

## Inhibition of lymphocyte proliferation mediated by

### *Helicobacter suis* $\gamma$ -glutamyl transpeptidase

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*Helicobacter (H.) suis* has been shown to cause gastric disease, both in pigs and humans. In the present study, we investigated the effect of *H. suis*  $\gamma$ -glutamyl transpeptidase (GGT) on the proliferation of lymphocytes. Incubation of Jurkat T cells with the enzyme resulted in a reduction of nearly 60% of cellular proliferation. Both cell death and cell cycle arrest were shown to be involved in this process. The inhibitory effect on purified mouse splenocytes was even more pronounced. Prior to and during *H. suis* GGT treatment, CD4<sup>+</sup> and CD8<sup>+</sup> T cells were stimulated with anti-CD3/CD28 mAb, and CD19<sup>+</sup> B cells were stimulated with anti-IgM mAb and IL-2. Incubation of stimulated cells with 1  $\mu$ g/ml *H. suis* GGT reduced the proliferation with about 80% for CD4<sup>+</sup> and CD8<sup>+</sup> T cells and with more than 95% for B cells. Supplementation of treated Jurkat cells with known *H. suis* GGT substrates was able to modulate the observed effects. Glutamine was able to restore the normal proliferation of the cells whereas supplementation with reduced glutathione (GSH) aggravated the inhibition of lymphocyte proliferation induced by *H. suis* GGT. In conclusion, this is the first report of a *H. suis* virulence factor involved in immune evasion. We showed that modulation of lymphocyte proliferation inhibition by *H. suis* GGT depends on the interaction of the enzyme with 2 important substrates, glutamine and glutathione. Inhibition of lymphocyte proliferation mediated by *H. suis* may be of importance for the chronic persistence of the bacterium in its preferred niche.