

hefA plays an important role in multidrug resistance of *Helicobacter pylori*

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Three RND efflux systems had been identified in *H pylori*, namely hefABC, hefDEF, and hefGHI, each of which consisted of a translocase, an accessory protein. But the contribution of efflux proteins to antibiotic resistance is not well established. 27 putative translocases also had been identified in the *H pylori* 26695 genome, but only four putative *H pylori* OEPs or TolC homologs were identified. While they could not quantitate the operons expression levels of the efflux systems in multidrug resistance strains of *H pylori*.

A research article to be published on September 7, 2008 in the *World Journal of Gastroenterology* addresses this question. The research team led by Prof. Zheng from Zhengzhou University used fluorescence real-time quantitative PCR to study the levels of mRNA expression of hefA in MDR strains and its parent strains. To further evaluate the contribution of hefA in multidrug resistance of *H pylori*, the article also constructed an *H pylori* mutant strain (Δ H. *pylori* LZ1026), and detected the susceptibility to 10 antimicrobials of the Δ H *pylori* LZ1026 with a more sensitive method of twofold agar dilution tests.

Six multidrug-resistant strains (including 5 clinical isolates and *H pylori* NCTC11637) were selected, and their MICs showed a significant (\geq 4-fold) increase than their parent strains. The expression levels of hefA gene in the MDR strains were significantly higher compared with their parent strains ($P = 0.033$). An *H pylori* LZ1026 mutant was successfully constructed and the Δ H *pylori* LZ1026 was more susceptible to four of the 10 antibiotics. All 20 strains displayed transcripts for hefA that

confirmed the in vitro expression of these genes.

The results revealed that the relative expression of hefA in the induced multidrug resistant strains were higher than those in their wild susceptible isolates. It has shown that similar to other gram-negative organisms, the H pylori hefA mutant displayed increased susceptibilities to antibiotics. It confirmed that high expression of the hefA plays an important role in multidrug-resistance of H pylori. H pylori contains an active multidrug efflux mechanism and therefore compound efflux needs to be taken into account when determining resistance mechanisms in this organism.

Source: World Journal of Gastroenterology

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