Helicobacter pylori. Where do we go from here?

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The discovery of *Helicobacter pylori* has changed the vision and management of gastroduodenal diseases. We must also acknowledge the introduction of new concepts following this discovery. Among them is the use of stable isotopes in clinical diagnosis, the use of bacterial markers of chronic infection to follow human migrations, and the theory that stem cells are at the origin of gastric adenocarcinoma and other possible carcinomas. The role of *H. pylori* as a potential cause of cancer was highlighted by IARC already in 1994, but little was known about the cells from which cancer arises. The model of a chronic infection by *Helicobacter felis* in mice allowed JM Houghton to propose that mesenchymal stem cells are at the origin of gastric carcinomas. Our laboratory began a research programme in this field at 3 levels: 1) mice in order to repeat the previous experiment with several *H. pylori* strains (not only *H. felis*), 2) cell cultures to analyze the different steps of the process and 3) detection of cancer imitating cells from human gastric tumour resection. This programme is still ongoing but preliminary data have been generated. Mice eradicated and reconstituted with bone marrow from GFP+ transgenic mice allowed us to have a marker for stem cells. After one year of infection, certain *H. pylori* strains were shown to induce mesenchymous stem cell homing in the gastric mucosa, as foci of GFP^+ epithelial cells can be visualized, confirming the first step of the process. The analysis of the different steps of the carcinogenesis process undertaken in vitro shows that epithelial cells infected by the same *H. pylori* strains are chemotactic on

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mesenchymous stem cells and also that stem cells can follow a mesenchymous-epithelial differentiation. Furthermore, cancer initiating cells, which exhibit specific markers, can be obtained by inoculating tumour cells in immunodeficient mice. These first results are in favour of the theory proposed by JM Houghton.

In another field, i.e. *H. pylori* eradication, a European survey of antimicrobial resistance shows us that clarithromycin resistance is over 20% especially in Southern European countries. Levofloxacin-based triple therapy can be an alternative but it may also induce resistance in case of failure. The future may lie in a new fluoroquinolone: finafloxacin which exhibits interesting properties of an increase in activity at low pH and also a lack of selection of resistant mutants in case of failure. Trials are currently underway.

The long term infection caused by *H. pylori* remains an exciting model to solve important questions in carcinogenesis but the basic question of *H. pylori* eradication remains a current problem.