



Effects of Exosomes Derived From *Helicobacter pylori* Outer Membrane Vesicle-Infected Hepatocytes on Hepatic Stellate Cell Activation and Liver Fibrosis Induction

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Liver fibrosis is a multifactorial disease with microbial and non-microbial causes. In recent years, *Helicobacter pylori* infection has been thought to play a critical role in some extra-gastrointestinal manifestations especially liver disorders. Outer membrane vesicles (OMVs) are one of the most important discussed *H. pylori* virulence factors. In the current study, four different clinical strains of *H. pylori* were collected and their OMVs were purified using ultra-centrifugation. To investigate their effects on liver cell exosomes, co-incubation with hepatocytes was applied. After a while, hepatocyte-derived exosomes were extracted and incubated with hepatic stellate cells (HSCs) to investigate the HSC activation and fibrosis marker induction. The expression of α -SMA, TIMP-1, β -catenin, vimentin, and e-cadherin messenger RNAs (mRNA) was assessed using real-time RT-PCR, and the protein expression of α -SMA, TIMP-1, β -catenin, vimentin, and e-cadherin was evaluated by Western blotting. Our results showed that infected hepatocyte-derived exosomes induced the expression of α -SMA, TIMP-1, β -catenin, and vimentin in HSCs and e-cadherin gene and protein expression was downregulated. In the current study, we found that *H. pylori*-derived OMVs may aid the exosome alternation and modified exosomes may have a possible role in HSC activation and liver fibrosis progression.

Keywords: *Helicobacter pylori*, outer membrane vesicle, exosome, liver fibrosis, α -SMA

INTRODUCTION

Helicobacter pylori is a Gram-negative and microaerophilic bacterium which is able to colonize human gastric (Chmiela et al., 2017). According to the latest epidemiological studies, its prevalence is about 50% of the world population (Mezmale et al., 2020; Ziyadee et al., 2020). *H. pylori* is a causative agent of various diseases including peptic ulcer, chronic gastritis, gastric cancer, and lymphoid malignancies of the stomach (Topi et al., 2020; Kunovsky et al., 2021). A possible role of *H. pylori* pathogenesis in extra-gastric diseases including cardiovascular disease has been studied in