H03: Genome Sequencing Reveals the Structure of a 32 kb ACRI12-1 Resistance Island in an Extensive-drug Resistant Clinical Strain of Acinetobacter baumannii

Soo-Sum Lean1, Zarizal Suhaili2, Chew Chieng Yeo2 and Kwai-Lin Thong1
1Institute of Biological Sciences, Faculty of Science, University of Malaya, 50603 Kuala Lumpur, Malaysia
2Faculty of Agriculture and Biotechnology, Universiti Sultan Zainal Abidin, 21300 Kuantan, Terengganu, Malaysia
*Corresponding author: soosumlean@gmail.com

Acinetobacter baumannii is an important nosocomial Gram-negative pathogen that is difficult to treat due to its increasing resistance towards almost all antimicrobials. Clusters of antibiotic resistance determinants in A. baumannii are often found in structures known as resistance islands (RIs). These RIs are usually transposable elements which can be transferred from one organism to another and thus play an essential role in the development of antimicrobial resistance. The objective of this study was to identify any RIs that may contribute to the extensive drug-resistance (XDR) phenotype in A. baumannii strain AC12, which was isolated from a tertiary hospital in Terengganu, Malaysia. Genome sequences were mapped to the reference RI using CLC Bio Genomics Workbench 5.0. Open reading frames (ORF) of ACRI12-1 were determined using ORF finder and gene function determined through BLAST. Visualization of the RI and gene orientations were carried out using the Artemis software. Whole genome analyses of A. baumannii AC12 revealed the presence of a 32,155 bp antibiotic resistance island that interrupts the comM gene and is designated here as ACRI12-1. This RI consists of the backbone of Tn6167 with two added copies of DTn6022, both of which are truncated variants of Tn6022 with a 2.85 kb fragment deleted. Drug resistance genes such as sup (encoding sulfate permease that confers resistance to sulfate components), blaOXA-23 (conferring β-lactam resistance), tetA(B) (conferring tetracycline resistance) and strA and strB (conferring streptomycin resistance) were found to be present in this RI. The blaOXA-23 gene in this RI was flanked by the insertion element ISAba1, which may increase the expression level of blaOXA-23 in A. baumannii by providing a strong promoter, thereby conferring resistance to carbapenems. The genetic structures in this RI thus explain the resistant phenotype of A. baumannii AC12 towards β-lactams, aminoglycosides and tetracyclines.

H04: ACA and its Anallogues: Apoptosis Via the Ubiquitin-proteasome System (UPS)

Liew Su Ki1, Mohamad Nurul Azmi2, Lionel In Lian Aun1, Khalijah Awang2 and Yoor Hasima Nagoor1
1Institute of Biological Science (Division of Genetics & Molecular Biology), Faculty of Science, University of Malaya, 50603, Kuala Lumpur, Malaysia
2Centre for Natural Product Research and Drug Discovery (CENARD), Department of Chemistry, Faculty of Science, University of Malaya, 50603, Kuala Lumpur, Malaysia

Twelve analogues (ACA-2 to -13) of 1(S)-1′-acetoxychavicol acetate (ACA) isolated from Alpinia conchigera were synthesized and evaluated for their anticancer activity. The MTT cell viability assay was used to determine the effects of these compounds on the proliferation of various human cancer cell lines. Among all tested compounds, ACA-1 and ACA-9 induced significant cytotoxic effects with IC50 values ranging from 4.0 to 30.0μM after 24 hours of treatment. Interestingly, ACA-9 exhibited a greater anticancer activity against liver HepG2 cells, oral HSC-4 cells, breast MCF-7 cells and bladder RT-112 cells, compared to the original ACA (ACA-1) structure. Furthermore, since the ubiquitin-proteasome system (UPS) is accepted as one of the effective targets in the treatment of cancer, an investigation on whether ACA-1 and ACA-9 could suppress tumor growth via this system was carried out. Human purified 26S proteasome assay was performed to provide evidence for the inhibitory effects of ACA analogues on three catalytic activities [chymotrypsin-like (CT-like), trypsin-like (T-like) and peptidylglutamyl peptide hydrolyzing-like (PGPH-like)] within the proteolytic core of the 26S.