Career Development Series 2023

How to Write a K-Award Application to Maximize Funding

Presentation will begin at 12:00 PM (PT)

ITHS | Institute of Translational Health Sciences
ACCELERATING RESEARCH. IMPROVING HEALTH.

UNIVERSITY of WASHINGTON

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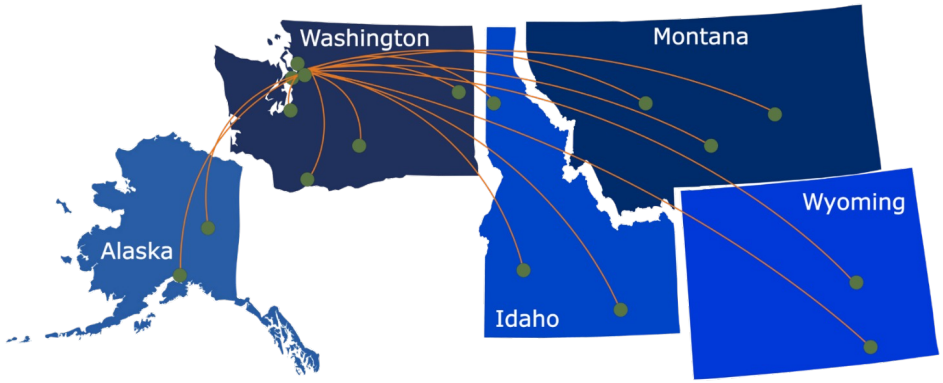


What We Offer:

1. **Research Support Services:** Members gain access to the different research services, resources, and tools offered by ITHS, including the ITHS Research Navigator.

2. **Community Engagement:** Members can connect with regional and community based practice networks

3. **Education & Training:** Members can access a variety of workforce development and mentoring programs and apply for formal training programs.

4. **Funding:** Members can apply for local and national pilot grants and other funding opportunities. ITHS also offers letters of support for grant submissions.

Contact ITHS

Director of Research Development

- Project Consultation
- Strategic Direction
- Resources and Networking

Melissa D. Vaught, Ph.D.
ithsnav@uw.edu
206.616.3875

Scientific Success Committee

- Clinical Trials Consulting
- Guidance on Study Design, Approach and Implementation
- Feedback on Design and Feasibility

https://www.iths.org/investigators/services/clinical-trials-consulting/

Feedback

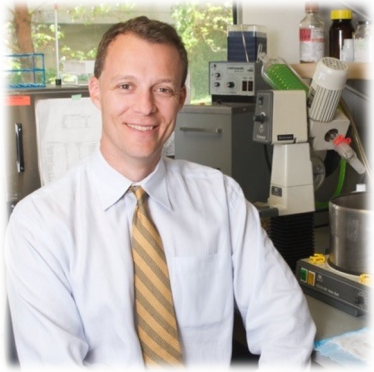
At the end of the seminar, a link to the feedback survey will be sent to the email address you used to register.

Career Development Series 2023

How to Write a K-Award Application to Maximize Funding

Presented by:

John K. Amory MD, MPH, MSc



Christy McKinney, PhD

Many thanks to Sheila Lukehart Phd for the slides!

ITHS | Institute of Translational Health Sciences
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Learning Objectives

At the end of the session, participants will be able to:

1. Select the K award mechanism for their circumstances
2. Develop a detailed career development section and research plan
3. Write a mentorship plan

NIH Career Development Awards

- NIH Structure
- Types of career development awards
- Getting information about K's
- Components of a K application
- Tips on writing a great application

NIH Structure

27 Institutes & Centers

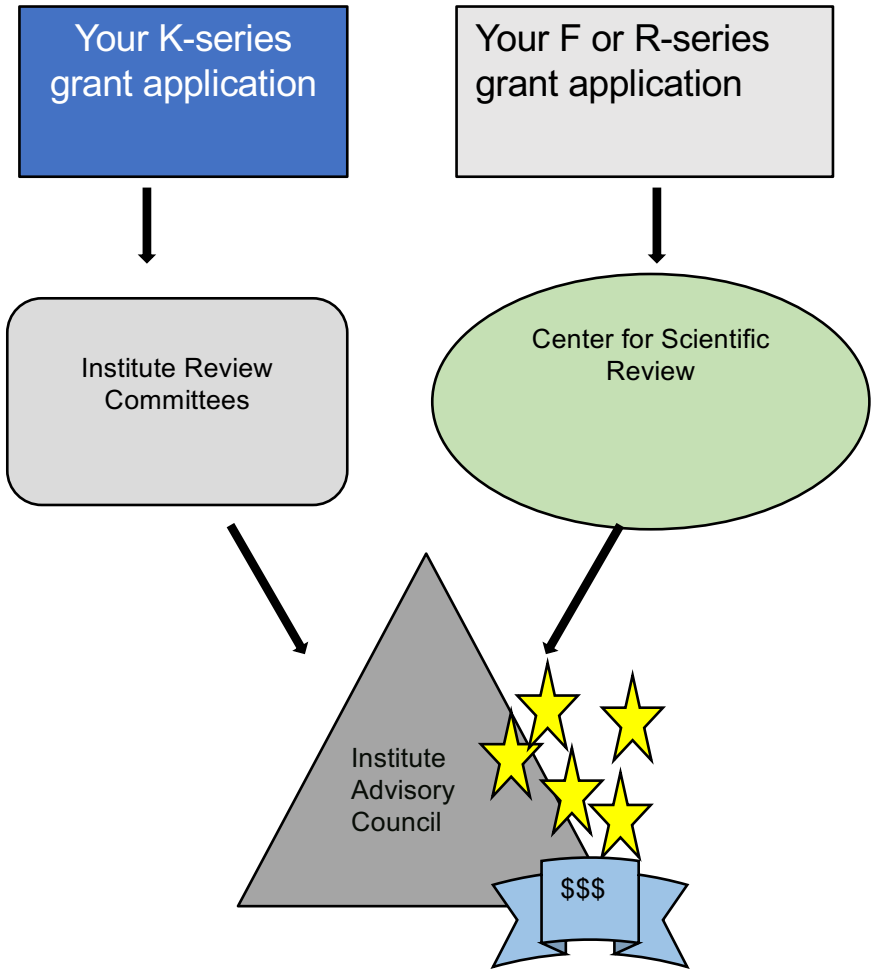
- NIAID → Divisions / Branches
- NCI
- NHLBI → Office of Research Training
- NINDS → Scientific Review Program
  - Review Committees--SRO
- NIAMS → Advisory Council
- Fogarty Int'l Center

