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学 位 論 文 の 要 旨

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論文題目　　　食品由来細菌の抗菌薬耐性に関する分子遺伝学的解析

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（Molecular Genetic Analysis of Antimicrobial Resistance in Foodborne Bacteria）
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Antimicrobial resistance (AMR) is a major public health challenge in many countries including Japan. In this study, the genetic attributes associated with antimicrobial resistance in foodborne bacteria were investigated.

Chapter 2 compared antimicrobial resistance among several *Escherichia coli* isolates obtained from meat samples in 2009 and 2021. The occurrence of antimicrobial resistance determinants especially cephalosporinases (AmpC) or extended-spectrum ß-lactamases (ESBL) was significantly higher among isolates obtained in 2009 than in 2021. Interestingly, a decreased rate of resistance to critical antimicrobials, including cephalosporins was observed between 2009 and 2021. More than 75% of the *E. coli* isolates belonging to different phylogroups obtained from the two years, exhibited multidrug resistance (MDR) phenotypes, although the differences were not statistically significant for comparisons.

In chapter 3, the overall rate of antimicrobial resistance in Gram-negative bacteria isolated from meat was evaluated. Different Gram-negative bacteria were isolated and grouped into Enterobacterales and non-Enterobacterales. Members belonging to the Enterobacterales were more prevalent than the non-Enterobacterales isolated in both 2009 and 2021. Overall, the most common resistance was observed against ampicillin, cefotaxime, cefoxitin, aztreonam, kanamycin, and tetracycline. Different plasmid replicon types were found within ESBL-producing *E. coli* isolates. AmpC ß-lactamases were dominantly found in Gram-negative bacteria obtained in 2009 than in 2021.

In chapter 4, I investigated the occurrence of antimicrobial resistance in supermarket retail seafood samples. Different seafood-borne bacteria carrying antimicrobial resistance determinants were mostly retrieved from fish, squid, and shrimp samples. Majority of the isolates were resistant to ampicillin, and some also conferred resistance to cephalosporins, which are currently among the recommended treatment of choice against severe infections. This study also evaluated the possibility of plasmid transfer that might play a role in the dissemination of antimicrobial resistance especially within aquatic environments.

Chapter 5 discussed the genetic and phenotypic characteristics of foodborne bacteria carrying mobile colistin resistance (*mcr*) genes. Six isolates were highly resistant to colistin and showed additional resistance to other antimicrobials. It was observed that only the meat isolates conferred clinical resistance to colistin. Whole genome sequencing (WGS) of six isolates revealed that some *mcr*-genes are encoded on the plasmid and some on the chromosome. The genetic context of the *mcr* alleles showed that the strains might have acquired these genes through genetic transposition by transposases.

In summary, this study showed that meat and seafood products carry different resistant bacteria. This calls for routine implementation of surveillance programs to track the status of AMR in food.