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REFERENCE CENTRE FOR DETECTION OF ANTIMICROBIAL RESISTANCE

Identification, molecular epidemiology, and antibiotic resistance characterization of *Acinetobacter* spp. clinical isolates

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A dissertation for the degree of Philosophiae Doctor

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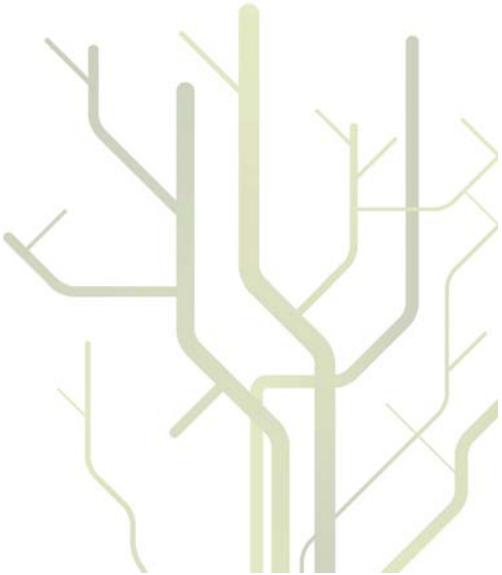

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Contents

List of papers

Paper I

Karah, N., B. Haldorsen, K. Hegstad, G. S. Simonsen, A. Sundsfjord, Ø. Samuelsen, and the Norwegian Study Group on *Acinetobacter*. 2011. Species identification and molecular characterization of *Acinetobacter* spp. blood culture isolates from Norway. J. Antimicrob. Chemother. **66:**738-744.

Paper II

Karah, N., B. Haldorsen, N. O. Hermansen, Y. Tveten, E. Ragnhildstveit, D. H. Skutlaberg, S. Tofteland, A. Sundsfjord, and Ø. Samuelsen. 2011. Emergence of OXA carbapenemase- and 16S rRNA methylase-producing international clones of *Acinetobacter baumannii* in Norway. J. Med. Microbiol. **60:**515-521.

Paper III

Karah, N., C. G. Giske, A. Sundsfjord, and Ø. Samuelsen. 2011. A diversity of OXA-carbapenemases and class 1 integrons among carbapenem-resistant *Acinetobacter baumannii* clinical isolates from Sweden belonging to different international clonal lineages. Submitted to Microbial Drug Resistance.

Paper IV

Karah, N., R. Smyth, B. Haldorsen, G. S. Simonsen, A. Sundsfjord, and Ø. Samuelsen. 2011. Performance of VITEK 2, BD Phoenix, and MALDI-TOF MS systems for species identification of *Acinetobacter* blood culture isolates. Manuscript ready for submission.

Abbreviations

G	Guanine
C	Cytosine
BJ	Bouvet and Jeanjean
TU	Tjernberg and Ursing
spp.	Species (plural)
16S rDNA	16S ribosomal DNA
16S-23S rDNA	16S-23S ribosomal DNA (intergenic spacer region)
Bp	Base pair
MDR	Multidrug-resistance/multidrug-resistant
Trp	Tryptophan
Lys	Lysine
Gly	Glycine
Val	Valine
Cys	Cysteine
Ser	Serine
Leu	Leucine
Ala	Alanine
Pro	Proline
Glu	Glutamic Acid
Phe	Phenylalanine

1. Introduction

1.1. The genus *Acinetobacter*

The Subcommittee on the "Taxonomy of *Moraxella* and Allied Bacteria" reached an agreement on the definition of the genus *Acinetobacter* in 1971 [1]. The genus *Acinetobacter* was initially classified in the family *Neisseriaceae* [1]. However, it has soon after been re-sorted into the family *Moraxellaceae* and the following taxonomic lineage: Cellular organisms; Bacteria; Proteobacteria; Gamma-proteobacteria; *Pseudomonadales*; *Moraxellaceae*; *Acinetobacter* (www.ncbi.nlm.nih.gov/Taxonomy) [1, 2]. The genus *Acinetobacter* can presently be defined as Gram-negative, strictly aerobic, non-fermenting, non-fastidious, non-motile, catalase-positive, and oxidase-negative coccobacillary bacteria with a DNA G and C content of 39% to 47% [1, 2]. Nonetheless, Gram staining of *Acinetobacter* can be variable and the morphologic characteristics may change depending on the growth phase [1].

1.2. *Acinetobacter* species

At least 33 species within the *Acinetobacter* genus have so far been identified, including 24 named species and 9 currently described as genomic species (gen. sp.) given that no phenotypic properties have been found to differentiate them from other species (Table 1) [3-21]. Several significant steps in the history of identifying novel *Acinetobacter* species have been achieved [3-21]. In 1986, twelve *Acinetobacter* genomic species within the *Acinetobacter* genus were identified by DNA-DNA hybridization [3]. Six of these DNA groups could be differentiated by phenotypic properties and were given the following formal species names: *A. calcoaceticus* (*Acinetobacter* gen. sp. 1), *Acinetobacter baumannii* (*Acinetobacter* gen. sp. 2), *Acinetobacter haemolyticus* (*Acinetobacter* gen. sp. 4), *Acinetobacter junii* (*Acinetobacter* gen. sp. 5), *Acinetobacter johnsonii* (*Acinetobacter* gen. sp. 7), and *Acinetobacter lwoffii* (*Acinetobacter* gen. sp. 8). The

study reported an uncertain genotypic and phenotypic differentiation of *Acinetobacter* gen. sp. 9 from *A. lwoffii*.

In 1988, one novel species was identified by DNA-DNA hybridization [4]. The new species was phenotypically distinguished from other *Acinetobacter* species and was named *Acinetobacter radioresistens*. Five novel genomic species (*Acinetobacter* gen. sp. 13BJ, *Acinetobacter* gen. sp. 14BJ, *Acinetobacter* gen. sp. 15 BJ, *Acinetobacter* gen. sp. 16, and *Acinetobacter* gen. sp. 17) were subsequently identified by DNA-DNA hybridization [5]. Biochemically, the novel DNA groups could not be separated unambiguously and therefore were not named. Simultaneously, three novel genomic species (*Acinetobacter* gen. sp. 13TU, *Acinetobacter* gen. sp. 14TU, and *Acinetobacter* gen. sp. 15TU) were identified by DNA-DNA hybridization [6]. The study also reclassified *A. radioresistens* and *Acinetobacter* gen. sp. 12 as one species.

In 1991, *Acinetobacter* gen. sp. 13BJ and *Acinetobacter* gen. sp. 14TU were found to represent one species [7]. The study also showed that strains belonging to *A. calcoaceticus*, *A. baumannii*, *Acinetobacter* gen. sp. 3 and *Acinetobacter* gen. sp. 13TU were so similar phenotypically that it was impossible to identify them to the species level by the use of biochemical tests. This similarity was in accordance with the observations that these four groups were genotypically more closely related to each other than to other DNA groups [6]. Accordingly, these four species were suggested to be grouped as the *A. calcoaceticus-A. baumannii* complex [7]. Then in 1993, two novel genomic species (*Acinetobacter* gen. sp. "between 1 and 3" and *Acinetobacter* gen. sp. "close to 13TU") were identified [8]. The two new species were included within the *A. calcoaceticus-A. baumannii* complex [8]. Successively, one novel species was identified and provisionally named as *Acinetobacter venetianus* [9, 10]. *A. venetianus* has recently been re-described and the name has accordingly been vaidated [11].

In 2001 and 2003, Nemec *et al*. identified three novel species (*Acinetobacter schindleri*, *Acinetobacter ursingii*, and *Acinetobacter parvus*) [12, 13]. Concurrently, seven novel species were identified (*Acinetobacter baylyi, Acinetobacter bouvetii, Acinetobacter*

towneri, Acinetobacter tandoii, Acinetobacter grimontii, Acinetobacter tjernbergiae, and *Acinetobacter gerneri*) [14]. However, *A. grimontii* was later re-classified within the *A. junii* species [15]. One novel species was identified and named as *Acinetobacter septicus* in 2008 although it was soon after re-classified within the *A. ursingii* species [16, 17].

Three novel species (*Acinetobacter soli*, *Acinetobacter beijerinckii*, and *Acinetobacter gyllenbergii*) were also identified in 2008 and 2009 by two different research groups [18, 19]. Furthermore, *Acinetobacter* gen. sp. 10, *Acinetobacter* gen. sp. 11, *Acinetobacter* gen. sp. 3, and *Acinetobacter* gen. sp. 13TU have recently been named *Acinetobacter berezinae*, *Acinetobacter guillouiae*, *Acinetobacter pittii*, and *Acinetobacter nosocomialis*, respectively, given that they can phenotypically be differentiated from other species within the genus *Acinetobacter* [20, 21].

Table 1. Type and reference strains for currently identified *Acinetobacter* spp. and their corresponding *rpoB* GenBank accession numbers

***Acinetobacter* species**[a]	**Type and reference strain**[b]	***rpoB* GenBank accession no.**[c]	**References**
Acinetobacter calcoaceticus (*Acinetobacter* gen. sp. 1)	B46^T = CIP 81.8^T = ATCC 23055^T = DSM 30006^T = LMG 1046^T = CCUG 12804^T = NCCB 22016^T = NIPH 2245^T = RUH 2201^T	DQ207474 = EF611388 = EU477149	[3, 16, 19, 20, 22]
Acinetobacter baumannii (*Acinetobacter* gen. sp. 2)	CIP 70.34^T = ATCC 19606^T = DSM 30007^T = LMG 1041^T = CCUG 19096^T = NCCB 85021^T = NIPH 501^T = RUH 3023^T	DQ207471 = EF611384 = EU477108	[3, 16, 19, 20, 22]
Acinetobacter pittii (*Acinetobacter* gen. sp. 3)	CIP 70.29 = ATCC 19004 = LMG 1035 = NIPH 519 = RUH 2206	EU477114	[3, 19-21]
Acinetobacter haemolyticus (*Acinetobacter* gen. sp. 4)	B40^T = CIP 64.3^T = ATCC 17906^T = DSM 6962^T = LMG 996^T = CCUG 888^T = NCCB 85026^T = NIPH 510^T = LUH 9705^T = CCM 2358^T	DQ207484 = EU477109 = EF611391	[3, 16, 19, 20, 22]
Acinetobacter junii (*Acinetobacter* gen. sp. 5 and *Acinetobacter grimontii*)	B10^T = CIP 64.5^T = ATCC 17908^T = DSM 6964^T = LMG 998^T = CCUG 889^T = RUH 2228^T = NIPH 551^T = CCM 2376^T	DQ207486 = EU477110 = EF611394[d]	[3, 14-16, 19, 20, 22]
***Acinetobacter* gen. sp. 6**	CIP A165 = ATCC 17979 = LMG 1026 = CCUG 26492 = NIPH 520 = RUH 2867	DQ207480 = EU477115	[3, 19, 20, 22]
Acinetobacter johnsonii (*Acinetobacter* gen. sp. 7)	B8^T = CIP 64.6^T = ATCC 17909^T = DSM 6963^T = LMG 999^T = CCUG 19095^T = NIPH 518^T = RUH 2231^T	DQ207485 = EU477113	[3, 19, 20, 22]
Acinetobacter lwoffii (*Acinetobacter* gen. sp. 8 and *Acinetobacter* gen. sp. 9)	CIP 64.10^T = ATCC 15309^T = DSM 2403^T = LMG 1029^T = CCUG 12805^T = NCCB 83025^T = NIPH 512^T = CCM 5581^T = RUH 2219^T	EU477111 = EF611395 = DQ060363[e]	[3, 16, 19, 20]
Acinetobacter berezinae (*Acinetobacter* gen. sp. 10)	CIP 70.12^T = ATCC 17924^T = LMG 1003^T = CCUG 26493^T = NCCB 82031^T = NIPH 521^T = RUH 2224^T	DQ207475 = EU477116	[3, 19, 20, 22]
Acinetobacter guillouiae (*Acinetobacter* gen. sp. 11)	B94^T = CIP 63.46^T = ATCC 11171^T = DSM 590^T = LMG 988^T = CCUG 2491^T = NCIB 8250^T = NIPH 522^T	DQ207476 = EU477117	[3, 19, 20, 22]
Acinetobacter radioresistens (*Acinetobacter* gen. sp. 12)	FQ-1^T = IAM 13186^T = CIP 103788^T = ATCC 43998^T = DSM 6976^T = LMG 10613^T = CCUG 56440^T = NIPH 513^T = RUH 2865^T = CCM 3588^T	DQ207489 = EU477112 = EF611400	[3, 4, 6, 16, 19, 20, 22]
***Acinetobacter* gen. sp. 13BJ** (*Acinetobacter* gen. sp. 14TU)	CIP 64.2 = ATCC 17905 = LMG 995 = CCUG 887 = NIPH 1860 = RUH 2218 = LUH 9704	DQ207478 = EU477149	[3, 5, 6, 19, 20]
***Acinetobacter* gen. sp. 14BJ**	Bouvet 513 = CCUG 14816 = NIPH 2112 = LUH 1726	EU477147	[5, 19, 20]
***Acinetobacter* gen. sp. 15BJ**	SEIP 23.78 = CCUG 26494 = NIPH 1866 = LUH 1729	EU477133	[5, 19, 20]

Table 1. Type and reference strains for currently identified *Acinetobacter* spp. and their corresponding *rpoB* GenBank accession numbers (cont.)

***Acinetobacter* species**[a]	**Type and reference strain**[b]	***rpoB* GenBank accession no.**[c]	**References**
***Acinetobacter* gen. sp. 16**	CIP 70.18 = ATCC 17988 = LMG 1031 = CCUG 996 = NIPH 1872	DQ207477 = EU477135	[5, 19, 20, 22]
***Acinetobacter* gen. sp. 17**	Bouvet 942 = SEIP Ac87.314 = CCUG 34437 = NIPH 1867 = LUH 1736	EU477134	[5, 19, 20]
Acinetobacter nosocomialis (*Acinetobacter* gen. sp. 13TU)	CIP 70.11 = ATCC 17903 = DSM 30010 = LMG 993 = CCUG 26488 = NIPH 523 = RUH 2210	EU477118	[6, 19-21]
***Acinetobacter* gen. sp. 15TU**	M 151a = CCUG 26390 = NIPH 546 = LUH 1090	EU477119	[1, 6, 19, 20]
***Acinetobacter* gen. sp. 'between 1 and 3'**	Gerner-Smidt 10095 = CCUG 34786 =NIPH 817 = LUH 1469	EU477122	[8, 19, 20]
***Acinetobacter* gen. sp. 'close to 13TU'**	Gerner-Smidt 10090 = CCUG 34785 =NIPH 973 = LUH 1472	EU477126	[8, 19, 20]
Acinetobacter venetianus	RAG-1^T = ATCC 31012^T = LMG 19082^T = CCUG 45561^T = NIPH 1925^T = LUH 3904^T	EU477136	[10, 19, 20]
Acinetobacter ursingii (*Acinetobacter septicus*)	CIP 107286^T = ATCC BAA-617^T = DSM 16037^T = LMG 19575^T = NCCB 100021^T = CCUG 45559^T = NIPH 137^T = LUH 3792^T	DQ231239 = EF611406 = EU477105	[12, 16, 17, 19, 20, 22]
Acinetobacter schindleri	CIP 107287^T = ATCC BAA-618^T = DSM 16038^T = LMG 19576^T = NCCB 100022^T = CCUG 45560^T = NIPH 1034^T = LUH 5832^T	DQ207490 = EU477128 = EF611402	[12, 16, 19, 20, 22]
Acinetobacter parvus	CIP 108168T =DSM 16617T = LMG 21765T = CCUG 48800T = NIPH 384T = LUH 4616T	DQ207488 = EU477107 = EF611399	[13, 16, 19, 20, 22]
Acinetobacter baylyif	NIPH 2312 = ADP1	EU477155 = CR543861	[19, 20, 23]
Acinetobacter bouvetii	4B02^T = CIP 107468^T = DSM 14964^T = CCUG 50766^T = NIPH 2281^T = CCM 7196^T	DQ207473 = EU477150 = EF611387	[14, 16, 19, 20, 22]
Acinetobacter towneri	AB1110^T = CIP 107472^T = DSM 14962^T = CCUG 50769^T = NIPH 2286^T = CCM 7201^T	DQ207493 = EU477154 = EF611405	[14, 16, 19, 20, 22]
Acinetobacter tandoii	4N13^T = CIP 107469^T = DSM 14970^T = CCUG 56317^T = NIPH 2284^T = CCM 7199^T	DQ207491 = EU477152 = EF611403	[14, 16, 19, 20, 22]
Acinetobacter tjernbergiae	7N16^T = CIP 107465^T = DSM 14971^T = CCUG 50768^T = NIPH 2285^T = CCM 7200^T	DQ207492 = EU477153 = EF611404	[14, 16, 19, 20, 22]
Acinetobacter gerneri	9A01^T = CIP 107464^T = DSM 14967^T = CCUG 56316^T = NIPH 2282^T = CCM 7197^T	DQ207482 = EU477151 = EF611389	[14, 16, 19, 20, 22]
Acinetobacter soli	B1^T = CCUG 59023^T = KCTC 22184^T = JCM 15062^T	Not determined	[18]

Table 1. Type and reference strains for currently identified *Acinetobacter* spp. and their corresponding *rpoB* GenBank accession numbers (cont.)

***Acinetobacter* species**[a]	**Type and reference strain**[b]	***rpoB* GenBank accession no.**[c]	**References**
Acinetobacter beijerinckii	CCUG 51249^T = NIPH 838^T = LUH 4759^T	EU477124	[19, 20]
Acinetobacter gyllenbergii	CCUG 51248^T = NIPH 2150^T = RUH 422^T	EU477148	[19, 20]

[a]gen. sp., genomic species; commonly accepted names are presented in bald; other putative names are presented in parenthesis.

[b]CIP, Collection de l'Institut Pasteur (France); ATCC, American Type Culture Collection (the United States of America); DSM, Deutsche Sammlung von Mikroorganismen (Germany); LMG, Laboratorium voor Microbiologie Gent (Belgium); CCUG, Culture Collection, University of Gothenburg (Sweden); NCCB, The Netherlands Culture Collection of Bacteria (The Netherlands); NIPH, National Institute of Public Health (Czech Republic); LUH and RUH, collection of Leiden University Medical Center (The Netherlands); CCM, Czech Collection of Microorganisms (Czech Republic); IAM, collection of Institute of Applied Microbiology, University of Tokyo (Japan); SEIP, collection of Service des Enterobacteries de l'Institut Pasteur (France); KCTC, Korean Collection for Type Cultures (Korea); JCM, Japan Collection of Microorganisms (Japan); ^{T}, type strain.

[c]Nucleotide similarity was compared only for zone 1 (between positions 2916 and 3267) of the *rpoB* gene.

[d]Incorrectly deposited under the name *A. johnsonii* DSM 6964 (GenBank accession no. EF611394).

[e]Different from DQ207487 of *A. lwoffii* CIP 64.10^T.

[f]*rpoB of A. baylyi* type strain B2^T = CIP 107474^T = DSM 14961^T = LMG 24678^T = CCUG 50765^T; GenBank accession nos. DQ207472 and EF611386 were found to carry sequences that may have resulted from intragenic recombination events [23].

1.3. Species identification

Identification of *Acinetobacter* isolates to the species level has been problematic [24]. Phenotypic schemes are generally insufficient [1, 7, 24]. Furthermore, phenotypic identification by commercial colorimetric systems has been associated with poor accuracy [24, 25]. For instance, one study conducted in 2009 reported an incorrect speciation of 75% of the isolates using the VITEK 2 GNI identification system [25]. On the other hand, molecular identification of *Acinetobacter* species by DNA-DNA hybridisation most likely represents the reference standard method for precise identification [1, 3]. However, this method is not appropriate for practical work in routine clinical laboratories since it is time-consuming, labour-intensive, and not widely available [1].

Other genotypic methods have, therefore, been proposed for fast and yet accurate identification of *Acinetobacter* species either by whole-genome fingerprinting or by restriction enzyme or sequence analysis of a particular gene/genetic region (Table 2) [24]. Alternatively, protein fingerprinting using a matrix-assisted laser desorption ionization-time-of-flight (MALDI-TOF) mass spectrometer has been found to represent a promising molecular method for rapid identification of *Acinetobacter* species with high-throughput capability [26]. The study showed that the MALDI-TOF Mass Spectrometry system was able to separate a total of 552 well-characterized *Acinetobacter* strains into distinct clusters representing 15 different species [26].

Detection of the $bla_{\text{OXA-51-like}}$ gene intrinsic to *A. baumannii* and detection of an internal 208-bp fragment from the *16S-23S rDNA* intergenic spacer region specific of *A. baumannii* represent two PCR-based molecular methods recommended for rapid sorting of *A. baumannii* isolates [27, 28]. Similarly, detection of the $bla_{\text{OXA-134-like}}$ gene intrinsic to *A. lwoffii* could be a putative method for rapid sorting of isolates belonging to this particular species [29].

Table 2. Molecular methods for *Acinetobacter* species identification

	Method	Reference
1.	Whole-genome DNA-DNA hybridisation	[3]
2.	Whole-genome fingerprinting	
	Amplified fragment length polymorphism (AFLP)	[30]
3.	Restriction enzyme analysis of a particular gene/genetic region	
	16S rDNA (ARDRA)[a]	[31]
	16S-23S rDNA intergenic spacer region	[32]
	recA	[33]
4.	Sequence analysis of a particular gene/genetic region	
	16S rDNA	[34]
	16S-23S rDNA intergenic spacer region	[35]
	gyrB	[36]
	recA	[37]
	rpoB	[22]
5.	Analysis of amplicon base composition of several genes (loci)	
	Multilocus PCR followed by electrospray ionization mass spectrometry (PCR/ESI-MS)	[38]
6.	Sequence analysis of several genes (loci)	
	Multilocus sequence typing (MLST)	[39]
7.	Whole-protein fingerprinting	
	Matrix-assisted laser desorption ionization-time-of-flight (MALDI-TOF) mass spectrometry	[26]

[a]Amplified ribosomal DNA restriction analysis

1.3.1. Partial *rpoB* sequence analysis

The degree of polymorphism of housekeeping protein-encoding genes, such as the *recA*, *gyrB*, and *rpoB* genes, has been found higher than that of the non-protein-encoding *16S rDNA* gene [22]. Accordingly, sequence analysis of these genes provides a method with a better level of resolution for the identification and taxonomic classification of various bacterial species. Sequence analysis of four zones of the RNA polymerase β-subunit (*rpoB*) gene and its flanking spacers has been proposed as a useful molecular method for identification of *Acinetobacter* species (Figure 1) [22].

Sequence analysis of the highly discriminative zone 1, spanning 352 bp between positions 2901 and 3250 on the *rpoB* gene, has in particular been found to represent a reliable and rapid identification method for *Acinetobacter* species [22]. The method, named partial *rpoB* gene sequence analysis, has later on been validated on both a collection of *Acinetobacter* reference strains and a collection of *Acinetobacter* clinical

isolates [40]. All the clinical isolates were separated into distinct *Acinetobacter* species with sequence similarities of ≥97.4% with their respective type strains [40]. Recent studies on the delineation of novel *Acinetobacter* species have exploited the sequence analysis of a slightly modified *rpoB* zone 1, spanning 352 bp between positions 2916 and 3267 [19, 20].

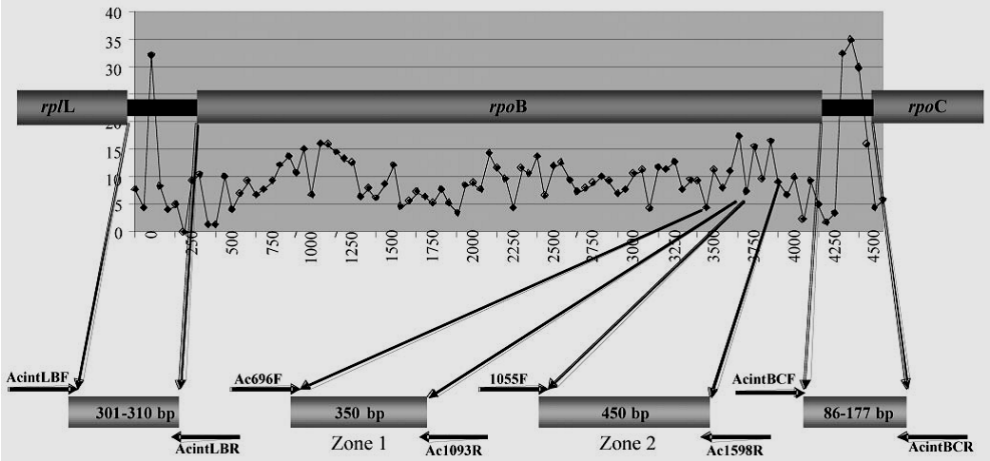

Figure 1. Graphical representation of range site variability in *rpoB* gene and spacer sequences of *Acinetobacter* species in the present study using SVARAP software. The *x* axis indicates the positions of nucleotides, and the *y* axis indicates the percent variabilities for 50 nucleotides. Primers that amplified spacers *rplL-rpoB* and *rpoB-rpoC* and hypervariable partial sequences of *rpoB* bordered by conserved regions are shown (reproduced from reference [22] with permission from American Society for Microbiology).

1.4. Clinical significance

Although cases of community-acquired infections caused by *Acinetobacter* spp. have been reported, the primary pathogenic role of these bacteria is undoubtedly to cause hospital-acquired infections, mainly among patients at intensive care units (ICU) [1]. *Acinetobacter* spp. have been implicated in ventilator-associated pneumonia, catheter-related blood stream infections, urinary tract infections, cerebrospinal-shunt-related meningitis, and wound infections [1]. The risk factors that predispose individuals to get infected with *Acinetobacter* spp. include: (i) patients with major trauma, particularly burns, and patients after major surgeries, (ii) previous antimicrobial therapy, (iii)

prolonged hospital and ICU stay, and (iv) utilization of mechanical ventilators, drainage tubes, and indwelling catheters [24]. Of important note, the human skin and respiratory and gastrointestinal tracts represent important and common sites of colonization by *Acinetobacter* spp. [41]. Accordingly, careful clinical judgment is required to differentiate between infection and colonization cases [42].

1.5. Skin, mucus membranes, and gastrointestinal tract colonization

Acinetobacter species are apparently the only group of Gram-negative bacteria that may be natural residents of human skin [43]. The human skin can thus be a natural reservoir and a probable source of infections of various *Acinetobacter* species [43, 44]. A study from Germany reported high carriage rates of *Acinetobacter* spp. on human skin and mucus membranes among inpatients (~75%) and control non-hospitalized persons (~43%) (Table 3) [43]. The most frequently isolated species in that study were *A. lwoffii* (47%) and *A. johnsonii* (21%). Unpredictably, the clinically important *A. baumannii* and *A. nosocomialis* species (0.5% and 1%, respectively) were not found to be common human skin colonizers [43].

