**Supplementary File 1.**

# CARBAPENEMASES: CLASSIFICATION, OCCURRENCE, STRUCTURE AND CATALYTIC MECHANISM

## Carbapenem hydrolysing class D beta-lactamases (CHDL)

CHDLs are the most common factor of carbapenem resistance in *A. baumannii* strains. These enzymes are referred as OXAs (oxacillinases) due to their ability to hydrolyse oxazolylpenicillin – oxacillin much faster than benzylpenicillin [1, 2]. Currently, more than 400 OXA enzymes have been described, within variants possessing carbapenemase activity. Among *A. baumannii* there have been identified so far six groups of OXA carbapenemases represented by: OXA-51-like, OXA-23-like, OXA-40/24-like, OXA-58-like, OXA-143-like, and OXA-48-like [3, 4]. The estimated sequence identities between members of OXA carbapenemases subgroups and enzymes belonging to each subgroup were more than 90% and less than 70%, respectively. Taking into consideration the structure of these enzymes, four essential motifs have been described. Till date the crystal structures of OXA-23, OXA-40/24, OXA-58, OXA-48, and OXA-146 have been determined. The general structure of class D carbapenemases comprises of two domains of which one includes helixes, and the second has a mixed alpha/beta domain [5]. The enzymes have in common three highly conserved active site elements represented by: 1) the tetrad – Ser70-X-X-Lys (X represents a variable residue, containing the active site serine; Ser70 according to the class D beta-lactamase numbering), 2) Ser118-X-Val/Ile, which is equivalent to the invariable Ser-Asp-Asn motif in class A beta-lactamases and Tyr-Ala/Ser-Asn in AmpC beta-lactamases, 3) Lys216-Thr/Ser-Gly element, that is common to the vast majority of serine-active beta-lactamases. Additional conserved motifs in class D beta-lactamases are represented by the triad Tyr/Phe144-Gly-Asn and the tetrad Trp232-X-X-Gly that have no analogues in either class A or AmpC beta-lactamases [6]. The enzymatic reaction of class D carbapenemases considers acylation and deacylation of beta-lactam, facilitated by the conserved lysine residue. In these groups of enzymes, the covalent acyl-enzyme intermediate is not formed.

**OXA-51-like group.** The largest group of OXA-type beta-lactamases (currently consisting of 95 closely related enzymes) is represented by OXA-51-like family. These enzymes are innate to *A. baumannii* and are encoded on the chromosome of this bacterium [3]. The kinetic studies performed by Smith and co-authors revealed the low catalytic efficiency for carbapenems, which was attributed to low affinity of the OXA-51 enzyme for

these antimicrobial agents. Further analysis concerning the structure of the enzyme revealed that low affinity towards carbapenems is derived from the presence of transient steric barrier which is formed by the occurrence of site chain of Trp222 in the enzymes active site. The research concerning the substitution of the Trp222Met showed that single amino acid substitution relieves the mentioned above steric hindrance and elevates the affinity of the mutant enzyme for carbapenems. The mutant enzyme exhibited tenfold rise in the affinity and an increase the level of resistance to these antimicrobials. Therefore, it was concluded that in the near future the OXA-51 family may become one of the most important carbapenemase, resulting with important clinical consequences among *A. baumannii* infections [7]. While natural low-level expression of OXA-51-like beta-lactamases have little impact on carbapenem susceptibility, the insertion sequence (IS*Aba1*) mediated overproduction can lead to carbapenem resistance [8]. Analysis performed by Figueiredo and co-authors revealed the fiftyfold increase of $bla_{\text{OXA-66}}$ expression (member of $bla_{\text{OXA-51-like}}$ gene family) in the isolate carrying IS*Aba1*. Moreover, the authors demonstrated that inactivation of a $bla_{\text{OXA-66}}$ gene in *A. baumannii* resulted in higher susceptibility to carbapenems [9]. The cases of *A. baumannii* strains resistant to carbapenems only due to the overexpression of OXA-51-like were reported inter alia in Spain and Korea, but this mode of resistance according to current knowledge remains globally infrequent [10, 11].

