Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is "None", please specify "None" as your response. "Not applicable" is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format.

1. **Grantee Institution:** Drexel University

2. **Reporting Period (start and end date of grant award period):** 1/1/2009 - 12/31/2010

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Anne Martella

4. **Grant Contact Person's Telephone Number:** (215) 895-6471

5. **Grant SAP Number:** 4100047631

6. **Project Number and Title of Research Project:** 7- *Piezoelectric Microcantilever Sensors (PEMS) to Detect Methicillin-Resistant Staphylococcus aureus (MRSA)*

7. **Start and End Date of Research Project:** 1/1/2009 - 12/31/2010

8. **Name of Principal Investigator for the Research Project:** Richard Rest, PhD

9. **Research Project Expenses**.

   9(A) Please provide the amount of health research grant funds spent on this project for the entire duration of the grant, including any interest earned that was spent:

   $ 32,333

   9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project	Cost
Rest	PI	1.39%	$ 2579.94
Shih	co-PI	2%	$ 2604.70

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project
Purohit	graduate student	25%
Wu	graduate student	25%

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost
None		

10. Co-funding of Research Project during Health Research Grant Award Period. Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes_____ No ____x_____

If yes, please indicate the source and amount of other funds:

11. Leveraging of Additional Funds

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes_____ No ____x_____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert "not funded" in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If

you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
NONE	☐NIH ☐ Other federal (specify:_____) ☐ Nonfederal source (specify: _____)		$	$

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes ____x_____ No _____

If yes, please describe your plans:

No definite plans as of this report. Since the results of these initial studies funded by the CURE funds were positive, and supported our hypothesis that piezoelectric cantilever sensors can detect MRSA with high sensitivity and specificity, Dr. Shih (co-PI) and Dr. Rest (PI) will discuss applying for additional funding at some later date.

12. Future of Research Project. What are the future plans for this research project?

See answer to no. 11(B) above. There is no MRSA research presently ongoing in either the Rest lab or the Shih lab.

13. New Investigator Training and Development. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes ____x_____ No_____

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male			1	
Female			1	
Unknown				
Total			**2**	

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic			2	
Unknown				
Total			**2**	

	Undergraduate	Masters	Pre-doc	Post-doc
White				
Black				
Asian			2	
Other				
Unknown				
Total			**2**	

14. Recruitment of Out-of–State Researchers. Did you bring researchers into Pennsylvania to carry out this research project?

Yes_____ No ____x_____

If yes, please list the name and degree of each researcher and his/her previous affiliation:

15. Impact on Research Capacity and Quality. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes ____x_____ No_____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

The research funding allowed us to test a new hypothesis – i.e., that we could specifically, and with high sensitivity, detect MRSA with antibody-bound piezoelectric microcantilevers – in an area of research that was not previously performed in either the PI's or co-PI's laboratories. We were excited to see that the hypothesis was valid, and that we can pursue this brand new line of research in the future. Thus, the funding most certainly broadened research activities at Drexel University. An additional advantage of this funding was that future pursuit of this research will help train new investigators in team-based research spanning several disciplines, including bioengineering, microbiology, immunology and infectious disease. Team-based approaches are an integral and important part of biomedical research in the future, and are being supported by the NIH and NSF.

16. Collaboration, business and community involvement.

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes_____ No _____x_____

If yes, please describe the collaborations:

16(B) Did the research project result in commercial development of any research products?

Yes_____ No ____x_____

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes_____ No _____x_____

If yes, please describe involvement with community groups that resulted from the research project:

17. Progress in Achieving Research Goals, Objectives and Aims.

List the project goals, objectives and specific aims (as contained in the grant application's strategic plan). Summarize the progress made in achieving these goals, objectives and aims for the entire grant award period. Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below,

no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

Piezoelectric Microcantilever Sensors (PEMS) to Detect Methicillin-Resistant Staphylococcus aureus (MRSA) - The purpose of the project was to develop a real-time, highly-sensitive, highly-specific, portable, cost-effective sensor that can be used to detect MRSA in patient samples in the field (doctors' offices, hospitals, university and college infirmaries, and others), leading to an improved treatment outcome measured by decreased mortality and morbidity.

