Genetic Cassettes Profiling of Class I Integron and Antimicrobial Susceptibility Profiles Among *Pseudomonas aeruginosa* Isolates Collected from Patients in North of Iran

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Abstract

**Background:** *Pseudomonas aeruginosa* is an opportunistic nosocomial bacterium, especially in infection wards and among patients with burns. The present study addressed the molecular investigation of the gene cassettes of Class I integrin (*intI*) and its relationship with multiple drug resistance in clinical samples of *P. aeruginosa* isolated from Babol hospitals in north of Iran.

**Objectives:** This study aimed to detect the frequency of *intI* and gene cassettes in the clinical isolates of *P. aeruginosa*.

**Methods:** In this study, from 75 clinical samples, 30 strains were identified using specific biochemical methods. After determining antibiotic susceptibility using disk diffusion and agar dilution, the frequency of the *intI* gene and its gene cassettes were determined using the polymerase chain reaction (PCR) method.

**Results:** The highest resistance rate was observed for cefotaxime, ampicillin, and nitrofurantoin using disk diffusion and agar dilution methods. The molecular analyses revealed that 60% of the isolates had the *intI* genes. The frequency of the *aadB*, *dfrA1*, and *bla-OXA30* genes were 61, 66, and 33%, respectively.

**Conclusions:** The high resistance of *Pseudomonas* isolates is due to the presence of *intI* and its gene cassettes. Considering their high resistance to cefotaxime, gentamicin, ampicillin, and imipenem in hospitals, selecting appropriate drugs or generally changing the treatment course for patients is possible to prevent the spread of resistance inducing genes and the development of nosocomial infections.

**Keywords:** *Pseudomonas aeruginosa*, Class I Integron, Gene Cassette, Antibiotic Resistance

1. Background

*Pseudomonas aeruginosa* obligates aerobic Gram-negative bacillus and is the second most common cause of infective diseases in different hospitals’ wards including intensive care units. This organism becomes resistant to antimicrobial agents via various mechanisms, including altering the microorganism’s permeability against drugs, enzymatic resistance, efflux pump, receptor altering for drugs, and achieving a secondary metabolic pathway (1). Resistance to antibiotics in this bacterium occurs through mutation or further horizontal transfer through conjugation by plasmid and the transposons carrying antibiotic resistance genes (1, 2).

In this case, the plasmids and transposons carry antibiotic resistance genes and transfer them from one cell to another. In 1986, a DNA sequence with genes for resistance to different antibiotics was found. These regions have been identified at the other sites of various plasmids and are similar to transposons. Integrons are genetic units encompassing genes and transferring them while placed inside mobile factors, called gene cassettes (3). They have an integrase gene (*intI*), one member of the tyrosine recombinase family (4, 5). The integron structure consists of two fixed protected areas, called 3' and 5', located on both sides of a variable region (genetic cassette) containing one or several antibiotic resistance genes (6, 7). Gene cassettes usually contain one drug resistance gene and one protected site, providing the grounds for integrase identification through attachment and cutting processes.

Further, various studies have reported that integrons usually have more than one gene cassette, in which case these bacterial isolates have the multidrug resistance
(MDR) pattern (4, 8). Gram-negative bacilli containing int1 and its gene cassettes have aroused concerns among physicians and infection specialists regarding infection control. The resistance of this bacterium to a wide range of antibiotics, especially the common antibiotics used in hospitals, has complicated the detection of proper therapeutic methods and the use of infection control instruments (8, 9).

2. Objectives

This study aimed to detect the frequency of int1 and gene cassettes in the clinically isolates of P. aeruginosa from Babol, north of Iran, and investigate their correlations with antibiotic resistance patterns in hospitalized patients.

3. Methods

3.1. Clinical Samples

In this cross-sectional study, 30 clinical samples of P. aeruginosa were collected from patients admitted to Aya-tollah Rohani Hospital, Babol, north of Iran, from 2016 to 2017. This project was a part of another project (10) (Code of Ethics: MUBABOL.REC.1394.162). The bacterial isolates were collected from the hospital laboratory. Pseudomonas aeruginosa was recognized using conventional biochemical and microbiological tests.