**OXA-23-like group.** The first identified acquired class D beta-lactamase with carbapenemase activity was OXA-23. It was detected in *A. baumannii* isolate collected in Edinburg, United Kingdom [12]. The ability of this enzyme to hydrolyse carbapenems, comparing to other CHDLs, is significant [1]. Till date, the OXA-23-like group includes 19 enzymes, known to be located on plasmids and chromosomes, mainly in *A. baumannii* isolates. Furthermore, the members of this group were also detected among other Gram-negative bacterial species, represented inter alia by: *A. junii*, *A. radioresistens*, *A. pittii*, *Proteus mirabilis*, *Acinetobacter* phenon 5, *Acinetobacter* phenon 6/ct 13TU, *A. nosocomialis*, *Acinetobacter* genomic species 10/11, *A. lwoffii*, *Klebsiella pneumoniae*, and *A. baylyi*. These carbapenemases are predominantly spread via plasmid-mediated transfer [4, 8]. Furthermore, the expression of OXA-23-like enzymes may be enhanced by the presence of IS*Aba1* upstream of $bla_{\text{OXA-23-like}}$ gene [13]. The OXA-23-like enzymes are capable of hydrolysing oxyiminocephalosporins, aminopenicillins, piperacillin, oxacillin, and aztreonam as well as carbapenems. Additionally, taking into consideration the OXA-23 turnover rate for subjected to the study carbapenems (imipenem, meropenem, ertapenem, and doripenem) the highest value was noted for imipenem [4]. Moreover, tight binding of the carbapenems by OXA-23

enzyme is associated with the presence of a hydrophobic bridge across the top of the active site, which is formed by phenylalanine 110 and methionine 221 [4, 14]. Clonal studies concerning carbapenem resistance among OXA-23 carrying strains revealed that the presence of the gene is efficient enough to confer the resistance. Furthermore, the high level of resistance can be accomplished due to the co-existence of OXA-23 and other resistance mechanisms, e.g. AdeABC efflux pump [4]. The spread of beta-lactamases belonging to OXA-23-like group has been reported worldwide and *A. baumannii* strains carrying these enzymes are isolated in Italy [15], Poland [16], France [17], Spain [18], Japan [19], Egypt [20], Australia [21], the United States of America [22], Brazil [23], and others [24].

**OXA-40/24-like group.** Further group of acquired carbapenemases belonging to class D beta-lactamases is OXA-40/24-like. The first discovered member of OXA-40/24-like group was OXA-24 enzyme, currently renamed to OXA-40. This beta-lactamase originated from *A. baumannii* outbreak strain from hospital in Spain [25]. OXA-40 was also the first CHDL enzyme identified in *A. baumannii* in the United States of America [26]. The OXA-40/24-like group comprises till date of 7 enzymes, mostly identified in *A. baumannii*, but lately also encoded on plasmids or chromosomes of Gram-negative bacteria, represented by other species of *Acinetobacter* genus as well as *P. aeruginosa* and *K. pneumoniae* [4]. The OXA-40/24 enzymes are able to hydrolyse the penicillins, and display the weaker activity towards cephalosporins and carbapenems. While, within OXA-40/24 group the kinetic parameters substantially differ, the OXA-40 exhibits the highest activity versus carbapenems [4]. The studies concerning insertional inactivation or insertion of cloned $bla_{\text{OXA-40}}$ gene, confirmed the significant role of OXA-40 in the resistance to carbapenems [27]. Taking into consideration the structure of apo OXA-24, it was suggested that the ability of the enzyme to hydrolyse carbapenems is facilitated by an entrance tunnel resembling entry to the active site formed by side chains of residues Tyr112 and Met223 [14]. *Acinetobacter baumannii* strains carrying OXA-40/24 enzymes have been isolated worldwide, including countries, such as: Spain [28], Portugal [29], Finland [30], Poland [31], Croatia [32], Turkey [33], Egypt [34], Iran [35], and the United States of America [36].

