



Fig. S5: Overview of the protein level regulation mediated by HP1021 revealed by MS/LC-MS. a Volcano diagram of proteins differentially expressed in the wild-type strain after 60-min oxidative stress (WTS_60) compared to the non-stressed WT strain (WTS_60-WT). **b** Volcano diagram of proteins differentially expressed in the wild-type strain after 120 min of oxidative stress (WTS_120) compared to the non-stressed wild-type strain (WTS_120-WT). **c** Volcano diagram of proteins differentially expressed in the Δ HP1021 mutant strain after 60 min of oxidative stress (Δ HP1021S_60) compared to the non-stressed Δ HP1021 mutant strain (Δ HP1021S_120). **d** Volcano diagram of proteins differentially expressed in the Δ HP1021 mutant strain after 120 min of oxidative stress (Δ HP1021S_120) compared to the non-stressed Δ HP1021 mutant strain after 120 min of oxidative stress (Δ HP1021S_120) compared to the non-stressed Δ HP1021 mutant strain after 120 min of oxidative stress (Δ HP1021S_120) compared to the non-stressed Δ HP1021 mutant strain after 120 min of oxidative stress (Δ HP1021S_120) compared to the non-stressed Δ HP1021 mutant strain after 120 min of oxidative stress (Δ HP1021S_120) compared to the non-stressed Δ HP1021 mutant strain (Δ HP1021S_120- Δ HP1021S_120) compared to the non-stressed Δ HP1021 mutant strain (Δ HP1021S_120- Δ HP1021S_120) compared to the non-stressed Δ HP1021 mutant strain (Δ HP1021S_120- Δ HP1021S



Fig. S6: *H. pylori* N6 Clusters of Orthologous Groups (COG). a COG groups of genes differently transcribed in the wild-type strain under oxidative stress (WTS) compared to the non-stressed wild-type strain (WTS-WT). b COG groups of genes differently transcribed in the Δ HP1021 mutant strain compared to the wild-type (WT) strain (Δ HP1021-WT). c COG groups of proteins expressed differently transcribed in the Δ HP1021 mutant strain compared to the wild-type (WT) strain (Δ HP1021-WT). c COG groups of proteins expressed differently transcribed in the Δ HP1021 mutant strain compared to the wild-type (WT) strain (Δ HP1021-WT). a-b Chi-squared test determined the P value; significantly affected COGs (P \leq 0.05) are marked with black stars.



Fig. S7: HP1021 controls *katA* and *kapA* expression. a ChIP-seq data profile of the *katA* and *kapA* genes. Read counts were determined for *H. pylori* N6 WT, WTS and Δ HP1021 strains. The y-axis represents the coverage of the DNA reads, while the x-axis represents the position of the genome (in bps). The main peak of the binding site is marked with a thick black line under the x-axis. **b** RNA-seq data profile of *katA* and *kapA* genes. The genomic locus for *H. pylori* N6 WT, WTS and Δ HP1021 strains with the WTS-WT and Δ HP1021-WT expression comparison; values above the black dashed lines indicate a change in the expression of $|\log_2 FC| \ge 1$; FDR ≤ 0.05 . **c** Western blot analysis of HP1021 in *H. pylori* P12 wild-type and mutant strains. Lysate of each *H. pylori* strain (approximately 1.4×10^8 cells per well) was resolved in a 10% SDS-PAGE gel visualized by the TCE-UV method. **d** HP1021 was detected in bacterial lysates by a rabbit polyclonal anti-6HisHP1021 IgG. The SDS-PAGE and Western blot were performed as previously². M, PageRuler Prestained Protein Ladder (Thermo Fisher Scientific). **e** Liquid cultures (10 µl) of *H. pylori* P12 of similar cell density (OD₆₀₀ ~1) were treated with an equal volume of 30% H₂O₂. Air bubbles produced by catalase are visible as white spots. A significant decrease in foam indicates lower catalase activity in the Δ HP1021 cells. **c-e** The experiments were repeated twice with similar results. Digital processing was applied equally across the entire image. Source data are provided with this paper.



Fig. S8: HP1021 controls *rocF* **expression. a** ChIP-seq data profile of the *rocF* gene. Read counts were determined for *H. pylori* N6 WT, WTS and Δ HP1021 strains. The y-axis represents the coverage of the DNA reads, while the x-axis represents the position of the genome (in bps). The main peak of the binding site is marked with a thick black line under the x-axis. **b** RNA-seq data profile of *rocF* gene. The genomic locus for *H. pylori* N6 WT, WTS and Δ HP1021 strains with the WTS-WT and Δ HP1021-WT expression comparison; values above the black dashed lines indicate a change in the expression of $|log_2FC| \ge 1$; FDR ≤ 0.05 .