3.2. Antibiotic Susceptibility Test

Following the Clinical and Laboratory Standards Institute (CLSI document M100) guideline (11), antimicrobial susceptibility was determined by the Mueller-Hinton agar plates (Merck, Germany) using the standard disk diffusion (DD) method for antimicrobials under gentamicin (GM, 10 µg), cefepime (CPM, 30 µg), amikacin (AK, 30 µg), ciprofloxacin (CIP, 5 µg), imipenem (IMI 10 µg), ceftaxime (CTX, 30 µg), ampicillin (AP, 10 µg), trimethoprim (TM, 5 µg), and nitrofurantoin (NI, 300 µg) (MAST Diagnostics, Merseyside, UK). Pseudomonas aeruginosa ATCC 27853 strain was used as a positive quality control. The results were evaluated according to the table of the CLSI2020 standard (11-14).

3.3. Antibiotic Susceptibility Assay by Agar Dilution Method (ADM)

After preparing stock solution according to the CLSI 2020 (11) standard for antibiotics, 1.5 × 10⁸ CFU/mL of microbial suspensions were cultured in specimens on Muller-Hinton agar containing the suspected antibiotics (MAST Diagnostics, Merseyside, UK) and incubated at 37°C for 18 - 24 h. A plate containing medium without antimicrobial agents was considered a negative quality control, and P. aeruginosa ATCC 27853 strain was used as a positive quality control. The data of variable region of type 1 integron amplicons and its nucleotide sequences were sequenced and analyzed, respectively, by the National Center for Biotechnology Information (NCBI) (Retrieved from: http://www.ncbi.nlm.nih.gov/BLAST/).

3.6. Sequencing of Class 1 Integron Gene

The data of variable region of type 1 integron amplicons and its nucleotide sequences were sequenced and analyzed, respectively, by the National Center for Biotechnology Information (NCBI) (Retrieved from: http://www.ncbi.nlm.nih.gov/BLAST/).

3.7. Statistical Analysis

Paired-sample t test and Spearman’s correlation tests were used to analyze the collected data with SPSS software version 21.01. In this study, P < 0.05 was set as the significance level.

4. Results

4.1. Bacterial Isolation

During one year (2016 - 2017), 30 clinical isolates of P. aeruginosa were collected from patients admitted to Aya-tollah Rohani Hospital (Babol, north of Iran).
Table 1. Primer Sequences and PCR Programs for Some Genes

| Gene    | Sequence Primer PCR Product | PCR Product | PCR Program |
|---------|-----------------------------|-------------|-------------|
| IntI    | F: TCTCGGGTACATCAAG; R: AGGAGATCGGAAGACCTC | 243 bp | 5 min at 94°C; 35 cycles (1 min at 94°C, 1 min at 53°C, and 30 sec at 72°C); 5 min at 72°C |
| aadB    | F: GGGCGGTCTGAGGAGTT; R: TATCGCGACCTGAAAGC | 329 bp | 5 min at 94°C; 35 cycles (1 min at 94°C, 1 min at 65°C, and 30 sec at 72°C); 5 min at 72°C |
| DfrA1   | F: GGAGTGCCAAAGGTGAACAGC; R: GAGGCGAAGTCTTGGGTAAAAAC | 367 bp | 5 min at 94°C; 35 cycles (1 min at 94°C, 1 min at 45°C, and 30 sec at 72°C); 5 min at 72°C |
| bla-OXA30| F: ATTATCTACAGCAGCAGCGCCAGTGC; R: TTCGACCCCAAGTTTCCTGTAAGTGC | 716 bp | 5 min at 94°C; 35 cycles (1 min at 94°C, 1 min at 50°C, and 30 sec at 72°C); 5 min at 72°C |

Table 2. Antibiotic Susceptibility of Integron-Positive and Integron-Negative Strains of Pseudomonas aeruginosa Compared to Disk Diffusion *