**OXA-58-like group.** The first described representative of this group was carried by the carbapenem-resistant *A. baumannii* isolate originated from the hospital in Toulouse, France [37]. While OXA-58 is considered to hydrolyse carbapenems at low-level, its expression may be enhanced by the presence of insertion sequences (e.g. IS*Aba3*, IS*Aba825*), resulting in carbapenem resistance in *A. baumannii* [38, 39]. Until now, four members of OXA-58-like group (OXA-58, OXA-96, OXA-97, OXA-164), located on plasmids or

chromosomes, have been described in this species [4]. *Acinetobacter baumannii* strains carrying these CHDLs were described worldwide, inter alia in: France [37], the United States of America [39], Turkey [38], and Germany [40]. The OXA-58 kinetic analysis disclosed similarity within the enzymatic spectrum with other OXA-type enzymes in *A. baumannii*, considering weak activity towards the penicillins and carbapenems and capability to hydrolyse cefpirome and cephalothin [4]. Taking into account the crystal structure of OXA-58 enzyme, it has been reported that the active site of the beta-lactamase lacs the hydrophobic bridge. Moreover, when compared with OXA-24/40 and OXA-48, the OXA-58 has a differently shaped active site. Comparative studies concerning catalytic efficiency for imipenem of OXA-48, OXA-58 and OXA-23, OXA-24/40 suggested that the role of the active site hydrophobic bridge may not be essential factor for more efficient deacylation of carbapenems in class D carbapenemases [41].

**OXA-143-like group.** An additional reported CHDL is OXA-143. This enzyme was first recovered from clinical isolate of *A. baumannii* in Brazil in 2004. Amino acid sequence analysis of $bla_{\text{OXA-143}}$ revealed diversified degree of identity to the previously described enzymes, following 88% with OXA-40, 63% with OXA-23 and 52% with OXA-58. The enzyme hydrolytically disintegrated penicillins, oxacillin, meropenem, and imipenem. Despite the fact that OXA-143 is characterised by low rates of hydrolysis, it is more probably that it significantly contributes to resistance to imipenem and meropenem. Taking into account genetic environment of plasmid encoded OXA-143 carbapenemase, it was not associated either with insertion sequences or integrons. Further studies concerning transformation of the *A. baumannii* reference strain resulted with $bla_{\text{OXA-143}}$ mediated carbapenem resistance [42]. Currently, four members of OXA-143-like group were described in *A. baumannii*: OXA-143 [42], OXA-182 [43], OXA-231 [44], and OXA-253 [44, 45] in strains from Brazil, Korea, Honduras, and Brazil, respectively.

**OXA-48-like group.** While OXA-48-like enzymes are the most frequently reported among *K. pneumoniae* and other Enterobacteriaceae, very recently there have been described the first detection of OXA-48-like-producing *A. baumannii*. The isolate derived from fecal flora of a nursing home resident in northern Portugal [46]. General structure of the OXA-48 enzyme is considered to resemble OXA-1, OXA-10 and OXA-13, although they differ structurally in the length and orientation of beta5-beta6 loop. Furthermore, it was also concluded that the short-loop connecting beta5- and beta6-strands may be responsible for the carbapenemase activity of the OXA-48 enzyme. The above-mentioned structure is situated within the active site of OXA-48, forming a narrow active site cleft [5, 47].

Table 1 presents acquired CHDLs described till date in *A. baumannii* strains (Table 1).