Another study from Europe similarly reported high carriage rates of *Acinetobacter* spp. on human skin of healthy humans (~44%) along with the predominance of *A. lwoffii* (Table 3) [44]. On the other hand, a study conducted in Hong Kong showed that the skin and mucus membranes carriage rates of *A. pittii* (32%), *A. nosocomialis* (14%), and *A. baumanni* (4%) in different groups of patients and healthy subjects were noticeably higher than those reported from Europe (Table 3) [45]. Interestingly, *A. baumannii* isolates recovered from the hands of individuals in the community were distinct from those recovered from patients in two hospitals in New York, the United States of America (USA), indicating that hospitals rather than the community represent a reservoir for nosocomially pathogenic *A. baumannii* [46].

A study conducted in 2005 investigated the carriage rate of *Acinetobacter* spp. in faecal specimens from non-hospitalized individuals from The Netherlands (Table 3) [47]. The study reported a carriage rate of ~25% (31/126 specimens). The predominant species was *A. johnsonii* (17.5%), followed by *A. guillouiae* (4%) whereas only one sample (0.8%) yielded an *A. baumannii* isolate. Accordingly, the human intestine was found not to constitute an important community reservoir of the clinically important *A. baumannii* species [47]. The colonization rate of multidrug resistant *A. baumannii* in faecal samples from hospitalized patients in an intensive care unit in Spain was 41% compared with only ≤ 1% in faecal samples from non-hospitalized individuals from the United Kingdom (UK) and The Netherlands [47, 48]. The Spanish study suggested that the multidrug resistant *A. baumannii* fecal colonization was mainly acquired during ICU hospitalizations [48]. Interestingly, a recent study showed that 6 of 7 patients with *A. baumannii* bloodstream infections were colonized in the gastrointestinal tract with genetically similar strains preceding their bacteremia [49].

Table 3. Distribution of *Acinetobacter* species on the human skin, mucus membranes, and gastrointestinal tract

Description of the *Acinetobacter* spp. collection	Distribution of *Acinetobacter* spp.	Method of identification[a]	Comments	Reference
138 *Acinetobacter* skin and mucous membrane culture isolates obtained between 1993 and 1994 from 30 patients (107 isolates) and 17 healthy controls (31 isolates) in Germany.	*A. lwoffii* (*n*=61) *A. johnsonii* (*n*=27) *A. radioresistens* (*n*=19) *A. pittii* (*n*=12) *A. junii* (*n*=8) *A. nosocomialis* (*n*=2) *A. baumannii* (*n*=1) *A. berezinae* (*n*=1) *Acinetobacter* gen. sp. 15TU (*n*=1) Unclassified (*n*=6)	ARDRA	The *Acinetobacter* skin and mucous membrane carriage rates were 75% (30/40) among inpatients and 43% (17/40) among control non-hospitalized persons. Twenty patients and 6 controls were colonized with two or more different *Acinetobacter* species at different body sites. One patient was colonized by 5 different *Acinetobacter* species at different body sites. In addition, 12 patients and 2 controls were colonized with two or more different *Acinetobacter* species at a same given body site.	[43]
112 *Acinetobacter* skin culture isolates obtained from 85 healthy volunteers from the United Kingdom.	*A. lwoffii* (*n*=68) *Acinetobacter* gen.sp. 15BJ (*n*=14) *A. radioresistens* (*n*=9) *A. pittii* (*n*=4) *A. haemolyticus*/*A. johnsonii* (*n*=2) *A. junii*/*Acinetobacter* gen. sp. 17 (*n*=1) *A. baumannii* (*n*=1) Unclassified (*n*=4)	ARDRA	The *Acinetobacter* skin carriage rate was ~44% (85/192) in healthy humans. 17 volunteers were colonised with two different *Acinetobacter* species (*n*=8) or with two different strains of one *Acinetobacter* species (*n*=9). Only 2 volunteers were colonised with the same *Acinetobacter* strain indicating a very low rate of cross-transmission between healthy subjects working in the same environment.	[44]

Table 3. Distribution of *Acinetobacter* species on the human skin, mucus membranes, and gastrointestinal tract (cont.)

Description of the *Acinetobacter* spp. collection	Distribution of *Acinetobacter* spp.	Method of identification[a]	Comments	Reference
349 *Acinetobacter* skin and mucous membrane culture isolates obtained between January 1997 and March 1998 from 49 patients, 62 nurses, and 90 new nurses and medical students from Hong Kong.	*A. pittii* (*n*=100) *A. nosocomialis* (*n*=60) *A. baumannii* (*n*=39) *Acinetobacter* gen. sp. 17 (*n*=23) *A. johnsonii* (*n*=10) *A . radioresistens* (*n*=10) *A. lwoffii* (*n*=7) *Acinetobacter* gen. sp. 15TU (*n*=8) *Acinetobacter* gen. sp. 15BJ (*n*=8) *A. calcoaceticus* (*n*=6) *A. berezinae* (*n*=3) *Acinetobacter* gen. sp. 16 (*n*=2) *A. junii* (*n*=1) *A. guillouiae* (*n*=2) *Acinetobacter* gen. sp. 13BJ (*n*=1) *Acinetobacter* gen. sp. 14BJ (*n*=1) Unclassified (*n*=67)	ARDRA	The *Acinetobacter* skin and mucous membrane carriage rates were 62% (49/79) among inpatients, 30% (62/210) among nurses (healthy hospital subjects), and 47% (90/192) among new nurses and medical students (healthy subjects from the community). 50% of the subjects who were positive at more than one site had different *Acinetobacter* species. 68% of the subjects who were positive at more than one site with the same *Acinetobacter* species showed that the isolates belonged to different strains.	[45]
35 *Acinetobacter* isolates obtained from faecal samples of non-hospitalized humans from The Netherlands.	*A. johnsonii* (*n*=22) *A. guillouiae* (*n*=5) *A. junii* (*n*=2) *A. ursingii* (*n*=2) *A. baumannii* (*n*=1) *A. pittii* (*n*=1) *A. lwoffii* (*n*=1) *A. berezinae* (*n*=1)	ARDRA	The *Acinetobacter* carriage rate in faecal samples of non-hospitalized humans was ~24.6% (31/126).	[47]

[a]ARDRA, amplified *16S rDNA* restriction analysis.

1.6. Species distribution in clinical isolates

In one of the first studies on the distribution of *Acinetobacter* species among human clinical isolates, *A. pittii* was predominant among *Acinetobacter* clinical isolates from Sweden [6]. Later on, species identification of 23 clinical isolates of the *A. calcoaceticus-A. baumannii* complex from Denmark showed somewhat equivalent distribution between *A. pittii* (8 isolates), *A. nosocomialis* (6 isolates), and *A. baumannii* (5 isolates) [8]. A study from Germany reported *A. baumannii* as the clinically predominant *Acinetobacter* species [50]. However, it is important to mention that identification of the strains at the species level in that study was done phenotypically.

Similarly, the majority of *Acinetobacter* isolates from patients in Belgium and The Netherlands were also found to belong to the *A. baumannii* species [42, 51]. Later on, many studies on the distribution of *Acinetobacter* species in clinical isolates have demonstrated the predominance of *A. baumannii* (Table 4) [40, 52-57]. However, studies from The Netherlands, Hong Kong, and Ireland have reported *A. pittii* as the most commonly detected species while studies from Korea and UK have shown high rates of occurrence of *A. nosocomialis* and *A. lwoffii*, respectively (Table 4) [25, 45, 58-60]. On the other hand, nosocomial infections caused by other *Acinetobacter* species, such as *A. johnsonii*, *A. junii*, *A. parvus*, *A. radioresistens*, *A. schindleri* and *A. ursingii* etc, have generally been less common and mainly represented as individual case reports. Clinial isolates from species other than the *A. calcoaceticus-A. baumannii* complex were mostly obtained in blood cultures and involved in catheter-related bloodstream infections and/or endocarditis [59, 61]. A review of the majority of the studies investigating the species distribution of *Acinetobacter* spp. in clinical isolates is presented in Table 4.

Table 4. Distribution of *Acinetobacter* species in human clinical isolates[a]

***Acinetobacter* spp. collection**	**Distribution of *Acinetobacter* spp.**	**Method of identification[b]**	**Comments**	**Reference**
85 *Acinetobacter* isolates obtained from different sources.	*A. baumannii* (*n*=21) *A. johnsonii* (*n*=12) *A. haemolyticus* (*n*=10) *A. lwoffii* (*n* =9) *A. pittii* (*n*=4) *A. junii* (*n*=4) *A. berezinae* (*n*=4) *A. calcoaceticus* (*n*=3) *A. guillouiae* (*n*=3) *Acinetobacter* gen. sp. 6 (*n*=2) *A. radioresistens* (*n* =2) Unclassified (*n*=11)	DNA-DNA hybridization	*A. calcoaceticus* isolates were all obtained from soil samples. It was not possible to undoubtedly separate *A. lwoffii* and *Acinetobacter* gen. sp. 9 into two species. Three of the unclassified isolates were described as "close to genospecies 1 to 3".	[3]
181 *Acinetobacter* isolates obtained from different sources.	*A. baumannii* (*n*=100) *A. lwoffii* (*n* =25) *A. haemolyticus* (*n*=13) *A. junii* (*n*=13) *A. pittii* (*n*=11) *A. johnsonii* (*n*=11) *A. calcoaceticus* (*n*=5) *Acinetobacter* gen. sp. 6 (*n*=1) *A. guillouiae* (*n*=1) *A. radioresistens* (*n* =1)	Phenotypic scheme	*A. calcoaceticus* isolates were all obtained from soil samples. *A. calcoaceticus*, *A. baumannii*, and *A. pittii* were phenotypically close to each other and far separated from all other species. *A. baumannii* and *A. pittii* were differentiated from each other only by growth at 44°C. Phenotypic tests were not able to differentiate *Acinetobacter* gen. sp. 9 from *A. lwoffii*.	[3]
27 proteolytic *Acinetobacter* clinical isolates differing phenotypically from the 12 previously described *Acinetobacter* species.	*Acinetobacter* gen. sp. 13BJ (*n*=9) *Acinetobacter* gen. sp. 16 (*n*=4) *Acinetobacter* gen. sp. 14BJ (*n*=3) *Acinetobacter* gen. sp. 15BJ (*n* =2) *Acinetobacter* gen. sp. 17 (*n*=2) Unclassified (*n*=7)	DNA-DNA hybridization	The five novel species (*Acinetobacter* gen. sp. 13BJ, *Acinetobacter* gen. sp. 14BJ, *Acinetobacter* gen. sp. 15BJ, *Acinetobacter* gen. sp. 16, and *Acinetobacter* gen. sp. 17) could not be separated unambiguously by biochemical tests from other species.	[5]

Table 4. Distribution of *Acinetobacter* species in human clinical isolates[a] (cont.)

Acinetobacter spp. collection	Distribution of *Acinetobacter* spp.	Method of identification[b]	Comments	Reference
23 clinical isolates phenotypically identified to the *A. calcoaceticus-A. baumannii* complex obtained from Denmark.	*A. pittii* (*n*=8) *A. nosocomialis* (*n*=6) *A. baumannii* (*n*=5) *Acinetobacter* gen. sp. "close to 13TU" (*n*=2) *Acinetobacter* gen. sp. "between 1 and 3" (*n*=2)	DNA-DNA hybridization	-	[8]
420 *Acinetobacter* clinical isolates obtained from 12 hospitals in Germany.	*A. baumannii* (*n*=275) *A. pittii* (*n*=50) *A. johnsonii* (*n*=26) *A. lwoffii* (*n*=21) *A. junii* (*n*=11) *A. haemolyticus* (*n*=8) *A. berezinae* (*n*=7) *A. guillouiae* (*n*=4) *A. radioresistens* (*n*=2) *Acinetobacter* gen. sp. 6 (*n*=1) Unclassified (*n*=15)	Phenotypic scheme of Bouvet and Grimont	*Acinetobacter* spp. were the second most common Gram-negative bacteria isolated from blood cultures accounting for 8.12% of all positive blood cultures, after *E. coli* (8.53%) and outnumbering *Pseudomonas* spp. (7.59%).	[50]
237 *Acinetobacter* clinical isolates obtained during 1990-1991 from different sources from patients hospitalized at one hospital in Belgium.	*A. baumannii* (*n*=128) *A. lwoffii* (*n*=18) *A. haemolyticus* (*n*=14) *A. pittii* (*n*=7) *A. johnsonii* (*n*=6) *A. calcoaceticus* (*n*=3) *Acinetobacter* gen. sp. 6 (*n*=2) *A. junii* (*n*=1) Unclassified (*n*=58)	Phenotypic scheme adapted from the scheme described by Bouvet and Grimont	*Acinetobacter* spp. accounted for ≤1% of positive cultures obtained from skin, respiratory tracts, and urinary tracts.	[51]
58 *Acinetobacter* clinical isolates collected during 1984 and 1985 from 43 patients in four intensive care units and six patients in other wards of a tertiary care hospital in The Netherlands.	*A. baumannii* (*n*=49) *A. pittii* (*n*=8) *A. calcoaceticus* (*n*=1)	SDS-PAGE	-	[42]

Table 4. Distribution of *Acinetobacter* species in human clinical isolates[a] (cont.)

***Acinetobacter* spp. collection**	**Distribution of *Acinetobacter* spp.**	**Method of identification[b]**	**Comments**	**Reference**
52 blood culture isolates of *Acinetobacter* species other than *A. baumannii* obtained between July 1990 and December 1991 at one institute in Germany.	*A. johnsonii* (*n*=14) *A. pittii* (*n*=12) *A. lwoffii* (*n*=10) *A. junii* (*n*=4) *A. berezinae* (*n*=4) *A. radioresistens* (*n*=4) *A. haemolyticus* (*n*=3) *Acinetobacter* gen. sp. 6 (*n*=1) Unclassified (*n*=3)	Phenotypic scheme adapted from the scheme described by Bouvet and Grimont	*Acinetobacter* spp. accounted for 8.1% of the positive blood cultures. *A. baumannii* accounted for 57% of these cultures while *Acinetobacter* species other than *A. baumannii* accounted for 43% of them.	[52]
38 *Acinetobacter* isolates including: 29 clinical isolates obtained during 1989/1990 from 21 patients, 6 environmental isolates also obtained during 1989/1990, and 3 clinical isolates obtained in 1998 from 3 patients. All the isolates were obtained from a Neonatal Intensive Care Unit at one university hospital in The Netherlands.	*A. pittii* (*n*=29) *A. baumannii* (*n*=3) *Acinetobacter* gen.sp. 13BJ (*n*=3) *A. junii* (*n*=1) Unclassified (*n*=2)	DNA-DNA hybridization	The isolation rate of *Acinetobacter* was 8/126 (6.7%) among the environmental samples.	[58]
91 *Acinetobacter* blood culture isolates obtained between January 1997 and March 1998 from 79 patients at one hospital in Hong Kong.	*A. pittii* (*n*=37) *A. baumannii* (*n*=18) *A. nosocomialis* (*n* =14) *Acinetobacter* gen. sp. 17 (*n*=3) *A. berezinae* (*n*=2) *A. lwoffii* (*n* =1) Unclassified (*n*=16)	ARDRA	-	[45]
129 *Acinetobacter* blood culture isolates obtained between 1995 and 1998 at 24 hospitals from the United States of America.	*A. baumannii* (*n*=111) *A. pittii* (*n*=11) *A. radioresistens* (*n*=4) *A. junii* (*n*=2) *A. guillouiae* (*n*=1)	Phenotypic scheme adapted from the scheme described by Bouvet and Grimont	*Acinetobacter* spp. accounted for 1.5% of all nosocomial bloodstream infections. Intra-hospital clonal spread of a single strain occurred in 5 hospitals.	[53]
244 *Acinetobacter* clinical isolates obtained in November 2000 from 28 hospitals in Spain.	*A. baumannii* (*n*=226) *A. pittii* (*n*=15) Unclassified (*n*=3)	ARDRA	7/15 of *A. pittii* isolates grew at 44°C. Identification of these isolates was confirmed by *16S rDNA* sequencing.	[54]

Table 4. Distribution of *Acinetobacter* species in human clinical isolates[a] (cont.)

75 *Acinetobacter* clinical isolates obtained between 2003 and 2005 from 75 patients at one medical center in the United States of America.	*A. baumannii* (*n*=73) *A. pittii* (*n*=1) *A. johnsonii* (*n*=1)	PCR/ESI-MS	The *A. pittii* and *A. johnsonii* two isolates contained $bla_{\text{OXA-51-like}}$ genes which could imply uncertain species identification.	[55]
232 non-duplicate consecutive *Acinetobacter* isolates obtained between November 2004 and November 2005 from different sources (sputum, urine, wound, blood, and throat) at two hospitals in Korea.	*A. baumannii* (*n*=142) *A. nosocomialis* (*n*=60) *A. pittii* (*n*=14) *A. berezinae* (*n*=4) *A. junii* (*n*=2) *A. johnsonii* (*n*=1) *Acinetobacter* gen. sp. 14BJ (*n*=1) Unclassified (*n*=8)	ARDRA	Resistance rates to most antimicrobial agents were higher in *A. baumannii* than other *Acinetobacter* species, except for the resistance rate for imipenem which was higher in *A. nosocomialis* than other *Acinetobacter* species, including *A. baumannii*.	[56]
50 *Acinetobacter* clinical isolates obtained between 2004 and 2005 at a university hospital in Korea and identified by the VITEK GNI card as belonging to the ACB complex.	*A. baumannii* (*n*=40) *A. nosocomialis* (*n*=9) *Acinetobacter* gen. sp. "close to 13TU" (*n*=5) *A. pittii* (*n*=4)	ARDRA	-	[57]
99 *Acinetobacter* clinical isolates obtained between February 2001 and March 2005 from different sources (blood, bone, soft tissue, CSF etc.) from four public hospitals in Marseille, France.	*A. baumannii* (*n*=52) *A. pittii* (*n*=27) *A. haemolyticus* (*n*=10) *A. schindleri* (*n*=5) *A. lwoffii* 9 (*n*=4) *A. nosocomialis* (*n*=1)	Partial sequence analysis of *rpoB*	Isolates of *Acinetobacter* gen. sp. 'between 1 and 3' closely clustered with those of *A. calcoaceticus*. Isolates of *Acinetobacter* gen. sp. 'close to 13TU' closely clustered with those of *Acinetobacter* gen. sp. 13TU.	[40]
107 clinical isolates of *A. calcoaceticus-A. baumannii* complex obtained in 2005-06 from a Public Teaching Hospital in Houston, Texas, the United States of America.	*A. baumannii* (*n*=87) *A. pittii* (*n*=15) *A. nosocomialis* (*n*=3) Unclassified (*n*=2)	ARDRA	66 of the *A. baumannii* isolates belonged to two major PFGE clonal types. ≥ 90% of the *A. baumannii* isolates were multidrug resistant, compared to 15% of the non-*A. baumannii* isolates.	[62]

Table 4. Distribution of *Acinetobacter* species in human clinical isolates[a] (cont.)

***Acinetobacter* spp. collection**	**Distribution of *Acinetobacter* spp.**	**Method of identification[b]**	**Comments**	**Reference**
63 non-duplicate *Acinetobacter* clinical isolates collected from April through November 2007 at ICUs in Korea.	*A. baumannii* (*n*=44) *A. pittii* (*n*=9) *A. nosocomialis* (*n*=6) *A. junnii* (*n*=1) *A. berezinae* (*n*=1) *A. baumannii*-like species (*n*=2)	Partial sequence analysis of *rpoB*, ARDRA, and *gyrB*-based multiplex PCR	Nineteen *A. baumannii* isolates belonged to ST22 and a single PFGE clone.	[63]
114 *Acinetobacter* clinical isolates obtained between May 2005 and October 2007 at one hospital in Dublin, Ireland.	*A. pittii* (*n*=45) *A. baumannii* (*n*=25) *A. johnsonii* (*n*=12) *A. ursingii* (*n*=8) *A. lwoffii* (*n*=7) *A. calcoaceticus* (*n*=5) *A. guillouiae* (*n*=4) *A. nosocomialis* (*n*=2) *A. radioresistens* (*n*=2) *A. berezinae* (*n*=1) *A. haemolyticus* (*n*=1) *A. schindleri* (*n*=1) *A. tjernbergiae* (*n*=1)	Partial sequence analysis of *rpoB*	The study demonstrated the poor accuracy of the speciation of *Acinetobacter* species by the VITEK-2 GNI identification system, with 75% of isolates erroneously speciated.	[25]
96 *Acinetobacter* clinical isolates obtained from 10 university hospitals in Korea between November 2006 and August 2007. The isolates caused either bacteremia (*n*=60) or urinary tract infections (*n*=36).	*A. baumannii* (*n* = 59) *A. nosocomialis* (*n*=19) *A. pittii* (*n*=7) *A. junii* (*n*=5) *A. calcoaceticus* (*n*=2) *Acinetobacter* gen. sp. 16 (*n*=2) *A. berenziae* (*n*=1) *A. baylyi* (*n*=1)	Partial sequence analysis of *rpoB* and *gyrB*-based multiplex PCR	*A. nosocomialis* and *A. pittii* were more frequently isolated from patients with UTIs whereas *A. junii* was isolated exclusively from patients with bacteremia. Thirty-three *A. baumannii* isolates belonged to one sequence type (ST22).	[61]

Table 4. Distribution of *Acinetobacter* species in human clinical isolates[a] (cont.)

***Acinetobacter* spp. collection**	**Distribution of *Acinetobacter* spp.**	**Method of identification[b]**	**Comments**	**Reference**
359 *Acinetobacter* clinical isolates from 331 patients collected between 1999 and 2006 at the Leiden University Medical Centre, The Netherlands.	*A. baumannii* (*n*=129) *A. pittii* (*n*=93) *A. lwoffii* (*n* =38) *A. ursingii* (*n*=15) *A. johnsonii* (*n*=13) *A. junii* (*n*=12) *A. nosocomialis* (*n*=9) *A. calcoaceticus* (*n*=6) *A. beijerinckii* (*n*=5) *A. berezinae* (*n*=4) *A. guillouiae* (*n*=4) *A. radioresistens* (*n* =4) *Acinetobacter* gen. sp. 15TU (*n*=3) *A. haemolyticus* (*n*=3) *Acinetobacter* gen. sp. 14BJ (*n*=3) *A. gyllenbergii* (*n*=2) *Acinetobacter* gen. sp. "close to 13TU" (*n*=1) *Acinetobacter* gen. sp. "between 1 and 3" (*n*=1) *A. parvus* (*n*=1) *Acinetobacter* gen. sp. 16 (*n*=1) Unclassified (*n*=12)	AFLP	Profile similarity cut-off levels of 50%, 80%, and 90% were used for species, clone, and strain/cluster identification, respectively. *A. baumannii* and *A. pittii* were most frequently isolated from sputum and wound samples whereas *A. lwoffii* was mainly isolated from blood samples or intravascular lines. A large cluster of *A. baumannii* (involving 31 patients) and 16 small clusters of various species (involving in total 39 patients) were observed.	[64]
547 *Acinetobacter* clinical isolates obtained in 2008 from 19 different hospitals in six provinces of Korea.	*A. baumannii* (*n*= 388) *A. nosocomialis* (*n*=82) *A. pittii* (*n*=62) *A. berenziae* (*n*=13) *Acinetobacter* gen. sp. 13BJ (*n*=2)	ATB 32 GN system and sequence analysis of *16S–23S rDNA* intergenic spacer region	-	[60]

Table 4. Distribution of *Acinetobacter* species in human clinical isolates[a] (cont.)

***Acinetobacter* spp. collection**	**Distribution of *Acinetobacter* spp.**	**Method of identification[b]**	**Comments**	**Reference**
690 *Acinetobacter* clinical isolates obtained during 2008/2009 from 135 hospitals in the United Kingdom.	*A. baumannii* (*n* = 538) *A. lwoffii* (*n* =61) *A. ursingii* (*n* =28) *A. pittii* (*n*=12) *A. johnsonii* (*n*=11) *A. parvus* (*n*=9) *Acinetobacter* gen. sp. 13BJ (*n*=6) *A. radioresistens* (*n* =4) *A. baylyi*/*A guillouiae* (*n*=3) *A. calcoaceticus* (*n*=3) *A. nosocomialis* (*n*=2) *A. haemolyticus* (*n*=2) *A. junii* (*n*=2) *A. beijerinckii* (*n*=1) *A. berenziae* (*n*=1) *A. gyllenbergii* (*n*=1) *A. schindleri* (*n*=1) *Acinetobacter* gen. sp. 15TU (*n*=1) *Acinetobacter* gen. sp. 16 (*n*=1) Unclassified (*n*=3)	Partial sequence analysis of *rpoB*	*A. baylyi* and *A guillouiae* clustered too closely to be distinguished from one another. Three isolates did not cluster closely enough with any of the described species. For all three, the closest currently described species was *A. towneri*.	[59]

[a]Some studies included both clinical and environmental samples.
[b]ARDRA, amplified *16S rDNA* restriction analysis; SDS-PAGE, cell envelope protein sodium dodecyl sulphate-polyacrylamide gel electrophoresis; PCR/ESI-MS, polymerase chain reaction/electrospray ionization mass spectrometry; AFLP, Amplified fragment length polymorphism.

1.7. Antibiotic resistance

Treatment of *Acinetobacter* infections has conventionally involved the use of ß-lactams, aminoglycosides, and quinolones [1]. However, the increased use of these antibiotics has resulted in a widespread emergence of antibiotic resistant strains [1]. Carbapenems, a class of β-lactams with a broad-spectrum of antibacterial activity, have then widely been used as the mainstay for treatment of infections caused by such antibiotic resistant strains [24]. Unsurprisingly, *Acinetobacter* strains resistant to carbapenems have also rapidly emerged worldwide [24]. Different levels and patterns of antimicrobial susceptibilities have been found among different *Acinetobacter* species with several studies reporting a higher occurrence of multidrug resistance in *A. baumannii* compared with the non-*A. baumannii* species [59, 64, 65]. Furthermore, intra-species diversity of antimicrobial susceptibilities has also been reported with specific genotypes in the *A. baumannii* population demonstrating higher resistance rates to antimicrobial agents compared with other *A. baumannii* genotypes [61].

