

# Graduate Affairs & Research

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**COLLEGE OF PHARMACY**  
**UNIVERSITY OF OKLAHOMA**  
**HEALTH SCIENCES CENTER**

## Special points of interest:

- *Tips on writing your PHS398 Grant application*
- *Spotlight on newly awarded research at the College of Pharmacy*
- *New graduate students*

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## Anticipated revisions to the PHS398

The National Institutes of Health (NIH) is required to change their grant application packet at least once every four years. At a recent regional conference, NIH personnel presented revisions to the PHS 398 (which is used primarily for RO1, R21, R03 applications) that can be expected during 2004-2005.

### Instructions Section

There will be an extensive overhaul on the instructions, with a focus on clarity, simplicity and plain language. This non-form section will include 3 parts:

*Part I*—Instructions. Now this will truly just be application instructions.

*Part II*—Supplement instructions for preparing the human subjects section of the research plan.

*Part III*—Policies, assurances, definitions and other information will be printed here.

### Face Page

Some of you will be happy to find out that the title field will be increased to 81 characters. There will also be a data element for clinical trials. The Duns & Bradstreet number will also be reinforced.

### Form Page 2

There will be a newly created designated area for Stem Cell information (removed from the description field).

There will also be a new section called "Other Significant Contributors," which may include individuals that are committed to the scientific development or execution of the project, but not truly committing measurable effort.

More information on these changes will be coming soon.

## NSF Revises Grant Proposal Guide Effective September 1

The National Science Foundation (NSF) has revised its *Grants Proposal Guide*. The revisions are effective for proposals submitted on or after September 1, 2004 and supersede all previous editions.

In its announcement, NSF highlighted the following revisions:

- (1) a description of the various categories of funding opportunities as well as appropriate scenarios in which each are used;
- (2) new descriptive information on the types of submissions that may be required under NSF program solicitations; and
- (3) implementation of the enhanced capabilities of the FastLane for submission of proposal file updates. This 61-page revised guide is available only in PDF format at: [www.nsf.gov/pubs/2004/nsf04\\_23/nsf05\\_23.pdf](http://www.nsf.gov/pubs/2004/nsf04_23/nsf05_23.pdf).

***DID YOU KNOW***  
*that one of the three major initiatives in the NIH roadmap is the “re-engineering of the clinical research enterprise?”*

***Tips on writing your progress reports:***

1. *NIH is equally interested in what hasn't worked in your research as well as areas you have been successful.*
2. *Remember, the best evidence of productivity is your record of publication.*

## READING THE NIH ROADMAP FOR DIRECTION

Science published an article in its October 2003 issue (volume 302), written by Elias Zerhouni. Dr. Zerhouni is the director of the National Institutes of Health (NIH).

In this article, Dr. Zerhouni talks about the “NIH Roadmap”, which was designed to define priorities for the entire institution and particularly in its funding opportunities.

The website for the article is: <http://www.sciencemag.org/feature/plus/nihroadmap.pdf>

Developed with input from more than 300 nationally recognized leaders in academia, industry, government and the public, the NIH Roadmap provides a framework of the strategic investments that NIH needs to make to optimize its entire research portfolio. The NIH Roadmap builds on the tremendous progress in medical research achieved, in part, through the recent doubling of the NIH budget. In setting forth an ambitious vision for a more efficient and productive system of medical research, the NIH Roadmap focuses on the most compelling opportunities in three main areas: new pathways to discovery, research teams of the future and re-engineering the clinical research enterprise.

To be part of the NIH Roadmap, scientific initiatives had to be deemed of high potential impact, had to enhance the disease and mission-specific activities of all of NIH's 27 institutes and centers, and had to respond to the needs and concerns of the public. NIH will begin to implement all of the initiatives in fiscal year 2004. Some initiatives that build upon existing research efforts are expected to achieve their goals rapidly, while other newer or more complex endeavors are expected to take several years to come to fruition.

Any faculty member who is interested in knowing the direction of funding for NIH should take the time to read this article in the Journal of Science.

## TIPS ON WRITING YOUR PHS398 GRANT APP

At the recent regional conference in Seattle, NIH presenters gave some tips to improve grant applications.