**Ambler class B beta-lactamases**

These enzymes are often described as metallo-beta-lactamases (MBL) and possess one or two metal ions (usually zinc) in their active site, in the opposition to a serine residue present among A, C and D class enzymes. Due to zinc dependence, MBL catalysis is inhibited by metal-chelating agents e.g. EDTA (ethylenediaminetetraacetic acid) [3]. These enzymes confer resistance to a broad spectrum of beta-lactams including: penicillins, cephalosporins and carbapenems. Furthermore, MBLs are not inhibited by any clinically useful beta-lactamase inhibitors, such as clavulanic acid, tazobactam and sulbactam. Metallo-beta-lactamases have been detected in strains of *P. aeruginosa*, *A. baumannii* and other Gram-negative non-fermenters as well as Enterobacteriaceae [58]. The overall structure of MBLs enzymes is very similar and all the metallo-beta-lactamases possess the alpha-beta/beta-alpha sandwich fold consisting of two central beta-sheets and five alpha-helices on the external faces. At the external edge of the beta-beta sandwich the zinc-binding motifs composed of six residues are located [5]. Taking into account the amino acid sequence homology and metal requirement, the MBLs are classified into three subclasses – B1, B2, and B3. Comparing the substrate spectrum, B1 and B3 subclasses hydrolyse broad range of beta-lactams including penicillins, cephalosporins and carbapenems, while B2 subclass enzymes have a narrow spectrum that involves carbapenems [5]. The subclass B1 contains the larger number of described so far metallo-beta-lactamases, including clinically important enzymes belonging to IMP, VIM, NDM, and SIM families [59]. The B1 metallo-beta-lactamases carry two Zn ions, with one tightly and the other loosely coordinated. However, the subclass B3 have two Zn ions, but with similar binding affinity. The subclass B2 beta-lactamases require only one zinc ion for maximal enzymatic activity, moreover the simultaneous binding of another zinc ion results with reduction of the enzymatic activity [5]. In case of B1 and B3 subclasses the role of the ligands for both metal ions is played by one water or OH-ion. Furthermore, the nucleophilic attack on the beta-lactam carbon present in the carboxyl group is considered to be associated with the Zn1 and Zn2 that stabilise and activate the OH-ion. In consequence, the formation of the intermediate characterised as transient, non-covalent, tetrahedral as well as stabilised by zinc ions is performed. Moreover, it is considered that the cleaved beta-lactam ring nitrogen protonation and disintegration of the tetrahedral intermediate is related with Zn1 and Zn2 [5]. Despite the fact that MBLs are not as much prevalent among *A. baumannii* as OXA enzymes, they exhibit significantly higher hydrolytic activity against carbapenems [60].

Currently four groups of these enzymes have been described in *A. baumannii* worldwide – IMP, VIM, SIM, and NDM [61].

**IMP (imipenemase).** The first report of IMP-type beta-lactamase considered the *P. aeruginosa* strain isolated in 1988 in Japan [62]. Currently, 42 variants of IMP have been described, predominantly in Asia and among *P. aeruginosa*. IMP enzymes are denoted with broad substrate specificity including high affinity for carbapenems and cephalosporins, but weak affinity towards 6-alpha-methoxy-penicillins [63]. Basing on the identity of the second sphere residue at position 262, IMP variants can be divided into two major groups: IMP-1-like and IMP-6-like. While IMP-1-like enzymes have Ser residue at 262 position the IMP-6-like exhibit a Gly residue at this position. Taking into consideration the differences in catalytic efficiencies, the IMP-1 possesses greater efficiency towards penicillins (in particular penicillin G and ampicillin), ceftazidime, cephaloridine, and imipenem than IMP-6 [64]. The first IMP metallo-beta-lactamase carried by *A. baumannii* was described in Brazilian teaching hospital [65]. At present, 9 variants of IMP enzymes have been reported in *A. baumannii*, predominantly occurring in Asia, but also in Europe and Southern America [61].