Project Overview

About 19,000 patients died in US hospitals in 2005 of rapidly progressing MRSA infections, and almost 100,000 developed serious infections … leading to more deaths than to AIDS, tuberculosis and viral hepatitis combined. Blacks, the elderly and males are at highest risk. These tragic consequences of MRSA disease have continued to increase nationally. It is imperative that a rapid, sensitive MRSA detection assay be developed. The translational aspect and long term goal (~3 years) of the project is to develop a real-time, highly-sensitive, highly-specific, portable, cost-effective detection system that can be used for MRSA diagnosis of patient samples in the field, leading to improved treatment outcomes measured by mortality and morbidity. The short term goal was to develop an antibody-based, bench-top *p*iezo*e*lectric *m*icrocantilever *s*ensor (PEMS) to detect MRSA. As part of an effort to fulfill this goal, the project had *2 specific aims*: (1) To acquire appropriate antibody (Immunoglobulin G, abbreviated IgG) specific for whole MRSA, MRSA surface components, and MRSA virulence factors, and (2) To attach the anti-MRSA IgG to the PEMS surface in order to optimize specific detection of well characterized MRSA strains, with high specificity and high sensitivity. Aim 2 will be done by modifying and fine tuning an existing lead magnesium niobate - lead titanate (PMN-PT) PEMS.

In addition to commercially available anti-MRSA antibodies, we proposed to use 3 MRSA strains to raise antibodies, and determine which antibodies have the highest specificity and avidity for MRSA binding. IgG will be tested in Enzyme Linked Immunosorbent Assays (ELISAs) against the immunizing MRSA strains, a panel of MRSA strains, and other relevant bacterial pathogens. Antisera will be raised in rabbits against whole UV-killed MRSA. Anti-MRSA IgG will be immobilized on the organic MPS insulation layer of PMN-PT PEMS via the bi-functional linker Sulfo-SMCC. In addition, MRSA will be targeted by multiple (array) PEMS to improve the sensitivity at very low MRSA concentrations. Different PEMS within the array will be bound with different antibodies, each specific to a particular MRSA target. To determine specificity, anti-MRSA IgG-coated PEMS will be challenged with the immunizing MRSA strain, a panel of additional MRSA clinical isolates, bacterial normal skin flora and other Gram positive and Gram negative bacteria causing skin and soft tissue infections (SSTI).

Expected Research Outcomes and Benefits

(i) Successfully acquire antibodies that are specific to MRSA and that bind MRSA but not other bacteria that cause skin or soft tissue infections (SSTI) similar to MRSA. Successfully bind functional anti-MRSA antibodies to the sensor (PEMS) surface and demonstrate that the antibody-coated sensor (MRSA PEMS) recognizes MRSA but not other bacteria that cause SSTI.

(ii) If the above outcomes are accomplished, then we are well on our way to developing a commercial product that can rapidly detect MRSA. Our hypothesis is that more rapid detection of MRSA infection will lead to more rapid antibacterial treatment and thus decreased morbidity and mortality.

Completed Research

Detection of Methicillin Resistant *Staphylococcus aureus* (MRSA)

Fabrication of Piezoelectric microcantilever sensors (PEMS)
Lead magnesium niobate-lead titanate (PMN-PT)/Cu piezoelectric microcantilever sensors (PEMS) were fabricated from freestanding PMN-PT films of 8 µm thick.[1, 2]. A 15-30 nm thick chromium/gold bonding layer was first deposited on one side of the PMN-PT freestanding film to serve as an electrode for plating. A 2-3 µm thick copper layer was electroplated using a copper plating solution of copper sulfate. A 150-nm thick gold was evaporated on both sides of the film. The PMN-PT/Cu bilayer was then cut to the cantilever shape into 1mm by 2mm rectangular strips using a wire saw (Princeton Scientific Precision, Princeton, NJ). Two wires to the top and bottom electrodes were connected using conductive glue and the PMN-PT/Cu strips were finally glued to a glass slide to form the cantilevers (Figure 1).

Insulation
For electrical insulation, a PEMS was first cleaned with diluted piranha solution (1:40 in de-ionized (DI) water), then rinsed with DI water and ethanol. After that the PEMS was submerged in a 0.1 mM mercaptopropyltrimethoxysilane (MPS) (Sigma-Aldrich, MO) in ethanol (Fisher Scientific, NY) for 30 minutes for the initial coating. The PEMS was then dried in air followed by more MPS coating in a 1% MPS ethanol solution at pH 4.5 titrated with glacial acetic acid for 48 hours. Fresh 1% MPS ethanol solution at pH 4.5 was changed every 12 hours. Subsequently, the PEMS was rinsed with DI water and then with ethanol. After that the PEMS was heated at 60°C on a hot plate for 30 min followed by drying in a vacuum oven overnight.

Immobilization
1 µM solution of rabbit polyclonal antibody to Methicillin Resistant *Staphylococcus aureus* (R-MRSA; 1683 from Abcam Inc, Cambridge, MA) was mixed with 80 µM solution of a bi-functional linker Sulfosuccinimidyl-4-(*N*-maleimidomethyl) cyclohexane-1-carboxylate (Sulfo-SMCC) (Thermo scientific, IL) in a total volume of 300 µl. The solution was mixed well for 30 min at room temperature to covalently link the sulfo-SMCC to the antibody.

