Title of dissertation				
Detection and characterization of extended-spectrum β-lactamase (ESBL)-producing Escherichia coli isolated from retail raw foods and children with diarrhea in Khanh Hoa province, Vietnam				
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Body Text

Antimicrobial resistance (AMR) has become one of the most serious threats to global health. Misuse of antimicrobials in humans and animals may accelerate the emergence of AMR bacteria, which is especially critical in low-resource countries such as Vietnam. This study was aimed to detect and characterize ESBL-producing *E. coli* (ESBL-*Ec*) isolated from retail raw foods and children less than five years of age with acute diarrhea at a local area in Central Vietnam, Khanh Hoa province for better understanding of their molecular epidemiology.

In Chapter 1, ESBL-producing *E. coli* was isolated from retail raw foods and children with diarrhea in Khanh Hoa province, Vietnam, then antimicrobial resistance of the isolates were examined. I found that the prevalence of ESBL-*Ec* from chicken, pork, fish and shrimp was 66.4, 55.4, 42.0 and 19.6%, respectively. Besides, ESBL-*Ec* was also found in 45.9% of *E. coli* strains isolated from patients with diarrhea. A significant number of ESBL-*Ec* isolates were multiple resistant phenotypes. These results suggested that multidrug resistant ESBL-*Ec* could disseminate via retail raw foods and children with diarrhea in Vietnam.

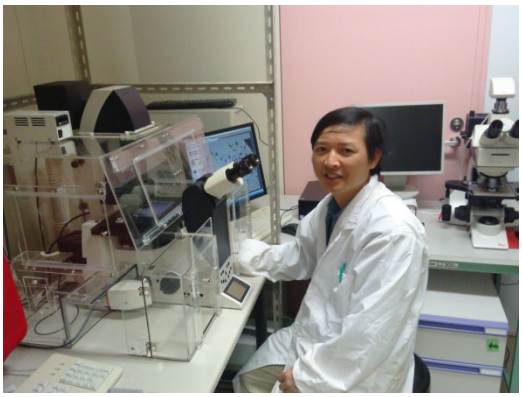
In Chapter 2, ESBL-*Ec* isolated from both foods and diarrheal patients were characterized for their ESBL genotype and virulence gene profile. The results indicated that the CTX-M type was remarkably dominant in ESBL-*Ec* isolated from retail raw foods (99.5%) and diarrheal patients (96.9%). The *astA* gene (29.3%) encoding heat-stable enterotoxin 1 (EAST1) was the most prevalent virulence gene in ESBL-*Ec* isolated from retail raw foods. Besides, the *eaeA* (6.5%) and *cdt* (5.2%) genes encoding intimin and cytolethal distending toxin (CDT) respectively, were also detected in ESBL-*Ec* isolated from chicken. Moreover, all *cdt* gene-positive *E. coli* (CTEC) produced a biologically active CDT, indicating that CDT might be potentially virulent. This finding also implied chicken as an important reservoir of CTEC in Vietnam. In ESBL-*Ec* isolated from patients, only *afaD-3* (31.2%) and *astA* (16.1%) genes were identified. Furthermore, the *afaD-3* positive strains showed adherence activity suggesting their potential association with acute diarrhea in children less than five years of age in the Central Vietnam. This is the first description of *cdt* and *afaD-3* genes in *E. coli* isolated in Vietnam.

In Chapter 3, the occurrence of mobile colistin resistance (*mcr*) genes (*mcr-1* to *mcr-8*) in ESBL-*Ec* isolated from raw foods retailed in markets and supermarkets and children with acute diarrhea at a local province in the Central Vietnam was investigated. 65 out of the 208 (31.3%) ESBL-*Ec* isolated from foods were positive for *mcr* genes including *mcr-1* (26.9%), *mcr-3* (0.5%) and both *mcr-1* and *mcr*-3 genes (3.9%). This is the first detection of *mcr-3* gene in *E. coli* isolated from fish and shrimp in Vietnam. PFGE analysis and O-genotyping revealed diverse genotypes implying particular clonal dissemination of *mcr*-harboring ESBL-*Ec* among retail raw foods in the Central Vietnam might be very limited. S1-PFGE and Southern hybridization illustrated that the *mcr-1* and *mcr-3* genes were located on either chromosomes or plasmids. A conjugation experiment indicated that the *mcr-1* or *mcr-3* gene was horizontally transferable. Two *mcr* genes existed individually or concurrently in ESBL-*Ec* isolates from retail raw foods, which might further complicate the antimicrobial-resistant situation in Vietnam, and is a possible health risk for humans.

This study revealed that MDR ESBL-*Ec*, some of which were potentially pathogenic to humans, were disseminated among diarrheal children and retail raw foods in the Central Vietnam. Especially, the CTX-M-type ESBLs were predominant in the ESBL-*Ec* strains. Noteworthy, a high prevalence of transferrable *mcr-1*- and/or *mcr-3*-harboring ESBL-*Ec* among retail raw foods was observed, which could contribute to the wide dissemination of *mcr* genes to bacteria in the environment, animals and humans. Moreover, co-existence of *mcr* genes with the genes encoding CTX-M enzymes in a bacterial cell was found in ESBL-*Ec*. Such conjunction may further exacerbate the co-occurrence and transmission of the drug-resistance genes into wider population, which may result in increased human health risk.

Photos

Mr. Quoc Phong Le was handed over Ph. D degree by Prof. Shinji Yamasaki and Director of Pasteur Institute in Nha Trang, July 2022



Research activities in Laboratory of Prevention of International Epidemics, Graduate School of Life and Environmental Sciences, Osaka Prefecture University, December 2019