CARBAPENEMASE-PRODUCING *ACINETOBACTER* spp. FROM ISRAEL, 2001-2006

EARLIEST REPORT OF bla_{NDM}

PREDATING THE OLDEST KNOWN bla_{NDM}-POSITIVE STRAINS

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ABSTRACT

Background: Carbapenem-resistant *A. baumannii* (CRAb) is a WHO priority 1 critical pathogen. Despite Israel being affected early by high CRAb rates, limited molecular data are available. We investigated the presence of carbapenemases among 198 Acinetobacter spp. clinical isolates from Israel between 2001 and 2006.

Methods: Strains from 3 archives underwent whole-genome sequencing (Illumina NovaSeq on all, MinION on a subset) and computational analyses: assembly (Unicycler), annotation (prokka), identification (Kraken, 16S rRNA), search for carbapenemases (ResFinder, BLDB curation). Figures were generated in Inkscape, plasmid alignment on AliTV.

Results: *A. baumannii* (Ab) represented 179/198 (90.4%) Acinetobacter spp. (Figure 1). Annual incidence varied from a minimum of 16 (2001) to a maximum of 62 (2004), with an average of 30. Eighty-four Ab (46.9%) carried a carbapenemase: 38 (45.2%) blaOXA-72 (blaOXA-24-like); 28 (33.3%) blaOXA-23-like (20 blaOXA-23 and 8 blaOXA-225); 18 (21.5%) bla_{OXA-58} (16 from 2001-2). Annual CRAb rate increased yearly from 2002 (32%) to 2006 (67%).

Eight species of non-baumannii *Acinetobacter* (NbA) accounted for 19 isolates (9.6%): *A. pittii* (n=6), *lwoffii* (n=4), *junii* (n=3), *ursingii* (n=2), others n=1: *A. gyllenbergii*, *johnsonnii*, *schindleri*, and *variabilis* (Figure 1). Two of three *A. junii* contained blaOXA-58, one of which, Ajun-H1-3, isolated in a blood culture in January 2004, also possessed bla_{NDM-1}. The pNDM-Ajun-H1-3 plasmid matched numerous BJ01-like plasmids reported from 2005 onwards in *Acinetobacter* spp. as well as Enterobacterales (Figure 2).

Conclusion: We retrospectively assessed carbapenemase diversity among *Acinetobacter* spp. in Israel from 2001-2006. Analysis of 179 Ab isolates predate observations elsewhere: rapidly rising CRAb rates, driven by the dissemination of $bla_{OXA-23-like}$ and $bla_{OXA-24-like}$ genes replacing bla_{OXA-58}.

Among 19 NbA, an *A. junii* isolated in 2004 carried two carbapenemases, bla_{OXA-58} and bla_{NDM-1}, making it the earliest NDM-positive isolate reported to date, preceding NDM-positive Acinetobacter spp. found in 2005 in India.

Further investigations into the origins of bla_{NDM} are needed to understand the conditions that led to its emergence and prevent similar issues from arising in the future.

FIGURE 1 : a) Breakdown of *Acinetobacter* according to species, including presence of oxacillinases and carbapenemases b) distribution over time separated between *A. baumannii* and non-*baumannii Acinetobacter*