**VIM (Verona integron-encoded metallo-beta-lactamase).** The first described VIM enzyme (VIM-1) was found in clinical isolate of *P. aeruginosa* in Verona, Italy, in the late nineties of the twentieth century. Moreover, the VIM-2 variant was found in 1996 in France. VIM metallo-beta-lactamases exhibit a broad substrate spectrum including: penicillins, cephalosporins and carbapenems. VIM enzymes show broader substrate specificity than IMP, in addition to their high affinity towards carbapenems and cephalosporins, they also hydrolyse 6-alpha-methoxy-penicillins. Variants of VIM are characterised with the sequence similarities ranging between 81% and 99.6%, and form two major clusters represented by VIM-1-like and VIM-2-like. The comparative studies of Rossolini and co-workers revealed that both VIM-1 and VIM-2 enzymes are efficient carbapenemases characterised with low $K_m$ and $K_{cat}$ values. This feature differentiates the VIM enzymes from the other carbapenemases with comparable hydrolytic efficiencies and high $K_m$ and high $K_{cat}$ values. Moreover, in the opposition to other B1 enzymes, VIM beta-lactamases are characterised with the absence of the conserved Lys224 [64]. Presently, the VIM enzymes are considered to be the most prevalent metallo-beta-lactamases worldwide, with phenomenal spreading potential including non-fermenters as well as Enterobacteriaceae. The first MBL belonging to this group was characterised among *A. baumannii* in 2002 in Korea [66, 67]. Out of twenty-five described so far allotypes of VIM enzymes, only five were currently reported among *A. baumannii* strains in Europe and Asia [61, 62, 64, 65–69].

**SIM (Seoul imipenemase).** Another group of MBLs is represented by SIM. These enzymes hydrolyse carbapenems, as well as penicillins, narrow- and extended-spectrum cephalosporins. SIM beta-lactamases are also characterised by lower prevalence and limited spread in comparison to IMP and VIM enzymes. The SIM-1 enzyme is also characterised with 69% and 64% identity to IMP-12 and IMP-9 MBL, respectively. Among *A. baumannii*, SIM-1 was first detected in clinical strain originating from tertiary-care hospital in Seoul, Korea [70]. Taking into consideration the occurrence of SIM-positive *A. baumannii* strains, their presence is currently limited to Korea.

**NDM (New Delhi metallo-beta-lactamase).** NDM is one of the most recently discovered carbapenemase, forming a novel group of MBLs [71]. The first described NDM enzyme – NDM-1, was detected in *K. pneumoniae* strain acquired from patient who was transferred from Indian hospital to Sweden [72]. NDMs have been reported worldwide, mostly in strains belonging to Enterobacteriaceae family but also in non-fermenters and Vibrionaceae. Owing to brisk international dissemination NDMs are considered to be in near future the most prevalent carbapenemases worldwide. While primary reports suggested that NDM-positive strains were epidemiologically associated with the Indian subcontinent, current data highlight also the other areas of endemicity which are the Balkans and the Middle East [63]. NDM enzymes are able to hydrolyse penicillins, carbapenems and cephalosporins. Taking into account sequence homology among described so far NDMs, it is considered that the enzymes are less diversified than variants of VIM and IMP. Comparative studies concerning the L3 loop of NDM-1 and IMP-1, VIM-2, and VIM-7, showed that the loop of NDM-1 is more open and hydrophobic. It was also proposed that L3 loop is considered to play a significant role in the binding of antimicrobials at the active site [5]. The first clinical isolate of *A. baumannii* carrying NDM enzyme was acquired from patient from intensive care unit of a tertiary-care hospital in Chennai, India in 2010 [73]. Till date *A. baumannii* NDM-positive strains have been recovered from patients in many countries throughout the world, including: Germany [74], Switzerland [75], France [76], Spain [77], Israel [78], the United Arab Emirates [79], Egypt [80], the United Kingdom, India, Bangladesh, and Pakistan [81]. The summarized data considering metallo-beta-lactamases carried by *A. baumannii* strains are presented in Table 2 (Table 2).

**Ambler class A carbapenemases**

Among currently described serine based Ambler class A beta-lactamases only a small number of enzymes represent carbapenemase activity. The carbapenem inactivation mechanism

mediated by these enzymes is associated with the acylation and deacylation steps [5]. These beta-lactamases include six groups of enzymes with the *K. pneumoniae* carbapenemases to be currently the most clinically-relevant [63].

