Grants 101 Part III

Structure & Behind the Scenes at a Study Section

Sheila Lukehart, PhD

July 18, 2014

Thanks to Bill Parks & Tom Hawn for slides and ideas

http://bytesizebio.net/index.php/2010/11/08/grant-writing-boot-camp/

Grants 101

- Research Administration—Monica Fawthrop
- Writing a Grant—Randall Curtis
- NIH Structure & Behind the Scenes at a Study Section—Sheila Lukehart

Topics covered here

- The NIH
  - Structure
  - How to navigate your way through NIH
  - Funding and success rates
- Grant Review Process
  - Mechanics of review
  - Psychology and tips

NIH Structure

NIH Structure

Director of NIH
Francis Collins, MD PhD

27 Institutes & Centers

NIH Structure—Contacts

27 Institutes & Centers

- NIAID
- NCI
- NHLBI
- NIGMS
- NIDDK
- Fogarty Int'l Center

Divisions / Branches

Program Officers ← **Your Contact**

- Before writing a K or R application
- After the research or training application has been reviewed

Office of Research Training ← Your Contact

- Before writing a K application

Scientific Review Program

Review Committees—SRO
CSR or Institute ← **Your Contact**

- Before the review

Institute Advisory Council

Funding Opportunities at NIH

- NIH Guide for Grants and Contracts
- NIH website

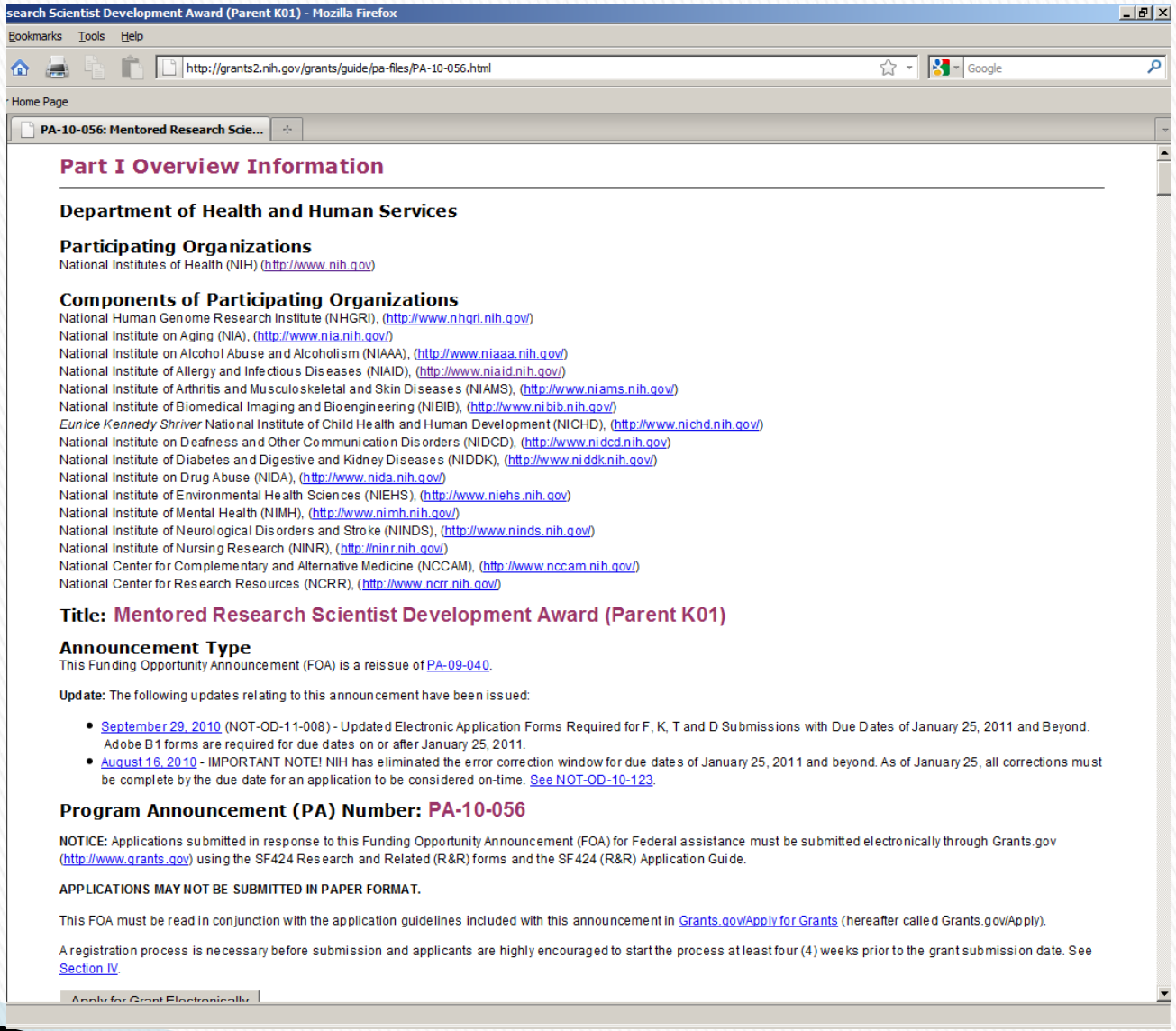
NIH Awards

- R-series Research Grants R03, R21, R01
- P-,U-series grants P01, U19
- Individual Training Awards
  - K-series K08, K23, K01, K99/R00, K22, K02, K24
  - F-series F31, F32, F33
- Contracts

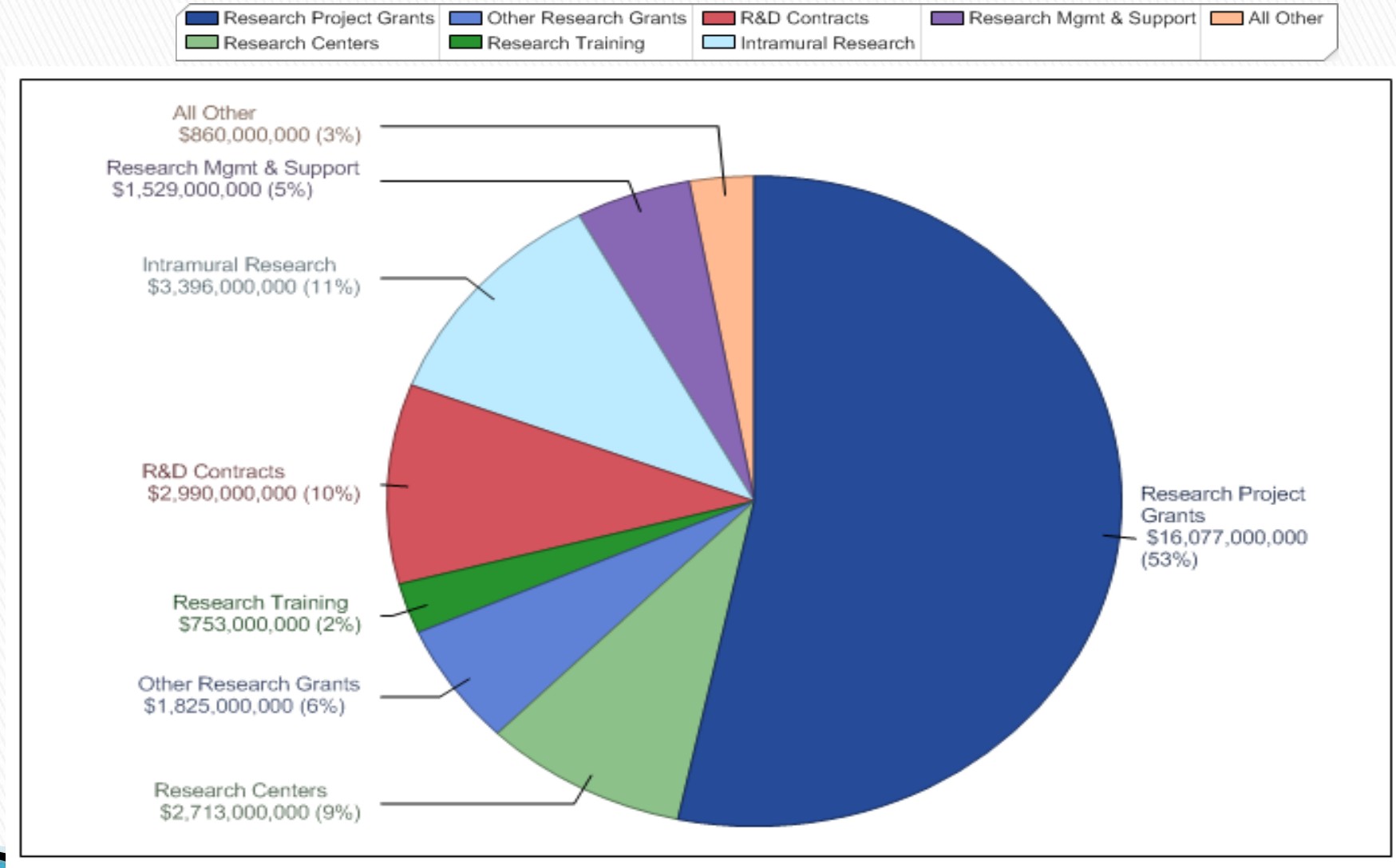
Program Announcement/Request for Applications