It is important to mention that incorrect or uncertain species identification has probably resulted in an inaccurately-reported occurrence of some resistance genes in specific *Acinetobacter* species. A study conducted in 1992 reported the characterization of an AmpC cephalosporinase produced by *A. calcoaceticus* strain CCM 5593 [66]. However, strain CCM 5593 actually belongs to *A. baumannii* according to the LMG catalogue provided by the Laboratory of Microbiology at University of Gent in Belgium (http://bccm.belspo.be/db/lmg_search_form.php). A study from USA reported the occurrence of bla_{TEM}, bla_{SHV}, and bla_{ADC} genes in an *A. pittii* isolate (AG073) and an *A. johnsonii* isolate (AJ075) [55]. However, the two isolates were found to contain the *A. baumannii*-intrinsic $bla_{\text{OXA-51-like}}$ gene which could probably imply uncertain species identification [28].

IMP-4 was reported to occur in an *A. junii* isolate [67]. However, the study used VITEK GNI card and API 20NE for species identification and these systems have repeatedly been associated with incorrect species identification of *Acinetobacter* isolates [24].

bla$_{ADC}$ might similarly be present in the chromosome of *A. lwoffii* although the species identification of the isolates was uncertain [68]. Furthermore, a recent review reported the occurrence of *bla*$_{CTX-M-43}$ in *A. baumannii* although the original article referred to the isolates as *Acinetobacter* spp. [2, 69].

1.7.1. Intrinsic resistance

Intrinsic resistance is defined as the inherent (not acquired) resistance against an antimicrobial drug which is a characteristic of all or almost all representatives of the species (http://www.eucast.org/expert_rules/). The antimicrobial activity of the drug is accordingly insufficient and the drug is clinically inadequate (http://www.eucast.org/expert_rules/). Consequently, antimicrobial susceptibility testing against the drug is unnecessary (http://www.eucast.org/expert_rules/). In this regard, *A. baumannii* and *A. calcoaceticus* are intrinsically resistant to ampicillin, amoxicillin-clavulanate, cefazolin, cefotaxime, ceftriaxone, ertapenem, trimethoprim, and fosfomycin according to the expert rules in antimicrobial susceptibility testing of the European committee on antimicrobial susceptibility testing (EUCAST) (http://www.eucast.org/expert_rules/). Due to the activity of sulbactam, *A. baumannii* does not have intrinsic resistance against ampicillin-sulbactam (http://www.eucast.org/expert_rules/).

1.7.2. Resistance to ß-lactams

Resistance to β-lactams in *Acinetobacter* involves: (i) the production of β-lactamases, (ii) alterations in the affinity to penicillin-binding proteins, (iii) decreased permeability of the outer membrane due to changes in the structure or number of porin proteins, and (iv) increased activity of efflux pumps (Figure 2) [70, 71].

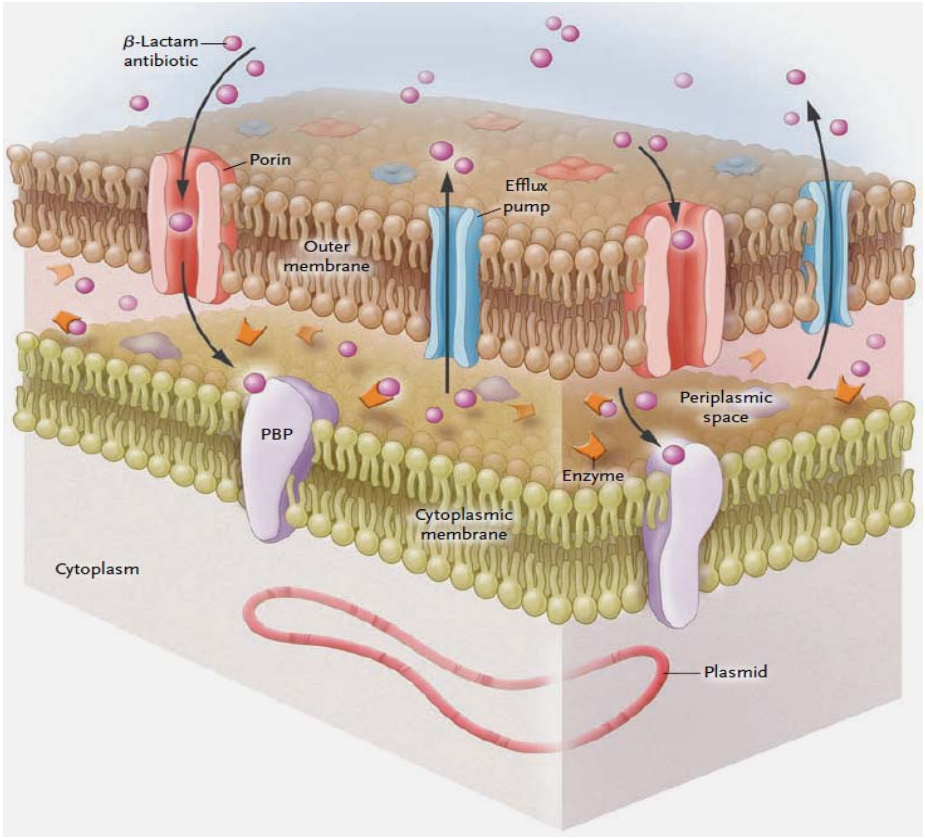

Figure 2. Mechanisms of β-lactam resistance. *Acinetobacter*, like other gram-negative bacteria, has an outer membrane and a cytoplasmic membrane, between which (the periplasmic space) β-lactamases (carbapenemases, AmpC β-lactamases, and extended-spectrum β-lactamases) reside. Penicillin-binding proteins (PBPs), located at the level of the cytoplasmic membrane, constitute the final targets of β-lactam antibiotics. To bind to these targets, antibiotics must traverse the outer membrane through porin channels (outer-membrane proteins) into the periplasmic space. Once in the periplasmic space, β-lactam antibiotics bind to PBPs or are actively expelled from the bacterial structure through efflux pumps. *Acinetobacter* can harbor integrons and transposons, genetic elements on the bacterial chromosome or on plasmids, that can carry multiple cassettes with resistant genes (e.g., extended-spectrum β-lactamases and metallo-β-lactamases) (reproduced from reference [70] with permission from The New England Journal of Medicine).

The over-expression of intrinsic and/or the horizontal obtaining of acquired β-lactamase genes encoding enzymes from the four different molecular classes (A-D) is the main mechanism of *Acinetobacter* resistance to β-lactams [70, 71]. A wide range of class A β-lactamases including the narrow-spectrum (TEM-1, TEM-2, CARB-5, and SCO-1), extended-spectrum (TEM-92, TEM-116, SHV-2, SHV-5, SHV-12, CTX-M-2, CTX-M-3, CTX-M-43, PER-1, PER-2, PER-6, VEB-1, VEB-1a, VEB-3, GES-11, and GES-12), and carbapenem-hydrolyzing (GES-14, KPC-2, KPC-3, KPC-4 and KPC-10) variants have been identified mainly in *A. baumannii* but also among *Acinetobacter* isolates from other

species [24, 69, 72-77]. Class A β-lactamase genes are generally considered to be less widespread among *Acinetobacter* than *Enterobacteriaceae* species [71]. However, assessment of the true prevalence of extended-spectrum class A β-lactamases in *Acinetobacter* might be underestimated since it has been hindered by difficulties with laboratory detection, especially in the presence of intrinsic AmpC enzymes [2, 78].

Class B β-lactamases (metallo-β-lactamases, MBLs) confer high levels of carbapenem resistance as well as resistance to all other ß-lactams except for aztreonam [79]. MBLs are characterized from other classes of β-lactamases by being susceptible to EDTA inhibition due to the requirement of zinc ions (Zn^{+2}) in the active site [79]. Several IMP (IMP-1, IMP-2, IMP-4, IMP-5, IMP-6, IMP-8, IMP-11) and VIM (VIM-1, VIM-2, VIM-4, and VIM-11) variants have been detected among isolates from the *A. baumannii-A. calcoaceticus* complex [57, 73, 79-82]. SIM-1 was first described in *A. baumannii* isolates from Korea [83]. The study reported a lower level of carbapenem resistance conferred by SIM-1 compared with that conferred by IMP and VIM variants [83]. To my knowledge, $bla_{\text{SIM-1-like}}$ genes have so far been found only among *Acinetobacter* isolates from Korea [83-85]. All different variants of bla_{IMP}, bla_{VIM}, and bla_{SIM} in *A. baumannii* isolates have regularly been located on class 1 integrons [79]. NDM-1 has mainly been found in *Enterobacteriaceae* isolates particularly from the Indian subcontinent but has also been detected in *A. baumannii* isolates from India as well as from other parts of the world [86-88]. Interestingly, resistance to carbapenems mediated by the coexistence of $bla_{\text{NDM-1}}$, bla_{OXA23}, and bla_{IMP} has been detected in pan-drug resistant *A. baumannii* isolates from China [88]. NDM-2, a variant of NDM-1 with only one amino acid substitution, has recently been described in an *A. baumannii* isolate recovered from a patient transferred to Germany from Egypt [89].

Class C β-lactamases (AmpC cephalosporinases) are enzymes able, when over-expressed, to hydrolyze most penicillins, cephalothin, cefazolin, cefoxitin, ceftazidime and ß-lactamase inhibitor/ß-lactam combinations, but generally not cefepime or carbapenems [90]. So far, the chromosomal-encoded AmpC cephalosporinase genes have only been identified in a few *Acinetobacter* species (*A. baumannii*, *A. pittii*, and *A. baylyi*) [54, 90].

Phylogenetic analysis demonstrated that AmpC cephalosporinases from *A. baumannii* and *A. pittii* are more closely related to each other than to the variants produced by other genera of bacteria [91]. Accordingly, these enzymes represent a distinct family of class C β-lactamases called "the *Acinetobacter*-derived cephalosporinases (ADCs)". Although the AmpC cephalosporinase from *A. baylyi* (designated as ADC-8) was considerably less homologous to ADC-5 from *A. pittii* and ADC-7 from *A. baumannii*, the phylogenetic proximity of all the ADC cephalosporinases, including ADC-8, appeared to evolve from a common ancestor [92]. The bla_{ADC} genes in *A. baumannii* are normally expressed at basal levels [90]. The key factor for high levels of expression of these genes is based on the presence of a strong promoter within an upstream insertion sequence known as IS*Aba1* [90]. ADC enzymes are the main mechanism responsible for resistance to ceftazidime and other extended-spectrum cephalosporins in *A. baumannii* [55]. To date, at least 44 bla_{ADC} genes have been identified [73].

Class D β-lactamases (OXA-type β-lactamases) are robust penicillinases given that all of them are able to significantly hydrolyze aminopenicillins (e.g. ampicillin and amoxicillin) and carboxypenicillins (e.g. carbencillin and ticarcillin) [93]. Some of the OXA-type β-lactamase variants also have the ability to hydrolyze extended-spectrum cephalosporins whereas other variants, described as OXA-type carbapenemases, are able to hydrolyze carbapenems [93]. Most of the extended-spectrum OXA-type β-lactamases are basically point mutation derivatives of related narrow-spectrum enzymes while all the so far identified OXA-type carbapenemases are remotely related to the non-carbapenem-hydrolysing OXA-type β-lactamases [93, 94]. OXA-20, OXA-21 and OXA-37 are the only narrow-spectrum OXA-type β-lactamases that have so far been identified in *Acinetobacter* isolates (*A. baumannii*) [93]. The genes for these three enzymes have been identified in the form of gene cassettes inserted into class 1 integrons [93]. None of the extended-spectrum OXA-type β-lactamases has yet been found in any *Acinetobacter* species [93]. In contrast, OXA-type carbapenemases, with the exception of $bla_{\text{OXA-48}}$, have almost exclusively been found among isolates of the genus *Acinetobacter* (several species) [25, 59, 73, 93, 95-98].

The OXA-type carbapenemase genes in *Acinetobacter* spp. can be divided into four phylogenetic subgroups of (*bla*$_{\text{OXA-23-like}}$, *bla*$_{\text{OXA-24-like}}$, *bla*$_{\text{OXA-51-like}}$, and *bla*$_{\text{OXA-58-like}}$) plus five discrete genes (*bla*$_{\text{OXA-134}}$, *bla*$_{\text{OXA-104}}$, *bla*$_{\text{OXA-143}}$, *bla*$_{\text{OXA-164}}$, and *bla*$_{\text{OXA-182}}$) (Figure 3). The variants within each of the four main subgroups have nucleotide sequence identities of ≥ 96% whereas the nucleotide sequence identities of the variants from different subgroups, including the discrete genes, range from 46% to 76% (Table 5). Exceptions include a 92% nucleotide sequence identity between *bla*$_{\text{OXA-143}}$ and *bla*$_{\text{OXA-182}}$ and ~88% nucleotide sequence identity between *bla*$_{\text{OXA-24-like}}$ subgroup with either *bla*$_{\text{OXA-143}}$ or *bla*$_{\text{OXA-182}}$ (Table 5).

The substrate profiles of OXA-type carbapenemases are diverse with most of them showing only a low hydrolytic activity against imipenem and yet a lower hydrolytic activity against meropenem [94]. The OXA-type carbapenemases additionally hydrolyse the narrow-spectrum penicillins (e.g. benzylpenicillin, ampicillin, piperacillin, ticarcillin) and cephalosporins (e.g. cefalotin and cefaloridine) efficiently. On the other hand, the extended-spectrum ß-lactams (e.g. ceftazidime, cefotaxime) and aztreonam are not or only very poorly hydrolyzed by these enzymes [94]. It is worth mentioning that the occurrence of OXA-type carbapenemase genes in *Acinetobacter* spp. represents vertical inheritance in specific species but horizontal acquisition in other species. The subgroup *bla*$_{\text{OXA-23-like}}$ for instance is intrinsically present and chromosomally located in *A. radioresistens* while it is acquired and most likely plasmid mediated in *A. baumannii*. The subgroup *bla*$_{\text{OXA-51-like}}$ and the variant *bla*$_{\text{OXA-134}}$ are intrinsically present in *A. baumannii* and *A. lwoffii*, respectively.

Table 5. Nucleotide sequence identities among the OXA-type carbapenemase subgroups and discrete genes in *Acinetobacter* spp.

bla_{OXA}	$bla_{OXA-164}$	$bla_{OXA-182}$	$bla_{OXA-143}$	$bla_{OXA-104}$	$bla_{OXA-134}$	$bla_{OXA-58-like}$	$bla_{OXA-24-like}$	$bla_{OXA-23-like}$	$bla_{OXA-51-like}$
$bla_{OXA-51-like}$	60-64%	67-69%	67-68%	75-76%	59-61%	49-53%	63-65%	61-63%	96-100%
$bla_{OXA-23-like}$	63-64%	69-70%	68-69%	61-62%	65-66%	49-52%	69-71%	96-100%	
$bla_{OXA-24-like}$	62-63%	87-88%	87%	64%	64-65%	51%	97-100%		
$bla_{OXA-58-like}$	49%	51%	53%	46-47%	53%	97-100%			
$bla_{OXA-134}$	66%	65%	63%	67%	100%				
$bla_{OXA-104}$	60%	62%	62%	100%					
$bla_{OXA-143}$	64%	92%	100%						
$bla_{OXA-182}$	67%	100%							
$bla_{OXA-164}$	100%								

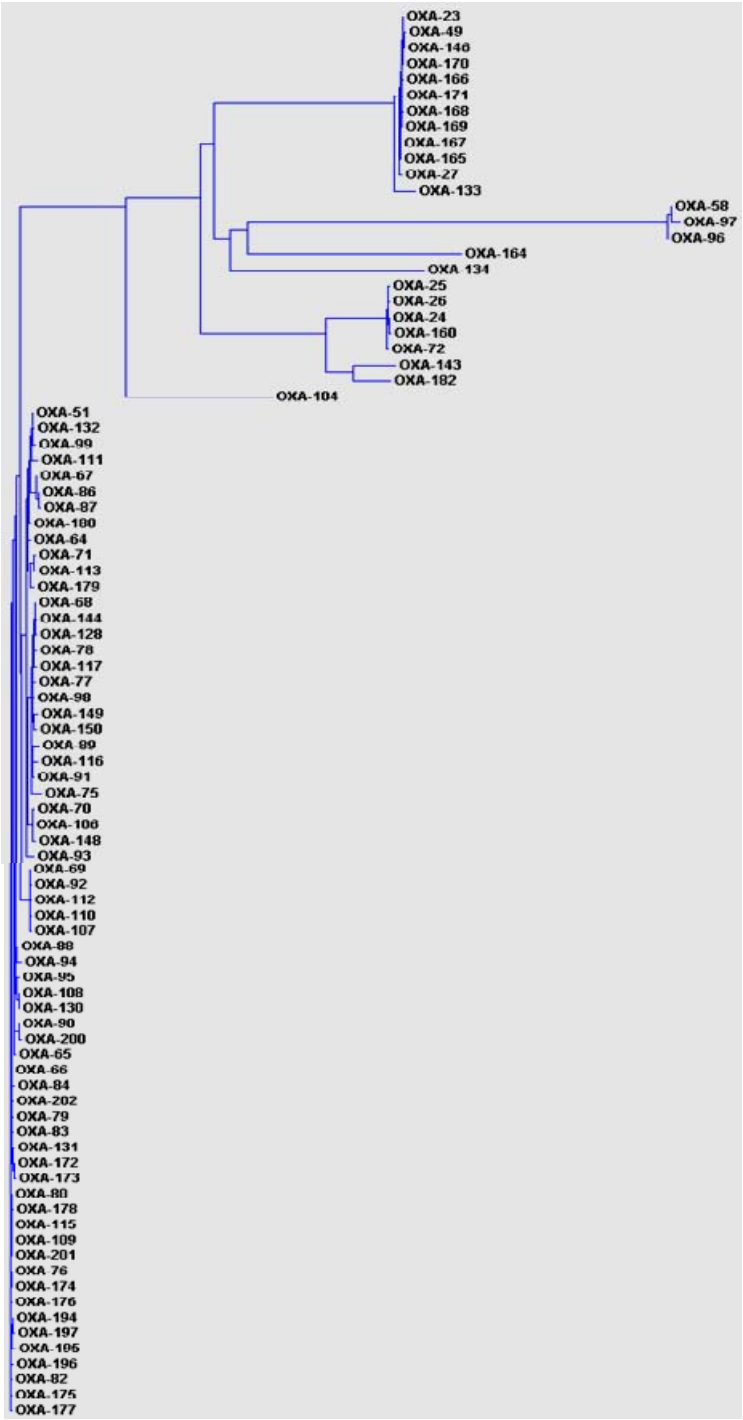

Figure 3. Dendrogram of 90 OXA-type carbapenemase genes identified in *Acinetobacter* spp. obtained using the online multiple sequence alignment program ClustalW. Branch lengths are to scale and proportional to the number of amino acid changes. The distance along the vertical axis has no significance.

1.7.3. Resistance to aminoglycosides

Enzymatic modification of aminoglycosides by acetyltransferases, nucleotidyltransferases and/or phosphotransferases accounts for the majority of aminoglycoside-resistant *Acinetobacter* isolates [99]. Several aminoglycoside-modifying enzymes have been detected in different *Acinetobacter* species (*A. baumannii*, *A. pittii*, *A. nosocomialis*, and *A. johnsonii*), including: (i) the phosphotransferases APH(3')-Ia, APH(3')-VIa, APH(3')-II (encoded by *aphA1*, *aphA6*, *aphA15*, respectively), (ii) the acetyltransferases AAC(3)-Ia, AAC(3)-IIa, AAC(6')-Ib, AAC(6')-Iad, AAC(6')-Im, and AAC(6')-II (encoded by *aacC1*, *aacC2*, *aacA4*, *aac*(*6'*)*-Iad*, *aac(6')-Im*, and *aac(6')-II*, respectively), and (iii) the nucleotidyltransferases ANT(2")-Ia, ANT(3")-Ia, and ANT(3")-Id (encoded by *aadB*, *aadA1*, and *aadA4*, respectively) [25, 73, 99-102].

The occurrence of a combination of two or more of aminoglycoside-modifying resistance genes and the association of some of these genes (such as *aacC1*, *aacA4*, *aadA1* and *aadB*) with class 1 integrons has been reported [99]. Nonetheless, reduction of accumulation of aminoglycosides is also fairly common in *Acinetobacter* isolates [71]. Lately, *A. baumannii* strains producing the 16S rRNA methylase ArmA enzyme have been identified [103]. ArmA is plasmid-encoded and characterized by conferring a high-level of pan-aminoglycoside resistance compared with a usually moderate-level of resistance against particular aminoglycosides resulting from production of the previously mentioned aminoglycoside-modifying enzymes [102]. The coexistence of *armA* with two carbapenem resistance genes, $bla_{\text{OXA-23}}$ and $bla_{\text{NDM-1}}$, has recently been reported in three clinical isolates from India [86].

1.7.4. Resistance to quinolones

Resistance to quinolones in *Acinetobacter* species is mostly due to chromosomal mutations in the quinolone resistance determining region (QRDR) of the *gyrA* and *parC* genes with the subsequent production of modified bacterial DNA gyrase and

topoisomerase IV enzymes [71]. Ser-83 and Ser-80 in GyrA and ParC, respectively, are the most frequently mutated amino acid residues in quinolone-resistant *A. baumannii* (Table 6) [104, 105]. A double mutation in the QRDRs of both GyrA and ParC is basically necessary to obtain high levels of quinolone resistance [105]. Nonetheless, quinolone resistance could also be due to decreased influx and/or increased efflux of quinolones [71]. Of note, plasmid-mediated quinolone resistance genes, including *aac*(6')-*Ib-cr* and *qnr*, have so far been not identified in *Acinetobacter* isolates [106].

Table 6. Amino acid substitutions in the quinolone resistance determining region (QRDR) of *gyrA* and *parC* implicated in quinolone resistance in *A. baumannii*

Amino acid substitutions	Reference
GyrA	
Gly-81 substituted by Val or Cys	[104, 107]
Ser-83[a] substituted by Leu	[104]
Ala-84 substituted by Pro	[104]
Glu-87 substituted by Gly	[108]
ParC	
Gly-78 substituted by Cys	[107]
Ser-80[a] substituted by Leu, Phe or Trp	[105, 108, 109]
Glu-84 substituted by Lys	[105]

[a]Mutations Ser-83 to Leu in GyrA and Ser-80 to Leu in ParC were also reported in quinolone-resistant isolates of *A. pittii* [54].

1.7.5. Role of IS*Aba* elements

Insertion sequences (IS) are the smallest (< 2.5 kb) and most abundant genetic elements capable of independent mobility (transposition) in microbial genomes [110]. IS elements can be responsible for the occurrence of insertion mutations, genome rearrangements, and enhanced spread of resistance and virulence determinants within species [110]. Several IS elements have commonly and probably exclusively been detected in the genus *Acinetobacter* (Table 7) (http://www-is.biotoul.fr) [111].

Studies have demonstrated the role of IS*Aba1* in providing a strong promoter resulting in over-expression of the intrinsic bla_{ADC} and $bla_{\text{OXA-51-like}}$ and the acquired $bla_{\text{OXA-23-like}}$ genes of *A. baumannii* [112-114]. IS*Aba1* most probably acts similarly with other resistance genes such as *sulI1* and $bla_{\text{OXA-58-like}}$, [111, 115]. IS*Aba2*, IS*Aba3*, IS*18*, and

IS*Aba825* might also provide strong hybrid promoters for $bla_{\text{OXA-58-like}}$ whereas IS*Aba4* may likewise be responsible for an enhanced expression of $bla_{\text{OXA-23-like}}$ [114-116]. Furthermore, sequence analysis of the genetic environment of $bla_{\text{NDM-1}}$ in one *A. baumannii* isolate from Germany revealed a chromosomal occurrence of $bla_{\text{NDM-1}}$ on a 10.5 kb genetic structure bracketed by two copies of IS*Aba125* [117]. The upstream IS*Aba125* element most likely provides a strong promoter for $bla_{\text{NDM-1}}$ expression [118]. Interestingly, the bla_{ADC} gene in the fully sequenced *A. baumannii* strain ACICU is also preceded by an IS*Aba125* element that could influence its expression [119].

IS*Aba1* might also be responsible for the mobility of $bla_{\text{OXA-23-like}}$ with either two copies bracketing the gene and forming a composite transposon defined as Tn*2006* or a single copy located at one side of the gene and forming a one-ended transposon defined as Tn*2008* [106, 114]. Similarly, a single copy of IS*Aba4* located at one side of $bla_{\text{OXA-23-like}}$ might mobilize it by forming a one-ended transposon defined as Tn*2007* [114]. An IS*Aba1*-mediated disruption of the *adeS* gene which regulates the expression of the multidrug AdeABC efflux pump was detected in two tigecycline-resistant isolates [120]. The insertional inactivation of *adeS* was probably responsible for a constitutive over-expression of the pump leading to increased resistance to various classes of antibiotics. Furthermore, IS*Aba825* and IS*Aba125* have been found responsible for reduced susceptibility to carbapenems by means of a natural insertional inactivation of the *carO* gene encoding an outer membrane channel associated with the influx of carbapenems *A. baumannii* [121].

Table 7. Insertion sequence (IS) elements in the genus *Acinetobacter* retrieved from the IS database homepage (http://www-is.biotoul.fr).

Name	Family	GenBank accession number	Origin
IS*Aba1*	IS*4*	AY758396	*A. baumannii*
IS*Aba2*	IS*3*	AY665723	*A. baumannii*
IS*Aba3*	IS*1*	AY665723	*A. baumannii*
IS*Aba4*	IS*982*	-	*A. baumannii*
IS*Aba5*	IS*5*	-	*A. baumannii*
IS*Aba6*	IS*982*	-	*A. baumannii*
IS*Aba7*	IS*5*	-	*A. baumannii*
IS*Aba8*	IS*21*	-	*A. baumannii*
IS*Aba9*	IS*982*	-	*A. baumannii*
IS*Aba10*	IS*5*	GQ379223	*A. baumannii*
IS*Aba11*	IS*701*	CP000521	*A. baumannii*
IS*Aba12*	IS*5*	-	*A. baumannii*
IS*Aba13* (IS*N1*)	IS*5*	NC_011586	*A. baumannii*
IS*Aba125*	IS*30*	AY751533	*A. baumannii*
IS*Aba825*	IS*982*	AY751532	*A. baumannii*
IS*Aca1*	IS*3*	AF121266	*A. calcoaceticus*
IS*1008*	IS*6*	AJ251307	*A. calcoaceticus*
IS*1236*	IS*3*	U03772	*A. calcoaceticus*
IS*Aha1*	IS*5*	-	*A. haemolyticus*
IS*Aha2*	IS*5*	-	*A. haemolyticus*
IS*17*	IS*5*	U95013	*A. haemolyticus*
IS*Ajo1*	IS*5*	-	*A. johnsonii*
IS*Alw1*	IS*5*	-	*A. lwoffii*
IS*1006*	IS*6*	NC_004361	*A. junii*
IS*Acsp1*	Tn*3*	-	*Acinetobacter* sp.
IS*1007*	IS*6*	AJ250860	*Acinetobacter* sp. LS56-7
IS*18*	IS*30*	AF043676	*Acinetobacter* sp. 13 BM2716

1.8. Epidemiology of *A. baumannii*

Among the different *Acinetobacter* species, *A. baumannii* has a remarkable ability to cause outbreaks of infections [24]. The occurrence of intra-hospital, local inter-hospital, and national *A. baumannii* outbreaks of infections have been reported worldwide [2]. Comparative typing of outbreak strains from geographically scattered European hospitals has demonstrated the occurrence of three extremely successful clones of *A. baumanni* named as "European clones I, II and III" [122, 123]. The three European clones have later on been found to disseminate globally and have accordingly been re-named as "international clones I, II and III" [39]. A significant shift towards international clone II, rather than international clone I, has lately been detected in the global *A. baumannii* population structure [124]. Multidrug resistance has been a frequent feature of the three clones although these clones have included strains with notable variations in their susceptibility patterns and underlying resistance genes [124]. However, a wide geographic distribution of several other clones, beyond international clones I to III, has also been detected [39, 125-127]. These clones have most likely played a supplementary role in the global dissemination of *A. baumannii* infections [39].