Center for Scientific Review

Divisions

- Study Sections--SRO

Application Pathway



Program Announcement

Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)	National Institutes of Health (NIH)
Components of Participating Organizations	National Heart, Lung, and Blood Institute (NHLBI) National Human Genome Research Institute (NHGRI) National Institute on Aging (NIA) National Institute on Alcohol Abuse and Alcoholism (NIAAA) National Institute of Allergy and Infectious Diseases (NIAID) National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) National Institute of Biomedical Imaging and Bioengineering (NIBIB) *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) National Institute on Deafness and Other Communication Disorders (NIDCD) National Institute on Drug Abuse (NIDA) National Institute of Mental Health (NIMH) National Institute of Nursing Research (NINR) National Center for Complementary and Alternative Medicine (NCCAM) Division of Program Coordination, Planning and Strategic Initiatives, Office of Research Infrastructure Programs (ORIP) Office of Behavioral and Social Sciences Research (OBSSR) Office of Dietary Supplements (ODS) **Special Note**: Because of the differences in individual Institute and Center (IC) program requirements for this FOA, prospective applicants strongly e the Table of IC-Specific Information, Requirements and Staff Contacts, to make sure that their application is responsive to the requirements of one NIH ICs.
Funding Opportunity Title	**Mentored Research Scientist Development Award (Parent K01)**
Activity Code	K01 Research Scientist Development Award - Research & Training
Announcement Type	Reissue of PA-11-190
Related Notices	• June 4, 2014 - Notice NOT-14-074 supersedes instructions in Section III.3 regarding applications that are essentially the same. • May 2, 2014 - See Notice NOT-OD-14-088. Notice of Clarification of Career (K) Award Eligibility. • February 27, 2014 - See Notice NOT-EB-14-003. Notice of Change to the Duration of Career Development Awards Supported by the NIBIB. • February 3, 2014 - See Notice NOT-HG-14-018. Notice of NHGRI Participation.
Funding Opportunity Announcement (FOA) Number	**PA-14-044**
Companion Funding Opportunity	None
Number of Applications	See Section III. 3. Additional Information on Eligibility.
Catalog of Federal Domestic Assistance (CFDA) Number(s)	93.242; 93.856; 93.855; 93.846; 93.213; 93.279; 93.839; 93.838; 93.837; 93.233; 93.361; 93.273; 93.286; 93.866; 93.351; 93.173; 93.865
Funding Opportunity Purpose	The purpose of the NIH Mentored Research Scientist Development Award (K01) is to provide support and "protected time" (three, four, or five years) supervised career development experience in the biomedical, behavioral, or clinical sciences leading to research independence. Although all of th Institutes and Centers (ICs) use this support mechanism to support career development experiences that lead to research independence, some ICs us individuals who propose to train in a new field or for individuals who have had a hiatus in their research career because of illness or pressing family ICs utilize the K01 award to increase research workforce diversity by providing enhanced research career development opportunities. Prospective ca encouraged to contact the relevant NIH staff for IC-specific programmatic and budgetary information: Table of IC-Specific Information, Requiremen Contacts.

READ THIS CAREFULLY!!

- Purpose
- Eligibility
- Deadlines
- Page limits
- Links to forms
- Required sections
- Review criteria
- Animal, human
- subjects info
- Contacts

Types of Early Career Training Awards

- US citizen, permanent resident
  - K08 } MD, DVM, DDS, other Clinical Doctorate
  - K23 } MD or PhD
  - K01 } MD or PhD
  - K22 } MD or PhD
  - K25
- US Citizen/PR or Non-citizen
  - K99/R00 Pathway to Independence: MD or PhD
  - K99/R00 MOSAIC Increases diversity

Some institutes don't offer all grant mechanisms

Mentored Career Development: K Awards

- **K08** Mentored Clinical Scientist Research Career Development Award
  - Laboratory focused research
    - Independent Clinical Trial not allowed (PA-20-203)
  - May use human samples
- **K23** Mentored Patient-Oriented Research Career Development Award
  - Patient oriented research
    - Independent Clinical trial not allowed (PA-PA-20-205)
    - Independent Clinical trial required (PA-20-206: not NIAID)
    - Independent basic experimental studies with humans required (PA-20-204)

Clinical doctoral degree: MD, DVM, PharmD
US citizen, permanent resident

K08 and K23 Mentored Research Career Development Awards

- 3 - 5 yr award
  - 3 yrs for more senior individual (e.g. MD MPH; MD PhD)
  - 5 yrs for more junior individual, but must justify a didactic 2 yr phase
- Salary: $100,000/yr* + Fringe Benefits
- Research Support:
  - $50,000/yr*
  - At least 75% effort committed to research

Health professional doctorate
US citizen, permanent resident
***May vary by institute**

K01 Mentored Research Scientist Development Award

- Focus varies by institute*
  - e.g., NIAID limits to epidemiology, modeling techniques, and outcomes research (PA-19-126); also NHP Research Models (PAR-20-258)
  - NIAMS: generally reserved for individuals interested in switching to a new research field, for individuals who have interrupted their career because of illness or pressing family care responsibilities, or for faculty at minority institutions who wish to enhance their capacity for independent research.
- MDs or PhDs
- 3 - 5 years
- Salary: $75,000/ yr* + Fringe Benefits
- Research Support: $25,000/yr*
- ≥75% effort on health-related research