READ THIS CAREFULLY!!

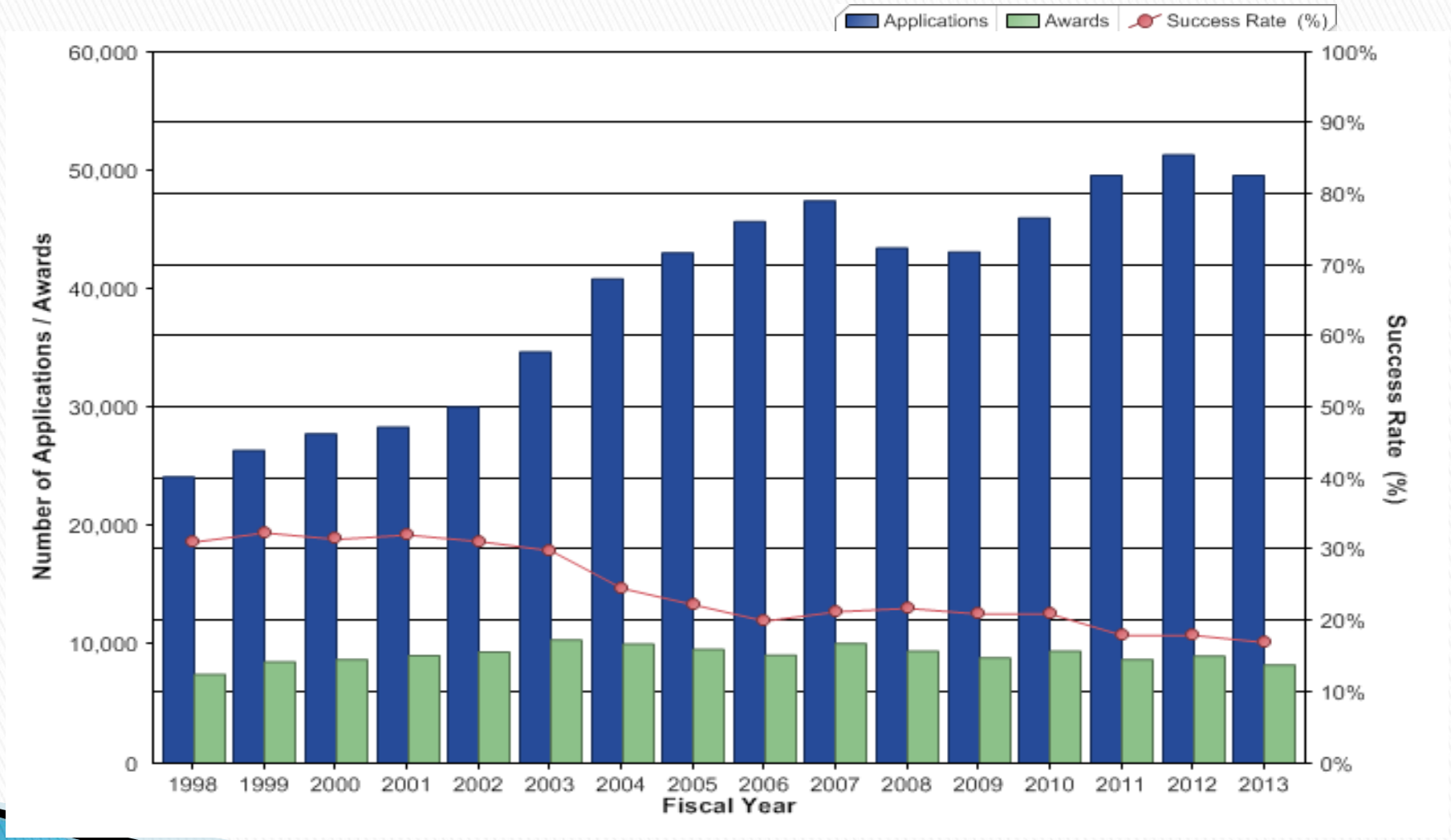
- Purpose
- Eligibility
- Deadlines
- Page limits
- Links to forms
- Required sections
- Review criteria
- Animals, humans
- Contacts