1.8.1. Molecular strain typing methods

Several molecular methods have been used to type *A. baumannii* strains at different scales [24]. A PCR-based typing scheme targeting three genes under selective pressure (*ompA*, *csuE* and $bla_{\text{OXA-51-like}}$) is a convenient method for rapid assorting of *A. baumannii* isolates into three major sequence groups (SG) corresponding to the previously mentioned international clones I (SG2), II (SG1), and III (SG3) [128]. Isolates can also be assigned into additional PCR-based sequence groups (SG4-SG7, putative SG8, SG9, and putative SG10-SG13) defined according to new combinations of the PCR amplicons (Table 8) (Papers II and III) [126, 129, 130]. Of note, the labels proposed for the PCR-based SGs don't correspond to the labels proposed by another typing approach based on comparitive sequence analysis of the same three genes [126, 127, 129].

Table 8. Sequence groups of *A. baumannii* defined according to combinations of amplicons in two multiplex PCRs targeting the *ompA*, *csuE* and $bla_{\text{OXA-51-like}}$ genes.

PCR-based sequence group (SG)	Group 1 multiplex PCR			Group 2 multiplex PCR			Reference
	***csuE* (702)**	**$bla_{\text{OXA-51-like}}$ (559)**	***ompA* (355)**	***csuE* (580)**	***ompA* (343)**	**$bla_{\text{OXA-51-like}}$ (162)**	
SG1 (international clone II)	+	+	+	-	-	-	[128]
SG2 (international clone I)	-	-	-	+	+	+	[128]
SG3 (international clone III)	+	+	-	-	+	-	[128]
SG4	-	+	+	-	-	-	[126]
SG5	-	-	+	-	-	-	[126]
SG6	+	-	-	-	+	+	[126]
SG7	-	-	+	+	-	-	[126]
SG8[a]	-	+	+	+	-	-	[129]
SG9	-	-	+	+	-	+	Paper II
SG10	-	+	-	+	+	-	[130]
SG11	-	-	-	-	+	+	[130]
SG12	-	+	-	-	-	-	Paper III
SG13	+	-	+	-	-	-	Paper III

[a]Assigned into group 6 according to the 3 locus sequence-based typing approach.

Sequence-based analysis of only the $bla_{\text{OXA-51-like}}$ gene can also be a useful typing method for *A. baumannii* isolates since evident correlation has been detected between particular $bla_{\text{OXA-51-like}}$ variants and particular epidemic lineages [131, 132]. In this regard, a study conducted on sixty *A. baumannii* isolates collected worldwide has demonstrated that isolates belonging to international clone II encoded $bla_{\text{OXA-51-like}}$ variants from the OXA-66 cluster while those belonging to international clone I encoded enzymes from the OXA-69 cluster [131, 132]. Furthermore, the study has shown that all isolates belonging to international clone III encoded $bla_{\text{OXA-71}}$ standing by itself without forming a cluster with other variants [131, 132].

Nevertheless, pulsed-field gel electrophoresis (PFGE) is still considered to be the `gold standard` for fine-scale typing of *A. baumannii* isolates [131]. PFGE, based on the generation of distinct patterns of chromosomal DNA, is able to detect the intra- and inter-hospital bacterial transmission providing a method especially suited for local short-term outbreak investigations [133]. However, it has a main disadvantage that data are hardly exchangeable among laboratories making it inappropriate for comparative epidemiological analyses of results obtained at different laboratories [133]. On the other hand, multilocus sequence typing (MLST), based on the comparative sequence analyses of loci from seven house-keeping genes, offers the possibility to transfer typing data

between laboratories and via the internet, making it an appropriate technique for global and long-term epidemiological studies [131].

Currently, two *Acinetobacter* MLST schemes are available for typing of *A. baumannii* strains. The Bartual scheme (http://pubmlst.org/abaumannii/) is based on DNA sequence comparisons of the internal fragments of seven housekeeping genes (*gltA*, *gyrB*, *gdhB*, *recA*, *cpn60*, *gpi*, and *rpoD*) [133]. However, analysis of *gyrB* and *gpi* sequences should be performed with caution since the phylogenetic trees generated for these two genes showed evidence of recombination and were inconsistent with those of the other five genes [131]. Similarly, the Pasteur scheme (http://www.pasteur.fr/recherche/genopole/PF8/mlst/) is based on DNA sequence comparisons of the internal fragments of seven housekeeping genes including three genes from the Bartual scheme (*gltA*, *recA*, and *cpn60*) plus four other genes (*fusA*, *pyrG*, *rpoB*, and *rplB*) [39]. The two schemes have generally showed compatible results although a recent study has reported a higher resolution of the Bartual MLST scheme providing a better association between epidemiological features, occurrence of acquired OXA genes, and temporal distribution of the isolates [134-136].

In general, PFGE and MLST should be considered as complementary tools to each other in epidemiological studies [137]. PFGE has a higher discriminatory power for small-sized local epidemiological studies while MLST has a better capability for grouping isolates mainly during large-sized global epidemiological analyses.

1.8.2. Epidemiological terminology

The definition of some terms, such as strain and clone, has repeatedly been discussed by epidemiological reviews [138]. For example, an isolate represents a general term used to describe a pure culture of bacteria, usually obtained by sub-culturing a single colony from a preliminary isolation plate, while a strain is a taxonomic term used to describe a subdivision of a species [139]. A strain can be defined as an isolate or group of isolates

that can be distinguished from other isolates of the same species by a number of phenotypic and/or genotypic characteristics [139]. An outbreak strain is a strain responsible for the occurrence of an outbreak of infections (an increased incidence of infections in a specific place during a given period that is above the baseline rate for that place and time frame) [139]. An outbreak strain will accordingly represent a group of epidemiologically, genotypically, and phenotypically related isolates [139]. Such isolates (outbreak isolates) are assumed to be a progeny of a recent single common precursor isolate.

Since PFGE is considered to be the `gold standard` for outbreak investigations, an outbreak strain can molecularly be defined as a group of isolates obtained within a limited time and place frames that show identical or related pulsotypes (PFGE restriction patterns). Currently, similarities among pulsotypes are usually determined using the band-based Dice coefficient. However, optimum settings for optimization and tolerance have not yet been agreed on. Cluster analysis of pulsotypes is commonly performed using the unweighted pair group method with mathematical averaging (UPGMA). A cut-off level of 90% can be proposed for strain delineation [140].

On the other hand, a clone is a group of epidemiologically unrelated (independently obtained from different sources, in different locations, and perhaps at different times) but genotypically and phenotypically related isolates [141]. Such isolates (epidemic isolates) are believed to be progeny of an old single common precursor isolate. Since MLST is the main tool for global population studies, a clone will practically be defined as a group of isolates obtained from more than one country and belong to one MLST sequence type or clonal complex. The occurrence in at least two countries is subjectively chosen to minimize the probability of a recent inter-hospital spread either by a direct patient transfer or by an intermediate circulation in the community [122]. The definition could be biased since it does not take into consideration the countries' size or the occurrence of import. Nonetheless, the occurrence of import should always be highlighted (Papers II and III). Of note, a clonal complex (CC) is a group of related sequence types (ST) sharing alleles at 5/7 or 6/7 of the loci (http://eburst.mlst.net/v3/instructions/2.asp). The terms

"clonal complex" and "clone" are not interchangeable; a clonal complex represents a clone only when it includes epidemiologically unrelated isolates obtained from more than one country.

1.8.3. Proposed nomenclature

The nomenclature of *A. baumannii* outbreak strains should probably include the time and place of occurrence and the pulsotype. Further phenotypic and/or genotypic characterization of the strain can then be used in order to describe the outbreak strain. For instance, outbreak strains can be designated as MDR- (for multidrug-resistance), *bla*$_{\text{OXA-24-like}}$-CR- (for *bla*$_{\text{OXA-24-like}}$-positive carbapenem-resistance), Tn*2006*-*bla*$_{\text{OXA-23-like}}$-CR- (for Tn*2006*-mediated *bla*$_{\text{OXA-23-like}}$-positive carbapenem-resistance) etc. It could also be valuable to include the corresponding ST and CC in the description of *A. baumannii* outbreak strains in order to allow a comprehensive assignment of these strains in a global context [142].

On the other hand, since the MLST allelic profiles are unambiguous and exchangeable, MLST provides an optimal naming system for *A. baumannii* clones rather than giving them roman numerals or letters [131]. The clones can be designated according to their STs and CCs together with their geographic distribution [39]. In contrast to outbreak strains, clones are believed to represent descendants of an old progenitor. Accordingly, the occurrence of broad intra-clonal diversity, with strains possessing a variety of phenotypic and genotypic resistance characteristics, can be anticipated [99]. Phenotypic and genotypic characterization of the clones could therefore be less essential than that of the outbreak strains. The higher discriminatory power of PFGE can also be exploited in the characterization of clones and probably the identification of sub-clones. However, since they are generally not interchangeable, PFGE data should be included with some caution [131].

1.8.4. MLST-based global population of *A. baumannii*

Analysis of a subset of 441 *A. baumannii* isolates, selected from other studies and from the MLST databases, might facilitate making an unbiased overview of the current structure of the global *A. baumannii* population [39, 60, 61, 72, 82, 127, 130, 131, 133-137, 142-146] (Papers II and III) (http://www.pasteur.fr/recherche/genopole/PF8/mlst/) (http://pubmlst.org/abaumannii/). The selection included one isolate per country per ST (geographically and genotypically divergent isolates) while other isolates from the same country with the same ST were rather considered as replicates of an outbreak strain and were excluded regardless if they were divergent by date of isolation or by their phenotypic and genotypic resistance characteristics. STs were grouped into CCs using eBURST V3 (http://eburst.mlst.net/) under stringent parameters (6/7 shared allels). However, an ST or CC would subjectively represent a clone only if included isolates from more than one country.

The collection included isolates typed using the Bartual's scheme (*n*=277), Pasteur's scheme (*n*=129), or both schemes (*n*=35) (Tables S1-S3). To differentiate between the two MLST schemes, STs and CCs were designated as ST^{B}/CC^{B} for the Bartual scheme and ST^{P}/CC^{P} for the Pasteur scheme. The isolates belonged to 246 Bartual's STs (ST1-88^{B}, ST90-110^{B}, ST112-187^{B}, ST189-197^{B}, $ST200^{B}$, and ST202-252^{B}) and 83 Pasteur's STs (ST1-32^{P}, ST34-59^{P}, ST77-86^{P}, ST94-106^{P}, $ST109^{P}$, and $ST110^{P}$) (http://pubmlst.org/abaumannii/) (http://www.pasteur.fr/recherche/genopole/PF8/mlst/).

Overall, the analysis assigned 243/441 of the isolates into 22 clones including sixteen international (≥two continents) clones, five European clones, and one Asian clone (Table 9) (Table 9 and Figures 4 and 5). On the other hand, 198/441 of the isolates were assigned into non-clonal STs or CCs (STs or CCs geographically restricted to one country).

1.8.4.1. International clone CC92^{B}/CC2^{P}

CC92^{B}/CC2^{P} was by far the largest *A. baumannii* clone with 88/441 of the isolates and a very broad international spread over 32 countries (Italy, Spain, Germany, UK, Greece, The Netherlands, Denmark, Czech Republic, France, Poland, Turkey, Norway, Sweden, Portugal, Ireland, Japan, China, Korea, Thailand, India, Malaysia, Philippines, Taiwan, Singapore, Vietnam, Lebanon, Brazil, South Africa, Reunion, Tahiti, New Caledonia, USA, and Australia). The Norwegian isolates were associated with import from other European or Asian countries (Paper II). CC92^{B}/CC2^{P} mainly included outbreak, MDR, and/or carbapenem-resistant (*bla*$_{\text{VIM-1}}$-, *bla*$_{\text{OXA-23-like}}$-, *bla*$_{\text{OXA-24-like}}$-, and/or *bla*$_{\text{OXA-58-like}}$-encoding) isolates. It also included several isolates producing the 16S rRNA methylase ArmA enzyme and one isolate resistant to colistin. Interestingly, an equine isolate was found to belong to this clone as well.

The occurrence of ST92^{B} isolates resistant to all antimicrobial agents available including colistin, polymyxin B, and tigecycline was also reported by a study from Korea although the isolates have not been submitted into the MLST database [63]. The intra-clonal diversity of phenotypic and genotypic resistance characteristics among isolates of CC92^{B}/CC2^{P} is most likely due to the scattered spread of these clones throughout the world resulting in an access to a wide range of varied pools of transmissible resistance elements [99]. The analysis confirmed the linkage between CC92^{B}/CC2^{P}, international clone II, and the *bla*$_{\text{OXA-66}}$, *bla*$_{\text{OXA-82}}$, *bla*$_{\text{OXA-83}}$, and *bla*$_{\text{OXA-109}}$ variants (OXA-66 cluster) of the intrinsic *bla*$_{\text{OXA-51-like}}$ gene [131, 132].

1.8.4.2. International clone CC109^{B}/CC1^{P}

CC109^{B}/CC1^{P} was the second major *A. baumannii* clone with 51/441 of the isolates and a broad international spread over 29 countries (Germany, Italy, China, Libya, the United Arab Emirates, Bahrain, Norway, Argentina, India, Japan, Bulgaria, UK, Australia, Korea, Poland, Slovenia, Croatia, Czech Republic, Ireland, Belgium, South Africa, Spain,

France, USA, Greece, The Netherlands, Lebanon, Turkey, and Algeria). One isolate from UK and the two Norwegian isolates were associated with import from Pakistan and India (Paper II) [131, 132]. Similar to the previous clone, CC109^{B}/CC1^{P} also included many outbreak, MDR, and carbapenem-resistant (*bla*$_{VIM-4}$-, *bla*$_{OXA-23-like}$-, and/or *bla*$_{OXA-58-like}$-encoding) isolates.

The clone was closely linked with international clone I and the *bla*$_{OXA-69}$, *bla*$_{OXA-107}$, *bla*$_{OXA-110}$ and *bla*$_{OXA-112}$ variants (OXA-69 cluster) [131, 132]. One isolate (K55-61) was assigned into CC1^{P} by Pasteur's scheme (ST94^{P}) but represented a singleton (ST194^{B}) rather than being a member of CC109^{B} by Bartual's scheme (Paper II). However, ST194^{B} is a DLV of several STs from CC109^{B}. Furthermore, this isolate interestingly contained *bla*$_{OXA-69}$ but belonged to sequence group 9, instead of international clone I (Paper II). This might probably indicate that sequence group 9 represents a sub-group of international clone I. One isolate of ST248^{B} (singleton) was reasonably found to encode *bla*$_{OXA-92}$ from the OXA-69 cluster since ST248^{B} is a DLV of several STs from CC109^{B} [132].

1.8.4.3. International (South and North American) clone CC131^{B}

CC131^{B} has so far been a South and North American clone with 18/441 of the isolates obtained from Argentina, Brazil, and USA. The clone included several hospital environmental isolates (personnel hand, cushion, bed-rail, soap dispenser etc.) (http://pubmlst.org/abaumannii/). A probable linkage could be present between CC131^{B} and the singleton ST79^{P} from the Pasteur's scheme [130]. Interestingly, two of the CC131^{B} isolates belonged to international clone II [130, 131]. The two isolates also encoded for *bla*$_{OXA-66}$ and *bla*$_{OXA-65}$ from the OXA-66 cluster [130, 131]. ST79^{P} and ST121^{B}, a DLV of several STs from CC131^{B}, included isolates recovered from Spain indicating that the distribution of this clone could probably be not restricted to South and North America [137].

1.8.4.4. International clone CC187^{B}/CC3^{P}

CC187^{B}/CC3^{P} was an international clone with 12/441 of the isolates obtained mainly from European countries (France, Germany, Spain, The Netherlands, Italy, and Belgium) as well as from Lebanon. CC187^{B}/CC3^{P} was closely linked with international clone III and the *bla*$_{\text{OXA-71}}$ variant of *bla*$_{\text{OXA-51-like}}$ genes [131, 132]. Many of the CC187^{B}/CC3^{P} isolates were MDR and/or carbapenem-resistant (*bla*$_{\text{OXA-58-like}}$-encoding) and were associated with outbreaks of infections. A canine isolate was assigned into ST13^{P} which was found to be a DLV of ST3^{P}. Of note, the less intra-clonal diversity within CC187^{B}/CC3^{P}, compared with CC92^{B}/CC2^{P}, was proposed to indicate short-term existence [99].

1.8.4.5. International clone CC104^{B}/CC15^{P}

CC104^{B}/CC15^{P}, another international clone, included 12/441 of the isolates obtained from 8 countries in Europe and South America (Norway, Portugal, Czech Republic, The Netherlands, Turkey, Spain, Argentina, and Brazil). The Norwegian isolate was however associated with import from Pakistan (Paper II). This clone included outbreak, MDR, carbapenem resistant (*bla*$_{\text{OXA-23-like}}$-and *bla*$_{\text{OXA-58-like}}$-positive), and *armA*-encoding isolates. The analysis detected a linkage between CC104^{B}/CC15^{P}, PCR-based sequence group 4, and encoded the intrinsic *bla*$_{\text{OXA-51}}$ and *bla*$_{\text{OXA-132}}$ variants (Paper II) [130, 134]. Two isolates from ST249^{B} and ST250^{B}, DLVs of CC104^{B}, were also found to encode the *bla*$_{\text{OXA-51}}$ variant [131]. Of note, *bla*$_{\text{OXA-132}}$ and *bla*$_{\text{OXA-51}}$ are one nucleotide different from each other (GenBank accession numbers EU547447 and AJ309734, respectively).

1.8.4.6. Other clones

The analysis also identified CC20^{B} as another international clone with 10/441 of the isolates recovered from Germany, Morocco, South Africa, Malaysia, Korea and China. Interestingly, the clone included one *bla*$_{OXA-23-like}$- and *armA*-encoding isolate [144]. In addition, another *bla*$_{OXA-23-like}$- and *armA*-encoding isolate belonged to ST248^{B} which was found to be a DLV of ST20^{B} [144]. Isolates from CC20^{B} encoded the intrinsic *bla*$_{OXA-51}$ and *bla*$_{OXA-68}$ variants. However, *bla*$_{OXA-51}$ and *bla*$_{OXA-68}$ did not belong to a one group of variants [132]. International clone CC110^{B} included 5/435 of the isolates obtained from Korea, Argentina, and USA. Interestingly, the CC110^{B} isolate from China was colistin resistant [144]. European clone CC32^{P} included 5/441 of the isolates obtained from Sweden, Denmark, Spain, and Portugal. One of the CC32^{P} isolates was *bla*$_{IMP-5}$-positive carbapenem-resistant.

Interestingly, clonal spread was also identified for a number of singleton STs (e. g. ST17^{B}, ST19^{B}, ST73^{B}, ST184^{B}, ST25^{P}, and ST49^{P}) [61]. This probably indicates a fast spread associated with limited time for these strains to genetically differentiate and create clonal complexes of many variants which might be a result of immaturity of these genotypes or due to a shortened life length possibly caused by an effective eradication. International clone ST73^{B} included only two isolates (2/435) with one of them being *bla*$_{OXA-23-like}$-positive carbapenem-resistant. International clone ST25^{P} included 6/441 of the isolates obtained from The Netherlands, Turkey, Greece, Italy, Sweden, and Singapore. The Swedish isolate was associated with import from Thailand (Paper III). Carbapenem resistance was prevalent in clone ST25^{P} since 5/6 of the isolates were *bla*$_{OXA-23-like}$-, *bla*$_{OXA-58-like}$-, and/or *bla*$_{OXA-24-like}$-positive carbapenem-resistant. Other clones are listed in Table 9.

1.8.4.7. Non-clonal STs and CCs

A large fraction of the isolates (~45%) was assigned into STs or CCs geographically restricted to one country. Interestingly, several clonal complexes such as CC164^{B}, CC(32/33/46/47)^{B}, and CC(85/86)^{B} etc. did not represent clones. For instance, CC164^{B} could basically represent a Korean 2008 outbreak strain although it included 5 isolates from 5 different STs. Many STs were found to include sporadic (not associated with an outbreak) strains. However, a number of non-clonal STs, such as ST96^{B} and ST78^{P}, were found to include outbreak strains [127, 142]. ST12^{B} included one isolate (RUH 875) from international clone I although RUH 875 was assigned into completly different ST by another study [39, 131-133]. Interestingly, non-epidemic ST2^{B} and ST134^{B} included isolates encoding the *bla*$_{\text{OXA-96}}$ variant [130, 131, 133].

The occurrence of isolates of international clone II within non-epidemic singleton ST252^{B} and ST59^{P} was unexpected. In contrast to what has previously been reported, ST59^{P} and CC2^{P} diverged by 4 or 5 of the seven allels [39]. Furthermore, *bla*$_{\text{OXA-108}}$ encoded by the ST252^{B} isolate was also not related to the OXA-66 cluster [132]. This could probably indicate a long-termed descent from a single ancestor, lack in the discriminatory power of the PCR-based clonal lineage typing method, or occasional inaccuracy in experimental results.

Finally, the identification of many singleton STs demonstrated a high genetic diversity of the population structure of *A. baumannii* [143]. Such broad diversity has previously been reported using other typing techniques [42, 147].

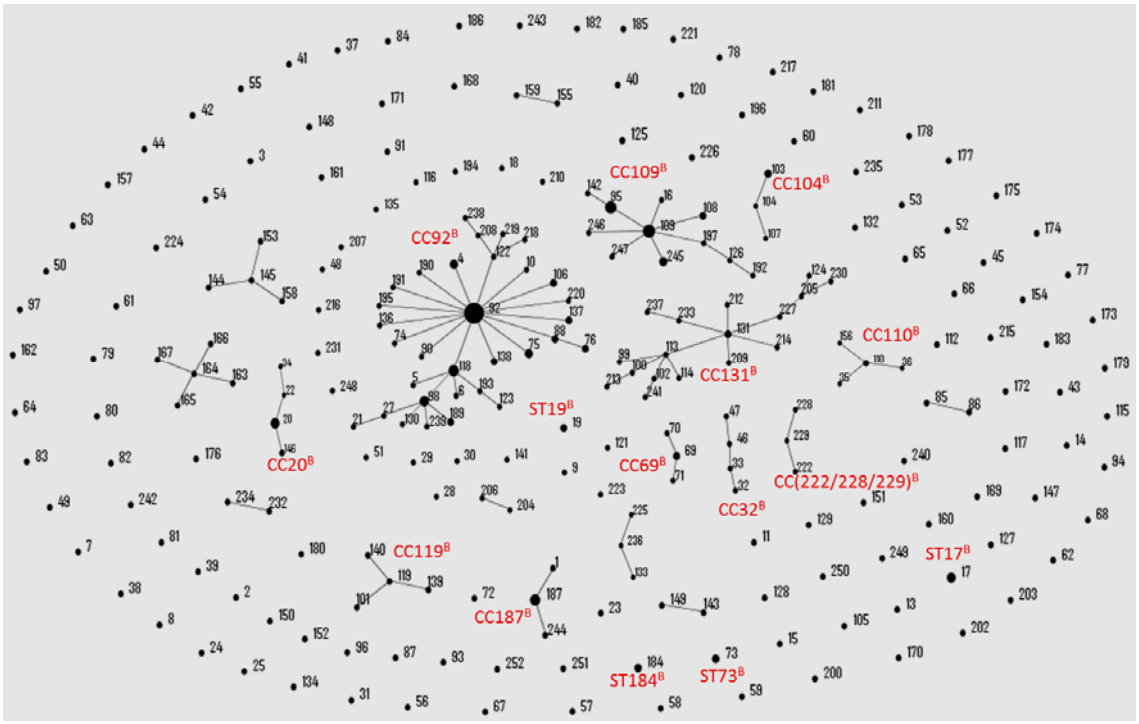

Figure 4. eBURST of 313 *A. baumannii* isolates investigated by the Bartual`s MLST scheme (Tables S1 and S3). Each circle corresponds to one sequence type (ST). Circle size increases logarithmically with the number of isolates of each ST. Each line indicates that the connected circles correspond to STs sharing 6/7 of the allels. Each group of circles linked by at least one line corresponds to one clonal complex (CC). Distance between circles does not correspond to the number of allelic mismatches among the corresponding STs. Each circle or group of circles highlighted in red corresponds to one clone.

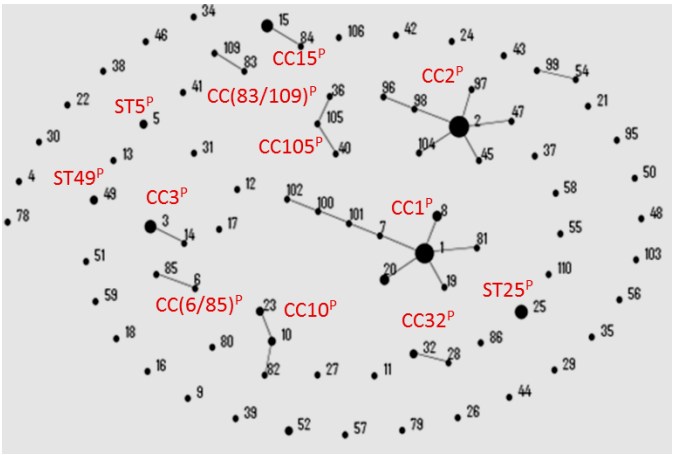

Figure 5. eBURST of 129 *A. baumannii* isolates investigated by the Pasteur`s MLST scheme (Table S2). Each circle corresponds to one sequence type (ST). Circle size increases logarithmically with the number of isolates of each ST. Each line indicates that the connected circles correspond to STs sharing 6/7 of the allels. Each group of circles linked by at least one line corresponds to one clonal complex (CC). Distance between circles does not correspond to the number of allelic mismatches among the corresponding STs. Each circle or group of circles highlighted in red corresponds to one clone.

