002, and then went to graduate school at Blaise Pascal University (Clermont-Ferrand II, France), where graduated with a PhD in 2007. My PhD work was focused on Enterohemorragic *E. coli* pathogenesis and more specifically on studying factors modulating toxin production by EHEC. Since 2008, I have been working at the Vanderbilt University (Nashville, TN, USA) as a postdoctoral fellow where I study gastric cancer carcinogenesis induced by Helicobacter pylori and especially which bacterial and host factors could be responsible for the development of gastric cancer.
My primary research interests are in the microbiology and infectious diseases of the gastrointestinal tract, with a special focus on host-pathogen and interbacterial interactions.

Selected Publications

- **de Sablet T**, Chaturvedi R, Asim M, Piazuelo MB, Barry DP, Verriere TG, Sierra JC, Hardbower DM, Delgado AG, Schneider BG, Israel DA, Romero-Gallo J, Nagy TA, Morgan DR, Murray-Stewart T, Bravo LE, Peek RM Jr, Fox JG, Woster PM, Casero RA Jr, Correa P, Wilson KT. 2014. Increased Helicobacter pylori-associated gastric cancer risk in the Andean region of Colombia is mediated by spermine oxidase. *Oncogene*. Sep 1.

- Gobert AP, Verriere T, Asim M, Barry DP, Piazuelo MB, **de Sablet T**, Delgado AG, Bravo LE, Correa P, Peek RM Jr, Chaturvedi R, Wilson KT. 2014. Heme Oxygenase-1 Dysregulates Macrophage Polarization and the Immune Response to *Helicobacter pylori*. *J Immunol*. Aug 8. pii: 1401075.

- Gobert AP, Verriere T, **de Sablet T**, Peek RM, Chaturvedi R, Wilson KT. Heme oxygenase-1 inhibits phosphorylation of the Helicobacter pylori oncoprotein CagA in gastric epithelial cells. *Cellular Microbiol*. 15(1):145-56.

- **de Sablet T**, Piazuelo MB, Shaffer CL, Schneider BG, Asim M, Chaturvedi R, Bravo LE, Sicinschi LA, Delgado AG, Mera RM, Israel DA, Romero-Gallo J, Peek RM Jr, Cover TL, Correa P, Wilson KT. Phylogeographic origin of Helicobacter pylori is a determinant of gastric cancer risk. Gut. 60(9):1189-95.

Epithelial response to enteric infections

Enteric apicomplexa are found worldwide and affect both animal farm production and human health. Infection of intestinal epithelial cells (IEC) by these protozoan parasites leads to various consequences such as malabsorption and diarrhea. The physiopathological consequences for the host depend on the particular infecting isolates as they can span a wide range of virulence. It is necessary to better characterize the mechanisms by which virulent strains of enteric protozoans impact major physiological functions of the intestinal epithelium, especially for economically important parasites affecting the livestock such as *Eimeria spp*. and the zoonotic agent *Cryptosporidium*. Within the IEC, the only host cell used for their development, these parasites utilize different subcellular locations (apical and extracytoplasmic for *C. parvum*, and cytoplasmic for the *Eimeria spp*.) and may affect the proper functioning of IEC differently.

It is known that protozoans can disrupt intestinal epithelium and thus, affect barrier function. The mechanisms involved in this process are still poorly understood and need to be investigated. Our project is to study the modulation of tight and adherens junction proteins during *C. parvum* and *Eimeria* infections. We plan to study the role of Nitric Oxide, polyamines, as well as cytokines in the regulation of intraepithelial permeability.

Pathogenic bacteria can elicit a chloride secretory response by stimulating the apical chloride secretory channel (Cystic Fibrosis Transmembrane Receptor) and chloride secretion has been observed in IEC after *C. parvum* infection. This gives us a good rationale to investigate the capacity of *C. parvum* strains to affect kinases activities regulating CFTR activation, either directly or via the induction of host factors.

This project will provide a better understanding of the molecular mechanisms involved in the physiopathology resulting from virulent enteric protozoan infection, a first step to develop new strategies against the dramatic consequences of these parasitic diseases.

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Team: CIMEN: Control and immunology of neonatal enteric diseases
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Institutions: INRA, Université François Rabelais – Tours

Key words: parasitology, immunology, neonate, epithelial cell, dendritic cell

UMR1282 ISP Infectology and Public Health, led by Dominique Buzoni-Gatel, is a recognized large joint research unit (15 teams) linking INRA and François Rabelais University of Tours, which aims to understand and control infections or infectious diseases. Within ISP, the team CIMEN (Control and Immunology of Neonatal Enteric Diseases) led by Fabrice Laurent, studies neonatal enteric infection by the protozoan parasite cryptosporidium parvum. Research is undertaken on ruminants and on the mouse model to (i) decipher the immune mechanisms leading to protection, (ii) to better understand host-pathogen interactions and (iii) to develop new strategies of control.

Cryptosporidium parvum

http://www7.tours.inra.fr/Pole_Sante_Animale/infectiologie_et_sante_publique/equipes/controle_et_immunologie_des_maladies_enteriques_du_nouveau_ne

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