OC-019

CLASSICAL AND ALTERNATIVE PATHWAY NUCLEAR FACTOR-κB SIGNALLING DIFFERENTIALLY REGULATE GASTRIC EPITHELIAL RESPONSES TO HELICOBACTER *FELIS* INFECTION

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Introduction Classical pathway NF-κB signalling is implicated in the pathogenesis of several inflammation associated cancers, including colitis associated colon cancer and *Helicobacter* associated gastric cancer. However, the role of individual NF-κB family members and the function of alternative pathway NF-κB signalling have not previously been assessed in this context. We have therefore investigated whether abrogation of classical and alternative pathway NF-κB signalling altered murine responses to *Helicobacter felis* infection.

Methods 6-week-old female NF-κB1 null ($p50^{-/-}$), NF-κB2 null ($p52^{-/-}$), c-Rel null and C57BL/6 mice were infected with *H. felis* by oral gavage and culled 6 weeks later. Tissues were processed for histological analysis and immunohistochemistry.

Results *H. felis* infection of wild-type mice resulted in gastric atrophy (29% fewer parietal cells were observed in infected than in control mice ($p < 0.05$, 1-way ANOVA and Holm Sidak post hoc test)), a 1.5-fold increase in the number of Ki67 positive proliferating cells and no significant change in the number of active caspase 3 positive apoptotic cells. Animals with abrogated classical pathway NF-κB signalling also developed gastric atrophy after *H. felis* infection. However, whereas infected c-Rel null animals showed similar parietal cell, proliferation and apoptotic indices to infected wild-type mice, $p50^{-/-}$ animals developed more severe pathology with significantly increased inflammation scores ($p < 0.05$, Mann–Whitney U) and a more marked 62% reduction in parietal cell number ($p < 0.05$, 1-way ANOVA). This was associated with significant 2.1-fold and 7.6-fold increases in the number of proliferating and apoptotic cells, respectively ($p < 0.05$, 2-way ANOVA). By contrast, infected $p52^{-/-}$ mice showed much lower inflammation scores than wild-type mice ($p < 0.05$, MWU) following *H. felis* infection and did not develop gastric atrophy, with only 3% parietal cell loss ($p < 0.05$, 1-way ANOVA). In addition, these mice showed no significant changes in proliferation or apoptosis following infection with *H. felis*, and demonstrated similar proliferation and apoptotic indices to untreated wild-type mice.

Conclusion NF-κB1 mediated signalling protects the gastric mucosa from *Helicobacter* induced atrophy, whereas alternative pathway NF-κB signalling is required for the development of both inflammation and atrophy following infection with this organism. This supports the hypothesis that classical and alternative pathway signalling differentially affect long-term outcomes, including carcinogenesis, following *H. felis* infection in C57BL/6 mice.

Competing interests None.

Keywords gastric atrophy, *H. pylori*, NF-κB.