US citizen or permanent resident
*Varies by institute

K25 Mentored Research Scientist Development Award

- Focus varies by institute* (PA-19-124)
  - quantitative (e.g., statistics, economics, computer science, physics, chemistry) and engineering backgrounds
  - Re-focus skills on health and disease
- MDs or PhDs
- 3 - 5 years
- Salary: $75,000/ yr* + Fringe Benefits
- Research Support: $20,000/yr*
- ≥75% effort on health-related research

US citizen or permanent resident

*Details vary by institute—be sure to look at the information for your own institute

K99/R00 Pathway to Independence

- PhD or MD
- Transition award: includes support for postdoc and moving to Assistant Professor position
- No more than 4 years of postdoctoral research* experience at the time of submission (or resubmission)
- 3-5 years of support
- Has mentored postdoc phase K99 (1-2 years)
- Independent Asst. Prof. phase R00 (up to 3 years)
- Non-citizens eligible

Uses and rules vary by institute—check with your institute

K99/R00 Pathway to Independence

K99 years (PA-19-130)

- Apply for K99 phase with specific postdoc career development and research plan, include broad description of independent phase
- Provides salary support ($75K) and benefits
- Modest research support ($25K/year)

Uses and rules vary by institute—check with your institute

K99/R00 Pathway to Independence

R00 years

- Total cost cannot exceed $249,000* per year
- Includes salary, benefits, research costs, **and indirect costs**

*~$160K direct costs

Uses and rules vary by institute—check with your institute

Things to do ahead of time

- Develop a research project with your mentor
- Obtain preliminary data to support hypotheses
- Publish papers
- Develop a good mentoring team

Administrative Issues: Their Rules and Yours

- Figure out what kind of application you will be writing—discussion with mentor
- Read the Program Announcement and Instructions—and read them again!
- Talk with a NIH Training Officer
- Talk with your dept'l or division administrator

Preparing to write the application

- Read the instructions!
  - Program Announcement—has link to forms
  - Instructions

  https://grants.nih.gov/grants/how-to-apply-application-guide.html

  General Instructions

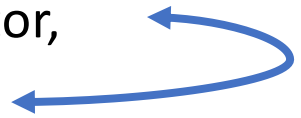
  Specific instructions for K applications
- Be aware of page limits
- Look at grant tutorials online
- Read a successful application (or two!)

Timeline: Writing the application

- Start planning and writing very early
- Talk with the administrator who will assist with application
- Talk with your mentor
- Have your mentor and others read the full application early

Timeline for Writing a Grant Application

>4 months ahead	Read NIH website about grants Talk with NIH official Decide on grant mechanism Discuss with your mentor and grants administrator
Week -12 to -14	Think, read, cogitate about career development and research plans
Week -10	Draft Specific Aims, give to mentor, meet to discuss, revise
Week -6	Give full draft of to mentor and others; request letters



Timeline for Writing a Grant Application

Week -6	Work on business pages (biosketch, equipment, facilities, RCR, HS, VA, biohazards, authentication of reagents, etc)
Week -5	Revise draft
Week -3	"Final" draft to mentor
	Begin to route business pages
Week -2	Finished text sent to Institutional Grants Office
Week -1	Submit to agency
Due Date	It's there on time!!!

Mechanics: Writing the application

- Use formal language—no slang or jargon
- Use correct grammar, punctuation
- No typos!
- Pay attention to required fonts, margins, page limits
- Leave white space on the pages-not solid text

Boring—and causes tired eyes……

these two lipoproteins as adhesins. The strain expressing both DbpA and DbpB acquired the ability to bind epithelial cells while only DbpB showed specificity for glioma cells *in vitro* (5). Later studies with the neuroborreliosis patients validated our results since antibodies mainly against DbpB were present in CSF after colonization by Lyme spirochetes (4, 12). Therefore, we anticipate that our *in vitro* experiments in the initial screen using non-infectious *B. burgdorferi* will identify surface localized *T. pallidum* adhesins. This non-adherent strain offers a cleaner background to study binding mechanisms since it does not express *B. burgdorferi* adhesins. Candidate adhesins identified from this experiment will help us select 3-4 surface proteins to express in the infectious, bioluminescent *B. burgdorferi* strain. ¶

We will first select the best luciferase reporter system and most useful promoter to express this reporter for *in vivo* imaging in the small animal model. Then, we will express and characterize the promising *T. pallidum* proteins, identified from the initial screen, in the infectious, sequenced *B. burgdorferi* strain to assess adherence to placental and neuronal cell lines *in vitro*. These results will form a foundation for our *in vivo* assessment of *T. pallidum* proteins in colonization of placenta and neuronal tissues. Hence, using the gain of function approach *in vitro* will allow us to test its validity also in the mouse model of infection. ¶

1A. Identification and characterization of *T. pallidum* adhesins with affinity for placental and/or neuronal tissues and other virulence factors. We have selected several genes of *T. pallidum* for the initial screen to determine them as candidate adhesins in this study. We will obtain clones containing these genes from Drs. Sheila Lukehart and Arturo Centurion at University of Washington at Seattle (please see their letters of support). We will also produce respective recombinant tagged proteins in *E. coli* and generate polyclonal antibodies against the proteins for which antisera are not available from our collaborators. ¶

