Geographic containment and virulence-resistance trade-offs drive the evolution of hypervirulent *Klebsiella pneumoniae*

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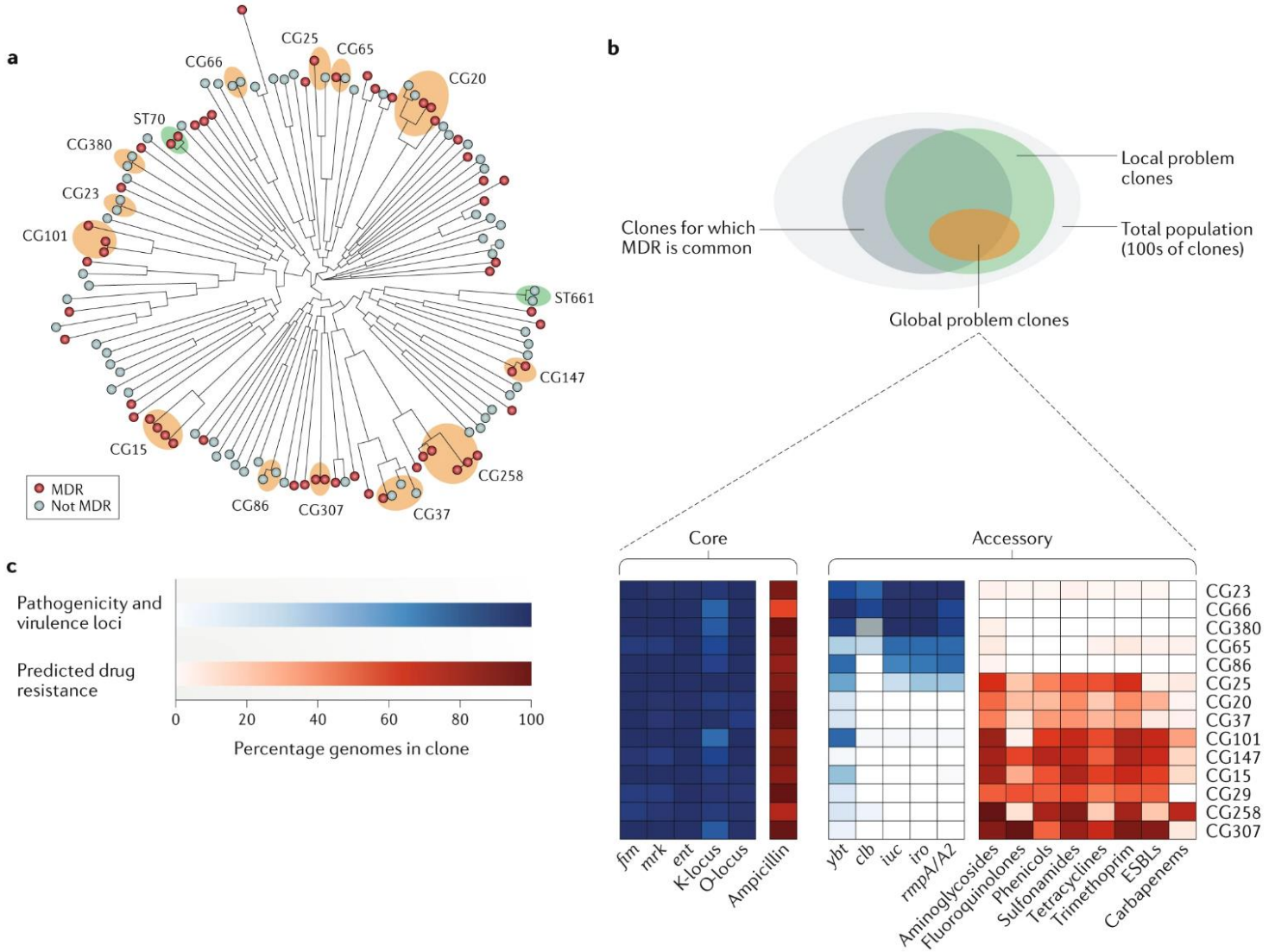
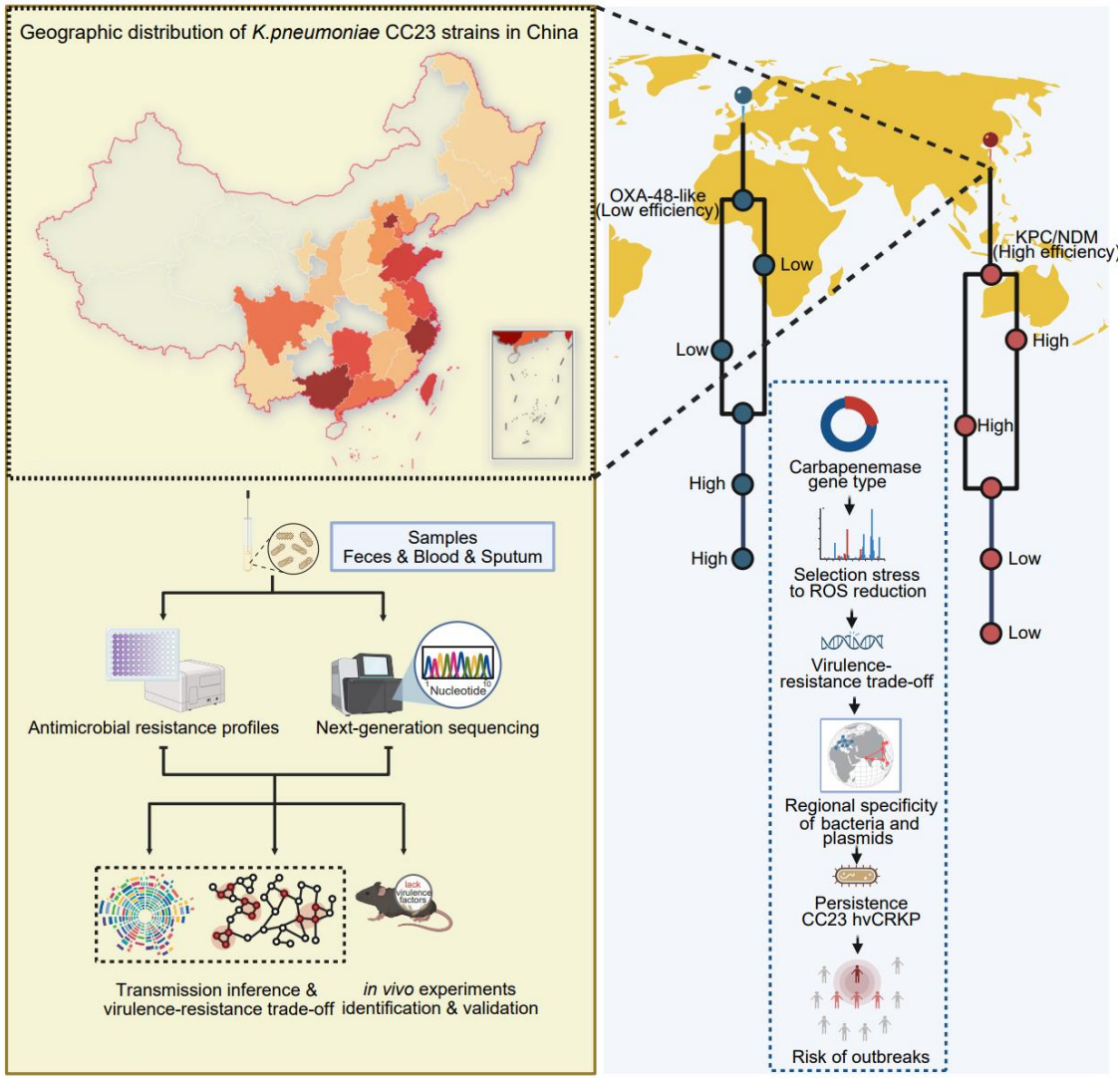
Background