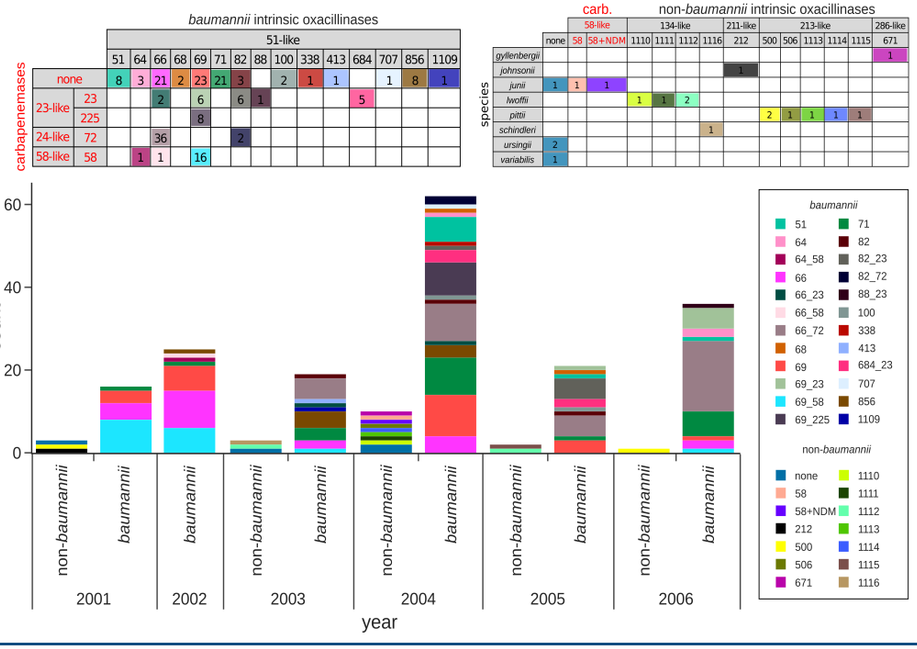
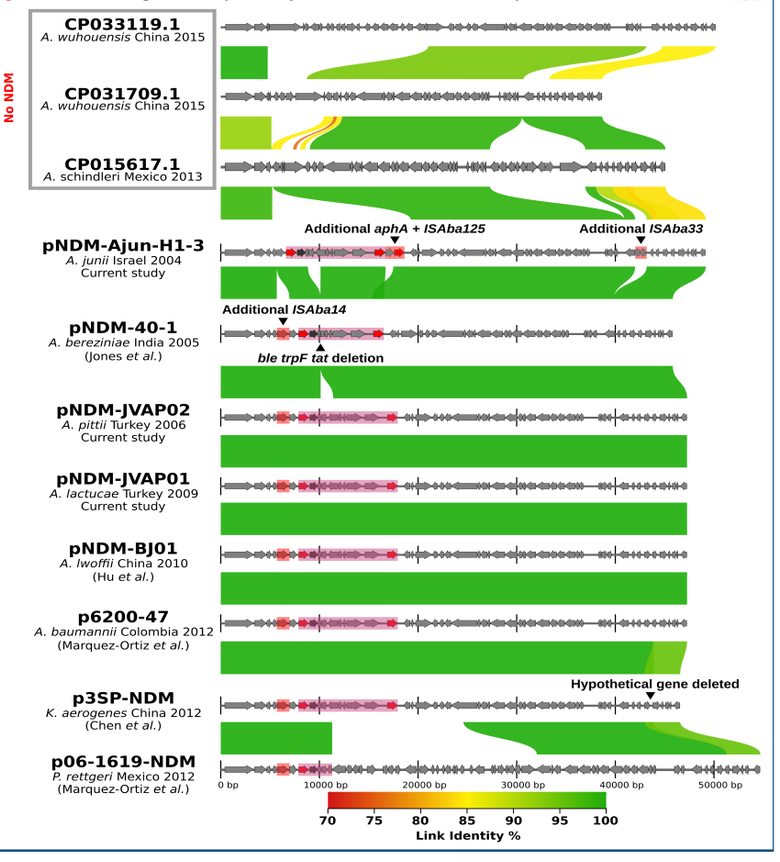


Figure 2: Plasmid alignment of pNDM-Ajun-H1-3 with other BJ01-like plasmids with or without bla_{NDM}



KEY TAKE-HOME MESSAGES

- bla_{NDM} is the most prevalent carbapenemase gene worldwide
- prior to our study, the earliest known bla_{NDM}-positive strains were *Acinetobacter* spp. from 2005 in India (Jones *et al.*)
- we identified the earliest bla_{NDM}-positive strain, an *A. junii* from 2004 from Israel
- this finding further supports the claim that *Acinetobacter* spp. are the likely source of bla_{NDM} before this gene spread to more common human pathogens
- it also suggests bla_{NDM} may have originated elsewhere than in India

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