Filtered microcentrifugation was then used to remove excess SMCC reagent. The PEMS was then immersed in the 300 µl remaining SMCC-antibody solution for 30 min to covalently bind antibody to the PEMS surface followed by rinsing with phosphate buffered saline (PBS) (Mediatech. Inc, VA). A different *S. aureus* antibody was also tested to compare the effect of a different antibody to the same MRSA, i.e., 1683.

Experimental Procedures

The PEMS was placed in a flow cell during detection (Fig 2). The total volume of the flow cell was 1.8 ml. A closed container with a 3 ml volume was used as a reservoir. PBS was circulated through the channel at a rate of about 0.7 ml/min and the frequency of the resonance peak around 680 KHz was monitored until it reached a stable baseline with a resonant frequency change of less than 200 Hz over 30 min. Increasing concentrations of MRSA were put into the flow system in sequence, which takes 30 mins for each concentration. The sequence of MRSA concentrations went from low to high:$1x10^3$/ml; $4x10^3$/ml; $7x10^3$/ml and $1x10^4$/ml. A validation step was also performed on a glass slide using gold-coated glass slides with an MPS layer using the same immobilizing method.

Experimental Results

The resonance spectrum of the PEMS is shown in Figure 3 in air and in liquid. The main peaks in air and in PBS overlapped indicating a good insulation in PBS. For the $1x10^3$/ml MRSA (1683) sample, the PEMS shows a frequency shift of 300 Hz (Fig 3). For continuous concentration increments, the frequency shift from detection signals are: 600 HZ for $4x10^3$/ml; 700Hz for $7x10^3$/ml; 700Hz for $1x10^4$/ml. The detection time is 10 to 20 min for each concentration (Fig 4).

Anti - *S. aureus* antibody (against a non-MRSA strain) was also tested to compare with the anti-MRSA-antibody using the same strain of MRSA strain 1683 at a concentration of $1x10^4$/ml. After insulation, the PEMS spectra peaks almost overlapped indicating good insulation (Fig 5). Of greatest importance, the PEMS immobilized with anti-*S. aureus* (non-MRSA) antibody did not show any response while the anti-MRSA antibody showed a 200 Hz clear response (Fig 5). This indicates that the anti-*S. aureus* antibody does not bind to MRSA 1683, while anti-MRSA antibody does and shows a reliable, sensitive and specific detection response.

Scanning Electron Microscopy (SEM) pictures were taken to verify the detection results. As shown in Figure 6, a dense binding layer of MRSA can be seen, indicating anti-MRSA antibody binds to MRSA effectively (Fig 6), consistent with the PEMS detection results.

Conclusions

We successfully fabricated piezoelectric microcantilever sensors (PEMS) using lead magnesium niobate-lead titanate (PMN-PT) freestanding films that we processed. After insulation and immobilization of anti-MRSA antibody, successful demonstration of MRSA detection was accomplished. On the other hand, PEMS immobilized with anti-SA antibody did not respond to MRSA indicating that PEMS is sensitive enough to differentiate the anti-MRSA and anti-SA antibodies. It is concluded that PEMS is a suitable technology for detection of MRSA in a direct manner.

References:
1. W.Y. Shih, H. Luo, H. Li, C. Martorano, and W.H. Shih, Appl. Phys. Lett. **89**, 242913 (2006).
2. H. Luo, Ph.D. thesis, Drexel University, Philadelphia, PA, 2005.