Table 9. The geographic distribution of MLST-designated *A. baumannii* clones

***A. baumannii* clone**[a]	**Geographic distribution**[b]
$CC92^{B}/CC2^{P}$	International clone with 88 isolates recovered from 32 countries in Europe, Asia, Africa, Australia, North America, and South America
$CC109^{B}/CC1^{P}$	International clone with 51 isolates recovered from 29 countries in Europe, Asia, Africa, The Middle East, Australia, and South America
$CC131^{B}$	South and North American clone with 18 isolates recovered from Argentina, Brazil, and USA
$CC187^{B}/CC3^{P}$	International clone with 12 isolates recovered from 6 European countries and Lebanon
$CC104^{B}/CC15^{P}$	International clone with 12 isolates obtained from 8 countries in Europe and South America (One isolate was exported from Pakistan)
$CC20^{B}$	International clone with 10 isolates recovered from 7 countries in Europe, Asia, and Africa
$CC110^{B}$	International clone with 5 isolates recovered from Korea, Argentina, and USA
$CC32^{P}$	European clone with 5 isolates recovered from Sweden, Denmark, Spain, and Portugal
$CC119^{B}$	International clone with 4 isolates recovered from Korea, Thailand, and Argentina
$CC69^{B}$	International clone with 4 isolates recovered from Korea and Australia
$ST25^{P}$	International clone with 6 isolates recovered from Europe and Asia
$CC10^{P}$	International clone with 5 isolates recovered from 4 European countries and Australia
$CC(222/228/229)^{B}$	International clone with 3 isolates recovered from Brazil and Japan
$ST17^{B}$	International clone with 3 isolates recovered from Germany, China, and Korea
$CC105^{P}$	International clone with 3 isolates recovered from Czech Republic and China
$ST19^{B}$	European clone with 2 isolates recovered from Germany and UK
$ST73^{B}$	International clone with 2 isolates recovered from Australia and Korea
$ST184^{B}$	Asian clone with 2 isolates recovered from China and Korea
$ST5^{P}$	European clone with 2 isolates recovered from Poland and Sweden[b]
$CC(6/85)^{P}$	European clone with 2 isolates recovered from UK and Greece
$CC(83/109)^{P}$	European clone with 2 isolates recovered from Turkey and Sweden[c]
$ST49^{P}$	International clone with 2 isolates recovered from The Netherlands and USA

[a]$CC110^{B}$ and $CC(222/228/229)^{B}$ were DLVs of each other; $CC69^{B}$ and $ST19^{B}$ were DLVs of $CC92^{B}$; $ST49^{P}$ was a DLV of $ST3^{P}$

[b]USA, the United States of America; UK, the United Kingdom.

[c]Could probably represent a polish outbreak-related or endemic strain since the isolate from Sweden was exported from Poland.

[d]Could probably represent an international clone since the isolate from Sweden was exported from Thailand.

2. Aims of the study

The main aim of paper I was to determine the distribution of *Acinetobacter* species in a nation-wide collection of consecutive blood culture isolates from Norway.

Papers II and III aimed to investigate the molecular epidemiology and antibiotic resistance characteristics of carbapenem-resistant clinical isolates of *A. baumannii* obtained in Norway and Sweden, respectively.

Paper IV was designed to compare the performance of three commercial systems (VITEK 2, BD Phoenix, and MALDI-TOF MS) for precise species identification of *Acinetobacter* clinical isolates.

3. Material

A collection of 113 consecutive blood culture isolates of *Acinetobacter* species was included in paper I. The isolates were collected between 2005 and 2007 from 111 patients by 19 diagnostic microbiology laboratories throughout Norway. Four isolates recovered from two patients were included since they were found to belong to different species.

Paper II included 11 carbapenem resistant *A. baumannii* clinical obtained between 2004 and 2009 from 11 patients from different specimens (blood, pus, respiratory secretions, abdominal cavity fluid and spinal fluid) by six different diagnostic microbiology laboratories in Norway. The study included all the isolates submitted to the Reference Centre for Detection of Antimicrobial Resistance in Norway based on carbapenem resistance according to guidelines issued by the Reference Centre.

Paper III included 13 *A. baumannii* clinical isolates collected between 2004 and 2007 from 11 patients from different cultures (blood, pus, respiratory secretions, and abdominal cavity fluid) by two laboratories in Stockholm and Kalmar, Sweden. Three isolates recovered from one patient were included since they were found to belong to different epidemiological lineages. All isolates were non-susceptible to imipenem or meropenem according to SRGA (Swedish Reference Group for Antibiotics) disk diffusion methodology (http://www.srga.org/RAFMETOD/BASMET.HTM) and breakpoints (http://www.srga.org/ZONTAB/zontab2a.htm).

Paper IV included 110/113 of the isolates described in paper I. Three isolates were excluded given that they were identified as ‘unclassified’ using partial *rpoB* sequence analysis (Paper I).

4. Main results

Paper I

- The study revealed that partial *rpoB* sequence analysis was able to correctly assign the majority of the isolates (110/113) into at least 12 different *Acinetobacter* species.
- Molecular identification revealed that *A. nosocomialis* (46.9%) and *A. pittii* (19.5%) were the most prevalent *Acinetobacter* species whereas *A. baumannii* only accounted for 8.8% of the isolates.
- The study represented the first report on the putative clinical relevance of *A. soli*.
- Less than 5% of the isolates expressed reduced susceptibility to one or more of the antimicrobial agents.
- $bla_{\text{OXA-23-like}}$ was detected in all three carbapenem-susceptible *A. radioresistens* isolates and in one carbapenem-resistant *A. baumannii* isolate. $bla_{\text{OXA-23-like}}$ was associates with an upstream IS*Aba1* element only in the *A. baumannii* isolate.
- A novel mutation, Ser-80 to Tyr, in the QRDR of ParC was identified in one *A. baumannii* isolate showing high-level resistance to ciprofloxacin, levofloxacin and nalidixic acid.

Paper II

- The isolates belonged to $CC2^{P}/CC92^{B}$/international clone II (*n*=7), $CC1^{P}/ST194^{B}$/SG9 (*n*=2), $CC1^{P}/CC109^{B}$/international clone I (*n*=1), and $ST15^{P}/CC104^{B}$/SG4 (*n*=1).
- Resistance to carpabenems was due the occurrence of acquired OXA-carbapenemase genes including: $bla_{\text{OXA-23-like}}$ (*n*=9), $bla_{\text{OXA-24-like}}$ (*n*=1), and $bla_{\text{OXA-58-like}}$ (*n*=1).
- Analysis of the genetic environment of $bla_{\text{OXA-23-like}}$ revealed a putative occurrence of Tn*2006* and Tn*2008* in seven and one isolates, respectively.
- High levels of aminoglycoside-resistance, detected in four isolates, were associated with identification of the 16S rRNA methylase *armA* gene.
- Class 1 integrons with six different variable regions carrying various combinations of eight resistance genes were detected in seven isolates.

Paper III

- The isolates belonged to ST2^{P}/international clone II (*n*=6), ST23^{P}/SG5 (*n*=2), ST25^{P}/SG12 (*n*=2), ST5^{P}/SG7 (*n*=1), and ST109^{P}/SG13 (*n*=2).
- Resistance to carpabenems was due the occurrence of acquired OXA-carbapenemase genes including: *bla*$_{\text{OXA-58-like}}$ (*n*=7), *bla*$_{\text{OXA-23-like}}$ (*n*=5), and *bla*$_{\text{OXA-24-like}}$ (*n*=1).
- IS*Aba825* was detected upstream of *bla*$_{\text{OXA-58-like}}$ in two isolates.
- None of the previously known IS elements were detected upstream of *bla*$_{\text{OXA-58-like}}$ in one isolate.
- Class 1 integrons with three different variable regions carrying various combinations of six resistance genes were detected in six isolates.

Paper IV

- VITEK 2 correctly identified 9 *A. baumannii* and 3 *A. lwoffii* isolates to the species level. BD Phoenix correctly identified 5 *A. baumannii* isolates to the species level. On the other hand, MALDI-TOF MS correctly identified 22 *A. pittii*, 10 *A. baumannii*, 8 *A. lwoffii*, 3 *A. ursingii*, 3 *A. radioresistens*, and 1 *A. calcoaceticus* isolates to the species level.
- Only MALDI-TOF MS was able to distinguish isolates of *A. pitti* from those of *A. baumannii*.
- None of the three commercial systems was able to identify isolates of *A. nosocomialis*.

5. Discussion

5.1. Species distribution in blood culture isolates from Norway

A. baumannii has frequently been considered the most clinically relevant *Acinetobacter* species worldwide [24]. However, our study revealed that only 10/113 (8.8%) of the consecutive blood culture isolates of *Acinetobacter* species from Norway belonged to *A. baumannii*. The study showed that *A. nosocomialis* and *A. pittii* were the most predominant *Acinetobacter* species with 53/113 (46.9%) and 23/113 (19.5%) of the isolates, respectively (Paper I). A drawback of my study was the lack of clinical data on each case, including the separation between colonization and infection, determination of injury severity scores, utilization of mechanical ventilation and catheterization, application of antimicrobial therapy, and outcomes.

The ability to persist on inanimate dry surfaces (humidifiers, hospital equipments, furniture, mattresses) and animate (human skin and mucus membranes) objects is probably a main factor in the long-term existence of particular *Acinetobacter* spp. in the hospital setting which subsequently results in a prolonged opportunity to infect patients [71]. However, although *A. baumannii* is the most prevalent *Acinetobacter* species in clinical samples, it is not the most prevalent *Acinetobacter* species in the hospital environment. *A. radioresistens* was more commonly detected than *A. baumannii* among environmental specimens obtained from pillows at one Dutch hospital [148]**.** Besides, *A. pittii* was more commonly detected than *A. baumannii* on the skin of patients and student nurses from Hong Kong [45]. *A. lwoffii* and *A. johnsonii* were the most commonly detected *Acinetobacter* species on skin and mucus membranes of inpatients and control non-hospitalized persons from Germany [43].

A study from USA showed that among 87 *A. baumannii* clinical isolates, 61 isolates (70%) were associated with infection and only 26 isolates (30%) were associated with colonization whereas among 20 non-*A. baumanni* clinical isolates, only 2 isolates (10%)

were associated with infection and 18 isolates (90%) were associated with colonization [62]. Accodingly, *A. baumannii* probably demonstrates an increased ability to infect, rather than to colonize, and then to cause an outbreak of infections, compared to other *Acinetobacter* species [24, 62]. The explanation could basically be that *A. baumannii* is genotypically more able to infect a vulnerable patient (probably following a temporary/prolonged colonization of the patient's gastrointestinal tracts) and then to cross-infect more patients (probably via a temporary/prolonged colonization of the hands of healthcare professionals or contamination of a medical device) compared to the non-*A. baumannii* species [24, 49].

Therefore, in addition to the incorrect and uncertain species identification applied by some studies, the reason why many studies from different countries have repeatedly reported *A. baumannii* to be more prevalent in clinical speciemens than other *Acinetobacter* species could, in my opinion, be because these studies have included replicates of the same strain. A recent Dutch study revealed that *A. baumannii* was involved in one large cluster (32 isolates) and nine small clusters (2-5 isolates) of isolates whereas other species (*A. ursingii*, *A. pittii*, *A. nosocomialis*, *A. berezinae*, and *A. beyerinckii*) were all together involved in only seven small clusters (2-5 isolates) [64]. The study showed that *A. baumannii* would be more prevalent than *A. pitti* if all the isolates were included. However, *A. baumannii* would be as common as *A. pitti* if the large cluster of *A. baumannii* was not included. Furthermore, *A. pitti* would exceed *A. baumannii* in the number of isolates if the small clusters were not included.

The limited contribution of *A. baumannii* in our collection of *Acinetobacter* blood culture isolates might therefore be due to (i) the presence of better conditions in the Norwegian clinical settings (less-crowded hospitals), (ii) the restricted use of antibiotics, and (iii) the application of more strict infection control regimes in Norway compared to other countries [149]. These factors will restrict the capacity of *A. baumannii* (more than other *Acinetobacter* species) to infect and cross-infect patients. Improvements in the health sector of some countries might, in my opinion, change the *Acinetobacter* species distribution in clinical isolates. However, epidemiological studies should, in my opinion,

never exclude replicate isolates as long as obtained from different patients since this would under-estimate the high ability of particular species (such as *A. baumannii*) to infect and cross-infect patients.

5.2. Predominance of CC92^{B}/CC2^{P}/international clone II

Analysis of the molecular epidemiology of *A. baumannii* clinical isolates obtained from Norway and Sweden yielded results consistent with other studies on the extensive distribution of CC92^{B}/CC2^{P}/international clone II worldwide (Papers II and III). Several factors and several approaches of evolution might be proposed to explain the predominance of this clone, and other clones, in the global population of *A. baumannii* (Figure 6).

The occurrence of a successful spread for isolates of CC92^{B}/CC2^{P}/international clone II might be due to a large clonal spread of one recent ancestor. The theory has been supported by a study from Korea showing that all the carbapenem-resistant ST92^{B} isolates obtained from five cities belonged to one outbreak pulsotype [144]. Furthermore, eight of nine carbapenem-resistant isolates of ST92^{B} obtained from three continents showed related PFGE patterns [135]. The nation-wide and worldwide spread of isolates is probably provoked by the massive increase of international travel, including transfer of patients among different countries.

On the other hand, the worldwide spread of CC92^{B}/CC2^{P}/international clone II could also be related to independent but parallel emergence of smaller clones expanding from several progenitors and probably one older ancestor. The carbapenem-resistant ST92^{B} isolates obtained from 16 cities in China (n=72) were distributed among at least three outbreak pulsotypes [142]. Furthermore, a number of carbapenem-resistant ST92^{B} isolates from China belonged to sporadic pulsotypes [144]. Similarly, distinct pulsotypes were assigned to isolates from the CC92^{B} obtained in Norway (Paper II). The similarity in resistance traits and determinants among isolates of distinct pulsotypes (proposed to be

independently-emerging) could be due to comparable selection pressures in different parts of the world [99]. Of note, using PFGE data to compare the two theories might consider by some authors as a main drawback since PFGE may lose its discriminatory power when analyzing isolates from geographically diverse areas [131].

One factor to explain the predominance of $CC92^{B}$/$CC2^{P}$/international clone II could be that specific genotypes probably have increased capacity for epidemic spread than other genotypes. In other words, particular strains are genotypically more able to spread than other strains. Nonetheless, the presence of determinants associated with increased capability of transmission, colonization, and/or invasion which may explain the epidemic behavior of these particular strains is so far unknown and has yet to be investigated [24].

Acquisition of antibiotic-resistance mechanisms and the evolution from antibiotic-susceptible to MDR- and carbapenem-resistant to pandrug-resistant $CC92^{B}$/$CC2^{P}$/international clone II is probably another essential factor in the predominance of $CC92^{B}$/$CC2^{P}$/international clone II. *A. baumannii* demonstrates a remarkable propensity to rapidly acquire resistance determinants to a wide range of antibacterial agents [150]. The acquisition of antimicrobial resistance determinants increases the ability of *A. baumannii* strains to survive in the hospital setting, providing them more time for dissemination and further clonal expansion [61]. $CC92^{B}$ isolates have frequently expressed higher resistance rates to all antimicrobial agents than the other genotypes [61]. However, it has not been investigated if particular genotypes (such as $ST92^{B}$) have a higher ability to acquire resistance genes compared to other genotypes.

The emergence of drug-resistant $CC92^{B}$/$CC2^{P}$/international clone II has most likely resulted from independent events of acquisition of various resistance determinants using different mobile elements [135]. Acquisition of $bla_{\text{OXA-23-like}}$ has, for instance, been a major mechanism of carbapenem-resistance in $CC92^{B}$/$CC2^{P}$/international clone II [144]. The identification of $bla_{\text{OXA-23-like}}$ in all *A. radioresistens* isolates has indicated intrinsic occurrence, and carbapenem-susceptible *A. radioresistens* has accordingly been proposed as the silent source of $bla_{\text{OXA-23-like}}$-based carbapenem-resistance in other *Acinetobacter*

spp [151] (Paper I). However, the identification of different genetic structures surrounding *bla*$_{\text{OXA-23-like}}$ (e. g. transposons Tn*2006* and Tn*2008*) indicates concurrent but independent events of acquisition of *bla*$_{\text{OXA-23-like}}$, probably due to comparable selective pressures related to comparable increased carbapenem usage in different geographic areas [106, 110, 135].

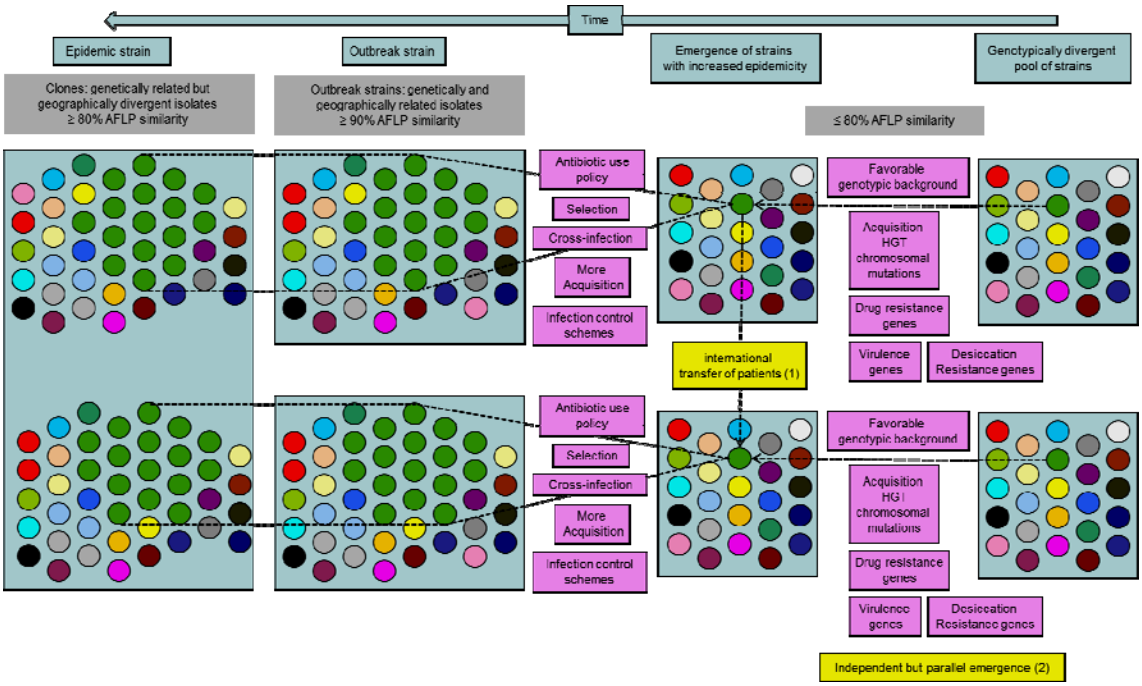

Figure 6. Predominance of CC92^{B}/CC2^{P}/international clone II. Favorable genetic background and acquisition of foreign genes are proposed to be main factors for the emergence of particular strains with increased epidemicity than other strains. International travel and independent but parallel emergence are probable hypotheses for the extensive worldwide distribution.

5.3. Class 1 integrons in *A. baumannii*

Integrons essentially consist of an integrase gene (*intI*) and an adjacent integration site (*attI*), together composing the 5` conserved segment (5`CS) [152] (Figure 7). In addition, class 1 integrons typically contain a combination of a truncated antiseptic-resistance gene (Δ*qacE*), a sulfonamide-resistance gene (*sulI*), and an open reading frame of unknown function (*orf5*), together representing the 3` conserved segment (3`CS) [153]. A variable region of gene cassettes can then be situated between 5`CS and 3`CS [153]. Importantly, gene cassettes are mobilized by the integrase enzyme (IntI) while class 1 integrons by themselves are non-mobile [152].

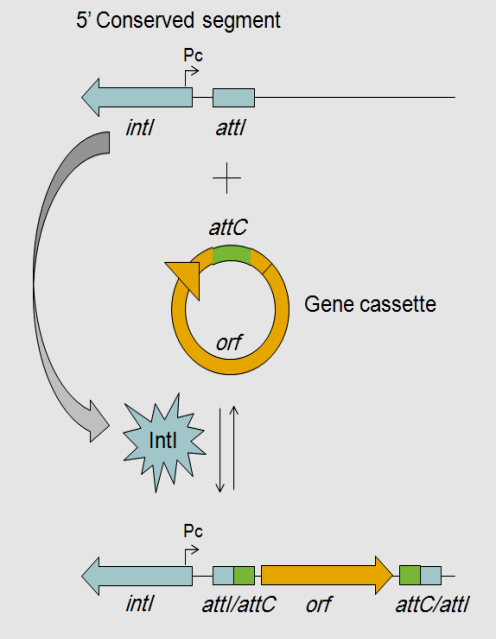

Figure 7. Outline of the process of integron-mediated insertion of a circular gene cassette. The integrase gene (*intI*) located in the 5` conserved ssegment (5`CS) encodes a site-specific recombinase enzyme (IntI). The Integrase mediates a recombination event between specific attachment sites (*attI* and *attC*). The inserted open reading frame (orf) is expressed by the strong promoter Pc located in the 5`CS.

The ability of class 1 integrons to capture various gene cassettes involved in antibiotic resistance has significantly contributed to the dissemination of multidrug-resistant bacterial strains worldwide [154]. In addition, analysis of the geographic distribution of

class 1 integrons with particular variable regions might be important in detecting the emergence and pattern of spread of particular clones of bacteria [99]. One aim of papers II and III was to detect and charaterize class 1 integrons among 24 multidrug- and carbapenem-resistant *A. baumannii* isolates obtained in Norway and Sweden. Our study revealed the occurrence of class 1 integrons with eight different variable regions (Table 10). Interestingly, particular class 1 integrons revealed a broad worldwide and multi-clonal distribution whereas other class 1 integrons showed a relatively less extensive continent-limited geographical spread.

Table 10. Class 1 integrons with 8 different variable regions detected in Papers II and III

Variable region	Isolate	Country (import) and year of isolation	Genetic background
*aacA*4-*orfO*-*bla*$_{OXA-20}$	K12-21	Norway (Greece), 2004	ST45^{P}/ST189^{B}/int. clone II
	AO-12066 (K51-54)	Sweden (no import), 2004	ST2^{P}/int. clone II
	AO-12327 (K51-63)	Sweden (Greece), 2005	ST2^{P}/int. clone II
	AO-15204 (K51-59)	Sweden (Greece), 2006	ST2^{P}/int. clone II
	AO-8058 (K51-53)	Sweden (Greece), 2007	ST2^{P}/int. clone II
aac(6')-*Im*-*aadA*1	K44-35	Norway (Thailand), 2007	ST2^{P}/ST190^{B}/int. clone II
*aacC*1-*orfP*-*orfP*-*orfQ*-a*adA*1	K47-42	Norway (China), 2007	ST2^{P}/ST191^{B}/int. clone II
*aacA*4-*catB*8-*aadA*1	K47-42	Norway (China), 2007	ST2^{P}/ST191^{B}/int. clone II
	K58-19	Norway (Italy), 2009	ST2^{P}/ST118^{B}/int. clone II
*aacC*1-*orfP*-*orfQ*-a*adA*1	K48-42	Norway (India), 2008	ST1^{P}/ST192^{B}/int. clone I
*arr*2-*cmlA*5	K71-71	Norway (Pakistan), 2009	ST15^{P}/ST103^{B}/SG4
aadB-*aadA*1-IS	AO-8866 (K51-58)	Sweden (Poland), 2006	ST5^{P}/SG7
bla$_{GES-11}$-*aacA*4-*dfrA*7	AO-21841 (K51-61)	Sweden (no import), 2006	ST25^{P}/SG12

Class 1 integron with the variable region *aacA*4-*orfO*-*bla*$_{OXA-20}$ was detected in five isolates obtained in Norway (*n*=1) and Sweden (*n*=4) (Papers II and III). Interestingly, all the five isolates belonged to international clone II. Furthermore, the Norwegian isolate and three of the Swedish isolates were associated with import from Greece. To my knowledge, the *aacA*4-*orfO*-*bla*$_{OXA-20}$ variable region has so far been detected only in *A. baumannii* isolates (http://www.ncbi.nlm.nih.gov/genbank/) [99, 155-159]. Furthermore, it has exclusively been detected in isolates obtained from Europe (France, Italy, Spain, Norway, and Sweden) with a frequent occurrence in Greece [99, 155-159] (Papers II and III). Interestingly, the Greek and Italian isolates reported by Nemec *et al*. and D'Arezzo *et al*. were found to belong to international clone II as well [99, 159]. Whole-genome sequence analysis of an Italian MDR *A. baumannii* clinical isolate "ACICU", also

belonging to international clone II, revealed an interesting occurrence of the *aacA*4-*orfO*-$bla_{\text{OXA-20}}$ variable region within a chromosomal resistance island designated as AbaR2 [119].

The identification of class 1 integron with *aac*(6')-*Im*-*aadA*1 in a Norwegian isolate imported from Thailand (Southeast Asia) was, from a geographic point of view, fairly consistent with previous studies reporting the occurrence of this integron in *A. baumannii* isolates from Korea (East Asia) (unpublished study, GenBank accession no: CP001921) [101] (Paper II). However, the *aadA1* cassette was disrupted by IS*26* in the Korean isolates. Of note, the variable region *aac*(6')-*Im*-*aadA*1 has so far been detected only in *A. baumannii* isolates (http://www.ncbi.nlm.nih.gov/genbank/) [101] (Paper II). Interestingly, the Norwegian isolate (K44-35) belonged to international clone II indicating that geographical boundaries might be an important factor in the emergence of intra-clonal clusters of isolates (subclones) showing distinct genomic markers [99] (Paper II).