1. *Preliminary Data Section*—Be honest with yourself. Is this information enough to convince you?
2. *Budget Justification (Personnel section)* - This section can include additional skills or collaboration that applies to the research. There is no page limit to this area.
3. *Abstract Page*—Write your abstract in “plain language.” Also, NIH suggests that you alphabetize your key personnel.
4. *Title of Research Application*—NIH suggests not to include the words “animal”, “fetal” or “stem cell” in your title. Activist groups often do word searches on government websites and these hot-topic words in your application may show up and your research targeted by them.
5. *Differentiating between Other Support and Your Biosketch*—Remember, a biosketch reports present and past accomplishments. In your other support section of the biosketch, report present and pending funding.
6. *Consultant Letters*—Write the letter for the consultant. You know best how to sell the need for a consultant.

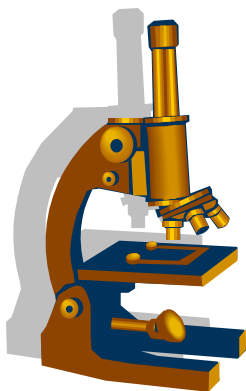
**NIH HOT TOPICS** - At the recent regional conference, NIH officials indicated the current “hot topics” in research include HIV/AIDS, obesity, cancer and bioterrorism.

## SPOTLIGHT ON CURRENTLY FUNDED COLLEGE OF PHARMACY RESEARCH

The College of Pharmacy were recently notified that two professors were awarded NIH multiple year awards.

**Randy Gallucci, Ph.D., Assistant Professor, Department of Pharmaceutical Sciences**, recently received an RO1 award from NIH for 5 years. His research is titled, "Identification of an IL-6 Induced Keratinocyte Motogen." His lay abstract follows:

In the United States, over 6 million individuals develop chronic skin ulcers annually. The augmentation of cutaneous wound healing has long been an elusive goal for health care professionals. Our previous studies indicate that mice deficient in the immune protein interleukin 6 (IL-6) display significantly delayed skin wound healing compared to wild type control animals. While the role of IL-6 is well documented in disease conditions such as psoriasis, little is known about the role this cytokine might play in regenerative responses such as wound healing. We have found that IL-6 appears to significantly induce the migration of epidermal cells also known as keratinocytes. However, this effect appears to be indirect and requires the presence of another skin cell called the dermal fibroblast.



Preliminary gene array experiments do not indicate the induction of a secreted protein known to induce keratinocyte migration.

In this application we propose to: 1) characterize and 2) identify the IL-6-induced dermal fibroblast produced migratory factor. Once identified, the motogenic potential of migratory

factor(s) will be assessed on isolated keratinocytes from IL-6KO and wild type mice. The results of these experiments will hopefully lead to the eventual development of a useful treatment for chronic wounds.



**Nathan Shankar, Ph.D., Associate Professor, Department of Pharmaceutical Sciences**, recently received an RO1 award from NIH for 5 years. His research is titled, "Role of *E. faecalis* Esp in Biofilms and UTI." His lay abstract follows:

Nosocomial (hospital acquired) infections by multiple antibiotic resistant bacteria are especially difficult to cure, pose a significant health risk and place an enormous burden on the economy. A leading cause of such nosocomial infections is the Gram-positive bacterium *Enterococcus faecalis*, which ranks high among the most commonly encountered pathogens infecting the bloodstream, surgical sites and urinary tract. In spite of *E. faecalis* being a leading cause of nosocomial infections, little is known about the bacterial factors involved in promoting persistence of enterococci in the nosocomial environment or at infection sites. We recently identified the first pathogenicity island in *Enterococcus faecalis*. Among the virulence traits that defined this element as a pathogenicity island is a gene encoding the surface protein Esp. Esp is enriched among infection-derived enterococcal isolates and has a unique architecture with multiple tandem

motifs, a feature characteristic of many bacterial surface protein adhesins involved in binding to host ligands. In previous studies we have determined that due to the variation in the number of tandem repeat units within the structural *esp* gene, *E. faecalis* cells may express Esp of varying size and structure at the cell surface. Preliminary studies indicate that alterations in the structure of Esp may influence its role in biofilm formation by enterococci on abiotic surfaces, and in colonization of the urinary bladder during infection. The specific aims of this proposal have been formulated to explore these dual functionalities of Esp. We propose to construct mutants lacking specific modular domains of Esp in an isogenic background, and assess the role of each domain in formation of enterococcal biofilms to determine which elements of Esp structure are essential for biofilm formation by *E. faecalis*. We also propose to construct and screen a library of transposon-insertion mutants to identify and characterize additional gene products that may play a role in the biofilm forming property of *E. faecalis*. Mutants identified in these studies will be evaluated to ascertain if mutations that affect biofilm formation also affect interaction with the host urothelium. Finally, urothelial cell receptors that may be bound by Esp will be identified and the role of the various Esp modular domains in colonizing urothelial surfaces will be determined.

