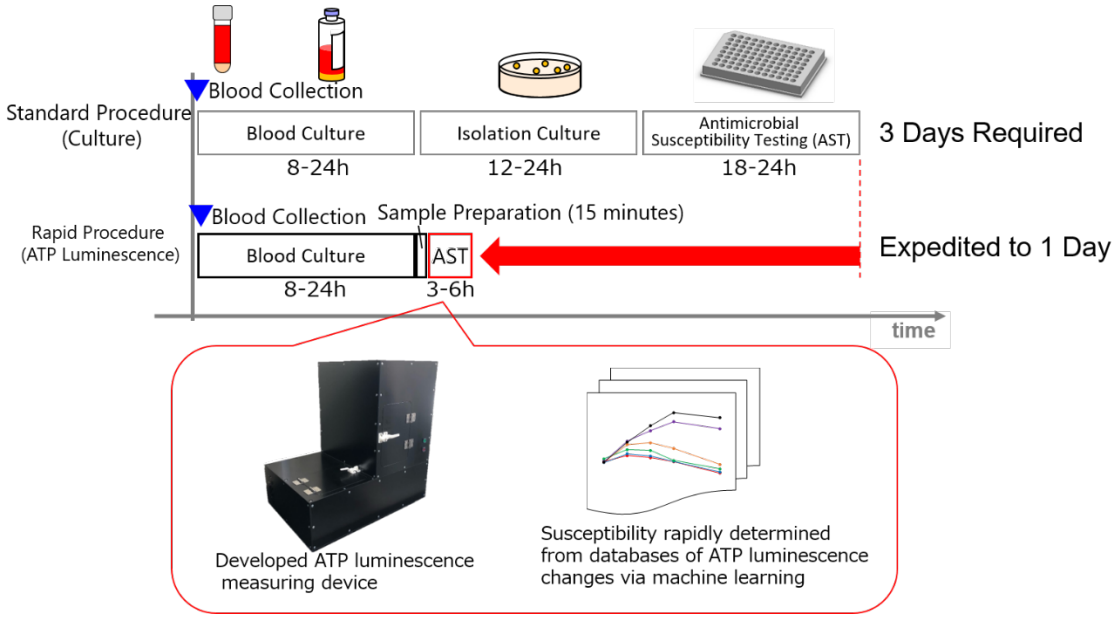
News Release

[dispatch] University of Toyama
Hitachi, Ltd.

October 3, 2019

Rapid Selection of Effective Antimicrobials for Patients with Septicemia using an ATP Luminescence Technique

Expedites testing procedure duration from blood collection to antimicrobial susceptibility testing from 3+ days to 1, optimizes antimicrobial treatment for patients with septicemia, and contributes to the prevention of spreading antimicrobial resistant bacteria



A research group led by Associate Professor Hideki NIIMI of the Graduate School of Medicine and Pharmaceutical Sciences for Research at the University of Toyama (National University Corporation) and Hitachi, Ltd. (TSE: 6501, "Hitachi") have developed a novel technique for rapid determination of effective antimicrobial treatment for patients with septicemia. The technique comprises of a simple sample preparation technique that eliminates all non-pathogen ATP in positive blood culture samples, a rapid ATP luminescence measurement[*1] technique, and a machine learning-based antimicrobial susceptibility testing (AST) analysis. Blood samples from patients at the University of Toyama and 63 *E. coli* strains were used, and a testing procedure using the new technique was verified. Results revealed that using standard

testing procedures, the total duration from blood collection to AST takes above 3 days, but this was expedited to about 1 day with our testing procedure. The rapid administration of effective antimicrobials to patients with septicemia would reduce mortality rate, medical costs due to shorter hospitalization days, and medicine administration periods and prevent the spread of antimicrobial-resistant bacteria[*2] due to overuse of antimicrobials.

Standard testing procedures for determining effective antimicrobial treatment for pathogens in septicemic patients involves a three-step culture process (i.e., blood culture, differential culture, and AST) and takes over 3 days from blood collection to AST stage. During this period, with the current situation being that doctors administer antimicrobials based on their own experience until the final results arrive, the severity of septicemia can easily increase, and a few hours delay in treatment can affect prognosis and mortality rate. Therefore, this involves a risk of potentially administering antimicrobials with no positive effects or inducing antimicrobial resistance due to the excessive administration of antimicrobials. Thus, a faster AST technique is required for more rapidly identifying effective treatments for septicemic patients.

Accordingly, the University of Toyama and Hitachi developed an effective technique for the rapid selection of effective antimicrobials, based on a sample preparation technique that reduces the time required for isolation cultures, a device that allows for rapid ATP luminescence measurements, and a machine learning-based AST technique. At the University of Toyama, blood-derived ATP, which often impedes AST, was greatly reduced using a simple sample preparation step of centrifugal separation and addition of ATP elimination reagent[*3] immediately after the start of the testing. A rapid AST procedure that reduces the time necessary for isolation cultures was made possible. At Hitachi, a rapid ATP luminescence measuring device, which can operate with a wide range of antimicrobials, was developed for creating a new AST procedure that uses ATP luminescence techniques. A rapid AST technique with accuracy equivalent to current standard procedures was made possible using machine learning to determine changes in bacterial ATP luminescence in response to various antimicrobials.

Conducting our new testing procedure on blood samples from septicemic patients at the University of Toyama, we obtained AST results in only 6 hours following the detection of positive blood cultures. Additionally, Hitachi obtained rapid AST results from 63 different *E. coli* strains using ATP luminescence techniques and machine learning. Results on 12 types of antimicrobials from our rapid AST technique matched with over 90% of those from the standard AST in 2 hours and 97.9% in 6 hours. These indicate that the time to obtain results from blood collection to AST can be expedited from the standard 3+ days to just 1.

Henceforth, the University of Toyama and Hitachi will continue to contribute to people's quality of life (QOL) by expanding the number of subject strains and antimicrobials, coordinating across multiple facilities, using clinical samples, and advancing the applicable elements of this testing procedure.

The results of this research have been published in *Scientific Reports* on October 2, 2019 (Atsushi MATSUI et al.) and will be presented at "IDWeek 2019" from October 2 to 6, 2019 in Washington, D.C.

*1 ATP luminescence measurement: a method in which bacteria are detected using luciferase (a luminous enzyme in fireflies) to induce luminescence in adenosine triphosphate (ATP), which is used as an energy source in all living organisms (including bacteria). Bacterial activities can be analyzed to a high degree of sensitivity by selectively detecting luminescence of ATP from living bacteria.
*2 Antimicrobial-resistant bacteria: bacteria against which antimicrobials have no effect, and its increase has become a global issue in recent years. The United Nations has adopted an action plan for preventing the spread of antimicrobial resistance, which also seeks to optimize usage for preventing overuse of antimicrobials.
*3 ATP elimination reagent: an enzyme that breaks apart ATP, which allows for the analysis of ATP derived only from living bacteria to a high degree of sensitivity by reducing additional ATP present outside of the target bacteria.

■ Contact details
Clinical Laboratory and Blood Center, Central Clinical Facility, Toyama University Hospital
Hideki NIIMI
Tel: 076-434-7759 (direct line)
e-mail: hiniimi@med.u-toyama.ac.jp

Research & Development Group, Hitachi, Ltd.
Contact Form:
https://www8.hitachi.co.jp/inquiry/hqrd/news/en/form.jsp

End

Information contained in this news release is current as of the date of the press announcement, but may be subject to change without prior notice.