Total NIH Budget Authority FY 2014



Research Project Grants: Competing applications, awards, and success rates



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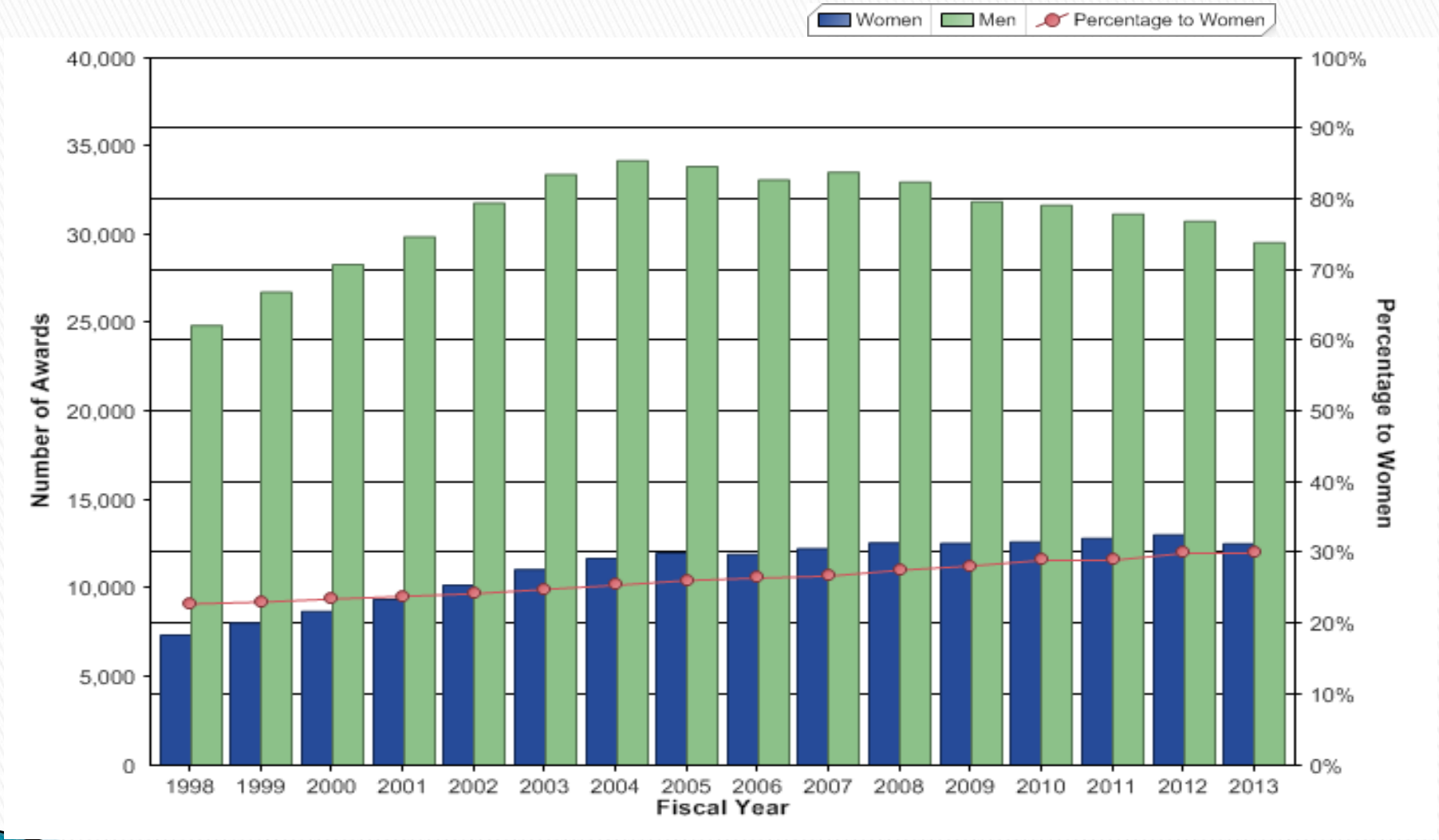
Research Grants: Awards, by gender