On the other hand, results of our work extended the broad worldwide distribution (Australia, China, Malaysia, and many European countries) of class 1 integrons with the variable regions *aacC*1-*orfP*-*orfP*-*orfQ*-a*adA*1 and *aacC*1-*orfP*-*orfQ*-a*adA*1 among *A. baumannii* isolates of both international clones I and II [99, 153, 156-163] (Papers II and III). The variable region *aacC*1-*orfP*-*orfQ*-a*adA*1 was also found in an equine isolate obtained from Ireland [164]. Interestingly, the variable region *aacC*1-*orfP*-*orfQ*-a*adA*1 has also been detected in *Klebsiella pneumoniae* (unpublished study, GenBank accession no: HM589045). Of note, the variable region *aacC*1-*orfP*-*orfP*-*orfQ*-a*adA*1 was located within the resistance islands AbaR1, AbaR5, and AbaR6 in *A. baumannii* strains AYE (France), 3208 (Australia) and D2 (Australia), respectively, whereas *aacC*1-*orfP*-*orfQ*-a*adA*1 was situated in AbaR3 and AbaR7 in *A. baumannii* strains AB0057 (USA) and A92 (Australia), respectively [150, 165-167].

The occurrence of these integrons in isolates from distinct clones and different worldwide locations indicates that these integrons are (i) remarkably stable, (ii) extremely valuable

for the host bacteria, and (iii) essential in the dissemination of particular antibiotic resistance genes [100]. Stability in this context refers to the occurrence of class 1 integrons with conserved and stable variable regions [99]. In other words, it means that the resistance genes located in class 1 integrons are transferred as part of the entire integron structure more often than as individual gene cassettes [168].

A scattered distribution (UK, Italy, and China) has been reported for class 1 integron with the variable region *aacA*4-*catB*8-*aadA*1 [160, 163, 169, 170] (Paper II). Similarly, a limited but dispersed distribution (Sweden, France, Turkey, Palestine, and Egypt) has been reported for class 1 integron with the variable region *bla*$_{\text{GES-11}}$-*aacA*4-*dfrA*7 [75, 78, 171] (Paper III). The *aacA*4-*catB*8-*aadA*1 variable region has also been identified in several other bacterial genera such as *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Burkholderia cepacia* (unpublished studies, GenBank accession no.: HM175870, HM175872, DQ141317, HM989924, and HQ880251, respectively), and *Stenotrophomonas maltophilia* [172] whereas the *bla*$_{\text{GES-11}}$-*aacA*4-*dfrA*7 variable region has so far been identified only in *A. bamannii* isolates (http://www.ncbi.nlm.nih.gov/genbank/) [75, 78, 171]. The occurrence of *aacA*4-*catB*8-*aadA*1 in different host genera also indicates the remarkabe stability and extreme valuability of this integron [168]. However, the less geographic distribution in the *A. baumannii* global society is probably due to a recent acquisition of *aacA*4-*catB*8-*aadA*1 compared to *aacC*1-*orfP*-*orfP*-*orfQ*-a*adA*1 and *aacC*1-*orfP*-*orfQ*-a*adA*1.

Class 1 integron with the variable region *aadB*-*aadA*1-IS has not been reported before in *A. baumannii* isolates; it has previously been detected only in a swine *E. coli* isolate from Germany and on a plasmid recovered from a wastewater treatment plant [173, 174] (Paper III). To my knowledge, class 1 integron with the variable region *arr2*-*cm1A5* with no other gene cassettes has been reported for the first time by our research group (http://www.ncbi.nlm.nih.gov/genbank/) (Paper II). The variable region *arr2*-*cm1A5* has subsequently been detected in an *A. baumannii* isolate from Kenya (unpublished study, GenBank accession no: HQ141279).

5.4. MALDI-TOF MS for precise *Acinetobacter* species identification

The capability of MALDI-TOF MS to accomplish species identification in less than one hour makes it particularly suitable for routine clinical laboratories (4). Previously, species identification of 552 well-characterized *Acinetobacter* strains representing 15 different species using the MALDI-TOF MS system has demonstrated a good capability for identification of most of the species [26]. A recent study from Spain demonstrated that MALDI-TOF MS was able to correctly identify both reference strains and clinical isolates belonging to *A. junii*, *A. haemolyticus*, *A. lwoffii*, *A. radioresistens*, *A. calcoaceticus*, *A. baumannii*, and *A. pittii* [175]. Only isolates belonging to *A. nosocomialis* were incorrectly identified by MALDI-TOF MS due to the lack of an *A. nosocomialis* reference strain in the database provided by the system "Bruker database". Nonetheless, the analysis identified unique MALDI-TOF MS patterns for every given species, including *A. nosocomialis*, allowing rapid and direct assertion of isolates into these species [175].

Our study showed that MALDI-TOF MS was suitable for precise species identification of isolates belonging to *A. baumannii* and *A. pittii* (the most prevalent *Acinetobacter* species in clinical isolates) as well as isolates belonging to *A. lwoffii*, *A. ursingii*, *A. radioresistens*, and *A. calcoaceticus* (*Acinetobacter* species encountered less frequently in clinical isolates) (Paper IV). MALDI-TOF MS incorrectly identified isolates belonging to *A. soli* and *Acinetobacter* gen. sp. "close to towneri" as *A. baylyi* and *A. towneri*, respectively. However, the closeness of these species demonstrated by MALDI-TOF MS was consistent with the outcomes of *rpoB* and *16S rDNA* sequence analyses, confirming the high capability of MALDI-TOF MS (Paper I). Similar to the previously mentioned study from Spain, the main drawback of MALDI-TOF MS was the incorrect identification of isolates belonging to *A. nosocomialis* since it has so far been not included in the BioTyper database (Table 11).

Table 11. List of the *Acinetobacter* spp. reference strains included in BioTyper database

Acinetobacter baumannii 13101_1 CHB	*Acinetobacter pittii* Serovar 7 DSM 9308 DSM
Acinetobacter baumannii B389 UFL	*Acinetobacter pittii* Serovar 8 DSM 9309 DSM
Acinetobacter baumannii DSM 30007T HAM	*Acinetobacter gerneri* DSM 14967T HAM
Acinetobacter baumannii DSM 30008 DSM	*Acinetobacter haemolyticus* DSM 6962T DSM
Acinetobacter baumannii DSM 30011 DSM	*Acinetobacter haemolyticus* LMG 1033 HAM
Acinetobacter baumannii LMG 994 HAM	*Acinetobacter johnsonii* 10036669_102 USH
Acinetobacter baylyi DSM 14959 DSM	*Acinetobacter johnsonii* 2_1 TUB
Acinetobacter baylyi DSM 14961T DSM	*Acinetobacter johnsonii* DSM 6963T DSM
Acinetobacter baylyi DSM 14963 DSM	*Acinetobacter johnsonii* DSM 6963T HAM
Acinetobacter bouvetii DSM 14964T DSM	*Acinetobacter junii* DSM 14968 HAM
Acinetobacter calcoaceticus B388 UFL	*Acinetobacter junii* DSM 1532 DSM
Acinetobacter calcoaceticus CCM 4503 CCM	*Acinetobacter junii* DSM 6964T HAM
Acinetobacter calcoaceticus CCM 4665 CCM	*Acinetobacter lwoffii* 2_Ring240 MHH
Acinetobacter calcoaceticus DSM 1139 DSM	*Acinetobacter lwoffii* B101 UFL
Acinetobacter calcoaceticus DSM 30006T HAM	*Acinetobacter lwoffii* B138 UFL
Acinetobacter guillouiae DSM 590 DSM	*Acinetobacter lwoffii* DSM 2403T DSM
Acinetobacter pittii Serovar 1 DSM 9337 DSM	*Acinetobacter lwoffii* LB_101249_09 ERL
Acinetobacter pittii Serovar 13 DSM 9312 DSM	*Acinetobacter parvus* DSM 16617T HAM
Acinetobacter pittii Serovar 14 DSM 9313 DSM	*Acinetobacter radioresistens* B381 UFL
Acinetobacter pittii Serovar 15 DSM 9314 DSM	*Acinetobacter radioresistens* DSM 6976T HAM
Acinetobacter pittii Serovar 18 DSM 9341 DSM	*Acinetobacter radioresistens* LMG 10614 HAM
Acinetobacter pittii Serovar 2 DSM 9306 DSM	*Acinetobacter schindleri* DSM 16038T DSM
Acinetobacter pittii Serovar 20 DSM 9317 DSM	*Acinetobacter* sp. DSM 11042 DSM
Acinetobacter pittii Serovar 21 DSM 9342 DSM	*Acinetobacter* sp. DSM 11652 DSM
Acinetobacter pittii Serovar 22 DSM 9318 DSM	*Acinetobacter* sp. DSM 30009 DSM
Acinetobacter pittii Serovar 23 DSM 9319 DSM	*Acinetobacter* sp. DSM 46612 DSM
Acinetobacter pittii Serovar 24 DSM 9320 DSM	*Acinetobacter tandoii* DSM 14970T HAM
Acinetobacter pittii Serovar 25 DSM 9343 DSM	*Acinetobacter tjernbergiae* DSM 14966 DSM
Acinetobacter pittii Serovar 26 DSM 9321 DSM	*Acinetobacter tjernbergiae* DSM 14971T HAM
Acinetobacter pittii Serovar 3 DSM 9307 DSM	*Acinetobacter towneri* DSM 14962T HAM
Acinetobacter pittii Serovar 4 DSM 9338 DSM	*Acinetobacter towneri* DSM 14969 DSM
Acinetobacter pittii Serovar 6 DSM 9340 DSM	*Acinetobacter ursingii* DSM 16037T HAM

Our study aimed to compare the performance of MALDI-TOF MS with two colorimetric semi-automated systems (VITEK 2 and Phoenix) for precise *Acinetobacter* species identification in routine clinical laboratories. Accordingly, the comparisions were performed based only on the concluding identification outcome provided by the system (for instance, no comparision was performed among MALDI-TOF MS patterns of different species). Overall, the study confirmed that MALDI-TOF MS represented a promising system for fast, simple, and reliable identification of members from the genus *Acinetobacter*. However, the system failed to correctly identify isolates of *A. nosocomialis* due to lack in the current database. Consequently, frequent updating of the supplementary databases is probably a major factor in improving the performance of the MALDI-TOF MS system.

6. Concluding remarks

Acinetobacter baumannii is an important opportunistic pathogen that has a considerable capacity to acquire mechanisms conferring resistance to a wide range of antimicrobial drugs.

The high proportion of *A. nosocomialis*, *A. pittii* in blood culture isolates from Norway points to the significant contribution of these species in the clinical setting and demonstrates the importance of molecular identification for precise *Acinetobacter* species identification.

The predominance of the highly-successful $CC92^{B}$/$CC2^{P}$/international clone II in the current global *A. baumannii* population has now been established. However, several other long-standing or recently-emerging *A. baumannii* clones have certainly played a major supplementary role in the worldwide spread of MDR *A. baumannii*.

The emergence of epidemic MDR *A. baumannii* clones in Norway and Sweden indicates the necessity of a screening programme for patients after hospitalization abroad, and strict infection control regimes to prevent further dissemination.

The protein-fingerprinting-based MALDI-TOF MS system offers a promising tool for the precise species identification of *Acinetobacter* isolates in routine clinical laboratories.

7. References

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Supplementary material

Table S1. Geographically and genotypically divergent 277 isolates selected for analyzing the global epidemiology of *A. baumannii*

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
1	62791	Spain/1993	Outbreak-related	1^B (1-1-1-1-1-1-6)	Pubmlst, [133]
2	A92	Spain	Carbapenem-S, bla_{OXA-69}	2^B (2-2-2-1-1-2-7)	[131, 132]
3	228620	Spain/2000	Outbreak-related	3^B (1-1-1-1-2-1-4)	Pubmlst, [133]
4	GEAC01/07	Italy/2007	MDR	4^B (1-12-3-2-2-7-3)	Pubmlst
5	A230	UK	Carbapenem-S, int. clone II, bla_{OXA-66}	4^B (1-12-3-2-2-7-3)	[131, 132]
6	A397	Greece	Carbapenem-I, int. clone II, bla_{OXA-66}	4^B (1-12-3-2-2-7-3)	[131, 132]
7	60127	Spain/1997	Outbreak-related	5^B (1-3-3-2-2-3-1)	Pubmlst, [133]
8	118151	Spain/1997	Outbreak-related	6^B (1-4-3-2-2-3-3)	Pubmlst, [133]
9[e]	RUH 134	The Netherlands/1982	Ref. strain, outbreak-related, int. clone II, bla_{OXA-66}	6^B (1-4-3-2-2-3-3) 98^B (1-12-3-2-2-3-3)	Pubmlst, [131-133]
10	61588	Spain/2000	Outbreak-related	7^B (3-3-3-2-3-3-8)	Pubmlst, [133]
11	61812	Spain/2000	Outbreak-related	8^B (4-4-4-4-4-5-9)	Pubmlst, [133]
12	62309	Spain/2000	Outbreak-related	9^B (1-3-3-2-2-6-8)	Pubmlst, [133]
13	2002-34100	Spain/2002	Outbreak-related	10^B (1-4-3-2-2-7-3)	Pubmlst, [133]
14	DSM 30008	.	Ref. strain	13^B (1-7-8-9-1-4-14)	Pubmlst, [133]
15	W 5420	Germany/1991	Outbreak-related	15^B (1-12-11-10-1-9-4)	Pubmlst, [133]
16	U 10247	Germany/1991	Outbreak-related	16^B (10-12-4-11-11-9-5)	Pubmlst, [133]
17	St 14733	Germany/1990	Outbreak-related	17^B (1-12-12-11-4-10-3)	Pubmlst, [133]
18	LS091	China/2005	-	17^B (1-12-12-11-4-10-3)	Pubmlst, [144]
19	B0706-077	Korea/2006-07	Carbapenem-S, colistin-S	17^B (1-12-12-11-4-10-3)	[61]
20	St 20820	Germany/1991	Outbreak-related	18^B (10-13-4-11-12-11-5)	Pubmlst, [133]
21	St 15598	Germany/1991	Outbreak-related	19^B (1-14-3-2-2-9-3)	Pubmlst, [133]
22	CGN-77	UK	Outbreak-related	19^B (1-14-3-2-2-9-3)	Pubmlst, [143]
23	St 17093	Germany/1991	Outbreak-related	20^B (1-15-13-12-4-12-2)	Pubmlst, [133]
24	HZ104	China/2005	MDR, $bla_{OXA-23-like}$ carbapenem-R, *armA*	20^B (1-15-13-12-4-12-2)	Pubmlst, [144]
25[f]	M08-20	Malaysia/2008-09	Imipenem-R	20^B (1-15-13-12-4-12-2)	[146]
26	A483	Morocco	bla_{OXA-51}	20^B (1-15-13-12-4-12-2)	[131, 132]
27	A187	South Africa	Carbapenem-S, bla_{OXA-68}	20^B (1-15-13-12-4-12-2)	[131, 132]
28	YMM14	Korea/2008	Carbapenem-S	20^B (1-15-13-12-4-12-2)	[60]
29	St 1650	Germany/1992	Outbreak-related	21^B (1-12-15-2-2-9-3)	Pubmlst, [133]
30	CGN-06	Germany/1991	Outbreak-related	22^B (1-15-13-12-4-12-37)	Pubmlst, [143]
31	CGN-81	Germany/1996	Outbreak-related	23^B (1-1-1-1-1-28-10)	Pubmlst, [143]
32	CGN-18	Denmark/1990	Sporadic	24^B (1-1-22-1-4-20-16)	Pubmlst, [143]
33	CGN-48	Germany/1991	Sporadic	25^B (1-1-41-6-23-31-26)	Pubmlst, [143]
34	CGN-09	Germany/1991	Outbreak-related	27^B (1-12-15-2-2-3-3)	Pubmlst, [143]
35	CGN-55	Germany/1996	Outbreak-related	28^B (1-12-3-2-2-35-4)	Pubmlst, [143]

Table S1. Geographically and genotypically divergent 277 isolates selected for analyzing the global epidemiology of *A. baumannii* (cont.)

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
36	CGN-52	Denmark	Sporadic	29[B] (1-12-3-28-2-29-4)	Pubmlst, [143]
37	CGN-56	Germany/1996	Outbreak-related	30[B] (1-12-3-29-2-34-4)	Pubmlst, [143]
38	CGN-39	Germany/1998	Outbreak-related	31[B] (1-12-39-25-21-3-25)	Pubmlst, [143]
39	CGN-44	Germany/1991	Sporadic	32[B] (1-12-4-11-4-28-2)	Pubmlst, [143]
40	CGN-46	Germany/1991	Sporadic	33[B] (1-12-4-11-4-29-2)	Pubmlst, [143]
41	CGN-23	Germany/1991	Sporadic	34[B] (1-15-13-12-4-49-37)	Pubmlst, [143]
42	CGN-71	USA/1995	Outbreak-related	35[B] (1-15-2-28-1-41-32)	Pubmlst, [143]
43	CGN-74	USA/1995	Outbreak-related	36[B] (1-15-2-28-1-44-32)	Pubmlst, [143]
44	CGN-15	Germany/1991	Sporadic	37[B] (1-19-21-17-1-18-14)	Pubmlst, [143]
45	CGN-19	Denmark/1990	Sporadic	38[B] (1-25-23-6-4-21-17)	Pubmlst, [143]
46	CGN-20	Germany/1991	Sporadic	39[B] (1-26-24-1-4-3-10)	Pubmlst, [143]
47	CGN-53	Denmark/1990	Sporadic	40[B] (1-3-6-1-4-34-10)	Pubmlst, [143]
48	CGN-30	Germany/1991	Sporadic	41[B] (1-31-31-24-4-10-21)	Pubmlst, [143]
49	CGN-54	Germany/1996	Sporadic	42[B] (1-34-14-28-22-35-2)	Pubmlst, [143]
50	CGN-82	Belgium	Outbreak-related	43[B] (1-42-49-10-1-48-23)	Pubmlst, [143]
51	CGN-68	USA/1995	Sporadic	44[B] (10-12-1-33-4-29-31)	Pubmlst, [143]
52	CGN-29	Denmark/1990	Sporadic	45[B] (10-12-30-24-4-9-20)	Pubmlst, [143]
53	CGN-79	Germany/1996	Outbreak-related	46[B] (10-12-4-11-4-29-2)	Pubmlst, [143]
54	CGN-76	Germany	Outbreak-related	47[B] (10-12-4-11-4-29-35)	Pubmlst, [143]
55	CGN-51	Denmark	Sporadic	48[B] (10-12-4-6-4-33-2)	Pubmlst, [143]
56	CGN-10	Germany/1991	Sporadic	49[B] (10-19-17-16-4-9-2)	Pubmlst, [143]
57	CGN-43	Germany/1991	Sporadic	50[B] (10-34-40-26-22-27-2)	Pubmlst, [143]
58	CGN-45	Germany/1991	Sporadic	51[B] (11-12-4-11-1-28-2)	Pubmlst, [143]
59	CGN-01	Denmark	Outbreak-related	52[B] (12-17-16-1-14-14-7)	Pubmlst, [143]
60	CGN-13	Germany/1991	Sporadic	53[B] (13-12-19-6-1-9-2)	Pubmlst, [143]
61	CGN-31	Germany/1998	Sporadic	54[B] (13-12-32-24-4-9-22)	Pubmlst, [143]
62	CGN-36	Germany/1991	Sporadic	55[B] (13-33-37-24-4-11-2)	Pubmlst, [143]
63	CGN-14	Germany/1991	Sporadic	56[B] (14-23-20-1-16-17-13)	Pubmlst, [143]
64	CGN-16	Germany/1991	Sporadic	57[B] (15-24-4-18-17-19-15)	Pubmlst, [143]
65	CGN-26	Germany/1991	Sporadic	58[B] (18-17-28-22-4-4-18)	Pubmlst, [143]
66	CGN-28	Germany/1991	Sporadic	59[B] (19-30-29-23-18-24-19)	Pubmlst, [143]
67	CGN-65	USA/1996	Outbreak-related	60[B] (2-21-12-32-26-39-2)	Pubmlst, [143]
68	CGN-33	Germany/1996	Outbreak-related	61[B] (20-12-34-24-1-9-2)	Pubmlst, [143]
69	CGN-34	Germany	Sporadic	62[B] (21-31-35-24–1-25-23)	Pubmlst, [143]
70	CGN-47	Germany/1991	Sporadic	63[B] (23-35-3-27-23-30-19)	Pubmlst, [143]
71	CGN-49	Germany/1991	Sporadic	64[B] (24-1-42-13-24-32-26)	Pubmlst, [143]
72	CGN-69	USA/1996	Sporadic	65[B] (28-38-45-1-16-40-5)	Pubmlst, [143]
73	CGN-64	USA/1995	Outbreak-related	66[B] (28-38-45-31-16-30-5)	Pubmlst, [143]
74	CGN-75	USA/1995	Outbreak-related	67[B] (29-41-48-11-1-45-10)	Pubmlst, [143]
75	CGN-12	Germany/1991	Sporadic	68[B] (3-22-18-1-1-16-12)	Pubmlst, [143]

Table S1. Geographically and genotypically divergent 277 isolates selected for analyzing the global epidemiology of *A. baumannii* (cont.)

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
76	C046	Korea/2003	Outbreak strain, carbapenem-R, ciprofloxacin-R, colistin-S	69^{B} (1-46-3-2-2-58-3)	Pubmlst, [72]
77	Q45	Australia/1998	Meropenem-S, amikacin-R, ciprofloxacin-R	69^{B} (1-46-3-2-2-58-3)	Pubmlst
78	C083	Korea/2005	Carbapenem-R	70^{B} (1-46-3-2-1-58-3)	Pubmlst, [72]
79	C077	Korea/2005	Carbapenem-R	71^{B} (1-46-3-2-2-58-4)	Pubmlst, [72]
80	C101	Korea/2006	Carbapenem-R	72^{B} (1-15-2-28-1-55-4)	Pubmlst, [72]
81	D015	Korea/2006	Carbapenem-R	73^{B} (1-47-53-1-1-59-32)	Pubmlst, [72]
82	Q18	Australia/2006	*bla*$_{OXA-23}$ meropenem-R, amikacin-S, ciprofloxacin-S	73^{B} (1-47-53-1-1-59-32)	Pubmlst, [145]
83	04-888	Japan/2004	-	74^{B} (1-3-3-2-2-75-3)	Pubmlst
84	09-946	Japan	-	75^{B} (1-3-3-2-2-11-3)	Pubmlst
85	F10	China/2005	MDR, *bla*$_{OXA-23}$ carbapenem-R, *armA*	75^{B} (1-3-3-2-2-11-3)	Pubmlst, [144]
86	K08-22	Korea/2008-09	*bla*$_{OXA-24-like}$ Imipenem-R	75^{B} (1-3-3-2-2-11-3)	[146]
87	04-93	Japan/2002	-	76^{B} (1-12-3-2-2-10-3)	Pubmlst
88	HK01-011	China/2008-09	*bla*$_{OXA-58}$ imipenem-R	76^{B} (1-12-3-2-2-10-3)	[146]
89	09-780	Japan/2008	-	77^{B} (1-1-66-12-33-76-21)	Pubmlst
90	09-775	Japan/2005	-	78^{B} (13-26-67-40-1-22-7)	Pubmlst
91	09-782	Japan/2009	-	79^{B} (34-12-68-41-32-7-46-79)	Pubmlst
92	09-785	Japan/2009	-	80^{B} (34-12-68-41-34-10-4)	Pubmlst
93	04-565	Japan/2004	-	81^{B} (1-54-69-11-4-69-45)	Pubmlst
94	07-791	Japan/2003	-	82^{B} (1-12-70-15-4-52-45)	Pubmlst
95	09-781	Japan/2009	-	83^{B} (21-12-2-15-35-77-4)	Pubmlst
96	08-943	Japan/2008	-	84^{B} (1-12-2-15-22-72-5)	Pubmlst
97	08-1648	Japan/2008	-	85^{B} (21-15-2-15-1-52-4)	Pubmlst
98	09-94	Japan/2008	-	86^{B} (21-15-2-15-1-78-4)	Pubmlst
99	04-774	Japan/2004	-	87^{B} (1-52-29-15-18-24-7)	Pubmlst
100	Ab08-13	Thailand/2008	-	88^{B} (1-3-3-2-2-10-3)	Pubmlst
101	ZS4	China/2005	-	88^{B} (1-3-3-2-2-10-3)	Pubmlst, [144]
102	ZP5	China/2005	MDR, *bla*$_{OXA-23}$ carbapenem-R, *armA*	90^{B} (1-3-3-2-2-62-3)	Pubmlst, [144]
103	ZF5	China/2005	MDR, *bla*$_{OXA-23}$ carbapenem-R, *armA*	91^{B} (22-15-13-12-4-62-2)	Pubmlst, [144]
104	ZY136	China/2005	MDR, *bla*$_{OXA-23}$ carbapenem-R, *armA*	92^{B} (1-3-3-2-2-7-3)	Pubmlst, [144]
105	B0707-093	Korea/2006-07	*bla*$_{OXA-23-like}$ carbapenem-R, colistin-R	92^{B} (1-3-3-2-2-7-3)	[61]
106	GEAO11/07	Italy/2007	-	92^{B} (1-3-3-2-2-7-3)	Pubmlst
107	Q17	Australia/2006	*bla*$_{OXA-23-like}$ meropenem-R, amikacin-R, ciprofloxacin-R	92^{B} (1-3-3-2-2-7-3)	Pubmlst, [145]
108	I05-06	India/2008-09	*bla*$_{OXA-58}$ imipenem-R	92^{B} (1-3-3-2-2-7-3)	[146]
109	HAP32	Malaysia/2008-09	*bla*$_{OXA-24}$ imipenem-R	92^{B} (1-3-3-2-2-7-3)	[146]
110	P08-009	Philippines/2008-09	*bla*$_{OXA-24}$ imipenem-R	92^{B} (1-3-3-2-2-7-3)	[146]

Table S1. Geographically and genotypically divergent 277 isolates selected for analyzing the global epidemiology of *A. baumannii* (cont.)

