BACTERIAL PATHOGENICITY

Vitamin B₆ hits *H. pylori* sweet spot

The vitamin B₆-dependent glycosylation of flagella is required for full *Helicobacter pylori* motility and virulence, according to a new paper from Richard Ferrero and colleagues in *mBio*.

Prolonged *in vitro* passage of *H. pylori* str. SS1 led to a loss of infectivity and a decreased bacterial burden in mice, and the genes that were significantly downregulated in the low-infectivity isolates were identified using global gene expression profiling. The authors focused on two genes, *pdxJ* and *pdxA*, that had been annotated as encoding homologues of PdxJ and PdxA, respectively, two *Escherichia coli* proteins involved in

the *de novo* synthesis of pyridoxal 5'-phosphate (PLP), the active form of vitamin B₆.

The authors found that *H. pylori* *pdxJ* could not be disrupted, indicating that it might be essential. Isogenic *H. pylori* *pdxA* mutants were created and showed slower growth than the parental strain. This growth defect could be restored by the addition of PLP or by introducing an intact copy of *pdxA*. Further work showed that *H. pylori* *pdxJ* and *pdxA* could cross-complement a PLP deficiency in *E. coli*, indicating that they encode proteins involved in vitamin B₆ biosynthesis. Moreover, mouse infection studies revealed that *H. pylori*

colonization was greatly reduced in the absence of a functional copy of *pdxA*.

What is the exact function of vitamin B₆ in colonization? In *H. pylori*, vitamin B₆ is a cofactor for PseC, an aminotransferase that is required for flagellar glycosylation. Analysis of bacterial motility on soft agar plates and in live-cell imaging assays found that *pdxA* mutants were non-motile, and electron microscopy showed that they lacked flagella. Analysis of whole-cell lysates and sheared flagellar preparations from wild-type and *pdxA* mutant *H. pylori* revealed that *pdxA* mutants could produce flagellin A but that it was not exported to the cell surface and was not glycosylated.

This is the first time that enzymes involved in vitamin B₆ biosynthesis have been identified as bacterial virulence factors, and the authors conclude that disruption of the vitamin B₆ synthesis pathway could lead to new therapeutics.

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A *Helicobacter pylori* *pdxA* mutant (left; showing impairment in flagellar assembly) and a *pdxA* mutant that has been complemented genetically (right; showing the presence of flagella). Image courtesy of A. Grubman and R. Ferrero, Monash Institute of Medical Research, Clayton, Australia.

ORIGINAL RESEARCH PAPER Grubman, A. et al. Vitamin B₆ is required for full motility and virulence in *Helicobacter pylori*. *mBio* 1, e100112-10 (2010)