We considered different features in selection of these proteins, such as; they (i) are known to be expressed during congenital syphilis or neurosyphilis on the basis of serological analysis, (ii) show specificity to a particular host receptor expressed in placenta and/or neuronal tissues, (iii) exhibit other potential activities important for pathogenesis, and (iv) were previously described membrane proteins with unknown function. Selected eight *T. pallidum* proteins, TP0171, TP0319, TP0435, TP0574, TP0954, TP0957, TP0971, and TP1037 have potential to contribute to neurosyphilis or congenital syphilitic manifestation. We will clone the genes along with their promoters in *B. burgdorferi* shuttle vector and transform the non-infectious *B. burgdorferi* B314 strain, which was also used to examine role of DbpA-DbpB, as described above (rationale). We will first assess the function of *T. pallidum* proteins expressed in *B. burgdorferi* as a surrogate system *in vitro*. Expression of *T. pallidum* genes in *B. burgdorferi* will be confirmed by Western blotting. Some of the selection criteria for candidate proteins are described here. ¶

(i) Several immunogenic proteins are identified but their functions not yet determined. TP0171 is a 15kD lipoprotein, which shows homology to proteins of *Listeria monocytogenes* and *L. innocua*, two pathogens causing adverse outcomes in pregnant women. TP0171 is a major membrane immunogen in *T. pallidum*. TP0435 (17kD) lipoprotein and TP0574 (previously known as TpN47) are two highly immunogenic proteins used in diagnosis of syphilis. However, their localization on the spirochete surface remains questionable and their roles have not been examined. This study will unequivocally determine their subcelluar localization in the spirochete and will help us evaluate their roles. If one or more of these proteins are present on the spirochete's surface in our initial screen, they will be selected for further experiments. ¶

(ii) Based upon a comprehensive analysis of the available information, we anticipate that TP0954 protein may located on the outer membrane and may facilitate colonization of placenta and neuronal tissues by *T. pallidum*. If so proved, it will provide a model molecule to study molecular basis of congenital spirochete transmission and neurosyphilis. We anticipate that TP0954 encoded protein will be located on the surface of the *T. pallidum* since it possesses a potential signal peptide. In addition, the predicted 3D-structure of this protein using the Hiden Marko models (HMM) program with Protein Data Bank (PDB) shows similarity with several surface proteins in other organisms. These similar proteins include the PilF outer membrane lipoprotein of *Pseudomonas aeruginosa*, peroxisomal targeting signal 1 binding domain of *Trypanosoma brucei* Peroxin 5 protein, and yeast mitochondrial outer membrane translocon protein Tom70p. All possess tetratricopeptide repeats. Finally, one peptide of TP0954 showed 54% similarity with defined chondroitin sulfate A-binding variable domain of PfEMP1 *Plasmodium falciparum*. Furthermore, PfEMP1 of malaria parasite displayed on infected red blood cells (RBCs) promotes adherence of the RBC to placenta. Interestingly, we have previously shown that DbpB lipoprotein of *B. burgdorferi* shows affinity to chondroitin sulfates and mediates binding to the glial cells. Later analyses of cerebrospinal fluid from neuroborreliosis patients confirmed intrathecal (in situ) expression of DbpB by Lyme spirochetes (4, 12). This collective information strongly supports inclusion of this protein in this proposal. ¶

(iii) TP1037 encoded protein is designated as hemolysin III in the genome. Any organ can be affected due to *T. pallidum* dissemination after infection of the fetus by this spirochete. Anemia is common in congenital syphilis and non-hemolytic anemia can persist for weeks even after treatment (21). It will be useful to determine if hemolysin III of *T. pallidum* is involved in this manifestation. Hemolysis on blood agar plates stimulated by *T. pallidum* hemolysin III will determine its enzymatic activity *in vitro*. These experiments will functionally establish its current predicted role on the basis of sequence homology with proteins of other pathogens. In addition, we will determine in our later experiments whether the expression of this hemolysin results in anemia in mice, similar to that seen in some syphilis patients and in congenital syphilis. ¶

(iv) We have selected three more proteins, which are known membrane proteins with unknown functions. First, Treponema-specific membrane lipoprotein (*tmpC* or TP0319) is an ABC-type nucleoside transport system that may transport purine nucleosides, which are essential for the survival of *T. pallidum* within its obligate human host. If it is not exposed to the surface of the spirochete in the initial analysis, it will serve as a negative control for all following experiments in the specific aim 2. Second, Dr. Norgard's group recently crystallized the membrane antigen (*tpd* or TP0971) of *T. pallidum*. It shows high affinity for human lactoferrin, suggesting its role as iron scavenger. These two proteins, TmpC and Tpd, are expressed at high levels in *T. pallidum* during infection (19) but their contribution to *T. pallidum* pathogenesis remains to be established. The current study will determine if they are located on the surface and potentially play a role in survival of the spirochetes in specific tissues during infection. Third, TP0957 encoded protein belongs to the extracellular solute-binding transporter superfamily that also includes sialic acid binding protein in other bacteria. Sialic acids are found widely distributed in mammalian tissues. They are also components of gangliosides and are found attached to the glycosphingolipid (ceramide and oligosaccharide). Since gangliosides are predominantly found in the nervous system, TP0957 could be a potential adhesin for neuronal tissues. ¶

Although some of these selected proteins were initially predicted to be periplasmic proteins, Hazlett and coworkers (2005) showed that several periplasmic proteins of *T. pallidum* can get exposed due to outer membrane destablization facilitated by outer membrane protein encoded by TP0453 (7). Therefore, it is useful to determine exact location of these proteins and assess their roles in colonization of neuronal and/or placental tissues. ¶

