CAS-040

APCCMI2025 BANGKOK

Plasmid carrying tandem amplification of *bla*$_{KPC-2}$ mediates carbapenem resistance with minimal fitness cost in hypervirulent *Klebsiella pneumoniae*

Yanyan Lu[1], Jianfeng Zhang[1], Jianping Jiang[1], Xiaobin Li[2], Yu Tang[3], Xiaoli Wang[4], Hongping Qu[4], Yanping Xu[5], Jieming Qu[5], Yiyi Hu[1], Zhewei Sun[1], Xin Lan[1], Yujia Wang[1], Leilei Wang[1], Liang Chen[6], Xiaogang Xu[1], Qinglan Guo[1], Minggui Wang[1*]

1、Institute of Antibiotics, Huashan Hospital, Fudan University, Shanghai, China

2、Department of Pulmonary and Critical Care Medicine, Zhuhai People's Hospital , Zhuhai, China

3、Department of Laboratory Medicine, Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China

4、Department of Critical Care Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

5、Department of Pulmonary and Critical Care Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

6、Center for Discovery and Innovation, Hackensack Meridian Health, Nutley, New Jersey, USA

ABSTRACT

Carbapenem-resistant hypervirulent *Klebsiella pneumoniae* (CR-hvKP) derived from hypervirulent *K. pneumoniae* (hvKP) acquiring a carbapenem-resistant plasmid, usually remains susceptible to carbapenems or exhibits loss of hypervirulence due to the substantial fitness burden. Here, we demonstrate that a KPC plasmid bearing tandem gene amplification (TGA) of *bla*$_{KPC-2}$ can transfer into hvKP, mediating changeable meropenem resistance ranging from susceptible to resistant. Meropenem resistance conferred by *bla*$_{KPC-2}$ TGA incurs a rare reduction in capsule production. Isolates harboring the *bla*$_{KPC-2}$ TGA plasmid can maintain hypervirulence while exhibiting meropenem resistance, leading to poorer outcomes of meropenem treatment in a mouse infection model, comparing with isolates bearing a simplex KPC plasmid. The formation of *bla*$_{KPC-2}$ TGA necessitates an IS26- *bla*$_{KPC-2}$ -IS26 structure. 42.0% (394/939) of KPC plasmids including 57.1% (8/14) of plasmids in ST23 CR-hvKP in GenBank harbor IS26- *bla*$_{KPC-2}$ -IS26-like structures. Our findings highlight that IS26- *bla*$_{KPC-2}$ -IS26 structure-mediated *bla*$_{KPC-2}$ TGA presents a critical threat in clinical practice and requires urgent and effective surveillance.