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
111	A401	Taiwan	Carbapenem-R, int. clone II, bla_{OXA-82}	92[B] (1-3-3-2-2-7-3)	[131, 132]
112	A484	UK	Carbapenem-R, int. clone II, bla_{OXA-83}	92[B] (1-3-3-2-2-7-3)	[131, 132]
113	A371	Czech Republic	Carbapenem-R, int. clone II, bla_{OXA-83}	92[B] (1-3-3-2-2-7-3)	[131, 132]
114	04-1278	Japan/2004	-	92[B] (1-3-3-2-2-7-3)	Pubmlst
115	GEBB14/07	Italy/2007	-	93[B] (1-12-13-6-11-1-4)	Pubmlst
116	GEBC16/07	Italy/2007	MDR	94[B] (2-12-12-1-1-4-4)	Pubmlst
117	GEAW22/07	Italy/2007	MDR	95[B] (10-12-4-11-1-9-5)	Pubmlst
118	CQ95	China/2005	-	95[B] (10-12-4-11-1-9-5)	Pubmlst
119	A384	Norway	Carbapenem-I, int. clone I, bla_{OXA-69}	95[B] (10-12-4-11-1-9-5)	[131, 132]
120	1A2	China/2005	Outbreak-related, MDR, $bla_{OXA-23-like}$ carbapenem-R, colistin-S	96[B] (1-43-50-31-1-50-26)	Pubmlst, [142]
121	4017355	Spain/2008	-	97[B] (1-17-8-10-28-51-38)	Pubmlst
122	A24	UK	Carbapenem-S, int. clone II, bla_{OXA-66}	98[B] (1-12-3-2-2-3-3)	[131, 132]
123	A392	Germany	Carbapenem-R, int. clone II, bla_{OXA-66}	98[B] (1-12-3-2-2-3-3)	[131, 132]
124	Ab21	Argentine/2000	-	99[B] (1-15-52-10-28-3-32)	Pubmlst
125	82	Argentina/2002	Environmental (bed-rail)	100[B] (1-15-52-10-28-55-32)	Pubmlst
126	Ab31	Argentine/2000	-	101[B] (1-15-12-6-28-12-40)	Pubmlst
127	Ab149	Argentine/1990	-	102[B] (1-15-52-10-28-12-32)	Pubmlst
128	Ab545	Argentine/1991	-	103[B] (12-17-12-1-29-3-39)	Pubmlst
129	Ab244	Argentine/1997	-	104[B] (12-17-12-1-29-57-39)	Pubmlst
130	Ab295	Argentine/1998	-	105[B] (31-45-51-6-30-53-6)	Pubmlst
131	R6	China/2007	-	106[B] (1-3-15-2-2-7-3)	Pubmlst
132	CYH13	Korea/2008	Carbapenem-S	106[B] (1-3-15-2-2-7-3)	[60]
133	Ab170	Argentine/1990	-	107[B] (1-17-12-1-29-57-39)	Pubmlst
134	Ab834	Argentine/2005	-	108[B] (10-12-4-6-4-9-5)	Pubmlst
135[f]	I02-18	India/2008-09	Imipenem-R	108[B] (10-12-4-6-4-9-5)	[146]
136	A63	Argentine	Carbapenem-S, int. clone I, bla_{OXA-69}	109[B] (10-12-4-11-4-9-5)	[131, 132]
137	04-1279	Japan/2004	-	109[B] (10-12-4-11-4-9-5)	Pubmlst
138	A442	Bulgaria	Carbapenem-S, int. clone I, bla_{OXA-69}	109[B] (10-12-4-11-4-9-5)	[131, 132]
139	A368	UK	Carbapenem-S, int. clone I, $bla_{OXA-112}$	109[B] (10-12-4-11-4-9-5)	[131, 132]
140	U557	Korea/2006-07	carbapenem-R, colistin-R	110[B] (1-15-2-28-1-52-32)	[61]
141	Ab253	Argentine/1997	-	110[B] (1-15-2-28-1-52-32)	Pubmlst
142	22	Argentina/2002	Environmental (bed-rail)	113[B] (1-15-52-10-28-56-32)	Pubmlst
143	Ab592	Argentine/1995	-	114[B] (1-15-52-10-28-57-32)	Pubmlst
144	GEBF02/08	Italy/2008	MDR	115[B] (2-1-12-1-1-4-5)	Pubmlst
145	GEBG03/08	Italy/2008	-	116[B] (1-15-4-11-4-4-2)	Pubmlst

Table S1. Geographically and genotypically divergent 277 isolates selected for analyzing the global epidemiology of *A. baumannii* (cont.)

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
146	GEBL06/08	Italy/2008	-	117[B] (1-15-2-2-1-4-5)	Pubmlst
147	GEBM07/08	Italy/2008	MDR	118[B] (1-3-3-2-2-3-3)	Pubmlst
148	TW01-010	Taiwan/2008-09	$bla_{\text{OXA-24-like}}$ imipenem-R	118[B] (1-3-3-2-2-3-3)	[146]
149	A343	UK	Carbapenem-S, int. clone II, $bla_{\text{OXA-109}}$	118[B] (1-3-3-2-2-3-3)	[131, 132]
150	Ab03-168	Thailand/2003	-	119[B] (1-15-12-6-28-59-40)	Pubmlst
151	24029815	Spain/2006	-	121[B] (1-17-52-10-28-63-32)	Pubmlst
152	ACAT195	USA/2008	-	122[B] (1-3-61-2-2-7-3)	Pubmlst
153	ACAT199	USA/2008	-	123[B] (1-35-61-2-2-3-3)	Pubmlst
154	ACAT1204	USA/2005	-	124[B] (1-17-60-10-28-66-32)	Pubmlst
155	Q47	Australia/1999	$bla_{\text{OXA-23}}$ meropenem-R, amikacin-R, ciprofloxacin-R	125[B] (1-52-59-12-1-18-44)	Pubmlst, [145]
156	Q55	Australia/2003	Meropenem-S, amikacin-R, ciprofloxacin-R	126[B] (10-53-4-11-4-64-5)	Pubmlst, [145]
157	Q22	Australia/2007	$bla_{\text{OXA-23}}$ meropenem-R, amikacin-S, ciprofloxacin-S	127[B] (1-33-57-11-26-11-6)	Pubmlst, [145]
158	Q29	Australia/2008	Meropenem-S, amikacin-S, ciprofloxacin-S	128[B] (2-44-58-1-1-54-41)	Pubmlst, [145]
159	Q44	Australia/2009	Meropenem-S, amikacin-S, ciprofloxacin-S	129[B] (1-38-42-37-4-11-43)	Pubmlst, [145]
160	Q56	Australia/2009	-	130[B] (1-12-3-2-2-65-3)	Pubmlst, [145]
161	256	Argentina/2002	Environmental (dispenser)	131[B] (1-15-60-10-28-56-32)	Pubmlst
162	Ab3135	Brazil/2007	$bla_{\text{OXA-23}}$ carbapenem-R, SG10, $bla_{\text{OXA-95}}$	132[B] (1-12-71-2-1-79-30)	Pubmlst, [130]
163	Ab3356	Brazil/2007	$bla_{\text{OXA-23}}$ carbapenem-R, SG11, $bla_{\text{OXA-69}}$	134[B] (2-12-73-12-1-9-47)	Pubmlst, [130]
164	09-1484	Japan/2009	-	135[B] (10-53-74-11-4-80-5)	Pubmlst
165	H401	China/2009	-	136[B] (1-3-3-2-2-16-3)	Pubmlst
166	LAMAB027	China/2009	MDR	137[B] (1-3-3-2-2-12-3)	Pubmlst
167	LAMAB020	China/2009	MDR	138[B] (1-3-3-2-2-50-3)	Pubmlst
168	K102-07	Korea/2008-09	$bla_{\text{OXA-24-like}}$ imipenem-R	138[B] (1-3-3-2-2-50-3)	[146]
169	KNSS0821 (KSS21)	Korea/2008	Carbapenem-S	139[B] (1-15-12-6-28-59-3)	Pubmlst, [60]
170	GYMC0812 (GY12)	Korea/2008	Carbapenem-S	140[B] (1-15-12-6-28-59-32)	Pubmlst, [60]
171	IJMC0822 (IJ22)	Korea/2008	Carbapenem-S	141[B] (1-47-3-2-2-7-30)	Pubmlst, [60]
172	IJMC0834	Korea/2008	-	142[B] (10-12-4-11-1-9-30)	Pubmlst
173	CHA0839 (CHA39)	Korea/2008	Carbapenem-S	143[B] (1-47-67-28-1-10-6)	Pubmlst, [60]
174	KNSM0820	Korea/2008	-	144[B] (21-35-2-28-22-52-4)	Pubmlst
175	IJMC0835	Korea/2008	-	145[B] (21-35-2-28-1-52-4)	Pubmlst
176	CNMC0810 (CN10)	Korea/2008	Carbapenem-S	146[B] (1-15-13-12-4-14-2)	Pubmlst, [60]
177[g]	Not found	China/2005	Carbapenem-S	146[B] (1-15-13-12-4-14-2)	[144]
178	IJMC0801	Korea/2008	-	147[B] (1-54-62-31-4-55-45)	Pubmlst

Table S1. Geographically and genotypically divergent 277 isolates selected for analyzing the global epidemiology of *A. baumannii* (cont.)

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
179	KNSS0841	Korea/2008	-	148[B] (1-3-65-45-4-4-26)	Pubmlst
180	YNMC0804 (YMM4)	Korea/2008	Carbapenem-S	149[B] (1-47-67-28-1-82-6)	Pubmlst, [60]
181	CSMC0818 (CS18)	Korea/2008	Carbapenem-S	150[B] (2-38-42-1-1-4-49)	Pubmlst, [60]
182	KNSM0822 (KSM22)	Korea/2008	Carbapenem-S	151[B] (21-12-2-28-32-83-4)	Pubmlst, [60]
183	KNSM0829 (KSM29)	Korea/2008	Carbapenem-S	152[B] (1-15-81-1-1-72-45)	Pubmlst, [60]
184	KYMC0814 (KY14)	Korea/2008	Carbapenem-S	153[B] (21-35-2-28-1-84-4)	Pubmlst, [60]
185	KSMC0830 (KS30)	Korea/2008	Carbapenem-S	154[B] (21-55-13-28-1-84-2)	Pubmlst, [60]
186	KMMC0807 (KMC7)	Korea/2008	Carbapenem-S	155[B] (1-57-78-12-1-25-51)	Pubmlst, [60]
187	CHA0815 (CHA15)	Korea/2008	Carbapenem-S	156[B] (1-15-2-28-1-25-32)	Pubmlst, [60]
188	CHA0826 (CHA26)	Korea/2008	Carbapenem-S	157[B] (1-31-79-43-4-25-50)	Pubmlst, [60]
189	CHA0833 (CHA33)	Korea/2008	Carbapenem-S	158[B] (21-35-2-28-1-85-4)	Pubmlst, [60]
190	CHA0851 (CHA51)	Korea/2008	Carbapenem-S	159[B] (1-57-78-12-1-10-51)	Pubmlst, [60]
191	YNMC0845 (YN45)	Korea/2008	Carbapenem-S	160[B] (1-56-2-44-1-52-6)	Pubmlst, [60]
192	IJMC0840 (IJ40)	Korea/2008	Carbapenem-S	161[B] (21-12-2-28-1-86-4)	Pubmlst, [60]
193	KMSS0815 (KSS15)	Korea/2008	Carbapenem-S	162[B] (40-1-83-6-4-7-13)	Pubmlst, [60]
194	KYMC0823 (KY23)	Korea/2008	Carbapenem-S	163[B] (33-12-40-26-32-91-5)	Pubmlst, [60]
195	CHA0818 (CHA18)	Korea/2008	Carbapenem-S	164[B] (33-12-40-26-32-84-5)	Pubmlst, [60]
196	CHA0827 (CHA27)	Korea/2008	Carbapenem-S	165[B] (33-12-40-26-25-84-5)	Pubmlst, [60]
197	CYMC0823 (CYM23)	Korea/2008	Carbapenem-S	166[B] (33-12-40-26-32-87-5)	Pubmlst, [60]
198	CSMC0830 (CS30)	Korea/2008	Carbapenem-S	167[B] (33-12-40-26-32-83-5)	Pubmlst, [60]
199	KNSM0811 (KSM11)	Korea/2008	Carbapenem-S	168[B] (1-12-65-45-4-88-26)	Pubmlst, [60]
200	MJMC0826 (MJ26)	Korea/2008	Carbapenem-S	169[B] (1-34-70-28-4-90-45)	Pubmlst, [60]
201	CHA0831 (CHA31)	Korea/2008	Carbapenem-S	170[B] (1-12-80-28-35-89-30)	Pubmlst, [60]
202	CHA0842 (CHA42)	Korea/2008	Carbapenem-S	171[B] (1-48-65-45-4-90-26)	Pubmlst, [60]
203	CCH0815 (CCH15)	Korea/2008	Carbapenem-S	172[B] (1-34-80-28-1-72-45)	Pubmlst, [60]
204	CHA0850 (CHA50)	Korea/2008	Carbapenem-S	173[B] (1-58-29-2-4-9-53)	Pubmlst, [60]

Table S1. Geographically and genotypically divergent 277 isolates selected for analyzing the global epidemiology of *A. baumannii* (cont.)

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
205	CSMC0841 (CS41)	Korea/2008	Carbapenem-S	174[B] (11-27-14-21-15-22-15)	Pubmlst, [60]
206	YMC42	Korea/2008	Carbapenem-S	175[B] (1-17-82-39-1-92-7)	[60]
207	CYH28	Korea/2008	Carbapenem-S	176[B] (21-48-58-42-36-83-4)	[60]
208	KS49	Korea/2008	Carbapenem-S	177[B] (33-21-12-49-1-54-7)	[60]
209	YMM05	Korea/2008	Carbapenem-S	178[B] (31-61-70-46-16-58-6)	[60]
210	KSMC0847 (KS47)	Korea/2008	Carbapenem-S	179[B] (35-62-75-28-35-7-30)	Pubmlst, [60]
211	MJMC0812 (MJ12)	Korea/2008	Carbapenem-S	180[B] (1-63-12-6-28-59-30)	Pubmlst, [60]
212	CYH0826 (CYH26)	Korea/2008	Carbapenem-S	181[B] (1-64-76-1-23-81-32)	Pubmlst, [60]
213	KNSM0807 (KSM07)	Korea/2008	Carbapenem-S	182[B] (35-60-77-11-26-11-48)	Pubmlst, [60]
214	KNSS0810	Korea/2008	-	183[B] (1-17-81-1-1-91-26)	Pubmlst
215	KNSS0836	Korea/2008	-	184[B] (36-31-70-28-4-54-4)	Pubmlst
216	LAMAB033	China/2009	MDR	184[B] (36-31-70-28-4-54-4)	Pubmlst
217	KYMC0822	Korea/2008	-	185[B] (37-53-13-47-32-64-52)	Pubmlst
218	SCMC0819	Korea/2008	-	186[B] (38-59-80-48-18-58-43)	Pubmlst
219	A20	France	Carbapenem-R, int. clone III, $bla_{\text{OXA-71}}$	187[B] (1-1-1-1-1-9-6)	[131, 132]
220	A377	Germany	Carbapenem-R, int. clone III, $bla_{\text{OXA-71}}$	187[B] (1-1-1-1-1-9-6)	[131, 132]
221	A329	Spain	Carbapenem-R, int. clone III, $bla_{\text{OXA-71}}$	187[B] (1-1-1-1-1-9-6)	[131, 132]
222	A387	Greece	Carbapenem-I, int. clone II, $bla_{\text{OXA-66}}$	189[B] (1-12-3-2-2-4-3)	[131, 132]
223	Mon2	Italy/2007	-	196[B] (2-21-12-32-26-63-5)	Pubmlst
224	Mon1	Italy/2008	-	197[B] (10-12-4-11-4-64-5)	Pubmlst
225	Ab08-26	Thailand/2008	-	200[B] (17-29-24-12-19-31-40)	Pubmlst
226	Ab04-32	Thailand/2004	-	202[B] (32-46-4-11-4-32-5)	Pubmlst
227	NYD625	USA/2008	-	203[B] (41-1-72-32-1-98-6)	Pubmlst
228	NYD644	USA/2009	-	204[B] (1-17-61-2-2-99-3)	Pubmlst
229	BJH07	USA/2008	-	205[B] (1-17-60-10-28-99-32)	Pubmlst
230	UCLA 2	USA/2009	-	206[B] (1-17-72-2-2-99-3)	Pubmlst
231	UCLA 3	USA/2009	-	207[B] (10-53-84-11-4-100-5)	Pubmlst
232	UCLA 11	USA/2009	-	208[B] (1-3-61-2-2-97-3)	Pubmlst
233	207	Argentina/2002	Environmental (bed-rail)	209[B] (1-15-60-39-28-56-32)	Pubmlst
234	AB104	Argentina/1992	-	210[B] (1-47-52-10-28-4-32)	Pubmlst
235	AB170	Argentina/1989	-	211[B] (1-52-62-39-4-4-38)	Pubmlst
236	202	Argentina/2002	Environmental (personnel hand)	212[B] (1-15-60-10-28-56-9)	Pubmlst
237	72	Argentina/2002	Environmental (personnel hand)	213[B] (1-52-52-10-28-55-32)	Pubmlst
238	AB17	Argentina/2002	-	214[B] (1-15-60-10-28-57-32)	Pubmlst
239	279	Argentina/2002	-	215[B] (12-17-72-1-26-3-7)	Pubmlst

Table S1. Geographically and genotypically divergent 277 isolates selected for analyzing the global epidemiology of *A. baumannii* (cont.)

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
240	49631	Argentina/2008	-	216[B] (10-12-32-11-12-9-5)	Pubmlst
241	287	Argentina/2006	-	217[B] (10-12-4-5-12-57-5)	Pubmlst
242	OXA-23 clone 1	.	-	218[B] (1-3-61-2-2-102-3)	Pubmlst
243	TUM10634	Japan/2007	-	219[B] (1-3-61-2-2-101-3)	Pubmlst
244	H07-988	Korea/2007	-	220[B] (1-3-3-2-1-7-3)	Pubmlst
245	TUM10639	Japan/2007	-	221[B] (33-57-86-10-1-103-6)	Pubmlst
246	TUM10641	Japan/2007	-	222[B] (1-15-87-28-1-104-32)	Pubmlst
247	LAMAB032	China/2009	MDR	223[B] (1-17-3-2-2-56-3)	Pubmlst
248	405 E4	China/2006	-	224[B] (1-34-72-6-1-18-45)	Pubmlst
249	C186	Brazil/2007	-	225[B] (12-17-72-1-29-99-39)	Pubmlst
250	I128	Brazil/2008	-	226[B] (12-17-72-1-29-16-54)	Pubmlst
251	I056	Brazil/2007	-	227[B] (1-15-60-10-28-99-32)	Pubmlst
252	I013	Brazil/2007	-	228[B] (1-15-87-28-1-16-32)	Pubmlst
253	C012	Brazil	-	229[B] (1-15-87-28-1-107-32)	Pubmlst
254	C581	Brazil	-	230[B] (1-17-60-10-28-108-32)	Pubmlst
255	I006	Brazil/2007	-	231[B] (10-12-88-11-4-98-5)	Pubmlst
256	252	Brazil	-	232[B] (21-48-89-50-36-109-4)	Pubmlst
257	282	Brazil	-	233[B] (1-15-60-10-28-106-32)	Pubmlst
258	596	Brazil	-	234[B] (21-48-89-42-36-109-4)	Pubmlst
259	440	Brazil	-	235[B] (1-69-90-2-1-79-30)	Pubmlst
260	487	Brazil	-	236[B] (12-17-72-1-29-102-39)	Pubmlst
261	597	Brazil	-	237[B] (1-15-60-10-28-106-4)	Pubmlst
262	546	Brazil	-	238[B] (1-3-61-2-38-97-3)	Pubmlst
263	A47	Germany	Carbapenem-S, int. clone II, $bla_{\text{OXA-66}}$	239[B] (1-12-3-2-2-55-3)	Pubmlst, [131, 132]
264	A37	Singapore	Carbapenem-S, $bla_{\text{OXA-64}}$	240[B] (1-15-2-15-1-52-16)	Pubmlst, [131, 132]
265	A60	Argentina	Carbapenem-S, int. clone II, $bla_{\text{OXA-65}}$	241[B] (1-15-52-10-28-12-16)	Pubmlst, [131, 132]
266	A135	Belgium	Carbapenem-S, $bla_{\text{OXA-111}}$	242[B] (1-28-49-10-1-24-4)	Pubmlst, [131, 132]
267	A457	Estonia	Carbapenem-S, $bla_{\text{OXA-106}}$	243[B] (1-50-13-6-4-60-42)	Pubmlst, [131, 132]
268	A13	The Netherlands	Carbapenem-S, int. clone III, $bla_{\text{OXA-71}}$	244[B] (1-51-1-1-1-9-6)	Pubmlst, [131, 132]
269	A404	Poland	Carbapenem-I, int. clone I, $bla_{\text{OXA-110}}$	245[B] (10-12-4-11-4-4-5)	Pubmlst, [131, 132]
270	A443	Slovenia	Carbapenem-I, int. clone I, $bla_{\text{OXA-107}}$	245[B] (10-12-4-11-4-4-5)	Pubmlst, [131, 132]
271	A424	Croatia	Carbapenem-R, int. clone I, $bla_{\text{OXA-107}}$	246[B] (10-12-4-11-4-55-5)	Pubmlst, [131, 132]
272	A479	UK (exported from Pakistan)	Carbapenem-I, int. clone I, $bla_{\text{OXA-69}}$	247[B] (10-12-4-11-4-58-5)	Pubmlst, [131, 132]
273	A388	Greece	Carbapenem-S, $bla_{\text{OXA-92}}$	248[B] (10-18-4-11-4-11-5)	Pubmlst, [131, 132]
274	A374	The Netherlands	$bla_{\text{OXA-51}}$	249[B] (12-18-12-1-29-14-39)	Pubmlst, [131, 132]
275	A125	Northern Ireland	$bla_{\text{OXA-51}}$	250[B] (12-18-12-1-29-55-23)	Pubmlst, [131, 132]

Table S1. Geographically and genotypically divergent 277 isolates selected for analyzing the global epidemiology of *A. baumannii* (cont.)

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
276	A95	Italy	Carbapenem-S, $bla_{\text{OXA-98}}$	251^{B} (32-48-54-35-1-11-40)	Pubmlst, [131, 132]
277	A473	Poland	Carbapenem-I, int. clone II, $bla_{\text{OXA-108}}$	252^{B} (1-49-38-12-31-56-4)	Pubmlst, [131, 132]

[a]UK, the United Kingdom; USA, the United States of America.
[b]Ref., reference; Int., international; S, susceptible; I, intermediate; R, resistant; MDR, multidrug resistant; SG, sequence group.
[c]ST^{B}, sequence type according to Bartual's scheme.
[d]Pubmlst, http://pubmlst.org/abaumannii/.
[e]RUH 134 was assigned into two different STs by the reference articles.
[f]M08-20 and I02-18 were $bla_{\text{OXA-23-like}}$-, $bla_{\text{OXA-24-like}}$-, and $bla_{\text{OXA-58-like}}$-neg [146].
[g]Isolate was associated with no label and ST146 was designated as STn27 in the supplementary data of the reference article.

Table S2. Geographically and genotypically divergent 129 isolates selected for analyzing the global epidemiology of *A. baumannii*

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
1	LUH 3783	Czech Republic/1991	MDR, outbreak-related, int. clone I	1^P (1-1-1-1-5-1-1)	Pasteur MLST, [39]
2	LUH 6015	Italy/1998	MDR, outbreak-related, int. clone I	1^P (1-1-1-1-5-1-1)	Pasteur MLST, [39]
3	LUH 6224	Australia/1995	MDR, outbreak-related, int. clone I	1^P (1-1-1-1-5-1-1)	Pasteur MLST, [39]
4	LUH 7140	UK/2000	MDR, outbreak-related, int. clone I	1^P (1-1-1-1-5-1-1)	Pasteur MLST, [39]
5	LUH 8592	Bulgaria/2001	MDR, outbreak-related, int. clone I	1^P (1-1-1-1-5-1-1)	Pasteur MLST, [39]
6	LUH 9668	Ireland/2003	MDR, int. clone I	1^P (1-1-1-1-5-1-1)	Pasteur MLST, [39]
7	RUH 3247	Belgium/1990	MDR, outbreak-related, int. clone I	1^P (1-1-1-1-5-1-1)	Pasteur MLST, [39]
8	LUH 6050	South Africa	MDR, outbreak-related, int. clone I	1^P (1-1-1-1-5-1-1)	Pasteur MLST, [39]
9	LUH 5881	Spain/1998	MDR, outbreak-related, int. clone I	1^P (1-1-1-1-5-1-1)	Pasteur MLST, [39]
10	LUH 6125	Poland/1998	MDR, outbreak-related, int. clone I	1^P (1-1-1-1-5-1-1)	Pasteur MLST, [39]
11	AYE	France/2001	MDR, outbreak-related	1^P (1-1-1-1-5-1-1)	Pasteur MLST, [39]
12	AB0057	USA/2004	MDR	1^P (1-1-1-1-5-1-1)	Pasteur MLST, [39]
13	3887	Greece/2006	$bla_{\text{OXA-58}}$ and $bla_{\text{VIM-4}}$ imipenem-R, outbreak-related, int. clone I	1^P (1-1-1-1-5-1-1)	[82]
14	A1755	UK/2000	Sporadic, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, [39]
15	LUH 4629	Czech Republic/1996	MDR, outbreak-related, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, [39]
16	LUH 5682	The Netherlands/1993	MDR, isolated from horse, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, [39]
17	LUH 6024	Spain/1998	MDR, outbreak-related, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, [39]
18	RUH 3422	Denmark/1984	Antibiotic-S, sporadic, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, [39]
19	LUH 5868	France/1997	MDR, outbreak-related, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, [39]
20	LUH 6021	Poland/1998	MDR, outbreak-related, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, [39]
21	LUH 8143	Singapore/1997	MDR, outbreak-related, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, [39]
22	RUH 3381	Ireland/1989	MDR, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, [39]
23	LUH 6231	Australia/1999	MDR, outbreak-related, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, [39]
24	3979	Italy/2006	MDR, outbreak-related, $bla_{\text{OXA-58}}$ carbapenem-R, colistin-S, int. clone II	2^P (2-2-2-2-2-2-2)	[127]
25	3894	Greece/2006	$bla_{\text{OXA-58}}$ and $bla_{\text{VIM-1}}$ imipenem-R, outbreak strain, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, [82]
26	4026	Lebanon/2007	$bla_{\text{OXA-58}}$ imipenem-R, outbreak strain, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, [82]
27	ANT229	Turkey/2009	-	2^P (2-2-2-2-2-2-2)	Pasteur MLST
28	AO-12066 (K51-54)	Sweden/2004	MDR, $bla_{\text{OXA-58-like}}$ carbapenem-R, int. clone II	2^P (2-2-2-2-2-2-2)	Pasteur MLST, paper III
29	LUH 6009	France/1997	MDR, outbreak-related, int. clone III	3^P (3-3-2-2-3-1-3)	Pasteur MLST, [39]
30	LUH 6012	Italy/1998	MDR, outbreak-related, int. clone III	3^P (3-3-2-2-3-1-3)	Pasteur MLST, [39]
31	LUH 6028	Spain/1998	MDR, outbreak-related, int. clone III	3^P (3-3-2-2-3-1-3)	Pasteur MLST, [39]
32	LUH 9536	Belgium/1993	MDR, outbreak-related, int. clone III	3^P (3-3-2-2-3-1-3)	Pasteur MLST, [39]
33	4025	Lebanon/2005	$bla_{\text{OXA-58}}$ imipenem-R, int. clone III	3^P (3-3-2-2-3-1-3)	Pasteur MLST, [39]
34	LUH 8225	The Netherlands/2002	Antibiotic-S, sporadic	4^P (1-3-3-2-4-1-4)	Pasteur MLST, [39]
35	LUH 5703	Poland/1999	MDR, outbreak-related	5^P (4-1-2-2-4-1-5)	Pasteur MLST, [39]
36	AO-8866 (K51-58)	Sweden (exported from Poland)/2006	MDR, $bla_{\text{OXA-58-like}}$ carbapenem-R, SG7	5^P (4-1-2-2-4-1-5)	Pasteur MLST, paper III
37	A955	UK/2000	Sporadic	6^P (5-4-4-1-3-3-4)	Pasteur MLST, [39]

Table S2. Geographically and genotypically divergent 129 isolates selected for analyzing the global epidemiology of *A. baumannii* (cont.)