FIGURES

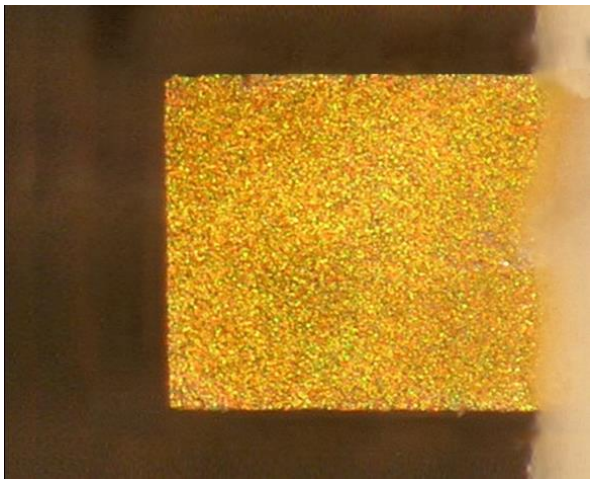

Figure 1: PEMS top view

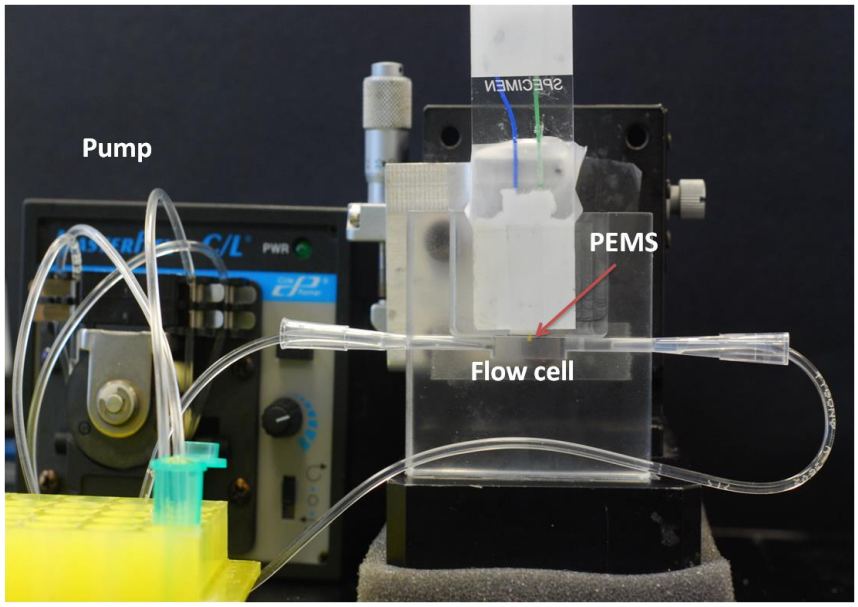

Figure 2: Flow cell set up

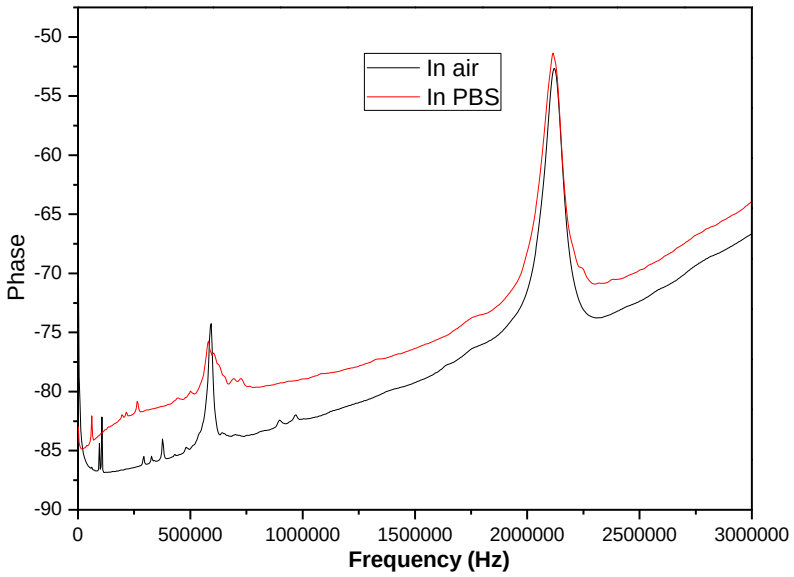

Figure 3: PEMS insulation results

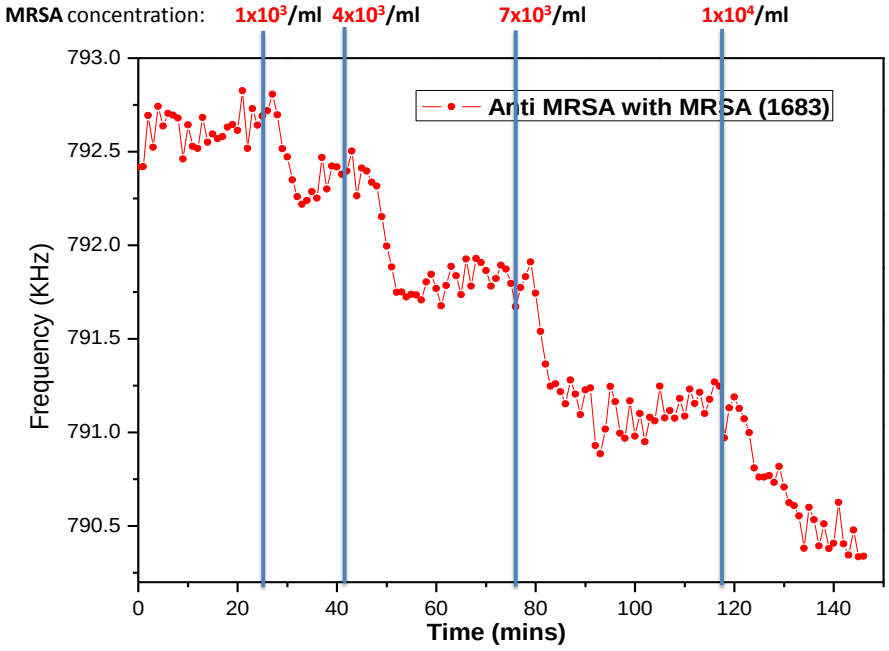

Figure 4: MRSA detection results using anti-MRSA antibody

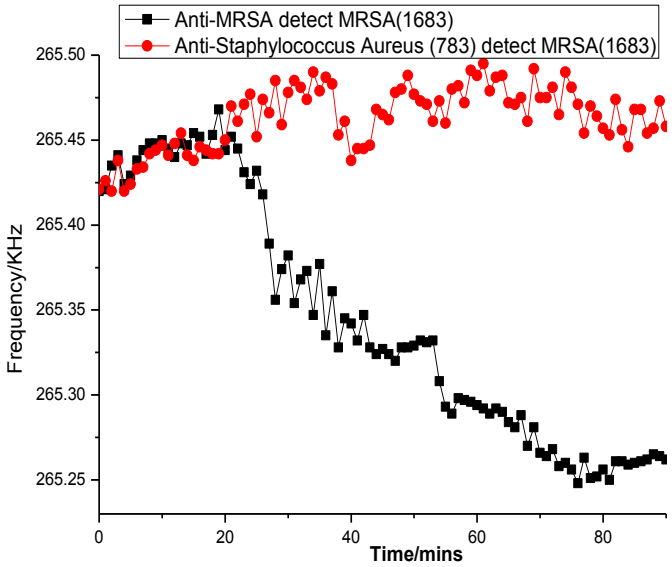

Figure 5: MRSA detection result using anti-MRSA and anti-SA antibody

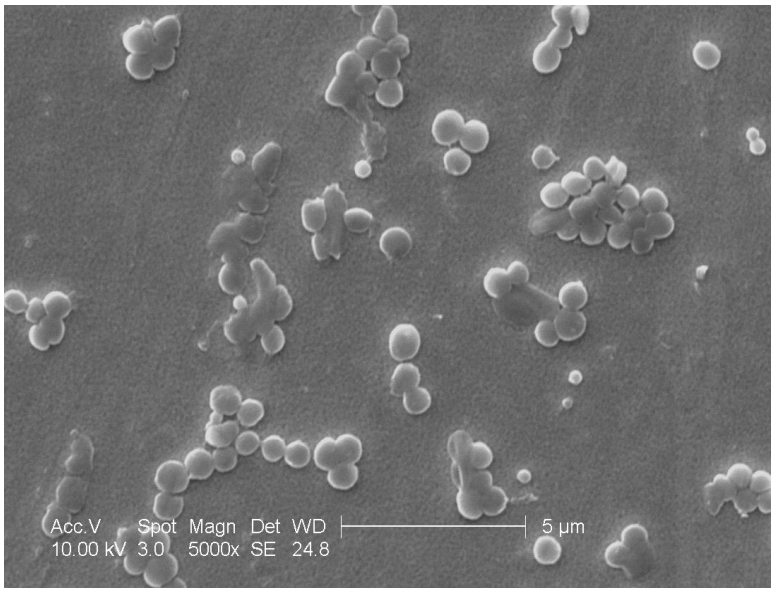

Figure 6: Section of an SEM micrograph of MRSA (1683) captured on glass slides with MPS using anti-MRSA antibody for immobilization

18. Extent of Clinical Activities Initiated and Completed. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be "No."

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
___x__ No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
____x_ No

If "Yes" to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both "No.")

18(C) How many hospital and health care professionals were involved in the research project?

_____Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

_____Number of subjects originally targeted to be included in the study
_____Number of subjects enrolled in the study

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:
_____Males
_____Females
_____Unknown

Ethnicity:
_____Latinos or Hispanics
_____Not Latinos or Hispanics
_____Unknown

Race:
_____American Indian or Alaska Native
_____Asian
_____Blacks or African American
_____Native Hawaiian or Other Pacific Islander
_____White

_____Other, specify:_____
_____Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

19. Human Embryonic Stem Cell Research. Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?
_____Yes
___x__ No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?
_____Yes
_____ No

19(C) Please describe how this project involved human embryonic stem cells:

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication, listed in the table, in a PDF version 5.0.5 format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the "Cognition and MRI in Older Adults" research project (Project 1), and two publications for PI Zhang for the "Lung Cancer" research project (Project 3), the filenames should be:

Project 1 – Smith – Publication 1 – Cognition and MRI
Project 1 – Smith – Publication 2 – Cognition and MRI
Project 3 – Zhang – Publication 1 – Lung Cancer
Project 3 – Zhang – Publication 2 – Lung Cancer

If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1. NONE				☐Submitted ☐Accepted ☐Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes ____x_____ No_____

If yes, please describe your plans:

When we can get together a bit more money, we will finish these studies and publish our results.