1B. Evaluation of *T. pallidum* proteins in adherence to cell lines derived from human placenta and neuronal tissue. Colonization of specific tissues *in vivo* often can be predicted on the basis of *in vitro* binding experiments conducted with relevant cell lines and the pathogen. The focus of this study is to identify proteins important in colonization of placental and/or neuronal tissues. Therefore, we will use the human epithelial cell line obtained from placental choriocarcinoma, CCL-98, and fibroblast cell line, CRL7464 as model for placental colonization, while neuronal cell line, PC12, and C6 glioma cell lines will be used to depict colonization of the central nervous system (CNS) during infection. Radiolabeled *B. burgdorferi* will be used in the binding experiments to assess the contribution of *T. pallidum* proteins in adherence with the gain of function approach. The wells without the cell line monolayers, and *B. burgdorferi* strain transformed with the shuttle vector alone will provide negative controls for specific mammalian cells and expressed *T. pallidum* protein, respectively. A significantly higher level of adherence by *B. burgdorferi* expressing specific *T. pallidum* protein(s) on their surface to these cell lines, as compared to *B. burgdorferi* control will identify them as adhesin(s). In addition, these results will suggest potential role of these proteins in colonization of specific tissues by *T. pallidum* during infection of humans. We have extensive experience in conducting these experiments with *B. burgdorferi* and found them to be very useful in identifying the bacterial adhesins and host receptors, and predicting their contribution in specific tissue colonization *in vivo*. ¶

Visual Appeal

- Open space
- Clear organization
- Use of Bold, CAPITALS, underlining to define sections

EXPECTED RESULTS AND INTERPRETATION Based upon our experience with TprK,[62] we expect that antibody specificity will be detected among different sequences for a given DR, and that the number of AA changes necessary to abrogate antibody binding will be few. We expect that antibodies will bind to sequences in the predicted loops, but these loops also contain conserved sequence in addition to the DR, so we cannot predict now whether there will be cross-reactive antibodies that bind the conserved regions of these loops. If so, this may have implications for the specificity of opsonization and neutralization, and may argue against a major role for TprC and D subspecies- and strain-specific immunity. The role of the conserved regions (within loops and separate from loops) in functional immunity, including cross-protection, will be explored formally using a complementary approach in Aim 4. Those results, along with results from Aims 2 and 3, will be evaluated together to reach conclusions or to develop further hypotheses.

LIMITATIONS AND ALTERNATIVE APPROACHES Completion of Aim 2 will require successful production and purification of a large number of recombinant proteins and peptides. OM proteins can be quite difficult to express in *E. coli*. We have been expressing Tpr proteins and other putative OM proteins from *T. pallidum* for ~15 years. The laboratory has used a number of different vectors, host strains, and growing conditions in order to optimize expression for individual molecules. We routinely express such proteins without the signal sequence to avoid toxicity to *E. coli*. Even so, the protein is often found in inclusions, which requires solubilization in urea or other agents before it can be purified (we typically use 6XHIS-tags for purification). Depending upon its intended use, the quality of the antibody that is produced following immunization with recombinant proteins is dependent upon the correct folding of the immunizing protein: If one wants an antibody simply to identify a protein in an immunoblot, correct folding is not necessary; if one wants antibody to recognize a 3-dimensional structure on an intact bacterium, however, correct folding may be critical. Lack of appropriate attention to this issue may be the reason that functional assay results obtained in one laboratory may not be successfully reproduced in another lab. For the proteins that are produced in this project, conditions for optimal folding will be determined, and the degree of correct folding will be evaluated by circular dichroism. Figure 5 shows an example of purified recombinant TprK (predicted to have a structure very similar to TprC and D) that has been optimally refolded in our lab; the spectrum is typical of a molecule rich in β-sheets, consistent with β-barrel structure. Purity of our recombinant proteins and peptides will be assessed by SDS-PAGE and immunoblotting (using anti-6xHIS and infection-immune rabbit serum). If further purification is needed, size exclusion chromatography will be used. Synthetic linear and cyclic peptides will be obtained commercially. We have considerable experience with performing ELISA and lymphocyte proliferation assays using whole recombinant proteins and synthetic peptides as antigens; we don't anticipate any problems with these assays. [56, 57, 59-61]

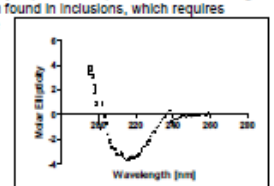


Figure 6. CD spectrum for purified refolded recombinant TprK, another likely OM protein of *T. pallidum*. The spectrum indicates abundant β-sheet composition.

Aim 3. Determine the role of the distinct regions of TprC and D in functional immunity, using homologous and heterologous *T. pallidum* strains as the targets of the functional assays.

RATIONALE AND PRELIMINARY DATA
Antibody can facilitate the killing of *T. pallidum* in two ways: opsonization for phagocytosis by macrophages,[63] and complement-mediated neutralization.[64] It is now widely believed that the major mechanism of clearance of *T. pallidum* from early lesions is by opsonophagocytosis, so the identification of the targets of opsonic antibody has been long-sought. Such targets are also surface-exposed antigens, so opsonization of *T. pallidum* has been used as a functional assay for surface-exposure of an antigen of interest. Several proteins have been reported to be opsonic targets in *T. pallidum*, including TprK,[44] although acceptance of these results has not been universal.[65] Data presented above indicate that several of the Tpr proteins, including TprC and TprD are also targets of opsonic antibody, and 3D