The emergence of hypervirulent carbapenem-resistant *Klebsiella pneumoniae* (hvCRKP) is altering the epidemiological landscape, with CC23-K1 as a key lineage.

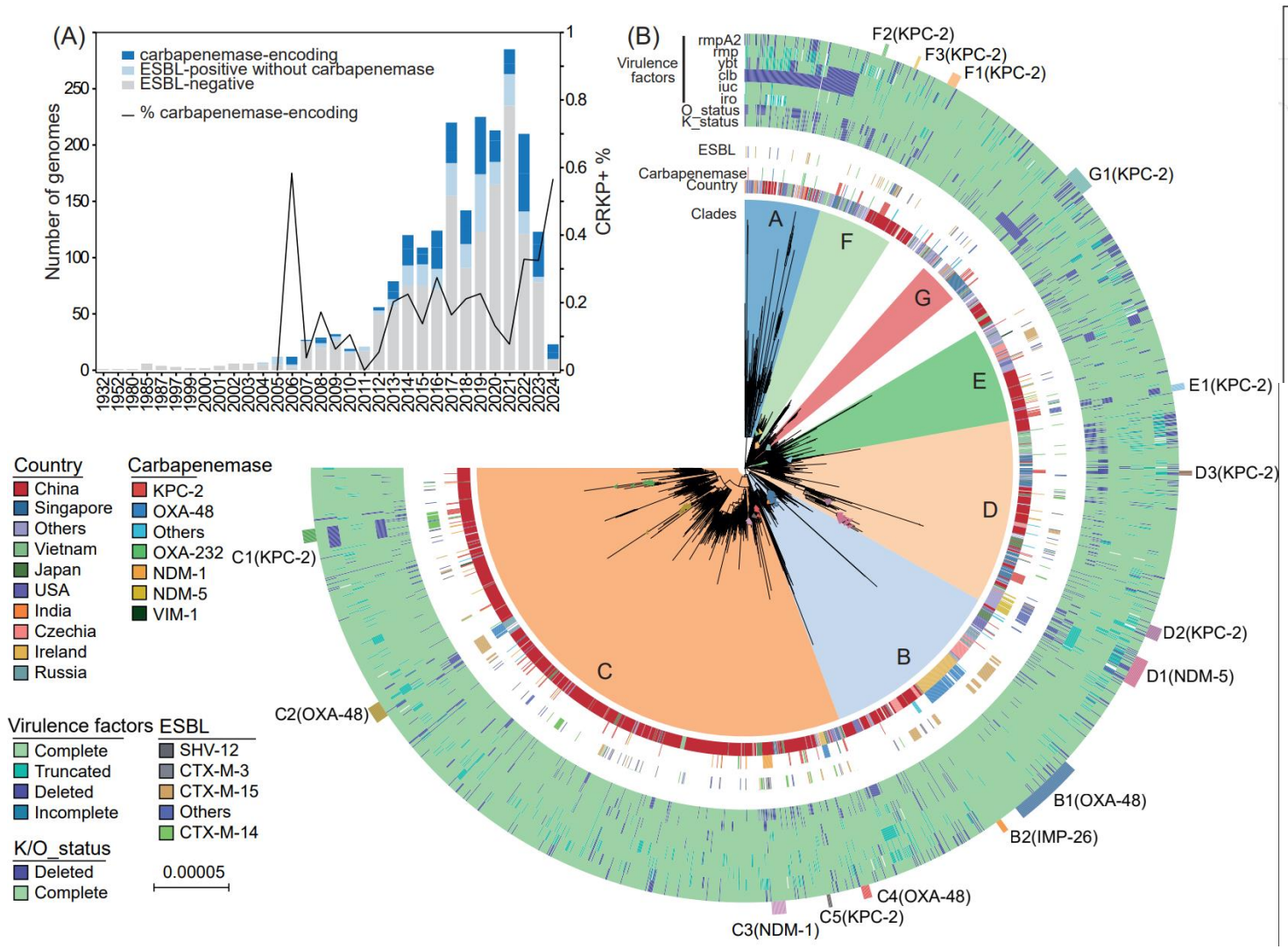
Wyres KL, Lam MMC, Holt KE. Nat Rev Microbiol. 2020

