A rapid diagnostic test to detect multiple resistance determinants against the important carbapenem antibiotics

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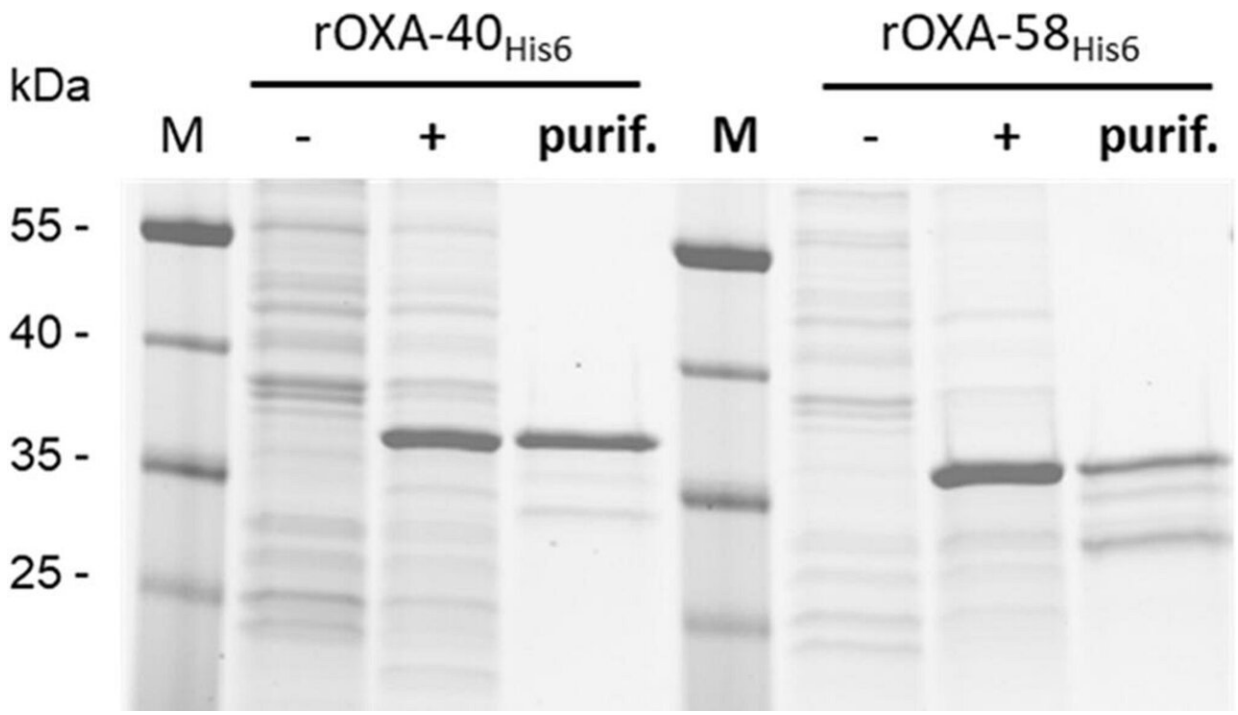

SDS-PAGE analysis of purified rOXA-40His6 and OXA-58His6. SDS-PAGE analysis of Coomassie-stained E. coli BL21 (DE3) lysate expressing rOXA-40His6 (32.8 kDa) and rOXA-58His6 (33.5 kDa) and His6-tag affinity chromatography-purified protein (purif.). Protein expression in E. coli BL21 (DE3) cells was non-induced (-) or induced with 1 mM IPTG (+). Credit: *Journal of Medical Microbiology* (2023). DOI: 10.1099/jmm.0.001681

Every year at least 700,000 people die as a result of infection with antibiotic-resistant bacteria—a figure which according to WHO forecasts could rise to ten million people by 2050 without new measures to combat the development and spread of resistance. In this context, rapid and targeted diagnosis of resistance is essential to determine appropriate antibiotic therapies and limit the spread of antibiotic resistance.

In 2018, DZIF scientists from the University of Cologne in cooperation with the Belgian company Coris BioConcept had developed a rapid diagnostic test (OXA-23 K-SeT) that uses OXA-23-specific antibodies to detect in Acinetobacter baumannii the widespread OXA-23 carbapenem resistance determinant within minutes. In a recent publication, the scientists now describe the further development of the rapid test into a multi-carbapenemase assay capable of detecting over 95 percent of carbapenem resistance in A. baumannii-infected patients.

In addition to OXA-23, the second-generation rapid test, called RESIST ACINETO, also detects the carbapenemases OXA-40 and OXA-58, as well as the metallo-beta-lactamase NDM, another enzyme that can cleave antibiotics from the carbapenem class.

"The RESIST ACINETO rapid test we co-developed screens samples for four resistance determinants simultaneously, detecting more than 95 percent of carbapenem-resistant A. baumannii strains," says Dr. Alexander Klimka, research group leader at the University of Cologne and lead author of the study.

"In a patient with an A. baumannii infection, the treating physician can use a RESIST ACINETO rapid test to determine within 15 minutes whether therapy with a carbapenem would be effective or not," says Dr. Paul Higgins, DZIF-scientist at the University Hospital Cologne.

The test, which has been marketed since May 2022, is based on the detection of carbapenemase enzymes in clinical isolates by binding highly specific antibody pairs. In a similar manner to the familiar COVID rapid tests, simultaneous binding of both antibodies to the respective enzyme results in a distinct color response.

The assay is not only rapid, but also comparatively inexpensive, easy to use, and does not require a specific reader, as is often necessary with other diagnostic methods. This makes the test particularly attractive for countries and regions that do not have an advanced medical infrastructure.

In further collaborative projects, the team now plans to develop rapid tests for the detection of other antibiotic-resistance determinants and bacterial species, as well as human pathogenic fungi and parasites.

In addition, the scientists are working on modifying the sensitivity and sample preparation so that they can also be used as point-of-care tests, i.e., without prior cultivation of the patient sample. This would not only improve the individual therapy, but also enable the early isolation of colonized or infected patients in order to prevent the spread of the respective pathogen.

The research is published in the *Journal of Medical Microbiology*.

More information: Sonja Mertins et al, Development of an immunochromatographic lateral flow assay to rapidly detect OXA-23-, OXA-40-, OXA-58- and NDM-mediated carbapenem resistance determinants in Acinetobacter baumannii, *Journal of Medical Microbiology* (2023). DOI: 10.1099/jmm.0.001681