Helicobacter pylori infection induces genetic instability of nuclear and mitochondrial DNA in gastric cells.

**Purpose:** Helicobacter pylori is a major cause of gastric carcinoma. To investigate a possible link between bacterial infection and genetic instability of the host genome, we examined the effect of H. pylori infection on known cellular repair pathways in vitro and in vivo. Moreover, various types of genetic instabilities in the nuclear and mitochondrial DNA (mtDNA) were examined. Experimental Design: We observed the effects of H. pylori infection on a gastric cell line (AGS), on C57Bl/6 mice, and on individuals with chronic gastritis. In AGS cells, the effect of H. pylori infection on base excision repair and mismatch repair (MMR) was analyzed by reverse transcription-PCR, Western blot, and activity assays. In mice, MMR expression was analyzed by reverse transcription-PCR and the CA repeat instabilities were examined by Mutation Detection Enhancement gel electrophoresis. Mutation spectra in AGS cells and chronic gastritis tissue were determined by PCR, single-stranded conformation polymorphism, and sequencing. H. pylori vacA and cagA genotyping was determined by multiplex PCR and reverse hybridization.

**Results:** Following H. pylori infection, the activity and expression of base excision repair and MMR are down-regulated both in vitro and in vivo. Moreover, H. pylori induces genomic instability in nuclear CA repeats in mice and in mtDNA of AGS cells and chronic gastritis tissue, and this effect in mtDNA is associated with bacterial virulence.

**Conclusions:** Our results suggest that H. pylori impairs central DNA repair mechanisms, inducing a transient mutator phenotype, rendering gastric epithelial cells vulnerable to the accumulation of genetic instability and thus contributing to gastric carcinogenesis in infected individuals.

**General information**

Publication status: Published
Organisations: Roskilde University, Institut Pasteur, University of Porto, Copenhagen University Hospital
Pages: 2995-3002
Publication date: 2009
Peer-reviewed: Yes

**Publication information**

Journal: Clinical Cancer Research
Volume: 15
ISSN (Print): 1078-0432
Ratings:
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 3.711 SNIP 1.696
Web of Science (2009): Indexed yes
Original language: English
DOI:
10.1158/1078-0432.CCR-08-2686
Source: PublicationPreSubmission
Source-ID: 93296416
Research output: Contribution to journal › Journal article – Annual report year: 2009 › Research › peer-review