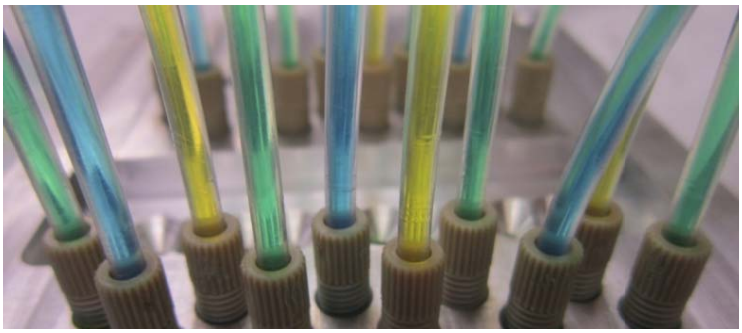
Fraunhofer USA

Rapid, stress-induced antibiotic susceptibility testing on a chip



Fraunhofer USA's Center for Manufacturing Innovation is seeking commercial partners to develop further a microfluidic platform that rapidly distinguishes antibiotic susceptible and antibiotic resistant bacteria.

OVERVIEW

Traditional culture-based methods for testing antibiotic susceptibility are lengthy and their accuracy depends on strict adherence to standard methods. Molecular methods can be useful in outbreaks, but are susceptible to failure caused by the high frequency of genetic mutation under selective pressure. The emergence and spread of bacterial resistance to ever increasing classes of antibiotics intensifies the need for fast phenotype-based clinical tests for determining antibiotic resistance.

TECHNOLOGY

Unlike standard susceptibility testing, our microfluidic platform does not rely on the passive observation of bacterial growth inhibition in the presence of antibiotics. Rather, it uses stress to distinguish between susceptible and resistant strains. Bacteria, immobilized on the bottom of a microfluidic channel, are subjected to mechanical shear stress created by flowing culture media (containing antibiotic) through the device. The combination of stress and antibiotic leads to rapid cell death in strains that are susceptible to the antibiotic. In contrast, resistant strains remain viable under the test conditions (see illustration on reverse side). Bacterial cell death is monitored via fluorescence using a dead cell stain, and rates of killing are automatically measured for the samples.

FIGURES OF MERIT

- Distinguishes susceptible and resistant bacteria after 30 min of applied stress.
- Reduces test times from *ca*. 24 h to 1 h.
- Multiplexed, microfluidic platform.
- Low cost disposables.

MARKETS & APPLICATIONS

- Clinical laboratories: Antibiotic susceptibility testing
- Pharmaceutical companies: Platform for screening and discovering new antibiotics
- Basic microbiological laboratories: Probing the stress responses of bacteria under various conditions

STAGE OF DEVELOPMENT

We have built a multi-channel microfluidic device capable of interrogating multiple bacterial strains and multiple antibiotics at the same time. Using model susceptible and resistant *S. aureus* strains, a metric has been established to separate susceptible and resistant strains based on normalized fluorescence values. We have demonstrated the successful development of a rapid microfluidic-based and stress-activated antibiotic susceptibility test by correctly designating the phenotypes of 18 clinically relevant *S. aureus* strains against oxacillin in a blinded study. We have also successfully applied our method to *E. coli*, *K. pneumonia*, and *S. aureus* against an unrelated antibiotic, gentamicin.

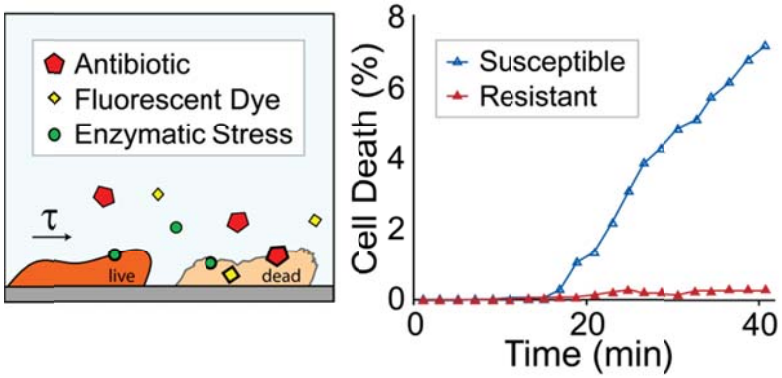
ADDITIONAL INFORMATION

Publications

Kalashnikov, M., Lee, J. C., Campbell, J., Sharon, A. & Sauer-Budge, A. F. (2012). A microfluidic platform for rapid, stress-induced antibiotic susceptibility testing of *Staphylococcus aureus*. Lab on a Chip, 12(21), 4523–4532.

Intellectual Property Status

Sauer-Budge, Sharon, Kalashnikov, Wirz. Method and device for rapid detection of bacterial antibiotic resistance/susceptibility. PCT/US2010/033523, filed May 5, 2010. US App# 13/283,892.



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