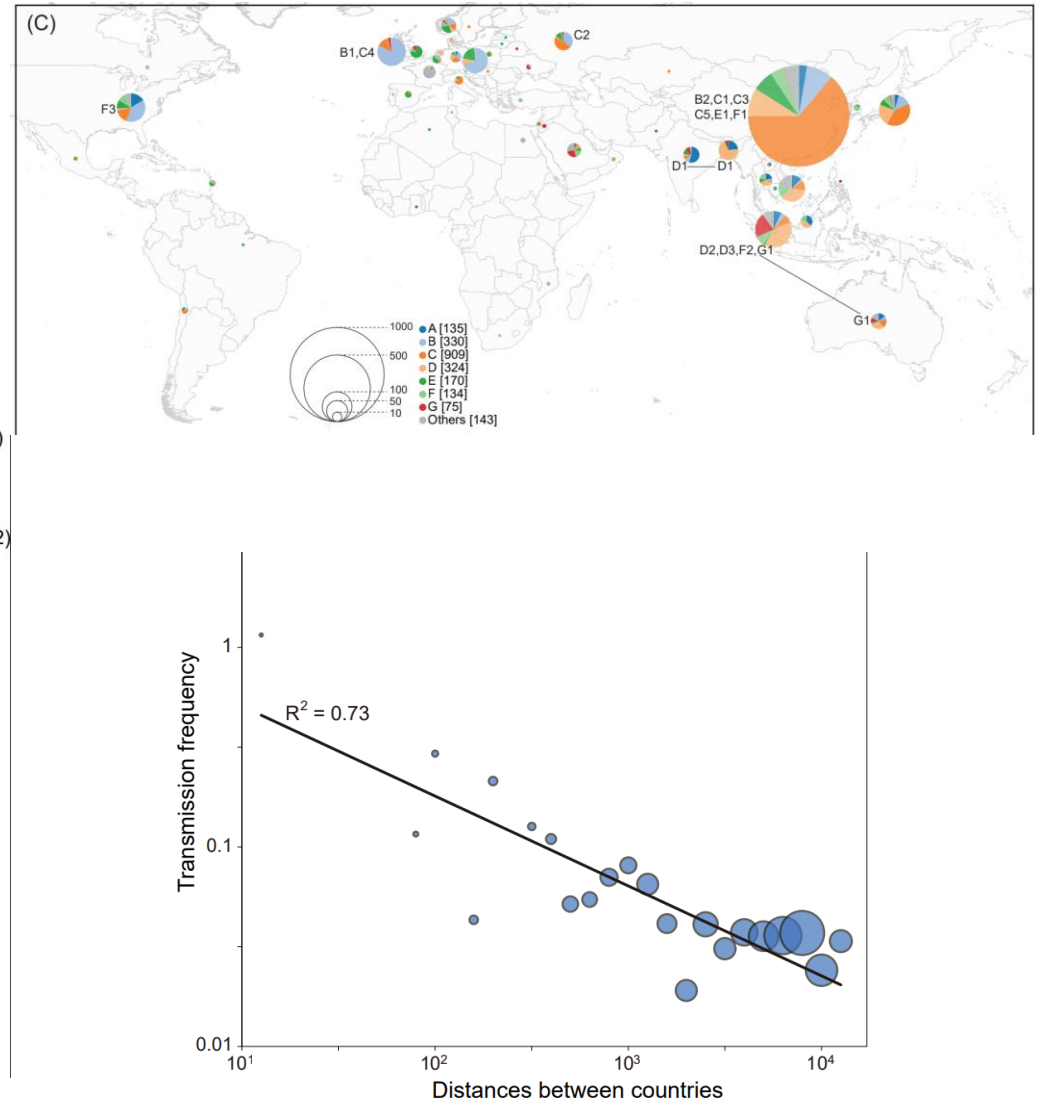
Highlights



- CC23-K1 hypervirulent *Klebsiella pneumoniae* exhibits strong geographic compartmentalization globally, with transmission patterns driven by geographic distance.
- Carbapenem resistance shows remarkable instability, with over 130 acquisition events and frequent losses.
- High-efficiency carbapenemases (bla_{KPC}/bla_{NDM}) are prevalent in Asia but incompatible with hypervirulent traits; in contrast, low-efficiency bla_{OXA-48} strains prevalent in Europe can preserve virulence determinants.
- *In vitro* and murine experiments indicate that capsule production hinders plasmid conjugation; the core genome shows adaptive signals related to metabolism and the electron transport chain (ETC).

