Evidence for conserved function of \( \gamma \)-glutamyltranspeptidase in Helicobacter genus.

Abstract:
The confounding consequences of Helicobacter bilis infection in experimental mice populations are well recognized, but the role of this bacterium in human diseases is less known. Limited data are available on virulence determinants of this species. In Helicobacter pylori, \( \gamma \)-glutamyltranspeptidase (\( \gamma \)GT) contributes to the colonization of the gastric mucosa and to the pathogenesis of peptic ulcer. The role of \( \gamma \)GT in H. bilis infections remains unknown. The annotated genome sequence of H. bilis revealed two putative ggt genes and our aim was to characterize these H. bilis \( \gamma \)GT paralogues. We performed a phylogenetic analysis to understand the evolution of Helicobacter \( \gamma \)GTs and to predict functional activities of these two genes. In addition, both copies of H. bilis \( \gamma \)GTs were expressed as recombinant proteins and their biochemical characteristics were analysed. Functional complementation of Escherichia coli deficient in \( \gamma \)GT activity and deletion of \( \gamma \)GT in H. bilis were performed. Finally, the inhibitory effect of T-cell and gastric cell proliferation by H. bilis \( \gamma \)GT was assessed. Our results indicated that one gene is responsible for \( \gamma \)GT activity, while the other showed no \( \gamma \)GT activity due to lack of autoprocessing. Although both H. bilis and H. pylori \( \gamma \)GTs exhibited a similar affinity to L-Glutamine and \( \gamma \)-Glutamyl-p-nitroanilide, the H. bilis \( \gamma \)GT was significantly less active.
Nevertheless, H. bilis ?GT inhibited T-cell proliferation at a similar level to that observed for H. pylori. Finally, we showed a similar suppressive influence of both H. bilis and H. pylori ?GTs on AGS cell proliferation mediated by an apoptosis-independent mechanism. Our data suggest a conserved function of ?GT in the Helicobacter genus. Since ?GT is present only in a few enterohepatic Helicobacter species, its expression appears not to be essential for colonization of the lower gastrointestinal tract, but it could provide metabolic advantages in colonization capability of different niches.