**KPCs (*Klebsiella pneumoniae* carbapenemases)** are serine-based enzymes, active against all beta-lactams, and not susceptible to commercially available beta-lactamase inhibitors. Till date twenty-two variants of KPC have been described [5]. The analysis of crystal structure of KPC-2 performed by Ke and co-authors revealed that subtle changes in the enzyme active site along with shifts in conserved amino acid positions which have a substantial effect on the substrate specificity [93]. KPC carbapenemases have been detected worldwide mainly in Enterobacteriaceae isolates, but also among *P. aeruginosa* and *A. baumannii* strains. The first report of KPC-positive *A. baumannii* took place in Puerto Rico. The PCR-based surveillance study conducted by Robledo and co-workers, performed in 17 hospitals, revealed the presence of 41 *A. baumannii* KPC producers. The authors emphasize the high potential of $bla_{\mathrm{KPC}}$ genes to spread among nosocomial pathogens in the hospitals of the Island [94].

**GES (Guiana extended-spectrum beta-lactamase)** enzymes are acquired beta-lactamases which have been reported in *P. aeruginosa*, Enterobacteriaceae and *A. baumannii* strains. Currently, the family includes twenty-four variants, all possessing the activity against broad-spectrum cephalosporins. Furthermore, several GES enzymes owing to the modification of the active site obtained the carbapenemase activity, within GES-2, -4, -5, -6, -11, -14, and -18 beta-lactamases hydrolysing imipenem efficiently [95]. Although, GES enzymes are not widely distributed throughout the world, there have been reports of *A. baumannii* strains carrying GES-11 and/or GES-14 beta-lactamases in France, Belgium, Turkey, and Kuwait [96–100].

## CARBAPENEMASE INHIBITORS

While production of beta-lactamases may cause a significant threat to effective therapy of *A. baumannii* infections, introduction of beta-lactamase inhibitors could be an effective strategy to conquer this clinical challenge. Unfortunately, among commercially available beta-lactamase inhibitors represented by clavulanic acid, sulbactam and tazobactam neither are effective against clinically relevant carbapenemases [101].

Further studies regarding novel beta-lactamase inhibitors represented by Avibactam (formerly NXL104), Relebactam (formerly MK7655) and RPX7009 are currently in progress [102]. The data concerning inhibition activity of Avibactam among carbapenem-resistant *A. baumannii* isolates, carrying class B and D carbapenemases, suggested the lack of the enzymes inhibition. Furthermore, research data regarding inhibition activity of Relebactam and RPX7009 are limited [103–105]. Therefore, extensive studies are carried out in order to develop effective inhibitors, particularly against class D and B carbapenemases [101].

**Inhibitors of class D enzymes**

One of the approaches to the inhibition of class D carbapenemases is represented by the use of modified penicillin sulphones. These mechanism-based beta-lactamase inactivators are characterised by high affinity for the enzymes active site and ability to form stable reaction intermediates. In the study of Drawz and co-authors, effective inhibition of OXA-40/24 enzyme was obtained by application of C-2-substituted 6-alkylidene penicillin sulphone (JDB/LN-1-255) [106]. Another approach to class D enzyme inhibition concerns application of boronic acid compounds. The first report on boronic acid-based beta-lactamase inhibitor (4,7-dichloro-1-benzothien-2-yl sulphonylaminomethyl boronic acid; DSABA) able to inhibit class D beta-lactamases was carried out by Tan and co-authors. The mechanism of DSABA action is based on docking into the catalytic pocket of serine hydrolases and forming of a transition-state tetrahedral complex with the serine hydroxyl group, resulting with shutting down the hydrolytic cycle of the enzyme. In these studies, the application of DSABA caused the reduction of MIC of imipenem against OXA-40 carrying *A. baumannii* strain [107].

