JS3-1:

Novel transferable multi-drug resistance plasmid and macrolide resistance genes from *Photobacterium damselae* subsp. *damselae* isolated from seawater of an aquaculture site

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The emergence of drug-resistant bacteria in aquaculture environments is a problem in terms of fish production and human public health. The transferability of drug resistance genes is thought to be responsible for the wide dissemination of the resistant bacteria in the environment; however, little is known about the gene transfer mechanisms in marine bacteria. *Photobacterium damselae* subsp. *damselae* is an indigineous marine bacterium known to be zoonotic pathogen which infects both fish and humans. Here, we show that a strain of *P. damselae* subsp. *damselae* 04Ya311, isolated from seawater at a coastal aquaculture site, harbors a novel transferable multiple drug resistance plasmid, pAQU1 containing seven drug resistance genes and a complete set of genes encoding the apparatus for the type IV secretion system. Phylogenetic analysis of the deduced amino acid sequence of relaxase demonstrated that pAQU1 belonged to a new cluster in the MOB_H plasmid family which were widely distributed among species of Enterobacteriaceae and Vibrionaceae. The “ pAQU group ” of plasmids which shared the backbone structure with pAQU1 were revealed and these plasmids were identified in the bacteria isolated from aquaculture environments in Japan and Taiwan. Further, *mef*(C) and *mph*(G), found on pAQU1 were determined to be novel macrolide resistance genes. These are located head-to-tail and show similarity to the known efflux pump and macrolide-2 ’ -phosphotransferase, respectively, and a novel mechanism conferring high-level macrolide resistance via combined expression of both proteins. The *mef*(C)-*mph*(G) were conserved on plasmids of the erythromycin resistant strains belonging to *Vibrio* and *Photobacterium* and these were conjugatively transferred to *E. coli* and integrated into its chromosome.

keywords:multi-drug resistance plasmids,pAQU1,transferability,macrolide resistance,mef(C),mph(G)