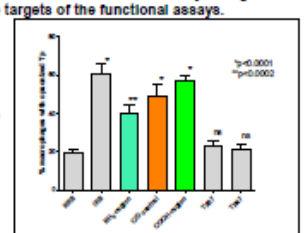
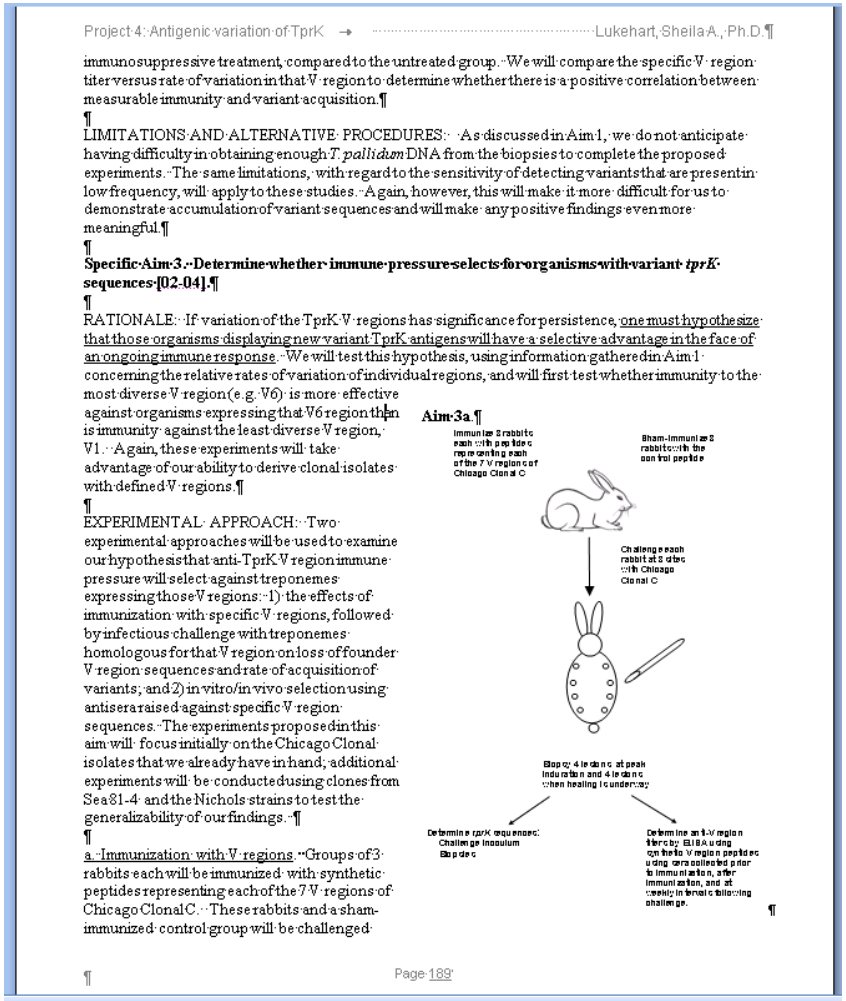


Fig. 6. Opsonization of *T. pallidum* Nichols strain by antisera directed to recombinant peptides of TprC/D.

Visual Appeal

- Figures and flow charts to explain experimental design



immunosuppressive treatment, compared to the untreated group. We will compare the specific V region titer versus rate of variation in that V region to determine whether there is a positive correlation between measurable immunity and variant acquisition.

LIMITATIONS AND ALTERNATIVE PROCEDURES: As discussed in Aim 1, we do not anticipate having difficulty in obtaining enough *T. pallidum* DNA from the biopsies to complete the proposed experiments. The same limitations, with regard to the sensitivity of detecting variants that are present in low frequency, will apply to these studies. Again, however, this will make it more difficult for us to demonstrate accumulation of variant sequences and will make any positive findings even more meaningful.

Specific Aim 3. Determine whether immune pressure selects for organisms with variant *tprK* sequences [02-04].

RATIONALE: If variation of the TprK V regions has significance for persistence, one must hypothesize that those organisms displaying new variant TprK antigens will have a selective advantage in the face of an ongoing immune response. We will test this hypothesis, using information gathered in Aim 1 concerning the relative rates of variation of individual regions, and will first test whether immunity to the most diverse V region (e.g. V6) is more effective against organisms expressing that V6 region than is immunity against the least diverse V region, V1. Again, these experiments will take advantage of our ability to derive clonal isolates with defined V regions.

EXPERIMENTAL APPROACH: Two experimental approaches will be used to examine our hypothesis that anti-TprK V region immune pressure will select against treponemes expressing those V regions: 1) the effects of immunization with specific V regions, followed by infectious challenge with treponemes homologous for that V region on loss of founder V region sequences and rate of acquisition of variants; and 2) in vitro/in vivo selection using antisera raised against specific V region sequences. The experiments proposed in this aim will focus initially on the Chicago Clonal isolates that we already have in hand; additional experiments will be conducted using clones from Sea81-4 and the Nichols strains to test the generalizability of our findings.

a. Immunization with V regions. Groups of 3 rabbits each will be immunized with synthetic peptides representing each of the 7 V regions of Chicago Clonal C. These rabbits and a sham-immunized control group will be challenged

Aim 3a.

Timeline: Writing the application

- Don't underestimate the time that it will take to do the "business" pieces of the application
- Be aware of SCRF/ UW OSP's timeline:
  - Final business 5-7 work days before due date
  - Final science 3 work days before due date
  - Absolute drop-dead deadline for "ready to submit" is 3 business days before due date

Business “Stuff”

- Cover letter/Assignment request
- Abstract, Project Narrative
- Face page
- Budget
- Budget Justification
- Resources, Equipment, Facilities
  - Include Biohazards!!!!