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project. Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

As we discussed in our original grant application, our ability to rapidly and specifically detect MRSA, with high sensitivity, should allow for faster diagnosis of disease caused by MRSA, and thus faster and more specific treatment. Such treatment should significantly decrease morbidity and mortality associated with MRSA disease. Much work remains to be done on this project, as we move forward with patient samples in the future.

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment. Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

See answers to #11(B) and #21 above.

23. Inventions, Patents and Commercial Development Opportunities.

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes_____ No___x_____

If "Yes" to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is "No.")

a. Title of Invention:

b. Name of Inventor(s):

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____

If yes, indicate date patent was filed:

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ No____

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes___ No____

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes_____ No_____x_____

If yes, please describe your plans:

24. Key Investigator Qualifications. Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages. *For Nonformula grants only – include information for only those key investigators whose biosketches were not included in the original grant application.*

BIOGRAPHICAL SKETCH	
NAME Richard F. Rest	POSITION TITLE Professor
eRA COMMONS USER NAME rickrest	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEARs	FIELD OF STUDY
Univ of Massachusetts, Amherst	B.S.	66-70	Microbiology
Univ of Kansas, Lawrence	Ph.D.	70-74	Bacterial Physiology
Univ of North Carolina, Chapel Hill	Postdoc	74-77	human neutrophil bactericidal activity

A. Positions and honors

2005-present, Director, Graduate and Postgraduate Professional Development, Drexel College of Medicine
1999-2001, Associate Dean, Biomedical Graduate Studies, MCP Hahnemann SOM
1994-present, Professor, Dept. of Path. and Lab. Med., Drexel Univ. Coll. of Med. (formerly MCP Hahnemann SOM)
1990-present, Professor, Dept. of Microbiology & Immunology, Drexel Univ College of Medicine
1983-1990, Associate Professor, Dept. of Microbiology & Immunology, MCP Hahnemann SOM
1983, Associate Professor (with tenure), University of Arizona
1977-1983, Assistant Professor, Dept. Molecular & Medical Microbiology, Univ Ariz Hlth Sci Ctr, Tucson
1974-1977, Post-doc, Dept Bacteriology & Immunology, UNC, Chapel Hill, Advisor: John K. Spitznagel
Research Career Development Award, NIH, 80-85
Ad hoc member/chair, various NIH study sections (SBIRs, BM1, BM2, ZRG-1, etc), 82-present
Member, Bacteriology and Mycology 2 (BM2) Study Section, NIH, 84-88
Editorial (advisory) board: Infection and Immunity, 88-present; J Infectious Diseases, 05-present
Sabbatical leave with Barry Eisenstein and Laurence Boxer, Univ Mich Med Sch, 8/89-8/90
Sabbatical leave with E. Richard Moxon, Oxford Univ, England, 8/96-8/97

B. Selected peer-reviewed publications

R.F. Rest and J. Frangipane. 1992. Growth of *Neisseria gonorrhoeae* in cytidine-3'-monophosphate-N-acetyl neuraminic acid (CMP-NANA) inhibits their nonopsonic (Opa-mediated) association with human neutrophils. Infect. Immun. 60:989-997.

Simon, D. and **R.F. Rest**. 1992. *Escherichia coli* expressing a *Neisseria gonorrhoeae* opacity associated (Opa) outer membrane protein invade human cervical and endometrial epithelial cell lines. PNAS (USA) 89:55112-55116.

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Gogotsi, Y, R. K. Dash, G. Yushin, B. E. Carroll, S. R. Altork, S. Sassi-Gaha and **R. F. Rest**. 2007. Bactericidal activity of chlorine-loaded carbide-derived carbon against *Escherichia coli* and *Bacillus anthracis*. J Biomed Materials Res: Part A, 84:607-613.

McGovern, J.-P., W. Y. Shih, **R. F. Rest**, M. Purohit, Y. Pandya, and W.-H. Shih. 2008. Label-Free Flow-Enhanced Specific Detection of *Bacillus anthracis* Using a Piezoelectric Microcantilever Sensor. The Analyst. 133:649-654.

