The complicated dialogue between *Helicobacter pylori* and p53

We recently read the interesting paper published in *GUT* elucidating the role of upstream stimulatory factor 1 (USF1) in *Helicobacter pylori (Hp)*-induced p53 degradation.[1] The work greatly broadens our knowledge of the interplay between *Hp* and p53 during gastric carcinogenesis. Here we propose some additional exploration, if incorporated in study design, can further deepen our understanding.

The significance of USF1 in gastric carcinogenesis should be acknowledged as the study showed that loss of USF1, on its own, exacerbated the severity of *Hp*-induced gastric lesions. However, the underlying mechanism probably warrants further investigation. The authors illustrated that USF1 defect accelerated gastric carcinogenesis through destabilising p53 and subsequently, leading to its degradation. Although mainly regulated at post-translational level, p53 can also be modulated through its transcriptional activity which was shown to be context-dependent.[2 3] Specifically, as a transcription factor, USF1 has been shown to be capable of binding to the p53 promoter.[4 5] In this article, the authors showed that the mRNA levels of *USF1* and *TP53* genes were significantly diminished by *Hp* (Figure 3[1]), therefore leading to the possibility of decreased transcriptional regulation of *TP53* by USF1. Thus, further research is encouraged to clarify, besides affecting p53 degradation, whether USF1 plays a transcriptional regulatory role in this context.

Additionally, it is premature, based on results in the current study (Figure 7), to draw a conclusion that *Hp*-induced accumulation of USF1 outside the nucleus is a 'point of no return'. Previous studies have shown that DNA double-strand breaks and impairment in mismatch repair induced by *Hp*, if transient, were repairable and reversible after the bacteria were removed and the cells were allowed to grow for another 48 hours.[6 7] Importantly, some clinical evidence also implied that *Hp* related lesions, including genomic instability, would be reversed 1 year after eradication therapy.[8] Taken together, it is possible that nuclear depletion of USF1 may partly, if not entirely, reversible as well and the observed irreversibility in the current study may be attributed to a lack of 'recovery period', as camptothecin (CPT) treatment was initiated immediately after several rinses. To permit an additional 48 hours for cellular growth before CPT is added and, meanwhile, keep a record of the dynamics of USF1 alterations is a potential way to provide a more holistic perspective.[9]

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