**Abstract**

**Host response and genotoxicity related to the *H. pylori* infection in a mouse model**

*H. pylori* is an important etiological factor in the development of gastric carcinoma. Carcinogenesis process is likely to result from an accumulation of mutations involving genes that guarantee the stability of the genome. The aims of our studies were i) to analyze the role of the *H. pylori* infection in the induction of genotoxic events in gastric epithelial cells, as DNA damages, genetic instabilities and mutations ii) to identify host, bacterial and environmental factors potentially responsible for the genesis of precancerous lesions at the gastric level.

Using a transgenic rodent mutagenesis assay, allowing the detection of mutation in any organs, the induction of a 5-fold mutagenic effect after 6 months of infection with the *H. pylori* strain SS1 have been evidenced, as compared to the non-infected mice. It is correlated with a high incidence of AT->CG and GC->TA transversions, known to result from oxidative DNA damages. Infected-mice exhibited a severe gastritis with an increased expression of the inducible Nitric Oxide Synthase (iNOS) responsible for the production of NO•, also known for their DNA damaging properties. In addition to the induction of mutations, the *H. pylori* infection led to instabilities in CA repeats microsatellite regions. After 12 months of infection, hyperplasia developed in the gastric mucosa. Concomitantly an extension of cell proliferation correlated with an induction of apoptosis as showed by the activation of Caspase 3 have been observed.

This transgenic mouse model is a powerful tool to investigate the influence of host factors on the inflammatory and genotoxic host response to the *H. pylori* infection.
The influence of a deficiency in the DNA repair gene *Ogg1*, encoding a DNA glycosylase responsible for the excision of the oxidative DNA lesions 8-oxoguanine, has been investigated. *Ogg1*−/− mice have been orally infected with *H. pylori* SS1 for 1, 3 and 6 months and the serological response, histological lesions, mutant frequency and spectra of mutation have been assessed and compared to what previously observed in the wild-type genetic context. Results obtained in these conditions strengthened the relation between chronic inflammation and genotoxicity.

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**Curriculum Vitae**

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**Present Position:** Assistant Professor (Chargé de Recherche) Institut Pasteur

**Positions Held:**
- 1982 : DEA practical stay directed by Dr P.L.Boquet in the Department of Biochimie, Commissariat à l’Energie Atomique (CEA) Saclay.  
- 1983-1986: Doctoral Thesis Fellowship, of the Direction Générale de la Recherche Scientifique et Technologique (DGRST)“ Unit of Regulation of Genetic Expression ” Institut Pasteur (Advisor, Pr.A.Danchin)  
- 1986-2001: Research Engineer “Unit of Molecular Programmation and Genetic Toxicology ” Institut Pasteur (Advisor, Pr. M.Hofnung)  
- 2001-2002 : Assistant Professor “ Unit of Molecular Programmation and Genetic Toxicology ” Institut Pasteur (Advisor, Dr. JM.Clément)  
- 2003…: Assistant Professor “Unit of Pathogenesis of Mucosal Bacteria ” Institut Pasteur (Advisor, Pr. A. Labigne)

**Research Interest:**
My major interests are the analysis of the genotoxicity involved in the relation between infectious agents and cancer development, focusing on the *H. pylori* infection and the genesis of gastric cancerous lesions. The main goal is to gain insight in the mechanisms involved in early events by which the infection and the associated chronic inflammation lead to DNA damage, mutations, genetic instabilities and ultimately carcinogenesis. For that purpose, mouse models of infection have been developed allowing the analysis of the influence of host, bacterial and environmental factors on the genotoxic and inflammatory host response.

**Main Publications:**