| Antibiotics | Disk Diffusion Method (n = 30) | Integron Positive (n = 18) | Integron Negative (n = 12) | P Value |
|-------------|--------------------------------|---------------------------|---------------------------|---------|
| Gentamicin  | Susceptibility: 14 (46.6) Resistant: 16 (53.4) | 7 (38.9) Resistant: 11 (61.1) | 7 (58.3) Resistant: 5 (41.7) | 0.296   |
| Ciprofloxacin| 23 (76.7) Resistant: 7 (23.3) | 11 (72.2) Resistant: 5 (27.8) | 10 (83.3) Resistant: 2 (16.7) | 0.481   |
| Cefepime    | 2 (6.7) Resistant: 28 (93.3) | 1 (5.6) Resistant: 17 (94.4) | 1 (8.3) Resistant: 11 (91.7) | 0.795   |
| Trimethoprim| 3 (10) Resistant: 27 (90) | 0 Resistant: 18 (100) | 3 (25.0) Resistant: 9 (75.0) | 0.025*  |
| Cefotaxime  | 0 Resistant: 30 (100) | 0 Resistant: 18 (100) | 0 Resistant: 12 (100) | 0.00*   |
| Ampicillin  | 0 Resistant: 30 (100) | 0 Resistant: 18 (100) | 0 Resistant: 12 (100) | 0.00*   |
| Imipenem    | 23 (76.7) Resistant: 7 (23.3) | 14 (77.8) Resistant: 4 (22.2) | 9 (75.0) Resistant: 3 (25.0) | 0.860   |
| Amikacin    | 27 (90.0) Resistant: 3 (10) | 14 (77.8) Resistant: 4 (22.2) | 11 (91.7) Resistant: 1 (8.3) | 0.804   |
| Nitrofurantoin| 0 Resistant: 30 (100) | 0 Resistant: 18 (100) | 0 Resistant: 12 (100) | 0.00*   |

* Values are expressed as No. (%).  

4.2. Antibiotic Resistance Profile

All samples were examined for resistance to nine antimicrobials using DD. The resistance rates to NI, AP, CTX, CPM, TM, GM, CIP, IMI, and AK were 100, 100, 100, 93.3, 9, 13.7, 10.3, and 3.4%, respectively (Table 2).

The results of the ADM rates for NI, AP, CTX, TM, GM, CPM, CIP, IMI, and AK were 100, 96.7, 96.7, 90, 63.3, 56.7, 40, and 3.3%, respectively (Table 3). The multidrug resistance (MDR) phenotype of P. aeruginosa clinical isolates for intI and gene cassettes of aadB, dfrA1, and bla-OXA30 are presented in Table 4.

4.3. Gene Cassettes

60% (n : 18) carried intI gene among 30 P. aeruginosa isolates. The prevalence of aadB, dfrA1, and bla-OXA30 genes were 11 (61%), 12 (66%), 6 (33%), and 0 (0%), respectively.

4.4. Nucleotide Sequence Accession Number

The positive aadB and dfrA1strains were sequenced and established in the Gene Bank database as MH708573 and MH708574, respectively.

5. Discussion

Pseudomonas aeruginosa is an important opportunistic nosocomial bacterium with high resistance to most common antibiotics. For this reason, treating infections induced by this bacterium is challenging. The innate and acquired resistance to antimicrobial agents is involved in the mortality rate of patients suffering from infections induced by this bacterium (19). Integrons have been known as the primary mechanism to detect the gene of resistance to antibiotics in Gram-negative bacteria (20). The integrase gene sets the ground for resistance to common antibiotics, including ampicillin, gentamicin, trimethoprim, and cefotaxime (5). The findings of this study indicated that 18 isolates (60%) had the intI gene. Further, out of the samples with the intI gene, 61, 62, and 33% had the gene cassettes of aadB, dfrA1, and bla-OXA30.

The correlation between the presence of the intI gene and inducing resistance to each antibiotic was examined with SPSS software version 21.0 using the chi-square test. In the DD method, there is a significant correlation between the presence of intI gene and resistance to trimethoprim, cefotaxime, ampicillin, and nitrofurantoin. In the agar dilution method, there is a significant correlation.
between the presence of intI gene and resistance to gentamicin, ciprofloxacin, cefepime, trimethoprim, and nitrofurantoin separately (Table 2,3). In Brazil, Fonseca et al. (21) documented 45.5% of P. aeruginosa strains had the intI gene, and out of 29 isolates, 66% and 52% samples had aacA and bla-OXA30 genes. In another study, the intI gene frequency was 57.1%, and there was also a significant relationship between the gene cassettes in intI and antibiotic resistance (22). In another study by Nikokar et al. (23) on antibiotic resistance of the Int1 gene in P. aeruginosa, 47% of the strains were resistant to the antibiotic. However, most of the strains were insensitive to imipenem. The PCR results indicated that 45.3% of the isolates had the intI gene and that 69% of the strains were antibiotic-resistant. All studies suggest a significant relationship between the presence of intI and gene cassettes with antibiotic resistance (24).

