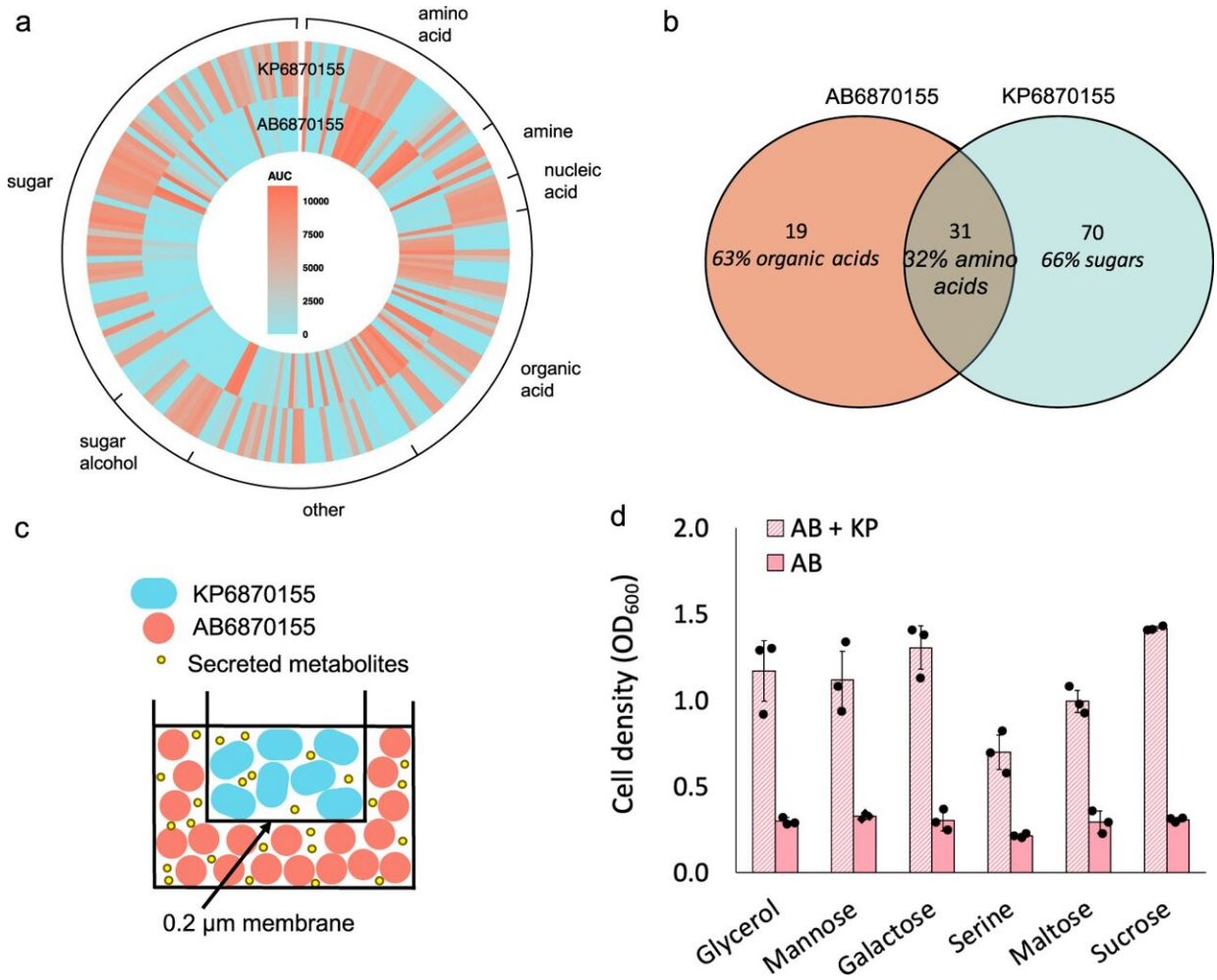
How teamwork makes superbugs more deadly and drug-resistant

February 13 2023



Carbon source utilization and cross-feeding between A. baumannii AB6870155 and K. pneumoniae KP6870155. a Carbon-source utilization activity calculated by AUC of AB6870155 (inner ring) and KP6870155 (outer ring) based on PM01-02 Biolog Phenotype Microarrays. b Venn diagram of C-source utilization from phenome data showing overlap between AB6870155 and KP6870155. c

Schematic of cross-feeding experiment utilizing Millicell culture inserts (Merck). d Growth of AB6870155 in Millicell plates with minimal media and select compounds (glycerol, mannose, galactose, serine, maltose, sucrose) provided as the sole carbon source in the presence (denoted as AB + KP) and absence of KP6870155 (denoted as AB) (n = 3 independent bacterial cultures). Data are presented as mean values + /− SD. Credit: *Nature Communications* (2023). DOI: 10.1038/s41467-023-36252-2

Some of the world's most deadly and drug-resistant pathogens work collaboratively to become more powerful and infectious, a new study has found.

Dr. Lucie Semenec and researchers from Macquarie University and University of Newcastle have characterized for the first time the mutually beneficial relationship between Klebsiella pneumoniae and Acinetobacter baumannii, microorganisms responsible for such conditions as pneumonia, urinary tract infections and bloodstream infections.

Due to their multiple drug resistance, these two notorious pathogens are on a World Health Organization priority list for urgent need of new antibiotics. These pathogens are commonly present in polymicrobial infections, acute and chronic diseases caused by various combinations of viruses, bacteria, fungi and parasites. Some studies in the U.S. and Europe have found them co-existing in about 40% of all hospitalized patients.

"This research is significant because diagnostic methods commonly look for the most dominant pathogen and therefore treatment is targeted at that," says Dr. Semenec.

"New drugs now can be informed in future research by the molecular

mechanisms we find in this work," says Dr. Semenec.

The *Nature Communications* study outlines how Klebsiella feeds Acinetobacter through its metabolic by-products. In return, Acinetobacter protects Klebsiella from high concentrations of drugs through antibiotic-degrading enzymes that it secretes.

"We have found that they have a mutually beneficial relationship to one another that enables Klebsiella to survive in antibiotic concentrations significantly higher than it can on its own," Dr. Semenec says.

Co-lead author, Associate Professor Amy Cain of Macquarie University, says the research highlights the pressing need for improved screening for mixed infections in hospital settings.

"It's important to understand that together these bugs are more infectious, more resistant to treatment and they feed off each other," she says.

The study investigated two strains previously co-isolated from a single lung infection and examined them using multiple screening and analysis mechanisms, from microscopy to genomics and infections in living organisms. It involved a team of researchers from the Center's Macquarie University and University of Newcastle nodes.

"Rather like photographing a sculpture from different angles so you can see it its entirety, we really needed a combination of methods to understand this interaction," Dr. Semenec says.

Caterpillar in vivo infection studies allowed the researchers to uncover that these two pathogens are more deadly when they co-infect. These experiments were performed using the ethical Galleria mellonella (greater wax moth larvae) animal model alternative at the Macquarie

Galleria Research Facility, the first of its kind in Australia.

More information: Lucie Semenec et al, Cross-protection and cross-feeding between Klebsiella pneumoniae and Acinetobacter baumannii promotes their co-existence, *Nature Communications* (2023). DOI: 10.1038/s41467-023-36252-2

Provided by Macquarie University