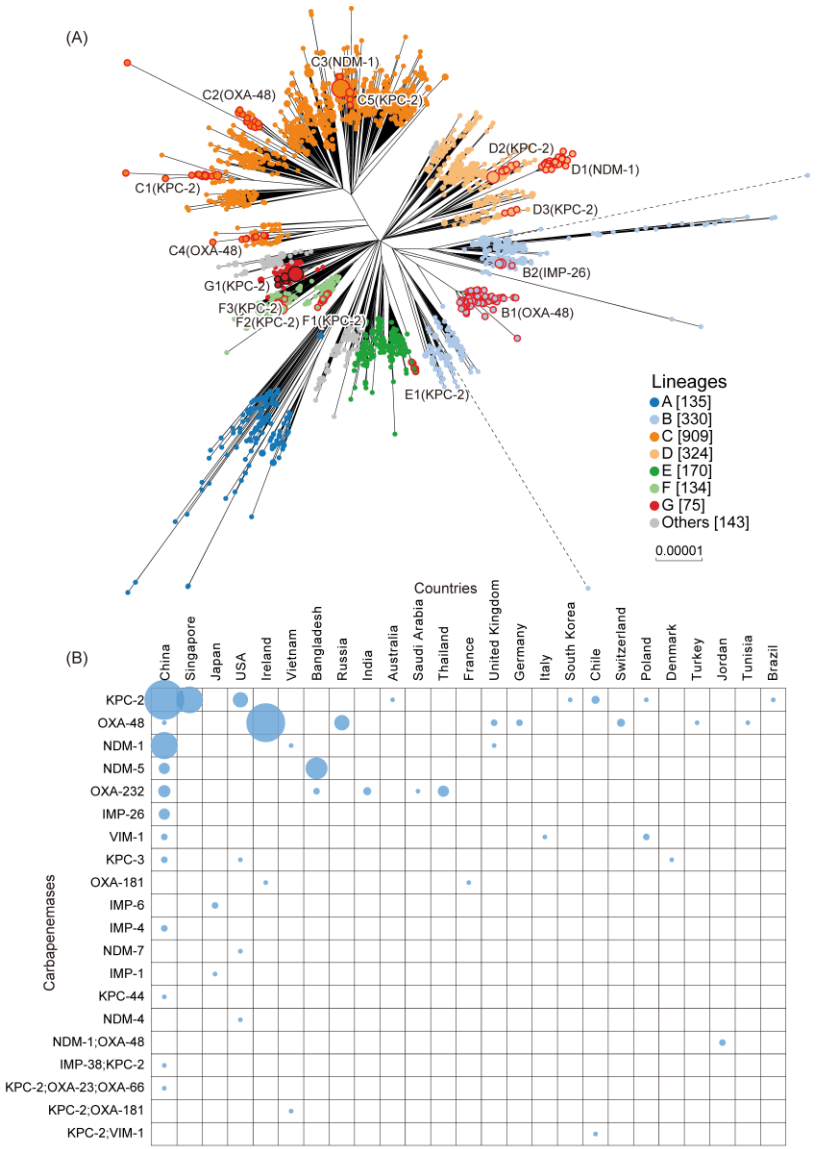
Global Population Structure and Geographic Distribution of CC23 *Klebsiella pneumoniae*