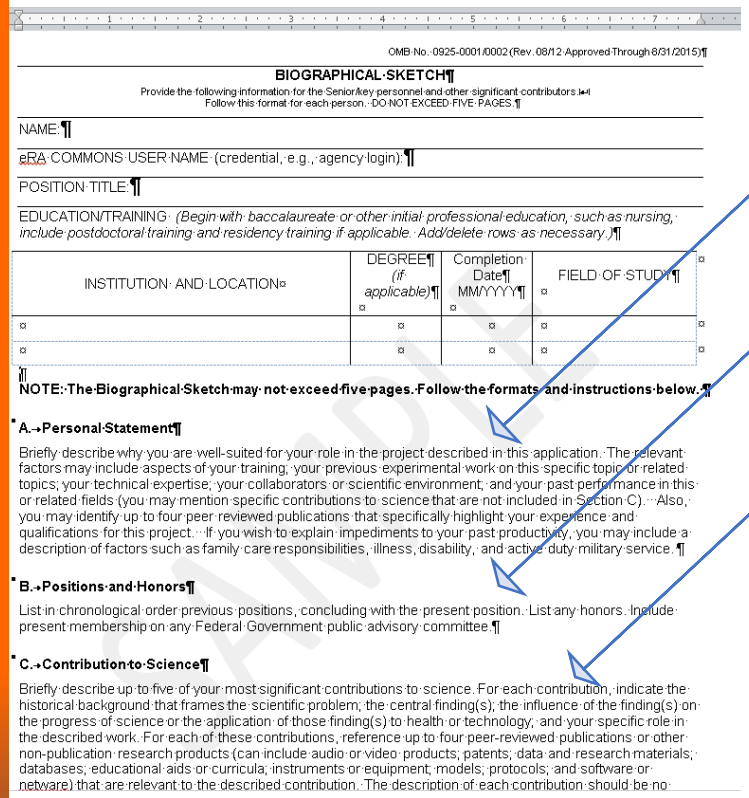
Additional non-science components for K's

- Biographical Sketch for Candidate
- Biographical Sketches for Mentor, Co-mentors
- Mentor's Statement*
- Current & Pending Support for Mentor*
- Co-mentor statements*

* Max 6 pages

- Letters of Reference
  - 3-5 letters from well-established scientists familiar with the candidate
  - May not be directly involved with the application

Biosketch



OMB No. 0925-0001/0002 (Rev. 08/12 Approved Through 8/31/2015)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME:

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE:

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (*if applicable*)	Completion Date MM/YYYY	FIELD OF STUDY

NOTE: The Biographical Sketch may not exceed five pages. Follow the formats and instructions below.

A. Personal Statement

Briefly describe why you are well-suited for your role in the project described in this application. The relevant factors may include aspects of your training, your previous experimental work on this specific topic or related topics, your technical expertise, your collaborators or scientific environment, and your past performance in this or related fields (you may mention specific contributions to science that are not included in Section C). Also, you may identify up to four peer reviewed publications that specifically highlight your experience and qualifications for this project. If you wish to explain impediments to your past productivity, you may include a description of factors such as family care responsibilities, illness, disability, and active duty military service.

B. Positions and Honors

List in chronological order previous positions, concluding with the present position. List any honors. Include present membership on any Federal Government public advisory committee.

C. Contribution to Science

Briefly describe up to five of your most significant contributions to science. For each contribution, indicate the historical background that frames the scientific problem; the central finding(s); the influence of the finding(s) on the progress of science or the application of those finding(s) to health or technology; and your specific role in the described work. For each of these contributions, reference up to four peer-reviewed publications or other non-publication research products (can include audio or video products; patents; data and research materials; databases; educational aids or curricula; instruments or equipment; models; protocols; and software or netware) that are relevant to the described contribution. The description of each contribution should be no

Tips and Pet Peeves

- **Keep the Personal Statement succinct**
  - **Make it clear when you joined the lab**
- **Honors—nothing from high school!!**
  - **AOA**
  - **Fellowships**
  - **Poster or travel awards**
- **Contributions to Science—include publications**
  - **Up to 5 contribution areas, with supporting publications**
  - **Complete citations, all authors**
  - **Name changed? Let us know.**
  - **Include link to My Bibliography, with total number of publications, # as FA**
- **Some leeway is OK for new investigators**
  - **OK to include manuscripts submitted and in press (clearly identify as such!!)**
  - **OK to add another heading for abstracts (e.g., Presentations)**

Components of K Applications

Components of K Applications

- Candidate Section (part of 12-page limit)
- Specific Aims (1 page)
- Research Plan (part of 12-page limit)
- Mentor's statement, Co-Mentors (6 pages)
- Institutional Environment (1 page)
- Institutional Commitment to Candidate (1 page)
- Human Subjects
- Vertebrate Animals

Components of K Applications

- Authentication of Reagents
- Select Agents
- Consortium/Contractual Arrangements
- Letters of Support (3-5)
- Resource Sharing Plans
- Data Management and Sharing Plan

Candidate, Aims, Research Strategy

- 12-pages + 2
- Candidate Section
- Training in Resp. Conduct of Research* (1 page)
- Specific Aims* (1 page)
- Research Strategy

* NOT included in the 12 page limit!!!

Candidate Section

- Candidate's Background
- Career Goals and Objectives
- Career Development/Training Activities

Specific to you and your proposal!

Candidate Background

- How did you get where you are?
- What inspired you?
- More than science/biosketch information
- Let the reviewers get to know you

Candidate Goals and Objectives

- Assess your own strengths & weaknesses
- Where do you want to be in 5, 10, 20 years?
- What do you need to learn to achieve your goals?

Candidate Career Development/Training

- Fill your training gaps
- Link to research plan/trajectory
- Didactic coursework (req'd for 5 yr award)
- Technical training
- What will you take with you to write an R01?
- Timeline for training activities

Candidate Career Development/Training

- Training in manuscript & grant writing, reviewing
- Budget and lab management
- Short-term rotation in special labs
- Attending scientific meetings, journal clubs
- Presenting work orally, posters
- Networking at meetings, conferences
- Measuring progress to independence

Training in the Responsible Conduct of Research

- Provide details per requirements: format, topics, faculty participation, duration, frequency

https://www.niaid.nih.gov/grants-contracts/guidance-responsible-conduct-research-rcr#advice

- Plans for future RCR training
- 1 page (not counted in limit)

Mentor's Statement of Support
(6 pages total)

- Evidence of successful training history (table of past trainees and current positions)
- Evidence of active productive research
- Evidence of support for proposed research
- Details about mentoring—e.g. frequency of meetings, topics addressed, etc
- Plan and metrics for transitioning candidate to independence

Co-Mentors' Statements of Support
(part of primary mentor 6 pages)

- Co-Mentors' statements should be specific about the expertise that they bring to the mentoring team
- Co-mentors are <u>different from collaborators</u>

Environment & Institutional Commitment to Candidate

- Institutional Environment (1 page)
  - Intellectual environment
  - Available facilities, resources relevant to applicant
- Institutional Commitment (1 page)
  - Usually letter from Chair/ Division Head
  - Guarantees ≥75% protected time for research training
  - Lab space, office, academic appointment
  - Optimal if commitment to faculty position, independent of receiving this award

The Science: Last But Certainly Not Least!