**Inhibitors of class B enzymes**

One of the promising groups of MBL inhibitors is represented by thiol derivatives (TD). The mechanism of TD mediated inhibition involves zinc halation and hydrolytic displacement. The TD group is represented by captopril – medication used in the therapy of blood pressure diseases. It turned out that this agent effectively inhibits metallo-beta-lactamases including NDM-1 and subclass B1, B2 enzymes in carried out *in vitro* studies [101, 108, 109].

Another novel MBL inhibitor, able to remove zinc ions, similarly to known *in vitro* chelators, is represented by aspergillomarasmine A (AMA) [110, 111]. This natural fungal product was described as a rapid and potent inactivator of several subclass B1 enzymes, represented by NDM-1 and VIM-2, while on contrary showed weak inhibition potential towards SPM-1 and IMP beta-lactamases. According to King and co-authors, AMA reinstated

meropenem activity against selected strains of Enterobacteriaceae, as well as *Acinetobacter* and *Pseudomonas* genus, expressing VIM and NDM-type alleles. This feature suggests that combination of AMA and a carbapenem antibiotic has therapeutic potential in challenging the threat of MBL-positive Gram-negative pathogens [110].

An additional MBL inhibitor – ME1071 (disodium 2,3-diethylmaleate), was first described by Ishii and co-workers [112]. This dicarboxylic acid derivative binds to the zinc ions, therefore preventing beta-lactam from access and resulting with certain MBL inhibition. In the study of Livermore and co-authors, ME1071 activity was examined against Enterobacteriaceae and *Acinetobacter* spp. isolates carrying several MBL enzymes (incl. IMP, VIM and NDM). The authors observed two patterns concerning ME1071 carbapenemase inhibition: 1) the reduction of MICs of carbapenems for strains carrying NDM-1 revealed weaker synergy than for isolates with IMP and VIM MBL, 2) the inhibitor potentiation towards *Acinetobacter* spp. isolates with NDM carbapenemases was weaker than against NDM-1-positive Enterobacteriaceae [113].

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**TABLES**

**Table 1**

Acquired carbapenem-hydrolysing OXA-type beta-lactamases carried by *Acinetobacter baumannii* strains

| Group | Enzymes | References |
|---|---|---|
| OXA-23-like | OXA-23 | [12] |
| | OXA-27 | [48] |
| | OXA-49 | [49] |
| | OXA-146 | [50] |
| | OXA-165-OXA-171 | [51] |
| | OXA-225 | [52] |
| | OXA-239 | [53] |
| OXA-40-like* | OXA-40/24 | [25] |
| | OXA-25 | [48] |
| | OXA-26 | [48] |
| | OXA-72 | [54] |
| | OXA-139 | [55] |
| | OXA-160 | [36] |
| OXA-58-like | OXA-58 | [37] |
| | OXA-96 | [56] |
| | OXA-97 | [57] |
| | OXA-164 | [40] |
| OXA-143-like | OXA-143 | [40] |
| | OXA-182 | [43] |
| | OXA-231 | [44] |
| | OXA-253 | [44, 45] |
| OXA-48-like | NFD | [46] |

*Also described as OXA-40/24-like

NFD – not fully described

**Table 2**

Metallo-beta-lactamases reported among *Acinetobacter baumannii* strains

| Group | Enzymes | References |
|---|---|---|
| IMP | IMP-1 | [82] |
| | IMP-2 | [83] |
| | IMP-4 | [84] |
| | IMP-5 | [85] |
| | IMP-6 | [86] |
| | IMP-8 | [65] |
| | IMP-10 | [87] |
| | IMP-11 | [88] |
| | IMP-19 | [89] |
| VIM | VIM-1 | [68] |
| | VIM-2 | [67] |
| | VIM-3 | [90] |
| | VIM-4 | [91] |
| | VIM-11 | [69] |
| SIM | SIM-1 | [70] |
| NDM | NDM-1 | [92] |
| | NDM-2 | [74, 78] |