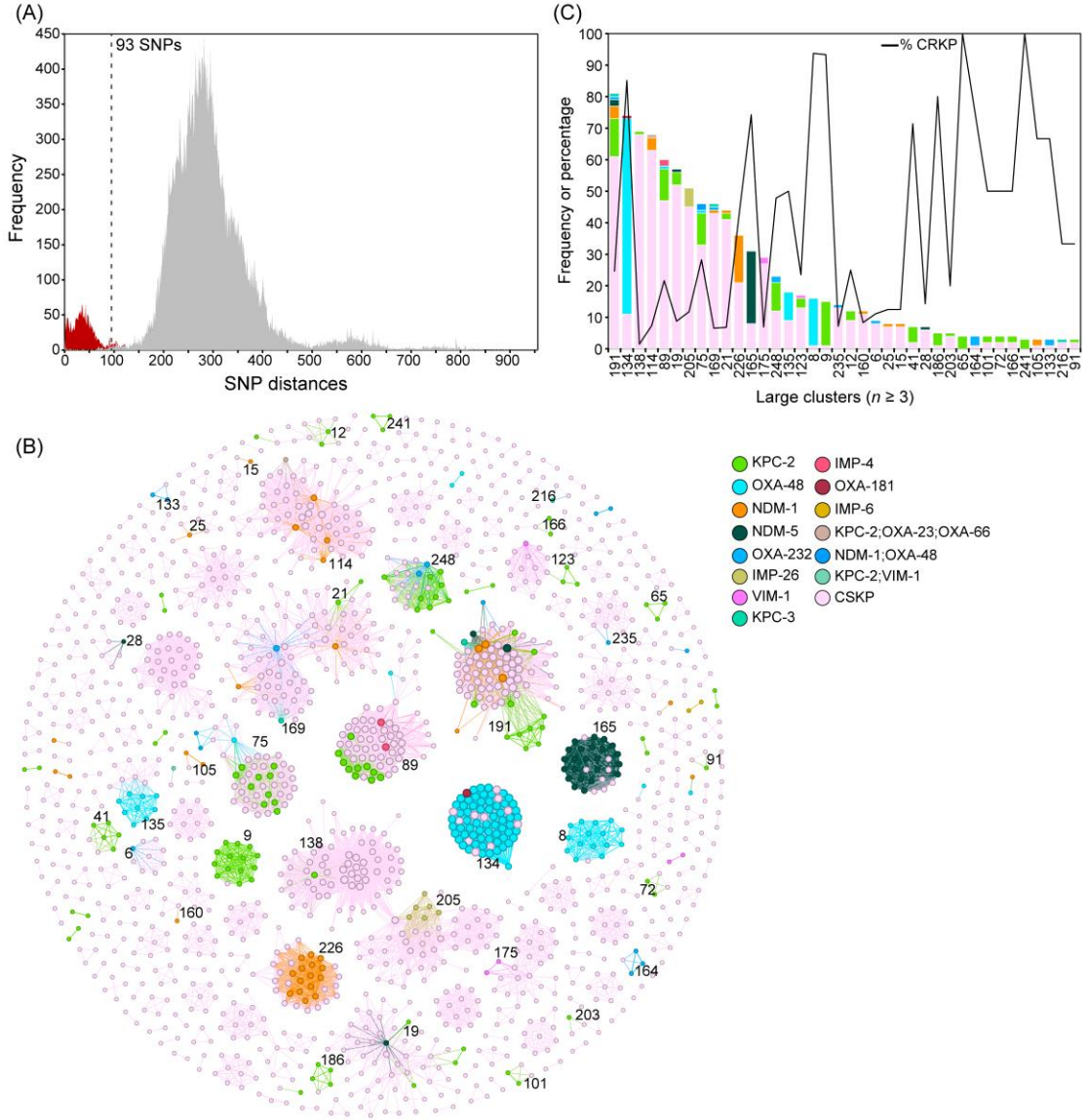




CC23-K1 has diversified into 7 major clades (A-G) with distinct regional distribution patterns and region-dependent transmission.

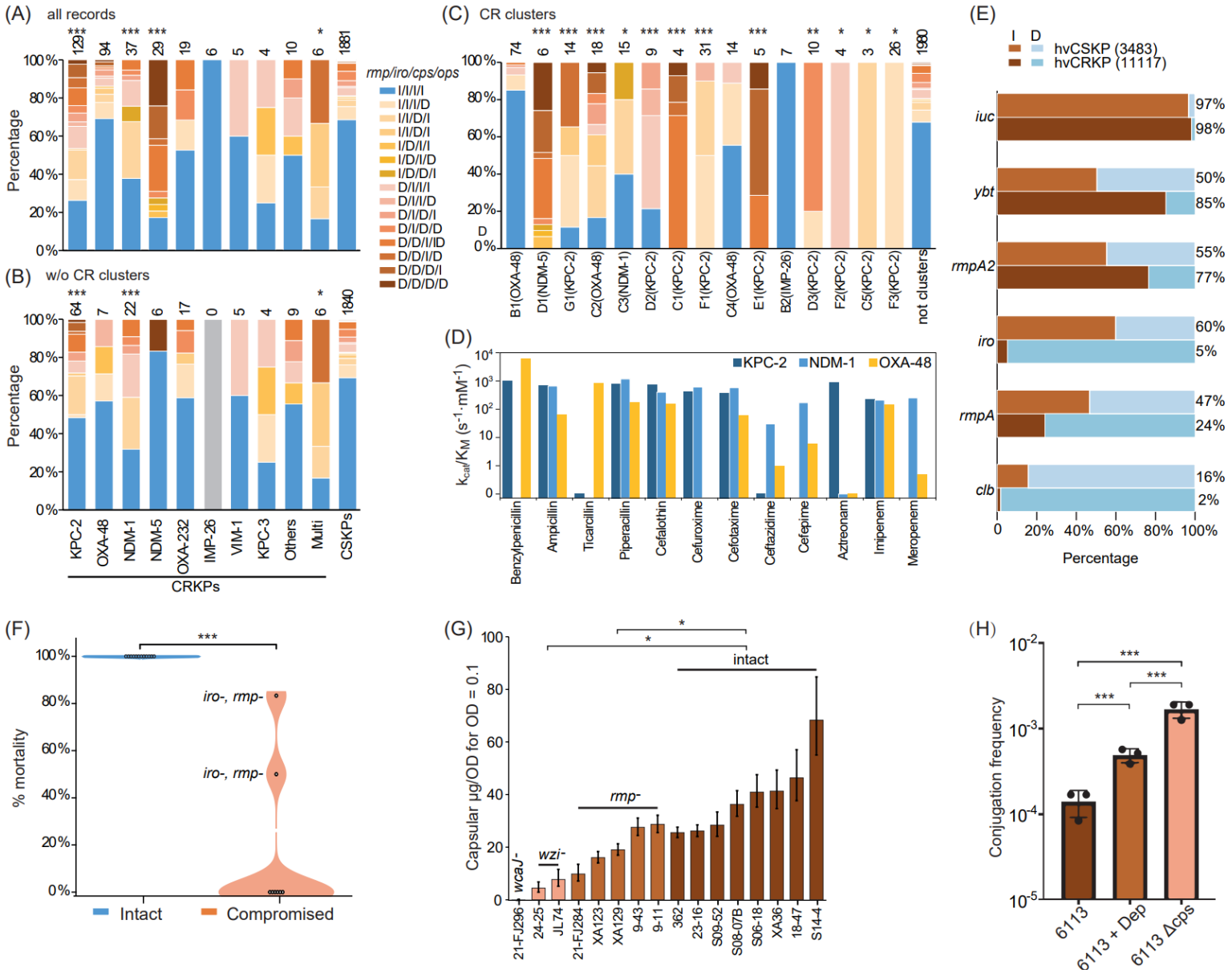
Repeated Acquisition and Loss of Carbapenem Resistance