- Schedule uninterrupted time to sit and think
- Think about the unknowns in your area
- Read the latest papers in your field as well as some well-written review articles—know the literature!!
- ID connections and patterns among your ideas
- *Follow your heart as well as your mind*

Research Plan

- Specific Aims—1 page (not in 12-page limit)
- Research Strategy
  - Significance
  - Innovation
  - Approach

Specific Aims

- **The most important page in the application**
- Start with an intriguing statement or question
- One page summary of the application
  - Why is this problem significant?
  - What is the hypothesis, and what data support it?
  - What are the exciting new preliminary data that support your aims?
  - What are you going to do?
  - What will your results mean for the field?
  - Consider a figure

https://www.biosciencewriters.com/NIH-Grant-Applications-The-Anatomy-of-a-Specific-Aims-Page.aspx

Specific Aims—1 page!!

- List your aims simply
  - 2-3 Specific Aims are sufficient…with hypotheses
- Don’t be too ambitious (limited research funds)
- Aim independence
- Aims guide the structure of your Research Plan

Significance (Background)

- **Assume you are not writing for an expert**
- Identify gaps in knowledge and weaknesses
- State how you will fill those gaps
- Tie the background to each Specific Aim
- Avoid selective citation of the literature
- Figures, tables, white space!
- Consider conceptual model / framework

Innovation

- What is new about your idea?
- Will it change the way people think about the topic?
- How will your results affect the future of research in your field?
- Will it affect research in other fields?
- Simply using a new method is not innovative
- Figures, tables, white space!

Approach: Research Design and Methods

Organize by Specific Aim

- Rationale and Hypothesis
- Preliminary data
- Experimental Design
- Expected Results & Interpretation
  - Statistical analysis, sample size
  - Relate expected results to the question
- Potential Pitfalls and Alternative Approaches
- Rigor and Reproducibility

Approach: Preliminary Data

- Show preliminary data relevant to each aim
- Highlight your data
- Include control/comparison data
- Use readable figures or tables
- Critically analyze the preliminary data and state how your proposal will clarify questions about it

Approach: Research Design & Methods

- Justify choice of methods, analyses, reference
- Details of methods are unimportant (boring)
- Collaborators and consultants- strong letters
- Alternatives considered, future directions, impact
- Timeline

Aim	Description	YR 1	YR 2	YR 3	YR 4	YR 5
1A	Role of matrilysin in ischemia-reperfusion repair					
1B	Neutrophil activation *in vivo*					
2A	Neutrophil binding to KC/syndecan-1 complexes					
2B	Requirement of syndecan-1 shedding					
2C	Syndecan-1 association with integrins					
3A	Binding sites of KC:syndecan-1 interaction					
3B	Neutrophil activation with disrupted KC/syndecan-1.					
3C	Inhibit KC/syndecan-1 interaction *in vivo*					

Other Considerations

- Be thorough in addressing all questions
  - Humans subjects
  - Vertebrate Animals
- Address or state “NA” to all categories
  - Select Agents, etc
- Bibliography
  - Clean up format—list all authors*

Review of K Applications

Reviewers' Criteria (see RFA)

- Overall Impact
- Candidate
  - Quality of academic record
  - Potential for independence
- Career Development Plan
  - Consistency with your prior experience and current/future goals

Reviewers' Criteria

- Research Plan
  - Appropriate training vehicle in pursuit of goals
  - Lead to independent funding opportunities
- Mentor(s), Consultants, Collaborators
  - Appropriate for developing candidate's independence
- Environment & Institutional Commitment
  - Commitment is not dependent upon this award

Additional Review Criteria*

- Study Timeline (Clinical Trials)
- Protection for Human Subjects
- Inclusion of Women, Minorities, & Children and Lifespan
- Vertebrate Animals
- Biohazards

* These criteria CAN affect the score

Will I be funded?

- Priority score posted on NIH Commons a few days after review
- Summary Statement 3-6 weeks later
- Pay lines are posted by Institutes
- Pay lines shift during the FY
- Discuss with program officer

What if you are not funded the first time?

- Read the comments carefully and put away
- Read the comments again 3-5 days later
- Don’t get discouraged
- Discuss options with your mentor
- Revision: One revised application can be submitted
- Listen to what the reviewers said!

Don’t give up!

- Unfunded first applications are common
- Learn from an unfunded submission and succeed next time
  - Study the criticisms in Summary Statement
  - Decide whether the problems are reparable
  - Attend diligently to each criticism
  - Keep a positive tone and attitude
- “Good” amended applications tend to do well

Response in Revised Application

One page Introduction

- Restate each criticism and explain how you revised the application in response
- Misunderstandings are *your* fault—if the reviewer missed a key fact in a figure or table, maybe it wasn't clear enough

Response in Revised Application, cont.

- Be diplomatic and positive (most reviewers' comments are useful)
- Don't argue with reviewers
- Avoid tone that says "The reviewer didn't know anything about this area"
- Avoid overstating your data

Thank You!

Open for Questions

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Feedback Survey

A link to the feedback survey has been sent to the email address you used to register.

Please get out your device, find that email, and spend a few moments completing that survey before you leave today.

Tip: If on a mobile device, shift view to landscape view (sideways) for better user experience.