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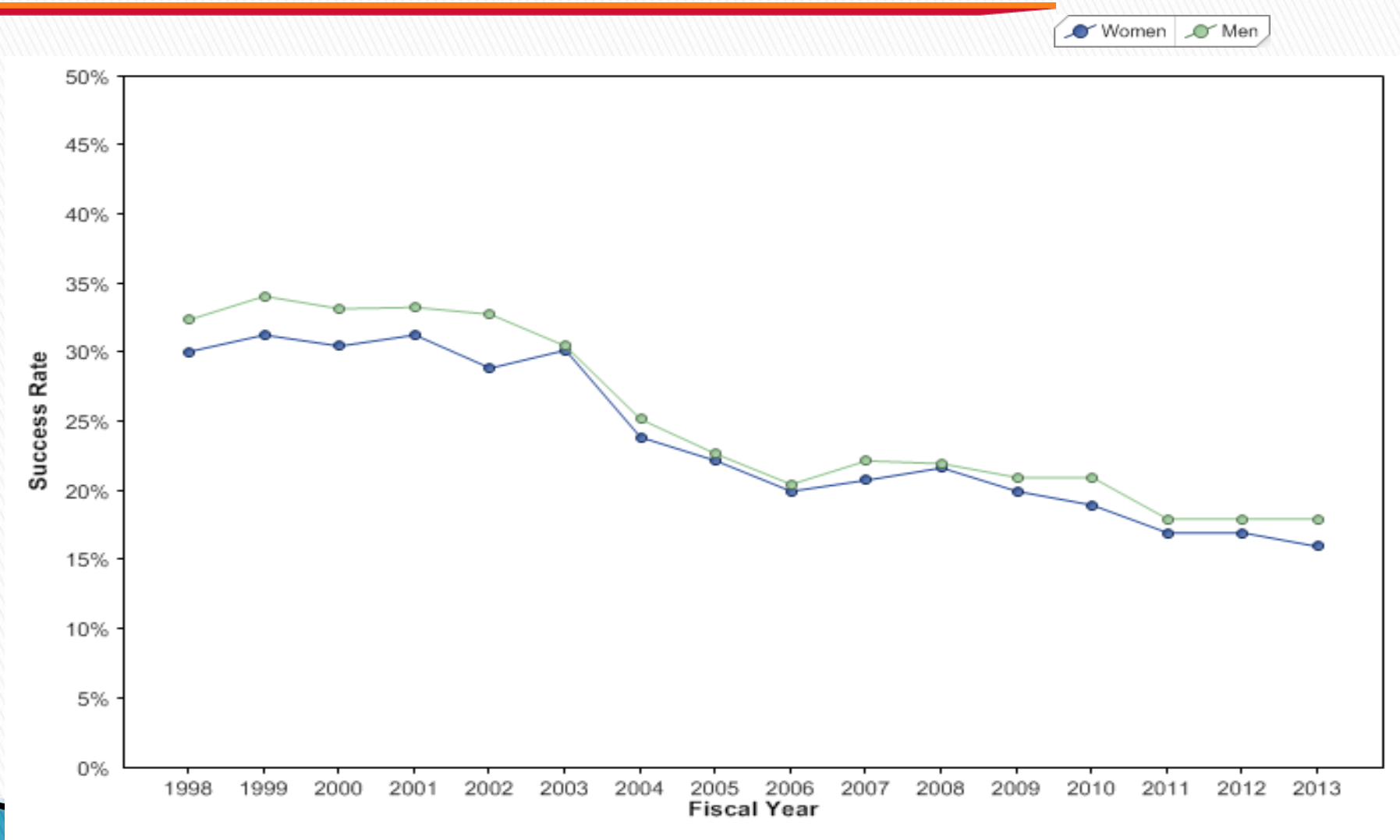
Research Project Grants
Success rates, by gender



