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Title: Cell-cell variation in expression of bla_{CTX-M-14}

Xiaorong 14722 Wang rong-100@163.com MD ¹, Yu 14723 Kang cangybwd@sina.com MD ¹, Shuchang 14724 An anshuchang@sohu.com MD ¹, Tong 14725 Zhao 93205660@qq.com ², Jichao 14726 Chen chen_htzxxy@sina.com MD ³, Rongrong 14736 Fu frr230@qq.com ¹ and Zhancheng 14758 Gao zcgao@bjmu.edu.cn MD ¹. ¹ Department of Respiratory & Critical Care Medicine, Peking University People's Hospital, Beijing, China ; ² Institute of Microbiology, Chinese Academy of Sciences, Beijing, China and ³ Department of Respiratory Medicine, The Central Hospital of China Aerospace Corporation, Beijing, China .

Body: Background: cell-cell variation in expression of their gene in isogenic population is frequently observed in microbes, which is recognized as one of the reasons for phenotype heterogeneity. The aim of this study is to investigate the heterogeneous resistance level in genetically identical cells which was originated from cell-cell variation in expression of bla_{CTX-M-14}. Methods: The transcriptional region of CTX-M-14 with or without the entire coding sequence of CTX-M-14 which were amplified from clinic strain isolated from patients with lower respiratory tract infection were subcloned to upstream of green fluorescent protein (GFP) gene to regulate expression of GFP followed by standard method. Applying flow cytometry measurement (FCM) to analyze the expression pattern of bla_{CTX-M-14} in single cell using GFP as the report genes. The expression pattern of cells after cultured with different ceftriaxone concentrations ranging from 0µg/ml to 2048µg/ml was also analyzed. Using the E-test method to measure the MIC to ceftriaxone. Results: Variation in GFP expression from cell to cell was seen (The fluorescence intensity of different cells vary largely, ranging from 10² to 10⁵). The resistance level to ceftriaxone was positively correlated with the expression level, with increment of the extracellular ceftriaxone concentrations, the proportion of cells with more GFP abundance increasing. We also found the epigenetic resistance phenotype mediated by the heterogeneous expression was non-strictly inheritable and have a transient property. Conclusions: Heterogeneous expression of antibiotic genes other than nucleotide alterations in genetically identical cells may be one of the reasons for diverse antibiotic resistance level.