McGovern, J-P, W. Y. Shih, M. Mattiucci, **R. F. Rest**, M. Purohit, K. Pourrezaei, B. Onaral, and W-H Shih. 2008. Array PZT/Glass Piezoelectric Microcantilevers for real-time detection of *Bacillus anthracis* with 10 spores/ml sensitivity and 1/1000 selectivity in bacterial mixtures. The Analyst. in press

C. Recent Research Support

W81XWH – 06-2-0044 Rest (co-I); Peter Ward, (PI) 8/05 – 9/09
US Dept of Defense Contract
Effects of Antioxidant Liposomes on Interactions of Bacillus anthracis with Human Macrophages: Role of Anthrax Toxins. These studies investigate the role of antioxidants in modulating the subcellular and cellular effects on the interaction of *B. anthracis* and its toxins with human macrophages.

U54 AI57168 Rest (co-I); Myron Levine (PI) 10/07 – 2/09
NIH, MARCE
Arp: a Bacillus anthracis Transcription Regulator. Pilot grant with Virginia Bioinformatics Institute (VBI), Virginia Tech to perform and interpret microarray analyses of a new, unique transcriptional regulator, *arp*, found only in the *B. cereus* group.

No Number Rest (PI) 2/08 – 1/12
TherimuneX Pharmaceuticals, Inc and Drexel University College of Medicine Collaborative Research Agreement
***PDAG: a Naturally Occurring Regulator of Inflammation*.** Studies involve investigation of the effects of a peptidyl diacylglyceride (PDAG) on innate immune functions in animals and humans, focusing on macrophage, neutrophil, dendritic cell and lymphocyte function.

1R43 AI077248 Thacker (PI); Rest (PI of subcontract) 9/09 – 8/11
NIAID/NIH
A Modulator of Innate Immunity for Preventing Hospital-Acquired Infections. SBIR. In conjunction with TherimuneX Pharmaceuticals, Inc, J. Thacker, President. Studies to investigate PDAG as a therapeutic for preventing hospital-acquired infections.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Shih, Wan Young	Associate Professor of School of Biomedical Engineering, Science, and Health Systems
eRA COMMONS USER NAME (credential, e.g., agency login)	
wyshih1	

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
National Tsing Hua University, Taiwan	B.S.	06/76	Physics
Ohio State University, Columbus, OH	Ph.D.	06/84	Physics
University of Washington, Seattle, WA	Postdoctoral	04/92	Materials Science & Engineering

Positions and Honors

1982-84 Grad. Res. Associate, Materials Res. Lab. & Dept. Physics, Ohio State Univ.
1984-85 Postdoc. Res. Associate, Materials Res. Lab. & Dept. Physics, Ohio State Univ.
1985-92 Res. Scientist, Dept. Materials Sci. & Eng., University of Washington, Seattle
1993-00 Research Scientist, Princeton Materials Institute, Princeton University, Princeton, NJ
1993-2005 Res. Associate Prof., Dept. Materials Sci. & Eng., Drexel University
2006- Assoc Prof, School of Biomedical Engineering, Drexel University

Honors

1999 The 1999 Edward C. Henry Electronics Division Best Paper Award for "Electromechanical Behavior of PZT-Brass Unimorphs," *J. Am. Ceram. Soc*. **82**[7], 1733-1740 (1999) by X. Li, W. Y. Shih, I. A. Aksay, and W.-H. Shih.
2002 Best Senior Design in Materials Sci. & Engineering, Drexel University
2003 106 Club, Drexel U.; Best Senior Design Project, Dept. Materials Sci. & Eng.
2009 Best Senior Design in School of Biomed, Drexel University

Selected Peer-reviewed Publications (Selected from 96 peer-reviewed publications)
Most relevant to the current application

1. J.-P. McGovern, W. Y. Shih, R. Rest, M. Purohit, Y. Pandya, and W.-H. Shih, "Label-Free Flow-Enhanced Specific Detection of *Bacillus anthracis* Using a Piezoelectric Microcantilever Sensor," *The Analyst*, **133**, 649-654 (2008), PubMed#18427687
2. Q. Zhu, W. Y. Shih, and W.-H. Shih, "Mechanism of Flexural Resonance Frequency Shift of a Piezoelectric Microcantilever Sensor During Humidity Detection," *Appl. Phys. Lett*., **92**, 183505 (2008), PMC2682738, NIHMSID#112993
3. J. Capobianco, W. Y. Shih, Q.-A. Yuan, G. P. Adams, and W.-H. Shih, "Label-free, All-electrical, In-Situ Human Epidermal Growth Receptor-2 Detection," *Rev. Sci. Instrum.*, **79**, 076101 (2008), PubMed#18681738, PMC2678786
4. Q. Zhu, W. Y. Shih, and W.-H. Shih, "Enhanced detection resonance frequency shift of a piezoelectric microcantilever sensor by a DC bias electric field in humidity Detection," *Sensors and Actuators B*, **138**, 1–4 (2009), NIHMSID#112322
5. J.-P. McGovern, W.-H. Shih, M. Mattiucci, R. Rest, M. Purohit, K. Pourrezaei, B. Onaral, and W. Y. Shih, "Array PZT/Glass Piezoelectric Microcantilevers for real-time detection of BA with 10 spores/ml sensitivity and 1/1000 selectivity in bacterial mixtures," *Rev. Sci. Instru.*, 80, 125104 (2009)