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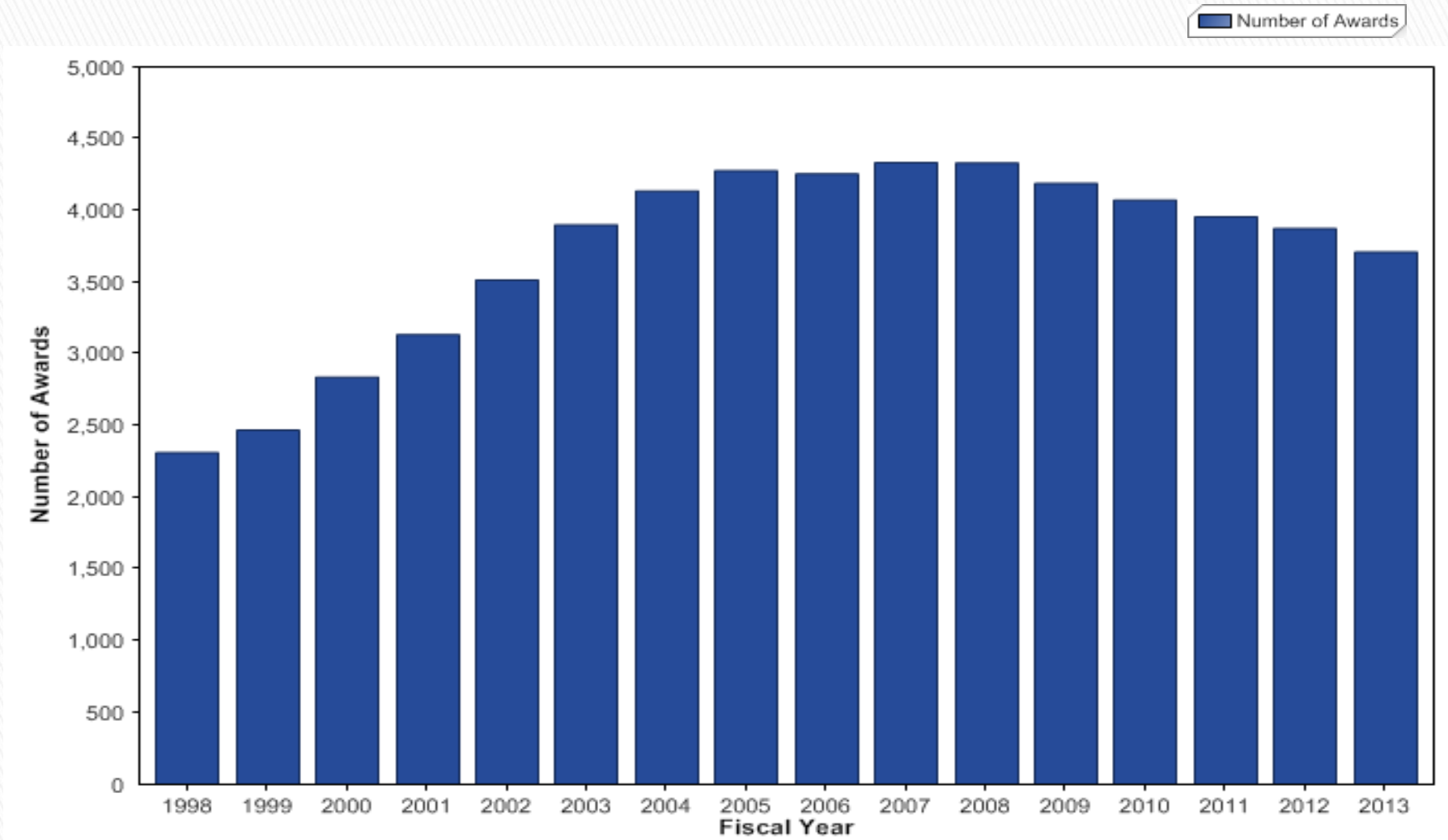
Research Career Development Awards



