Helicobacter pylori \(\gamma\)-glutamyltranspeptidase impairs T-lymphocyte function by compromising metabolic adaption through inhibition of cMyc and IRF4 expression.

Abstract:
Helicobacter pylori (H. pylori) is a human-specific pathogen that has evolved to cope with the immune response elicited against the infection. We previously reported that H. pylori \(\gamma\)-glutamyltranspeptidase (gGT) impairs T-lymphocyte proliferation and thus might act as immune regulatory factor. In this study, we analysed the underlying mechanism and its implications for H. pylori persistence. We found that H. pylori gGT compromised T-cell proliferation, activation and effector cytokine expression by specifically depriving the extracellular space of glutamine. When assessing signalling cascades and transcription factors affected by H. pylori gGT, we found that expression of cMyc and IRF4, both required for metabolic adaptation of T-lymphocytes, was highly sensitive to extracellular glutamine levels and downregulated upon gGT treatment. Moreover, we could confirm decreased IRF4 expression in T-lymphocytes infiltrating the stomach of infected individuals. Thus, our results suggest that H. pylori gGT-mediated glutamine deprivation in the gastric mucosa may suppress T-cell function thereby contributing to bacterial persistence.

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