6. J. Capobianco, W.-H. Shih, J.-H. Leu, C.F. Lo, , and W. Y. Shih, "Label Free Detection of White Spot Syndrome Virus Using Lead Magnesium Niobate-Lead Titanate Piezoelectric Microcantilever Sensors," *Biosensors and Bioelectronics,* **26**, 964–969 (2010).

Additional recent publications of importance to the field (in chronological order)

1. X. Gao, W. Y. Shih, and W.-H. Shih, "Vibration Energy Harvesting Using Piezoelectric Unimorph Cantilevers with Unequal Piezoelectric and Nonpiezoelectric Lengths," submitted to *Appl. Phys. Lett*. **97**, 233503 (2010)
2. H. Yegingil, W.-H. Shih, and W. Y. Shih, "Probing Model Tumor Interfacial Properties Using Piezoelectric Cantilevers," *Rev. Sci. Instrum*., **81**, 095104 (2010).
3. H. Li, W. Y. Shih, and W.H. Shih, "Lead-Free Piezoelectric Freestanding Films with Sheet Geometry-Enhanced High-Field Piezoelectric Coefficients," *J. Am. Ceram. Soc.*, **93**[7], 1852-1855 (2010)
4. H. Li, W. Y. Shih, and W.-H. Shih, "Highly Photoluminescent and Stable Aqueous ZnS Quantum Dots ," *Ind. Eng. Chem. Res.*, **49**, 578–582 (2010).
5. Q. Zhu, W. Y. Shih, and W.-H. Shih, "Mechanism of the Flexural Resonance Frequency Shift of a Piezoelectric Microcantilever Sensor in a DC Bias Electric Field," *Appl. Phys. Lett.*, **92**, 033503 (2008)

Patents (Selected from 8 published patents; 20 pending applications)

W.-H. Shih, H. Li, M. Schillo, and W. Y. Shih, "Synthesis of Water Soluble Nanocrystalline Quantum Dots and Uses Thereof," US Patent No. 7,335,345, February 26, 2008

W. Y. Shih, W.-H. Shih, and Z. Shen, "Piezoelectric Cantilever Sensors," US Patent 7,458,265, 12/2/08

W. Y. Shih, W.-H. Shih, A. Markidou, S. T. Szewczyk, and H. Yegingil, "All-electrical Piezoelectric Finger Sensor (PEFS) for Soft Material Stiffness Measurement," US Patent 7497133B2, 3/3/09

Research Support.

DoD CDMRP Concept Wei-Heng Shih (PI) 9/15/09-10/14/10
Near-Infrared Quantum Dots for Clear Margin Determination during Breast Cancer Surgery
The goal of this study is to demonstrate the use of antibody-conjugated quantum dots in imaging cancer cells.
Role: Co-Investigator

University City Science Center Wan Y. Shih (PI) 10/15/09-10/14/10
Portable, Low-Cost, Radiation-Free Breast Cancer Detector for Dense Breasts
The goal of this study is to collect in vivo measurement data on patients using the piezoelectric cancer detector
Role: PI

Coulter Foundation Translational Grant Wan Y. Shih (PI) 4/1/10-3/31/11
Development of a urine screening test for liver cancer
The goal of this project is to perform initial research on identifying potential liver cancer markers in urine and the detection of DNA hybridization using piezoelectric microcantilever sensor
Role: PI

Nanotechnology Institute Core Project Wan Y. Shih (PI) 9/1/07 to 3/31/10

Array Piezoelectric Nanocantilever Sensors to Detect Immune Responses to Therapeutic Monoclonal Antibodies and Breast Cancer Markers
The goal of this project is to develop and manufacture reliable piezoelectric microcantilever sensors for detecting breast cancer proteins and antibodies from immune response
Role: PI

Coulter Foundation Translational Grant Wan Y. Shih (PI) 4/1/08-3/31/10
Portable, Low-Cost Breast Cancer Detector
The goal of this project was to develop a piezoelectric device to monitor the elastic properties of soft tissues for tumor identification
Role: PI