Genomic Characterization of a Pandrug-Resistant Klebsiella pneumoniae Outbreak to Guide Monoclonal Antibody Discovery

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Antibiotic resistance (AMR) is a silent pandemic that, without innovative interventions, it is fated to escalate globally. While monoclonal antibodies (mAbs) are already recognised as transformative and safe biologicals in other medical fields,they are now gathering traction as a novel therapeutic stratecy to fight intractable AMR infections.
In this work we applied an antigen-agnostic strategy to isolate extremely potent human mAbs against Klebsiella pneumoniae sequence type 147 (ST147),a hypervirulent and pandrug-resistant lineage that is spreading globally. This approach successfully yielded human mAbs exhibiting bactericidal activity in the picomolar range.
The application of advanced bioinformatic and genomic analysis allowed us to predict the therapeutic breadth and escape potential of the pathogen. This in turn guided us to identify mAbs conferring robust *in vivo* cross-protection, effectively neutralizing not only the outbreak strain but also genetically and geographically distant carbapenem-resistant isolates.

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Short bio:

Giuseppe Maccari is Head of the AI, Bioinformatics and Biostatistics group at Fondazione Biotecnopolo di Siena. His research focuses on the characterization, design, and discovery of monoclonal antibodies and antigens to fight infectious diseases. His work bridges structural bioinformatics, computational immunology, and protein engineering through the application of advanced predictive deep-learning models and molecular dynamics. He has contributed to several international research projects and is actively involved in developing robust computational pipelines to refine therapeutic antibody design and support advancements in immunology.