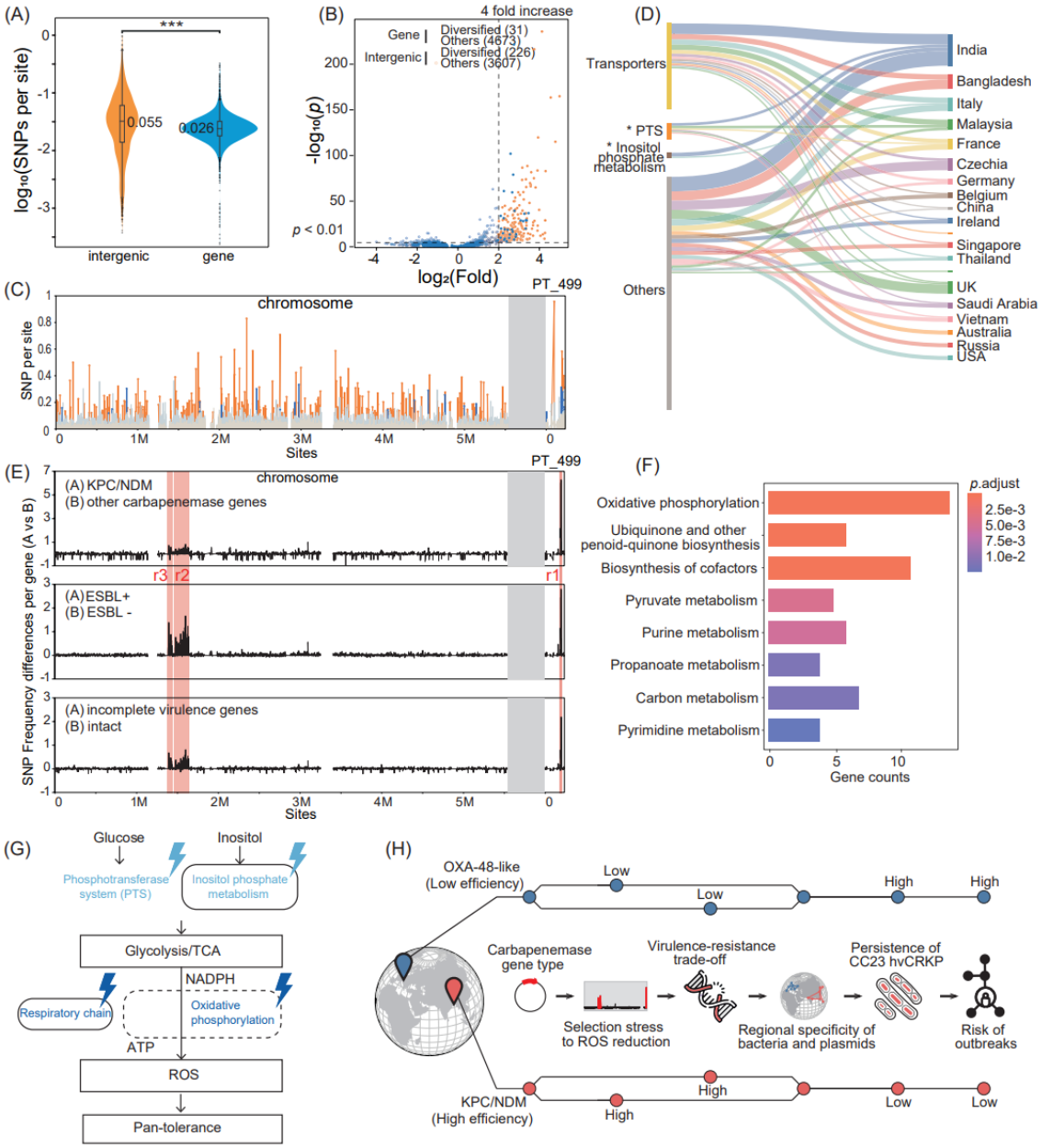
Carbapenem resistance in CC23-K1 is unstable, with at least 130 independent acquisitions and frequent losses.

