Antimicrobial resistance has been a looming threat ever since its conception and it has become one of the greatest global problems of the current era. Although various studies have been conducted to better understand the mutational triggers leading to antimicrobial resistance, the specific genomic path towards it have yet to be discerned. Here, we aim to elucidate the pathway of genomic evolution throughout the resistance induction of an A. baumannii strain towards ciprofloxacin, erythromycin, meropenem and imipenem, as well as comparing the mutations acquired clinically versus in vitro. Twenty-five (25) local clinical A. baumannii strains were isolated and screened for antimicrobial susceptibility, and their genome were sequenced using the Illumina GAIIx genome sequencer. The susceptible parent was then challenged with ciprofloxacin, erythromycin, meropenem and imipenem separately until growth is still possible beyond the Minimum Inhibitory Concentration (MIC) as defined by EUCAST standards. Once the resistance stability was confirmed, another sequencing run was done on the isogenic. Variant analysis was carried out using CLC Bio, and primers were designed to target the mutations of interest. PCR was then carried out on aliquots of the resistant mutants, each taken at increasing levels of antimicrobial tolerance throughout the challenging process. Phylogenetics and wgMLST analyses were carried out between the parent and resistant strain, as also the remaining isolates. Stable low and high-level resistant strains were successfully generated. Several genomic variants were identified in the high-level resistant strains. Validation of variant calling via PCR removed all miscalled variants. Comparative genome annotation revealed a high consistency in the genome structures of the clinical strains, despite non-consistent phylogenetic and synteny profiles. The mutation validation revealed several variations arising in genes responsible for signaling (yihG, bvgS and srrA), metabolic activities (atpD, ribonuclease I, and epsL) and cell structure maintenance (ftsI and yceG) in addition to targeted mutations (mexB, acrB and gyrA). Analysis of the mutation chronology shows that when exposed to erythromycin, A. baumannii incurs modifications to genes bvgS and srrA, on days 4, 6, and to ftsI and its ribonuclease I encoding gene on day 67. When exposed to ciprofloxacin, mutations developed in gyrA and yihG on days 28 and 48. Meropenem exposure on the other hand has led to variations in epsL, mexB, and atpD on days 4, 10 and 70. In contrast, meropenem exposure resulted in mutations to acrB on day 38, and two mutations in ftsI occurred on day 19 and 67. From the results it is deduced that the chronology of intrinsic mutations is dependent on the types and intensity of selective pressures enacted, even on the same bacteria. Antibiotic pressure under in vitro and in vivo conditions has also resulted in development of different mutations leading to similar resistance profiles. It was also found that a prolonged exposure to the drugs used in this study plays as much of a role as the sub-inhibitory concentration.

In recent years there has been a remarkable revision of the negative perceptions on knowledge traditionally held and practiced by indigenous peoples. A particular aspect of traditional knowledge that has been attracting much attention is indigenous people’s knowledge and uses of medicinal plants. This indigenous knowledge has attracted particular attention for the economic potential it brings from new drug development, as leads provided by indigenous use constitute an important cost-savings factor in research and development. However, knowledge of medicinal plants among indigenous communities is facing the threat of erosion due to rippling forces of globalization and modernization. Studies among the country’s indigenous communities have indicated that Malaysia is equally affected by this phenomenon. The impending loss of this valuable resource has stimulated policy intervention for affirmative action both at the international and national levels aimed at preserving, reinforcing, recording or adapting indigenous knowledge on medicinal plants, primarily through documentation and recording of medicinal plants species and their uses in traditional treatments. Malaysia’s recent membership to the 2003 Convention on Safeguarding Intangible Cultural Heritage provide an opportunity for an indigenous stakeholder lens at policy intervention towards ensuring viability of the knowledge. The findings indicated that in spite of a lack of awareness of policy on traditional knowledge of indigenous plants, there is high appreciation and value of the knowledge among the elder generation as a cultural heritage and as a first course of treatment for illnesses and ailments; and that awareness and education on the value of this traditional knowledge among the younger generation impacts upon intergenerational transmission of knowledge. The study also identified several constraints and factors affecting public education and awareness of government policies and programs, as well as inter-generational transmission of knowledge and management of this knowledge among rural populations. Suggestions by the younger generation on ways to facilitate inter-generational transmission were incorporated into a logic model to encourage viability of the knowledge among indigenous communities in Malaysia.