The long term goals of the proposed research are to be able to better identify and control infections by pathogenic enterococci and to identify new enterococcal targets for therapeutic intervention. |

# NEWS AND INFO ABOUT GRADUATE STUDIES AND RESEARCH

## CONGRATULATIONS TO PRESTINA THOMPSON!

Congratulations to Prestina Thompson (P2), who received the award for best basic science poster presentation at the Pharmacy Student Research Conference, June 4-5 at the University of Colorado School of Pharmacy. Her presentation was titled, "Bacteriophage Regulation of Mismatch Repair in *Streptococcus Pyogenes* SF370." Her faculty mentor is Mike McShan, Ph.D.

## STUDENTS ACCEPTED INTO THE PHARM.D/MS PROGRAM

We are pleased to announce that four students have officially been accepted into the College of Pharmacy Pharm.D./M.S. program. They include Prestina Thompson (Dr. McShan, mentor); G.T. Dolan (Dr. Shankar, mentor); Matt Brammer (Dr. Matsumoto, mentor and Dr. Gallucci, co-advisor); and Craig A. Trusley (Dr. Kupiec, mentor).

Three of these students just recently successfully completed a summer research session with their respective mentors.

## STUDENTS ACCEPTED INTO THE GRADUATE PROGRAM

Three students were accepted into the graduate program of the College of Pharmacy.

Shellie Gorman Keast, Pharmacy Administration. Shellie received her B.S. in Pharmacy in 1999, and her Pharm.D. in 2000—both from our College of Pharmacy.

Juliet Lurtz, Pharmacy Administration. Juliet received a B.A. in Philosophy from SMU in 1991, and a J.D. from Virginia in 1994.

Thi Nguyen, Pharmacy and Toxicology. Thi received her Pharm.D. degree from our College of Pharmacy in 2004.

## DR. HOFFMAN RECEIVES OCAST AWARD FOR NEXT THREE YEARS

The College of Pharmacy is pleased to announce that Holly Hoffman, Pharm.D., has received research funding through the Oklahoma Center for the Advancement of Science and Technology (OCAST) for the next three years.

Her research title is: Gene Expression in Wild-Type and Resistant Pneumococci. Her abstract summary follows:

Antimicrobial resistance in *Streptococcus pneumoniae* has increased dramatically over the last twenty years. Although resistance with the different classes of antimicrobials occurs through dissimilar mechanisms, the presence of gene mutations most commonly with penicillin resistance appears to be a marker for the acquisition of gene mutations consistent with resistance to other antimicrobial classes. Currently, it is unknown what alterations in gene expression occur following single-drug antimicrobial resistance. Furthermore, it is not known what additional changes in gene expression occur among multidrug-resistant pneumococci.

Our long term goal is to determine the relationship between changes in gene expression with single-drug and multidrug-resistant pneumococci to identify potential therapeutic drug targets. The objective of this application is to determine what genes are altered in *S. pneumoniae* following mutations that confer antibiotic resistance. The central hypothesis is that specific genes that control regulation, transport and signaling are involved in antibiotic resistance between the different antimicrobial classes.

The rationale for the proposed research is that once these genes are identified, they can be altered pharmacologically in new and innovative approaches for the treatment of individuals infected with singledrug- and multidrug resistant pneumococci.

The central hypothesis will be tested and the objective of this application will be met by pursuing two specific aims: 1) Identify the genes with altered expression in singledrug-resistant *S. pneumoniae* isolates compared to wild-type isolates, and 2) Identify the genes with altered expression in multidrug resistant *S. pneumoniae* isolates compared to singledrug-resistant and wild-type isolates.

This planned proposal is innovative because it employs a new technology that allows whole genome analysis simultaneously. It is our expectation that the proposed approach will identify the genetic mechanisms of antibiotic resistance in *S. pneumoniae*.

These outcomes will be significant because we will obtain an understanding of the complex interaction between regulators of gene expression following the occurrence of resistance with several antimicrobial classes