

# Metagenomic study of *Helicobacter pylori* microdissected from archived formalin-fixed paraffin-embedded biopsy sections

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## Background

Identification of microbial virulence factors that causing chronic diseases in host such as cancers is complicated, since the microbes present at the time of disease diagnosis might reflect adaption to the long-term altered environment, rather than what actually caused the disease. Hence, samples collected before or in the early stage of disease development, such as archived formalin-fixed and paraffin-embedded (FFPE) materials from not yet malignant stomachs, with long-term follow-up of disease outcomes, are valuable resources for identifying virulence strains. However, sequencing microbe genomes in decade-preserved formalin-fixed and paraffin-embedded (FFPE) biopsy is challenging due to the minute amounts of highly degraded microbial DNA and the interference by vast majority of human DNA.

## Materials and methods

Metagenomic profiles of *Helicobacter pylori* in two FFPE biopsies (both aged 15 years) from two patients were obtained by laser microdissection (LCM) and modified Roche 454 pyrosequencing. Frozen homogenized biopsies from these two patients were also available for comparison after re-culture.

## Results

*H. pylori* DNAs dissected from FFPE sections had highest identity with the culture DNAs from the same host (~ 98%) than with other reference genomes (93 ~ 95%) or with culture isolates from the other patient (94.7%).

## Conclusions

This method demonstrates the feasibility of using decade-preserved FFPE biopsies for metagenomic study of *H. pylori* virulence factors in a longitudinal epidemiological setting. Also, the results demonstrate an advantage of physical enrichment (i.e. by microdissection) over hybridization methods that rely on current knowledge of the genomics of this microbe and thus may miss novel genes.

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