5.1. Conclusions

The high resistance of P. aeruginosa isolates is due to the presence of intI and its gene cassettes. Considering their high resistance to cefotaxime, gentamicin, ampicillin, and imipenem in hospitals, selecting appropriate drugs or generally changing the treatment course for patients is possible to prevent the spread of resistance inducing genes and the development of nosocomial infections.

Footnotes

Authors’ Contribution: Study concept and design: E. F. Sh. and R. E. Sh.; analysis and interpretation of data: E. F. Sh.

## Table 3. Antibiotic Susceptibility of Integron-Positive and Integron-Negative Strains of Pseudomonas aeruginosa Compared to Agar Dilution Method *

| Antibiotic  | Agar Dilution Method (n = 30) | Integron-Positive (n = 18) | Integron-Negative (n = 12) | P-Value |
|-------------|-------------------------------|---------------------------|---------------------------|---------|
|             | Susceptibility | Resistant | Susceptibility | Resistant | Susceptibility | Resistant |                |
| Gentamicin  | 11 (36.7)       | 19 (63.3) | 3 (16.7)       | 15 (83.3) | 8 (66.6)       | 4 (33.4)  | 0.005 *        |
| Ciprofloxacin| 18 (60)         | 12 (40)  | 8 (44.4)       | 10 (55.6) | 10 (83.3)      | 2 (16.7)  | 0.033 *        |
| Cefepime    | 13 (43.3)       | 17 (65.7) | 3 (16.7)       | 15 (83.3) | 10 (83.3)      | 2 (16.7)  | 0.000 *        |
| Trimethoprim| 3 (10)          | 27 (90)  | 0              | 18 (100) | 1 (25)         | 9 (75)    | 0.025 *        |
| Cefotaxime  | 1 (3.3)         | 29 (96.7) | 0              | 18 (100) | 1 (8.3)        | 11 (91.7) | 0.213          |
| Ampicillin  | 1 (3.3)         | 29 (96.7) | 0              | 18 (100) | 1 (8.3)        | 11 (91.7) | 0.213          |
| Imipenem    | 18 (60)         | 12 (40)  | 11 (61.1)      | 7 (38.9) | 7 (58.3)       | 5 (41.7)  | 0.879          |
| Amikacin    | 29 (96.7)       | 1 (3.3)  | 17 (94.4)      | 1 (5.6)  | 12 (100)       | 0         | 0.406          |

* Values are expressed as No. (%).

## Table 4. MDR Phenotype of Pseudomonas aeruginosa Clinical Isolates for intI and Gene Cassettes of aadB, dfrA1, and bla-OXA30

