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学位論文全文に代わる要約
Extended Summary in Lieu of Dissertation

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Name

学位論文題目：
Title of Dissertation

Persistence of multi-drug resistance plasmid in seawater environment
(多剤耐性プラスミドの海水環境での残存)

学位論文要約：
Dissertation Summary

Antibiotics are generally present in environments at sub-lethal concentrations. The origins of antibiotics in natural environments are natural products of microorganisms and residues of contamination from human and veterinary medicine and aquaculture settings. A variety of antibiotics have been detected in the aquatic environments, which impose selective pressure on bacterial populations resulting prevalence of diverse antibiotic resistance mechanisms in bacteria. Thus, it is sure that antibiotics in environments play an important role contributing to occurrence and retaining of antibiotic resistance genes (ARGs). Multiple ARGs are frequently clustered on conjugative plasmids and confer variety of resistance mechanisms. Therefore, conjugative plasmids are the most important vectors of ARGs, and are directly linked to major outbreaks of antibiotic resistant infection.

Recent studies pointed out the effect of low selective pressure for ARGs and resistance plasmid dynamics in environments. However, there are no reports on the destiny of ARGs/plasmids in bacterial cells and outside cells under the absence of selective pressure and presence of grazing pressure. The knowledge of such black box in ARG-ecology is needed to consider the estimation of the gene risk and developing the mitigation protocol of antibiotic resistance issues.

Here, several defined microcosm experiments were used to examine the persistence of multi-drug resistance (MDR) plasmid/ARGs inside and outside bacterial cells in the presence or absence of antibiotics and protist grazers. The conclusive cartoon is shown in Figure 1. The box A and B are the results in this study by comparison to previous general opinion, and box C shows further studies arisen from present work.

It has been hypothesized so far that bacterial plasmids frequently impose a fitness burden on their host; thus, in the absence of selective pressure, resistance plasmids should be lost to reduce the fitness cost. However, present study indicated that MDR plasmids can stably persist in different bacterial hosts including non-culturable bacteria, even in the absence of antibiotics and in the presence of grazers. I could not clarify the role of the non-culturable cells in horizontal gene transfer, but the ARGs should be reserved in the non-culturable cells, which form high background of environmental ARGs pool.

It is common sense that bacterial cell is completely digested by grazing, and ARGs are thought to be decomposed in the digestion process. ARGs released into environments after bacterial lysis should also be rapidly hydrolyzed by physicochemical and biological reactions, and utilized by indigenous microbial communities. This study (Figure 1B) gave new evidences against the common sense. The extracellular ARGs were relatively stable and the releasing was not affected by selective pressure. This should be a cause of ubiquitous detection of ARGs in non-contaminated aquatic environments. The invisible ARG pool present in outside cells might work for dissemination of ARGs in the aquatic environments.

ARGs arrived in the sea from human land environments might become a source of ARGs invading to society of humans by flowing back. The transformation of released ARG/plasmid to indigenous marine bacterial communities as well as retaining and expression profiles should be further examined to enlarge our knowledge about the dynamics of resistance plasmid in aquatic environment. Risk assessment of ARGs exposure from aquatic ecosystems is needed in the future to progress the “one health concept and strategy”.

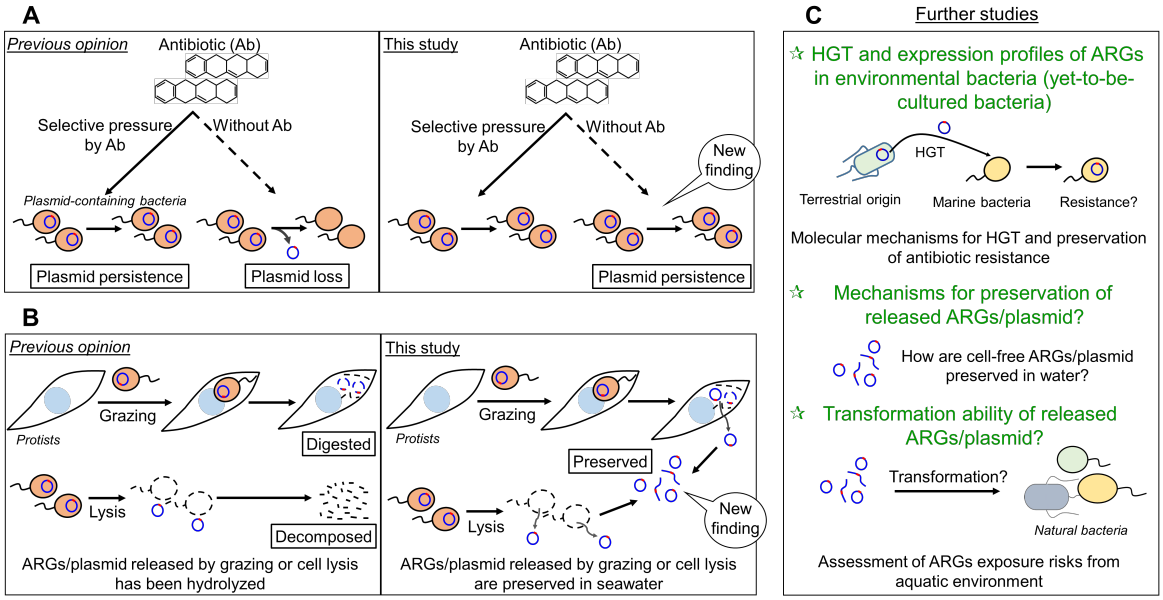

Figure 1 Dynamics of multi-drug resistance plasmid in seawater environment.

A, Previous opinion has hypothesized that resistance plasmid should be lost from bacterial cells in the absence of antibiotics. This study showed that MDR plasmid can be stable in different hosts including non-culturable cells, even in the absence of antibiotic. B, Previous opinion has hypothesized that extracellular ARGs/plasmid released by grazing or cell lysis should be decomposed or taken up by other microbes as organic nutrients. This study showed that extracellular plasmid can be preserved in seawater. Cellular plasmid is also retained under grazing stress by protist. C, Further studies are needed for; expression profile of plasmid in environmental bacteria which are non-culturable state; mechanisms of preservation of extracellular ARGs/plasmid; whether extracellular ARGs/plasmid can be transferred to environmental bacteria.

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