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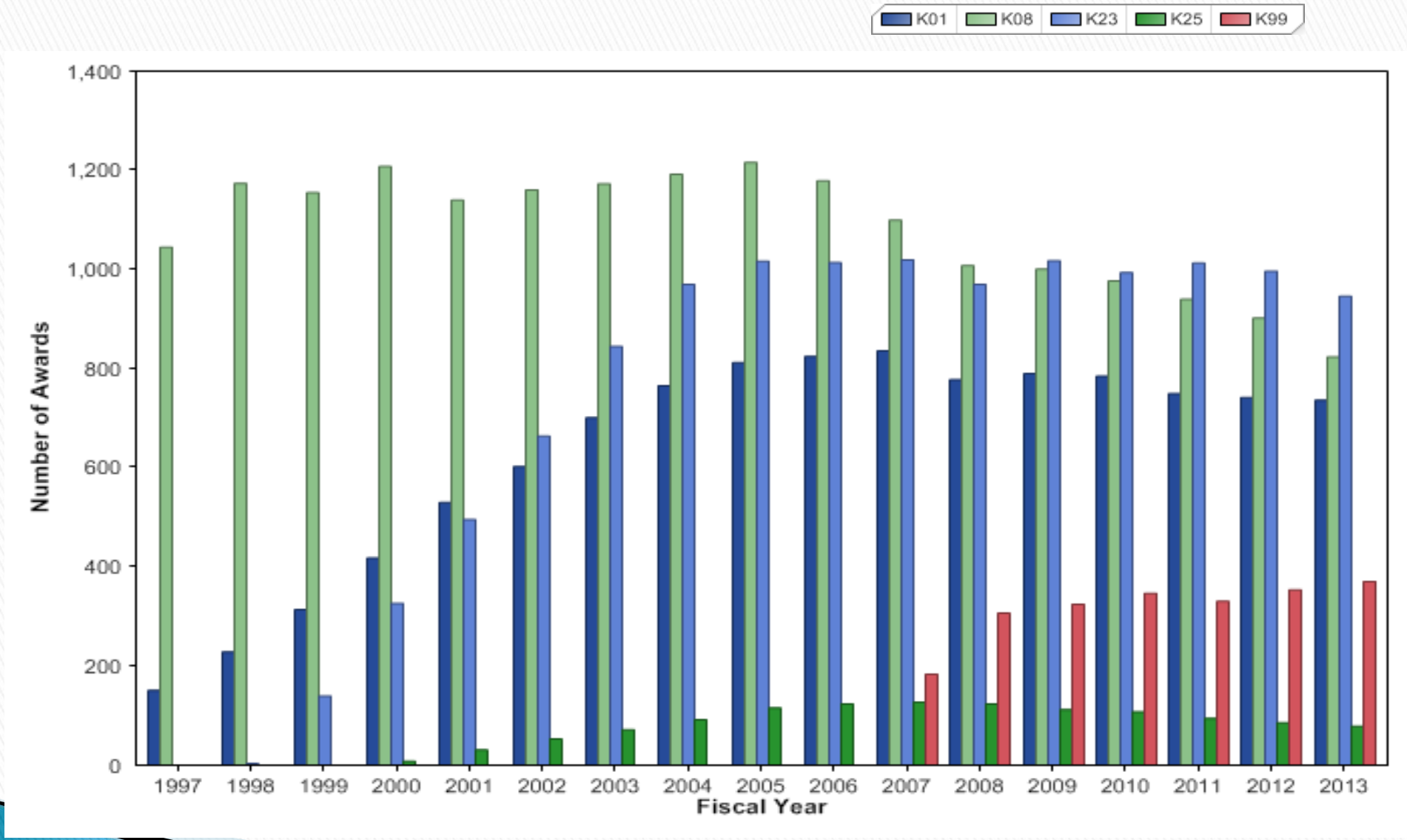
Research Career Development Awards



