European Association of Urology – press release

Biosensor chips identify effective antibiotic treatment up to x8 faster than current methods

Embargo until: Friday 24th March, 00.01 GMT (London)

Scientists have piloted silicon biosensor chips which can rapidly identify the best antibiotics for treating bacterial infections. The system can direct clinicians to the best antibiotic treatment in around 2 to 6 hours, rather than upwards of 2 days which is typical of conventional tests. The new technology, which is still in development, is being presented at the European Association of Urology congress in London.

The scale of the problem this test addresses is huge. Bacterial infections are still a major cause of death in the Western world, and because of over and mistreatment antibiotics resistant Bactria stains are increasing every day. In the UK, it is estimated that 300,000 patients a year acquire infections in hospital, with Over 9000 dying from bacterial infections[1]. In Europe generally, over 4 million people acquire a healthcare-associated infection every year[2], and in the US[3] around 100,000 die each year from hospital acquired infections. Up to 40% of these are Urinary Tract Infections (UTIs). It is vitally important for doctors to be able to identify which antibiotic works as rapidly as possible, but typically they need 24 hours to confirm the presence of bacteria, and at least another 24 to 36 hours to identify the correct antibiotic to use.

The team, led by Professor Ester Segal (Technion Israeli Institute of Technology, Haifa), has developed special silicon biosensor chips. Each chip contains thousands of nano wells, which are coated with a material which allows bacteria to stick to the chip. Once the bacteria have stuck to the well, technicians use reflected visual light to count the bacteria, and to see whether the colony is growing. They can then add a different antibiotic in various dilutions to each chip to see which best inhibits bacterial growth, giving results within 2 to 6 hours.

Professor Segal said "*So far we have used the system to rapidly identify antibiotics for a range of bacteria, such as E. Coli, which causes many urinary tract infections (UTIs)"*

Professor Sarel Halachmi (Bnai-Zion Medical centre, and the Faculty of Medicine, Haifa), said that *"We are currently at initial testing stages using commercial bacteria solution and also human bacteria isolated from urine samples, however we are not yet at the stage where we can roll this out for routine clinical use. But the system is accurate, simple economical, and significantly shortens the time to accurate treatment recommendation and will save lives in the future."*

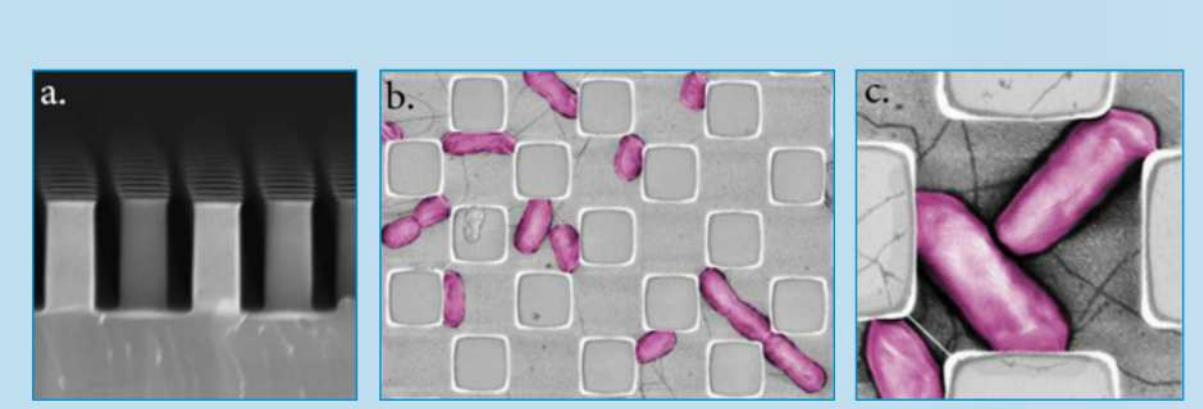
"Urinary Tract Infections (UTIs) for example, are a major health burden. Around half of all women in the West will have a UTI at some point. The major obstacle in the diagnosis and clinical management of UTI is the delay in our ability to isolate the bacteria causing the infection, and identify its susceptibility to certain antibiotics., We know that this silicon well system can significantly cut the time needed to identify the correct antibiotic, from a couple of days down to just a few hours. Using the best antibiotics will also help prevent the rise of antibiotic resistant bacteria which are one of the main problems in hospital acquired infections".

"Of course, there is more work to do before the system is generally available. We envisage the costs of the system being pretty low, with each analysis costing between $5 and $25, but this will come down over time. If our system can save an extra day in hospital, that alone will save at least $300 in most countries".

