



Dynamic Variation of Multiple CagA EPIYA-C Motifs in East-Asian *Helicobacter pylori*

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ABSTRACT

The polymorphic bacterial oncoprotein, CagA bears different types of C-terminal Glu-Pro-Ile-Tyr-Ala (EPIYA) motifs depending on its geographical distribution: ABD type for East-Asian and ABC type for Western *H. pylori*. The multiple EPIYA-C motifs were associated with a disease severity. Some East-Asian *H. pylori* isolates carried Western ABC-type CagA. Hence, to gain better understanding, whole genomes of four Korean *H. pylori* clinical isolates carrying ABC-type CagA were sequenced via Pac-Bio SMRT sequencing technology, and the phylogenetic analysis was performed, which identified that three of four isolates indeed belong to hpEastAsia group with typical East-Asian polymorphism of virulence factors and one is grouped to HpAfrica with typical Western polymorphism. Furthermore, the variation of multiple EPIYA-C motifs in East-Asian *H. pylori* background was investigated using a Korean clinical isolate, K154, belonging to hpEastAsia but possessing CagA EPIYA-ABCCCC. Due to the sequence homology for CagA multimerization sequence located at the EPIYA-C segment, we predicted the possibility of changing the number of C motifs via homologous recombination. To test this hypothesis, 287 single colonies after culturing 1st generation were screened for the detection of multiple EPIYA-C motifs by PCR-based screening method and further verified by DNA sequencing. Three out of 287 single colony isolates (1%) showed polymorphism in the number of EPIYA-C motifs *in vitro*: increasing EPIYA-C motifs in five and decreasing EPIYA-C motifs in three and even in complete deletion. The mechanism of dynamic change of EPIYA-C repeats may play a part in generating an intraspecies diversity in East-Asian *H. pylori*.

Keywords: *Helicobacter pylori*, CagA, geographic diversity