| Antibiotics resistant pattern | Number of Isolates | intI | aadB | DfrA1 | bla-OXA30 |
|------------------------------|--------------------|------|------|-------|-----------|
|CTX/SXT/AM/IM/IPM/GM/CP/FEP  | 1                  | 1    | -    | 1     | -         |
|CTX/SXT/AM/AN/IM/IPM/GM/FEP  | 2                  | 2    | 2    | 1     | 1         |
|CTX/SXT/AM/IM/CP/FEP         | 2                  | 2    | 2    | 2     | -         |
|CTX/SXT/AM/IPM/GM/CP/FEP     | 1                  | 1    | -    | 1     | -         |
|CTX/SXT/AM/CP/GM/CP/FEP      | 1                  | -    | -    | -     | -         |
|CTX/SXT/AM/GM/CP/FEP         | 8                  | 5    | 3    | 2     | 2         |
|CTX/SXT/AM/AN/CP/FEP         | 1                  | 1    | 1    | 1     | -         |
|CTX/SXT/AM/CP/CP/FEP         | 3                  | 3    | -    | 1     | -         |
|CTX/SXT/AM/IPM/GM/CP/FEP     | 3                  | 1    | 1    | 1     | 1         |
|CTX/SXT/AM/IPM/CP/FEP        | 5                  | 2    | 2    | 2     | 2         |
|CTX/AM/IPM/CP/FEP            | 1                  | -    | -    | -     | -         |
|CTX/AM/CP/CP/FEP             | 1                  | -    | -    | -     | -         |
|CTX/AM/CP/FEP                | 1                  | -    | -    | -     | -         |
|CTX/AM/GM                    | 1                  | -    | -    | -     | -         |
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References
1. Rajabnia R, Ashgharpour F, Ferdosi Shahandashti E, Khalilian M, Norkhomami S, Shafii M, et al. Class I Integron in Pseudomonas aeruginosa Isolates From Different Places and Devices of ICU in Babol, Iran. Jundishapur J Microbiol. 2013;6(2):e44850. doi:10.5812/jmm.44850.
2. Japoni A, Alborzi A, Kaliani M, Nasiri J, Hayati M, Farshad S. Susceptibility patterns and cross-resistance of antibiotics against Pseudomonas aeruginosa isolated from burn patients in the South of Iran. Burns. 2006;32(3):343-7. doi:10.1016/j.burns.2005.10.007. [PubMed: 16527415].
3. Fluit AC, Schmitz FJ. Resistance integrons and super-integrons. Clin Microbiol Infect. 2004;10(4):227-88. doi:10.1111/j.1469-7751.2004.00858.x. [PubMed: 1505915].
4. Deylam Salehi M, Ferdosi-Shahandashti E, Yahyapour Y, Khafri S, Pournejaf A, Rajabnia R. Integron-Mediated Antibiotic Resistance in Acinetobacter baumannii Isolated From Intensive Care Unit Patients, Babol, North of Iran. Biomed Res Int. 2017;2017:757923. doi:10.1155/2017/757923. [PubMed: 28804720]. [PubMed Central: PMC5540380].
5. Nourbakhsh F, Nourbakhsh V, Jafakesh MT. [Prevalence of class I, II and III integrons in the antibiotic-resistant isolates of A. baumannii detected from patients hospitalized in medical centers of Shahrrekord]. KOUJS Journal (FETJE). 2016;20(5):461-8. Persian.
6. Peng CF, Lee MF, Fu HT, Chen YJ, Hsu HJ. Characterization of class I integrons and antimicrobial resistance in CTX-M-3-producing Serratia marcescens isolates from southern Taiwan. Jpn J Infect Dis. 2007;60(5):250-6. doi:10.7888/jijid.1788862.
7. Stokes HW, Hall RM. A novel family of potentially mobile DNA elements encoding site-specific gene-integration functions: integrons. Mol Microbiol. 1989;3(12):1669-83. doi:10.1111/j.1365-2958.1989.tb00153.x. [PubMed: 2560819].
8. Moradian Kouchakzadeh F, Ferdosi Shahandashti E, Molana Z, Moradian Kouchakzadeh M, Ashgharpour F, Mojtahed A, et al. Molecular detection of integron genes and pattern of antibiotic resistance in pseudomonas aeruginosa strains isolated from intensive care unit, Shahid Beheshti Hospital, North of Iran. Int J Mol Cell Med. 2012;4(3):209-17. [PubMed: 24555780]. [PubMed Central: PMC3920509].
9. Lister PD, Wolter DJ, Hanson ND. Antibacterial-resistant Pseudomonas aeruginosa: clinical impact and complex regulation of chromosomally encoded resistance mechanisms. Clin Microbiol Rev. 2009;22(4):582-600. doi:10.1128/CMR.00040-09. [PubMed: 19828890]. [PubMed Central: PMC2727362].