Commenting, Professor Florian Wagenlehner (University Clinic, Giessen, Chair of the European Section of Infections in Urology), said:

"This work addresses a really urgent medical requirement; how do we rapidly identify the best antibiotic? The current culture based techniques have a delay of several days in producing results, which leads on the one hand to inappropriate antibiotic treatment, and on the other hand to an overuse of broad spectrum, last resort antibiotics.

There are several labs working on this topic, and there are several alternative methodologies being presented at the EAU conference, including a new method from our own lab. Developing the right test will save resources and lives and slow down emergence of antibiotic resistance"



(a) Photo of chip from the side
(b) Photo of chip from above, with bacteria
(c) Enlarged photo of chip from above, with bacteria

Credits: photo: by H. Leonard, property of Technion, Israeli Institute of Technology, Haifa, Israel

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Notes for Editors

PLEASE MENTION THE EUROPEAN ASSOCIATION OF UROLOGY CONGRESS IN ANY STORY RESULTING FROM THIS PRESS RELEASE

The 32nd European Association of Urology conference takes place in London from 24th to 28th March. This is the largest and most important urology congress in Europe, with up to 13,000 expected to attend. Conference website http://eau17.uroweb.org/

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How has this work been reviewed? This work has not gone through a journal peer-review process. This work is amongst the top-rated 150 abstracts (out of 1171 accepted from around 5000 submissions) from the EAU congress. It was reviewed for suitability and accuracy by members of the EAU communications group at more than one stage in development, and subsequently reviewed by a specialist in the field on behalf of the EAU.

1. https://www.nice.org.uk/guidance/qs61/chapter/introduction
2. http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/Pages/index.aspx
3. Klevens, R Monina et al. "Estimating Health Care-associated Infections and Deaths in U.S. Hospitals, 2002." Public Health Reports 122.2 (2007): 160–166.

This research was funded via an Israeli chief scientist competitive grant

ABSTRACT **Adhesive siliconmicropillar arrays for bacteria capture: A method for rapid antibiotic susceptibility testing**

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Introduction & Objectives

As antibiotic resistant bacteria are becoming a critical public health concern, numerous methods have been devised to determine the appropriate antibiotic to use for a patient's infection; however these tests are laborious, expensive and lengthy, typically taking 7-24 hours to peform. Though porous silicon has been already used as a biosensor for the rapid detection of bacteria at low concentrations, its typical pore size (<100 nm) is too small to capture and entrap microorganisms to monitor their growth over time. To circumvent this limitation, we have designed Si micropillar arrays that can effectively trap bacteria and exhibit optical reflectance patterns that monitor bacteria growth over time using Reflective Interferometric Fourier-Transform Spectroscopy (RIFTS), consequently allowing for real time monitoring of bacteria growth and its response to various antibiotics. Our aim of study was to use the novel system to isolate bacteria from liquid suspension, to detect bacterial growth and growth inhibition following antibiotic administration.

Material & Methods

Si micropillar arrays are fabricated by deep reactive ion etching of silicon wafers. Overexposure of light during the hard mask photoetching process leads to the formation of disconnected wells, forming arrays of pillars instead, as seen in the scanning electron microscopy,The optical signal from this architecture allows for the monitoring of bacteria infiltration in-between the micropillars. Attachment of wheat germ agglutination (WGA), which binds to N-acetylglucosamine, a key component in the bacterial cell wall. Binding by WGA to bacterial cell walls acts as an adhesive to capture bacteria as they flow through the micropillar surface. Escherichia coli (E. coli) K12 are briefly incubated in Luria-Bertani broth for 30 minutes prior to their study. The bacteria culture is diluted to a concentration of 1 x 107 CFU/mL in 0.1 M PBS and a five step process is used to optically monitor their growth within the Si micropillar arrays.

Results

We were able to to detect bacterial adhesion and growth curve within 2 hours. Following administration of antibiotics we completely inhibited the growth of the bacteria in the affected microcapilaries vs. continuation of bacterial growth in the non exposed areas. total time since the introduction of the bacteria to the device to the determination of its susceptibility to the antibiotics was 150 minutes.

Conclusions

We have designed a system capable of not only entrapping bacteria, but yielding a real-time output of bacteria growth using the optical reflectance of three dimensional structures optimized in their chemistry and morphology. This system reveals the effect of both antibiotic concentration and type of antibiotic on bacterial growth, enabling it to be used as a rapid method of antibiotic susceptibility testing capable of determining the MIC in less than 4 hours, approximately half the time of conventional methods. Current efforts are directed at increasing the sensitivity of the structure to shorten assay time. This optimized system will be multiplexed to run tens of samples at once and for a variety bacteria species, particularly those found in bodily fluid samples collected at the hospital.