Trade-off Between Virulence and Resistance



Strains carrying bla_{KPC}/bla_{NDM} often exhibit loss of virulence genes (>60%), while bla_{OXA-48} strains maintain integrity; experiments confirm that capsule production hinders plasmid transfer, and murine models show reduced virulence.

Impact of Virulence-Resistance Trade-off on the Core Genome



Highly mutated/resistance-associated regions are enriched in central metabolism and ETC pathways, potentially aiding bacterial survival under stress.

Summary

- CC23-K1 *Klebsiella pneumoniae* displays clear geographic compartmentalization and distance-dependent transmission, with its global dissemination influenced by geographic distance and local selective pressures.

- carbapenem resistance involves repetitive acquisitions and frequent losses, influenced by regional plasmid prevalence and antibiotic usage intensity.

- Strains carrying bla_{KPC} or bla_{NDM} often exhibit *cps*/*ops*/*iro*/*rmp* gene deletions and reduced virulence, while bla_{OXA-48} strains are more likely to retain intact virulence determinants; experiments confirm that capsule production physically hinders plasmid transfer.

- Core genome highly mutated regions are enriched in the phosphotransferase system (PTS), inositol metabolism, nuo/men genes, and other electron transport chain (ETC) pathways, potentially reducing reactive oxygen species (ROS) production and enhancing stress tolerance.

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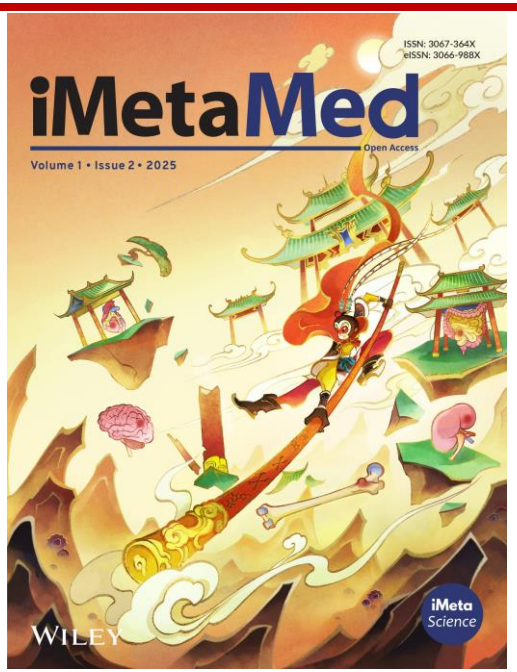

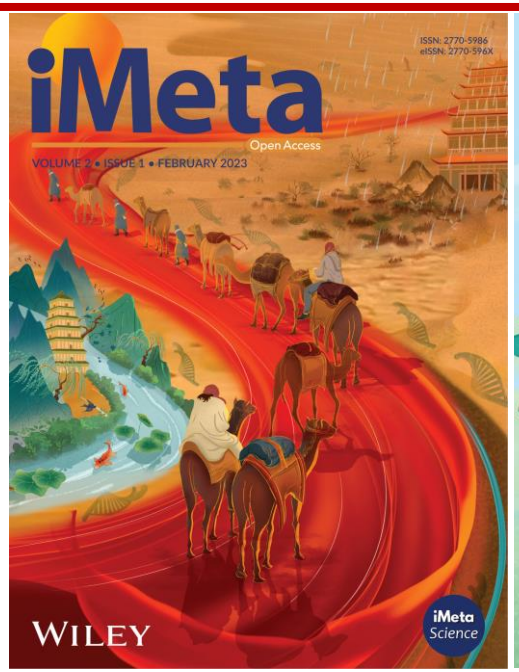

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