10. Akrami F, Shahandashti EF, Yahyapour Y, Sadeghi M, Khafri S, Pournejaf A, et al. Integron types, gene cassettes and antimicrobial resistance profile of Acinetobacter baumannii isolated from BAL samples in Babol, north of Iran. Microb Pathog. 2017;109:35-8. doi:10.1016/j.micpath.2017.05.005. [PubMed: 28479508].
11. Weinstein MP, Lewis JS, Bobenchik AM, Cusack S, Cullen S, Galas MF, et al. M 100 Performance Standards for Antimicrobial Susceptibility Testing. 30th ed. Pennsylvania, USA: Clinical & Laboratory Standards Institute; 2020. 332 p.
12. Ahangarkani F, Rajabnia R, Shahandashti EF, Bagheri M, Ramez M. Frequency of class I integrin in Escherichia coli strains isolated from patients with urinary tract infections in north of Iran. Mater Sociomed. 2015;27(1):10-2. doi:10.5455/msm.2014.27.10-12. [PubMed: 25870523]. [PubMed Central: PMC434837].
13. Moammedi F, Arabestani MR, Safari M, Roshanaii G, Alkhiani MY. [Prevalence of class 2, 3 and 3 integrons among extensive drug resistance Acinetobacter baumannii strains isolated from intensive care units in Hamadan, west province, Iran]. Iran J Med Microbiol. 2014;3(1):8-14. Persian.
14. Lyzaacz JB, Cannon CI, Pier GB. Establishment of Pseudomonas aeruginosa infection: lessons from a versatile opportunist. Microbes Infect. 2000;2(9):1051-60. doi:10.1016/S1286-4579(00)01329-4. [PubMed: 1096728].
15. Peymani A, Naserpour Farivar T, Rahimi H, Ranjbar M, Najafipour R. [Frequency of class I integron among multidrug resistant Pseudomonas aeruginosa isolates from the selected hospitals in Qazvin and Tehran, Iran]. Qum Univ Med Sci. J. 2014;8(3):46-9. Persian.
16. Nasiri H, Forouzandeh M, Rasaei MJ, Rabharizadeh F. Modified salting-out method: high-yield, high-quality genomic DNA extraction from whole blood using laundry detergent. J Clin Lab Anal. 2005;19(6):229-32. doi:10.1002/jcla.20083. [PubMed: 16302208]. [PubMed Central: PMC5808306].
17. Yousefi S, Nhaeii M, Farajzadeh S, Gholizadeh M, Akhi M, Shariyi Y, et al. Class 1 integron and Imipenem Resistance in Clinical Isolates of Pseudomonas aeruginosa: Prevalence and Antibiotic Susceptibility. Iran J Microbiol. 2010;2(3):115-21. [PubMed: 22437559]. [PubMed Central: PMC279777].
18. Sun J, Zhou M, Wu Q, Ni Y. Characterization of two novel gene cassettes, dfrA27 and aadA16, in a non-O1, non-O139 Vibrio cholerae isolate from China. Clin Microbiol Infect. 2010;16(8):1235-9. doi:10.1111/j.1469-0691.2009.03060.x. [PubMed: 19906275].
19. Bauer KA, West JE, O’Brien JM, Goff DA. Extended-infusion cefepime reduces mortality in patients with Pseudomonas aeruginosa infections. Antimicrob Agents Chemother. 2013;57(7):2907-12. doi:10.1128/AAC.02365-12. [PubMed: 23579547]. [PubMed Central: PMC3697364].
20. Molana Z, Ferdosi Shahandashti E, Ghavari S, Shafii M, Norkhomami S, Aghankhani F, et al. [Molecular investigation of class I integrin in Klebsiella Pneumoniae isolated from intensive care unit (Shahid Beheshti Hospital of Babol 2010)]. J Babol Univ. Medical Sci. 2012;13(3):6-7. Persian.
21. Fonseca EL, Vieira VV, Cipriano R, Vicente AC. Class 1 integrons in Pseudomonas aeruginosa isolates from clinical settings in Amazon region, Brazil. FEMS Immunol Med Microbiol. 2005;44(1):303-9. doi:10.1016/j.femsim.2005.01.004. [PubMed: 15907453].
22. Odonmosu BT, Adeniyi BA, Chandra R. Analysis of integrons and associated gene cassettes in clinical isolates of multidrug resistant Pseudomonas aeruginosa from Southwest Nigeria. Ann Clin Microbiol Antimicrob. 2013;12:29. doi:10.1186/2047-7101-12-29. [PubMed: 24143920]. [PubMed Central: PMC3842740].
23. Nikakor I, Tishayar A, Fakryan Z, Alijani K, Rehana-Banisaed S, Hossinpour M, et al. Antibiotic resistance and frequency of class I integrons among Pseudomonas aeruginosa, isolated from burn patients in Guilan, Iran. Iran J Microbiol. 2013;5(1):36-41. [PubMed: 2346682]. [PubMed Central: PMC3577559].
24. Koeleman JG, Stoof J, Van Der Bijl MW, Vandenbroucke-Grauls CM, Savelkoul PH. Identification of epidemic strains of Acinetobacter baumannii by integrase gene PCR. J Clin Microbiol. 2001;39(1):8-3. doi:10.1128/JCM.39.1.8-3.2001. [PubMed: 1136740]. [PubMed Central: PMC87671].