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
38	LUH 3782	Czech Republic/1991	MDR, int. clone I	7^{P} (1-1-1-2-5-1-1)	Pasteur MLST, [39]
39	RUH 0510	The Netherlands/1984	MDR, outbreak-related, int. clone I	8^{P} (1-1-1-1-1-1-1)	Pasteur MLST, [39]
40	700	Italy/1999	-	8^{P} (1-1-1-1-1-1-1)	Pasteur MLST
41	3886	Greece/2005	-	8^{P} (1-1-1-1-1-1-1)	Pasteur MLST
42	LUH 4633	Czech Republic/1993	Antibiotic-S	9^{P} (3-1-5-3-6-1-3)	Pasteur MLST, [39]
43	LUH 4641	Czech Republic/1994	MDR	10^{P} (1-3-2-1-4-4-4)	Pasteur MLST, [39]
44	LUH 6237	Australia/1981-91	Antibiotic-S, sporadic	10^{P} (1-3-2-1-4-4-4)	Pasteur MLST, [39]
45	LUH 4718	Czech Republic/1994	Antibiotic-S	11^{P} (1-2-6-2-3-4-4)	Pasteur MLST, [39]
46	LUH 4727	Czech Republic/1994	Antibiotic-S	12^{P} (3-5-7-1-7-2-6)	Pasteur MLST, [39]
47	LUH 5687	The Netherlands/1996	Antibiotic-S, Isolated from dog, int. clone III	13^{P} (3-1-2-2-4-1-3)	Pasteur MLST, [39]
48	LUH 5874	France/1997	MDR, outbreak-related	14^{P} (3-3-2-2-3-1-7)	Pasteur MLST, [39]
49	LUH 8406	Czech Republic/2001	MDR	15^{P} (6-6-8-2-3-5-4)	Pasteur MLST, [39]
50	LUH 6374	The Netherlands/2000	MDR, outbreak-related	15^{P} (6-6-8-2-3-5-4)	Pasteur MLST, [39]
51	LUH 8147	Argentina/1995	MDR, outbreak-related	15^{P} (6-6-8-2-3-5-4)	Pasteur MLST, [39]
52	3868	Turkey/2003	$bla_{\text{OXA-58-like}}$ imipenem-R, outbreak-related	15^{P} (6-6-8-2-3-5-4)	Pasteur MLST, [82]
53	Ab54	Spain/2003-04	Imipenem-R, outbreak-related	15^{P} (6-6-8-2-3-5-4)	[137]
54	LUH 6639	The Netherlands/2001	MDR, outbreak-related	16^{P} (7-7-2-2-8-4-4)	Pasteur MLST, [39]
55	SDF	France/<1999	Antibiotic-S, sporadic	17^{P} (3-29-30-1-9-1-4)	Pasteur MLST, [39]
56	LUH 8326	The Netherlands/2002	Antibiotic-S, sporadic	18^{P} (1-8-9-2-4-6-4)	Pasteur MLST, [39]
57	LUH 8605	Bulgaria/2002	MDR, sporadic, int. clone I	19^{P} (1-2-1-1-5-1-1)	Pasteur MLST, [39]
58	LUH 8723	The Netherlands/2003	MDR, outbreak-related, int. clone I	20^{P} (3-1-1-1-5-1-1)	Pasteur MLST, [39]
59	2979	Italy/2002	Imipenem-S, outbreak-related, int. clone I	20^{P} (3-1-1-1-5-1-1)	Pasteur MLST, [82]
60	3130	Lebanon/2004	$bla_{\text{OXA-58}}$ imipenem-R, outbreak-related, int. clone I	20^{P} (3-1-1-1-5-1-1)	Pasteur MLST, [82]
61	LUH 9415	The Netherlands/2004	Antibiotic-S, sporadic	21^{P} (3-3-2-2-4-4-8)	Pasteur MLST, [39]
62	RUH 1093	The Netherlands/1985	Antibiotic-S, sporadic	22^{P} (3-9-3-2-4-1-9)	Pasteur MLST, [39]
63	RUH 1316	The Netherlands/1964	Antibiotic-S	23^{P} (1-3-10-1-4-4-4)	Pasteur MLST, [39]
64	AO-11921 (K51-60)	Sweden/2006	MDR, $bla_{\text{OXA-58-like}}$ carbapenem-R, SG5	23^{P} (1-3-10-1-4-4-4)	Pasteur MLST, paper III
65	RUH 1317	The Netherlands/1985	Antibiotic-S	24^{P} (1-10-2-2-9-1-10)	Pasteur MLST, [39]
66	RUH 1486	The Netherlands/1985	Antibiotic-S, sporadic	25^{P} (3-3-2-4-7-2-4)	Pasteur MLST, [39]
67	3865	Turkey/2005	$bla_{\text{OXA-23}}$ and $bla_{\text{OXA-58}}$ imipenem-R, outbreak-related	25^{P} (3-3-2-4-7-2-4)	Pasteur MLST, [82]
68	3890	Greece/2003	$bla_{\text{OXA-58}}$ imipenem-R; outbreak-related	25^{P} (3-3-2-4-7-2-4)	Pasteur MLST, [82]
69	4190	Italy/2009	$bla_{\text{OXA-72}}$ imipenem-R, outbreak-related	25^{P} (3-3-2-4-7-2-4)	Pasteur MLST, [82]
70	AO-471 (K51-49)	Sweden (exported from Thailand)/2005	MDR, $bla_{\text{OXA-23-like}}$ carbapenem-R, SG12	25^{P} (3-3-2-4-7-2-4)	Pasteur MLST, paper III
71	DR25547 (LUH14601)	Singapore/1996	$bla_{\text{OXA-23}}$, $bla_{\text{OXA-64}}$	25^{P} (3-3-2-4-7-2-4)	Pasteur MLST
72	RUH 1907	The Netherlands/1986	Antibiotic-S, sporadic	26^{P} (1-2-11-5-3-1-11)	Pasteur MLST, [39]

Table S2. Geographically and genotypically divergent 129 isolates selected for analyzing the global epidemiology of *A. baumannii* (cont.)

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
73	RUH 2180	The Netherlands/1987	Antibiotic-S, sporadic	27[P] (3-3-12-2-9-7-4)	Pasteur MLST, [39]
74	RUH 2208	Sweden/1980-81	Antibiotic-S, sporadic	28[P] (1-1-2-2-10-4-4)	Pasteur MLST, [39]
75	RUH 3413	UK/1981	MDR, sporadic	29[P] (1-3-13-1-5-8-12)	Pasteur MLST, [39]
76	RUH 3423	Denmark/1990	Antibiotic-S, sporadic	30[P] (1-1-2-5-3-2-3)	Pasteur MLST, [39]
77	RUH 3424	Denmark/1990	Antibiotic-S, sporadic	31[P] (1-2-2-2-11-1-1)	Pasteur MLST, [39]
78	RUH 3425	Denmark/1990	Antibiotic-S, sporadic	32[P] (1-1-2-2-3-4-4)	Pasteur MLST, [39]
79	Ab55	Spain/2004-07	Imipenem-R, outbreak-related	32[P] (1-1-2-2-3-4-4)	[137]
80	RUH 3429	Sweden/1980-81	Antibiotic-S, sporadic	34[P] (8-1-14-3-12-1-13)	Pasteur MLST, [39][e]
81	LUH 4631	Czech Republic/1992	Antibiotic-S	35[P] (9-3-2-2-5-4-14)	Pasteur MLST, [39][e]
82	LUH 4707	Czech Republic/1992	Antibiotic-S	36[P] (1-2-2-2-3-1-2)	Pasteur MLST, [39][e]
83	LUH 4708	Czech Republic/1992	Antibiotic-S	37[P] (3-2-2-2-7-1-2)	Pasteur MLST, [39][e]
84	LUH 4709	Czech Republic/1993	Antibiotic-S	38[P] (3-2-15-6-6-4-5)	Pasteur MLST, [39][e]
85	LUH 4711	Czech Republic/1992	Antibiotic-S	39[P] (10-4-3-2-13-1-2)	Pasteur MLST, [39][e]
86	LUH 4722	Czech Republic/1996	Antibiotic-S	40[P] (1-2-2-2-5-1-14)	Pasteur MLST, [39][e]
87	LUH 4725	Czech Republic/1993	Antibiotic-S	41[P] (1-1-2-2-12-1-5)	Pasteur MLST, [39][e]
88	LUH 5684	The Netherlands/1994	Antibiotic-S, isolated from horse	42[P] (3-11-16-1-13-1-15)	Pasteur MLST, [39]
89	LUH 5685	The Netherlands/1994	Antibiotic-S, isolated from dog	43[P] (3-3-13-2-4-4-5)	Pasteur MLST, [39]
90	LUH 5691	The Netherlands/1997	Antibiotic-S, isolated from cat	44[P] (11-2-2-4-13-1-2)	Pasteur MLST, [39]
91	LUH 6011	Greece/1997	MDR, outbreak-related, int. clone II	45[P] (2-6-2-2-2-2-2)	Pasteur MLST, [39]
92	LUH 7852	Czech Republic/1994	MDR	46[P] (5-12-11-2-14-9-14)	Pasteur MLST, [39]
93	LUH 7855	Czech Republic/2000	MDR, outbreak-related, int. clone II	47[P] (2-13-2-2-2-2-20)	Pasteur MLST, [39]
94	LUH 8088	The Netherlands/2002	Antibiotic-S, sporadic	48[P] (3-14-2-2-15-4-5)	Pasteur MLST, [39]
95	LUH 9084	The Netherlands/2003	Antibiotic-S, sporadic	49[P] (3-3-6-2-3-1-5)	Pasteur MLST, [39]
96	AB900	USA/2003	Antibiotic-S	49[P] (3-3-6-2-3-1-5)	Pasteur MLST, [39]
97	LUH 9136	The Netherlands/2004	MDR, sporadic	50[P] (3-15-17-2-3-1-2)	Pasteur MLST, [39]
98	RUH 0414	The Netherlands/1978	Antibiotic-S	51[P] (3-16-6-2-16-4-2)	Pasteur MLST, [39]
99	RUH 1752	The Netherlands/1986	Antibiotic-S, outbreak-related	52[P] (3-2-2-7-9-1-5)	Pasteur MLST, [39]
100	RUH 1063	<1948	Antibiotic-S	52[P] (3-2-2-7-9-1-5)	Pasteur MLST, [39]
101	ATCC 17904	<1962	Antibiotic-S	54[P] (12-3-18-2-17-4-5)	Pasteur MLST, [39]
102	RUH 2688	The Netherlands/1987	Antibiotic-S, sporadic	55[P] (13-4-2-2-6-1-16)	Pasteur MLST, [39]
103	RUH 3410	UK/1982	Antibiotic-S, sporadic	56[P] (3-17-7-2-18-1-2)	Pasteur MLST, [39]
104	RUH 3414	UK/1988	Antibiotic-S, sporadic	57[P] (1-3-17-5-3-1-14)	Pasteur MLST, [39]
105	SB 1414	The Netherlands/1997	Antibiotic-S	58[P] (13-4-2-2-7-1-2)	Pasteur MLST, [39]
106	LUH 6049	Turkey/1997	MDR, int. clone II	59[P] (3-2-19-2-5-2-5)	Pasteur MLST, [39]
107	3978	Italy/2006	MDR, outbreak-related, bla_{OXA-58} carbapenem-R, colistin-S, SG8, bla_{OXA-90}	78[P] (25-3-6-2-28-1-29)	[127]
108	Ab1	Spain/2006-07	Imipenem-R, outbreak-related	79[P] (26-2-2-2-29-4-5)	[137]
109	Ab9	Spain/2005-07	Imipenem-R, outbreak-related	80[P] (1-1-10-1-4-4-5)	[137]
110	Ab20	Spain/1999-2000	Imipenem-R, outbreak-related	81[P] (1-1-1-1-5-1-2)	[137]
111	2977	Italy/2001	bla_{OXA-58} imipenem-R	82[P] (28-3-2-1-4-4-4)	[82]

Table S2. Geographically and genotypically divergent 129 isolates selected for analyzing the global epidemiology of *A. baumannii* (cont.)

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
112	3866	Turkey/2003	$bla_{\text{OXA-58}}$ imipenem-R, outbreak-related	83^{P} (26-4-2-2-9-1-4)	Pasteur MLST, [82]
113	3871	Turkey/2003	$bla_{\text{OXA-58}}$ imipenem-R	84^{P} (6-6-8-2-3-5-30)	Pasteur MLST, [82]
114	4389	Greece/2003	-	85^{P} (5-2-4-1-3-3-4)	Pasteur MLST
115	4381	Greece/2003	-	86^{P} (6-30-2-19-31-20-31)	Pasteur MLST
116	ANK29	Turkey/2009	-	95^{P} (1-3-2-2-4-24-2)	Pasteur MLST
117	ANK33	Turkey/2009	-	96^{P} (1-2-36-2-2-2-2)	Pasteur MLST
118	IZM35	Turkey/2009	-	97^{P} (2-2-36-2-2-2-2)	Pasteur MLST
119	ANK17	Turkey/2009	-	98^{P} (1-2-2-2-2-2-2)	Pasteur MLST
120	ANT750	Turkey/2009	-	99^{P} (12-3-18-2-4-4-5)	Pasteur MLST
121	D1	Turkey/2009	-	100^{P} (1-1-1-2-1-1-2)	Pasteur MLST
122	D10	Turkey/2009	-	101^{P} (1-1-1-2-1-1-1)	Pasteur MLST
123	D14	Turkey/2009	-	102^{P} (1-1-1-2-1-5-2)	Pasteur MLST
124	ML	Egypt/2010	MDR, $bla_{\text{NDM-2}}$ carbapenem-R	103^{P} (7-3-2-1-7-1-4)	Pasteur MLST, [89]
125	pla30155	China/2010	MDR	104^{P} (2-2-2-2-2-2-14)	Pasteur MLST
126	pla30104	China/2008	Antibiotic-S	105^{P} (1-2-2-2-5-1-2)	Pasteur MLST
127	pla30162	China/2010	Antibiotic-S	106^{P} (3-3-16-1-13-1-1)	Pasteur MLST
128	AO-2412 (K51-56)	Sweden (exported from Thailand)/2005	MDR, $bla_{\text{OXA-23-like}}$ carbapenem-R, SG13	109^{P} (26-4-2-2-9-1-5)	Pasteur MLST, paper III
129	Acb16	Romania/2010	$bla_{\text{OXA-58-like}}$	110^{P} (3-2-2-4-7-2-2)	Pasteur MLST

[a]UK, the United Kingdom; USA, the United States of America.
[b]Ref., reference; Int., international; S, susceptible; R, resistant; MDR, multidrug resistant; SG, sequence group.
[c]ST^{P}, sequence type according to Pasteur Institute's scheme.
[d]Pasteur MLST, http://www.pasteur.fr/recherche/genopole/PF8/mlst/.
[e]Sequence types ST34-ST41 in the Pasteur MLST database were inconsistently designated as ST33-ST40 in the reference article.

Table S3. Geographically and genotypically divergent 35 isolates selected for analyzing the global epidemiology of *A. baumannii*

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
1	RUH 2207	Sweden/1980	Antibiotic-S, sporadic	11^{B} (4-11-6-1-7-8-6) 53^{P} (1-1-2-2-3-4-2)	Pubmlst, Pasteur MLST, [39, 133]
2	RUH 875	The Netherlands/1984	Ref. strain, outbreak-related, int. clone I, bla_{OXA-69}	12^{B} (8-4-4-4-4-5-5) 109^{B} (10-12-4-11-4-9-5) 1^{P} (1-1-1-1-5-1-1)	Pubmlst, Pasteur MLST, [39, 131-133]
3	LUH 5875	The Netherlands/1997	Ref. strain, MDR, outbreak-related, carbapenem-S, int. clone III, bla_{OXA-71}	187^{B} (1-1-1-1-1-9-6) 3^{P} (3-3-2-2-3-1-3)	Pasteur MLST, [39, 72, 131, 132]
4	ATCC 19606 (DSM 30007)	The Netherlands/1911	Ref. strain, Antibiotic-S, sporadic	14^{B} (1-10-10-6-1-4-14) 26^{B} (1-10-36-22-20-4-24) 52^{P} (3-2-2-7-9-1-5)	Pubmlst, Pasteur MLST, [39, 133, 143]
5	ATCC 17978	1951	Ref. strain, Antibiotic-S	112^{B} (1-12-56-36-1-61-26) 77^{P} (3-2-2-2-3-4-28)	Pubmlst, Pasteur MLST, [39]
6	240	France/2003	bla_{OXA-23} (Tn*2006*) carbapenem-R, int. clone II	92^{B} (1-3-3-2-2-7-3) 2^{P} (2-2-2-2-2-2-2)	[135]
7	512	Tahiti/2004	bla_{OXA-23} (Tn*2006*) carbapenem-R, int. clone II	92^{B} (1-3-3-2-2-7-3) 2^{P} (2-2-2-2-2-2-2)	[135]
8	761	Vietnam/2005	bla_{OXA-23} (Tn*2006*) carbapenem-R, int. clone II	92^{B} (1-3-3-2-2-7-3) 2^{P} (2-2-2-2-2-2-2)	[135]
9	810	New Caledonia/2004	bla_{OXA-23} (Tn*2006*) carbapenem-R, int. clone II	92^{B} (1-3-3-2-2-7-3) 2^{P} (2-2-2-2-2-2-2)	[135]
10	863	Thailand/2006	bla_{OXA-23} (Tn*2006*) carbapenem-R, int. clone II	92^{B} (1-3-3-2-2-7-3) 2^{P} (2-2-2-2-2-2-2)	[135]
11	883	Reunion/2006	bla_{OXA-23} (Tn*2006*) carbapenem-R, int. clone II	92^{B} (1-3-3-2-2-7-3) 2^{P} (2-2-2-2-2-2-2)	[135]
12	859	South Africa/2006	bla_{OXA-23} (Tn*2006*) carbapenem-R, int. clone II	92^{B} (1-3-3-2-2-7-3) 2^{P} (2-2-2-2-2-2-2)	[135]
13	AS1	UAE/2006	bla_{OXA-23} (Tn*2006*) carbapenem-R, int. clone I	109^{B} (10-12-4-11-4-9-5) 1^{P} (1-1-1-1-5-1-1)	[135]
14	Ab14	Algeria/2004	bla_{OXA-23} (Tn*2007*) carbapenem-R, int. clone I	109^{B} (10-12-4-11-4-9-5) 1^{P} (1-1-1-1-5-1-1)	[135]
15	585	France/2004	bla_{OXA-23} (Tn*2006*) carbapenem-R, int. clone II	118^{B} (1-3-3-2-2-3-3) 2^{P} (2-2-2-2-2-2-2)	[135]
16	BEL	Belgium/2007	bla_{OXA-23} (Tn*2007*) carbapenem-R, int. clone I	245^{B} (10-12-4-11-4-4-5) 1^{P} (1-1-1-1-5-1-1)	[135]
17	614	Libya/2004	bla_{OXA-23} (Tn*2008*) carbapenem-R, int. clone I	95^{B} (10-12-4-11-1-9-5) 20^{P} (3-1-1-1-5-1-1)	[135]
18	AS3	UAE/2006	bla_{OXA-23} (IS*Aba1*) carbapenem-R, int. clone I	95^{B} (10-12-4-11-1-9-5) 20^{P} (3-1-1-1-5-1-1)	[135]
19	1190	Bahrain/2008	bla_{OXA-23} (IS*Aba1*) carbapenem-R, int. clone I	95^{B} (10-12-4-11-1-9-5) 20^{P} (3-1-1-1-5-1-1)	[135]
20	142HUC	Portugal/1999	bla_{OXA-40} carbapenem-R	98^{B} (1-12-3-2-2-3-3) 2^{P} (2-2-2-2-2-2-2)	[136]
21	65FFC (65HUC)	Portugal/1998	bla_{IMP-5} carbapenem-R, amikacin-S, ciprofloxacin-S	120^{B} (1-3-6-1-4-3-6) 32^{P} (1-1-2-2-3-4-4)	Pubmlst, [136]
22	K71-71	Norway (exported from Pakistan)/2009	MDR, $bla_{OXA-23-like}$ carbapenem-R, *armA*, SG4, bla_{OXA-51}	103^{B} (12-17-12-1-29-3-39) 15^{P} (6-6-8-2-3-5-4)	Pubmlst, Pasteur MLST, paper II
23	K58-19	Norway (exported from Italy)/2009	MDR; $bla_{OXA-23-like}$ carbapenem-R, *armA*, int. clone II; bla_{OXA-66}	118^{B} (1-3-3-2-2-3-3) 2^{P} (2-2-2-2-2-2-2)	Pubmlst, Pasteur MLST, paper II
24	K61-46	Norway (exported from Pakistan)/2009	MDR, $bla_{OXA-23-like}$ carbapenem-R, int. clone II, bla_{OXA-66}	137^{B} (1-3-3-2-2-12-3) 2^{P} (2-2-2-2-2-2-2)	Pubmlst, Pasteur MLST, paper II

Table S3. Geographically and genotypically divergent 35 isolates selected for analyzing the global epidemiology of *A. baumannii* (cont.)

No.	Isolate	Country and year of isolation[a]	Comment[b]	Sequence type[c]	Reference[d]
25	K12-21	Norway (exported from Greece)/2004	MDR, $bla_{\text{OXA-58-like}}$ carbapenem-R, int. clone II, $bla_{\text{OXA-66}}$	189^{B} (1-12-3-2-2-4-3) 45^{P} (2-6-2-2-2-2-2)	Pubmlst, Pasteur MLST, paper II
26	K44-35	Norway (exported from Thailand)/2007	MDR, $bla_{\text{OXA-23-like}}$ carbapenem-R, int. clone II, $bla_{\text{OXA-66}}$	190^{B} (1-3-3-2-2-52-3) 2^{P} (2-2-2-2-2-2-2)	Pubmlst, Pasteur MLST, paper II
27	K47-42	Norway (exported from China)/2007	MDR, $bla_{\text{OXA-23-like}}$ carbapenem-R, *armA*, int. clone II; $bla_{\text{OXA-66}}$	191^{B} (1-3-3-2-2-94-3) 2^{P} (2-2-2-2-2-2-2)	Pubmlst, Pasteur MLST, paper II
28	K48-42	Norway (exported from India)/2008	MDR, $bla_{\text{OXA-23-like}}$ carbapenem-R, int. clone I, $bla_{\text{OXA-69}}$	192^{B} (10-53-4-11-4-95-5) 1^{P} (1-1-1-1-5-1-1)	Pubmlst, Pasteur MLST, paper II
29	K55-13	Norway (exported from Cyprus)/2009	MDR, $bla_{\text{OXA-24-like}}$ carbapenem-R, int. clone II, $bla_{\text{OXA-66}}$	193^{B} (1-35-3-2-2-3-3) 2^{P} (2-2-2-2-2-2-2)	Pubmlst, Pasteur MLST, paper II
30	K55-61	Norway (exported from India)/2009	MDR, $bla_{\text{OXA-23-like}}$ carbapenem-R, SG9, $bla_{\text{OXA-69}}$	194^{B} (1-15-4-11-4-58-4) 94^{P} (1-2-2-1-5-1-1)	Pubmlst, Pasteur MLST, paper II
31	K58-15	Norway (exported from Thailand)/2009	MDR, $bla_{\text{OXA-23-like}}$ carbapenem-R, *armA*, int. clone II, $bla_{\text{OXA-66}}$	195^{B} (1-3-3-2-2-96-3) 2^{P} (2-2-2-2-2-2-2)	Pubmlst, Pasteur MLST, paper II
32	Ab2941	Brazil/2007	$bla_{\text{OXA-23-like}}$ carbapenem-R, int. clone II, $bla_{\text{OXA-66}}$	131^{B} (1-15-60-10-28-56-32) 79^{P} (26-2-2-2-29-4-5)	Pubmlst, [130]
33	Ab3222	Brazil/2007	$bla_{\text{OXA-23-like}}$ carbapenem-R, SG4, $bla_{\text{OXA-132}}$	133^{B} (12-17-72-1-29-67-39) 15^{P} (6-6-8-2-3-5-4)	Pubmlst, [130]
34	HGSA56	Portugal/2007-08	$bla_{\text{OXA-23-like}}$ carbapenem-R, int. clone II, $bla_{\text{OXA-66}}$	92^{B} (1-3-3-2-2-7-3) 2^{P} (2-2-2-2-2-2-2)	[134]
35	HGSAI40	Portugal/2008	$bla_{\text{OXA-58-like}}$ carbapenem-R, SG4, $bla_{\text{OXA-132}}$	103^{B} (12-17-12-1-29-3-39) 15^{P} (6-6-8-2-3-5-4)	[134]

[a]UAE, the United Arab Emirates.
[b]Ref., reference; Int., international; S, susceptible; R, resistant; MDR, multidrug resistant; SG, sequence group.
[c]ST^{B}, sequence type according to Bartual's scheme; ST^{P}, sequence type according to Pasteur Institute's scheme.
[d]Pubmlst, http://pubmlst.org/abaumannii/; Pasteur MLST, http://www.pasteur.fr/recherche/genopole/PF8/mlst/.

Paper I

Karah, N., B. Haldorsen, K. Hegstad, G. S. Simonsen, A. Sundsfjord, Ø. Samuelsen, and the Norwegian Study Group on *Acinetobacter*. 2011. Species identification and molecular characterization of *Acinetobacter* spp. blood culture isolates from Norway. J. Antimicrob. Chemother. **66:**738-744.

Paper II

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Paper III

Karah, N., C. G. Giske, A. Sundsfjord, and Ø. Samuelsen. 2011. A diversity of OXA-carbapenemases and class 1 integrons among carbapenem-resistant *Acinetobacter baumannii* clinical isolates from Sweden belonging to different international clonal lineages. Submitted to Microbial Drug Resistance.

Paper IV

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