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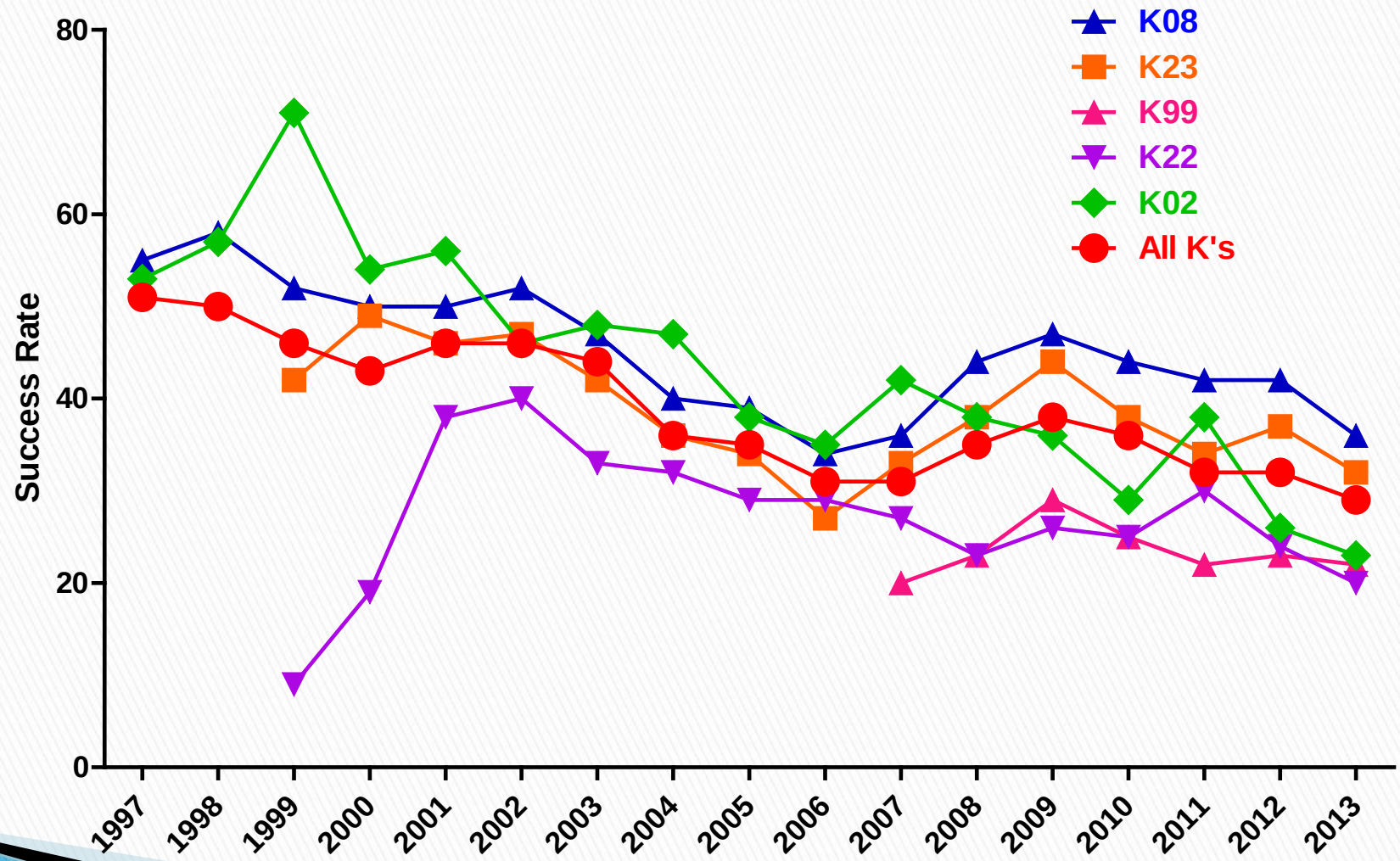
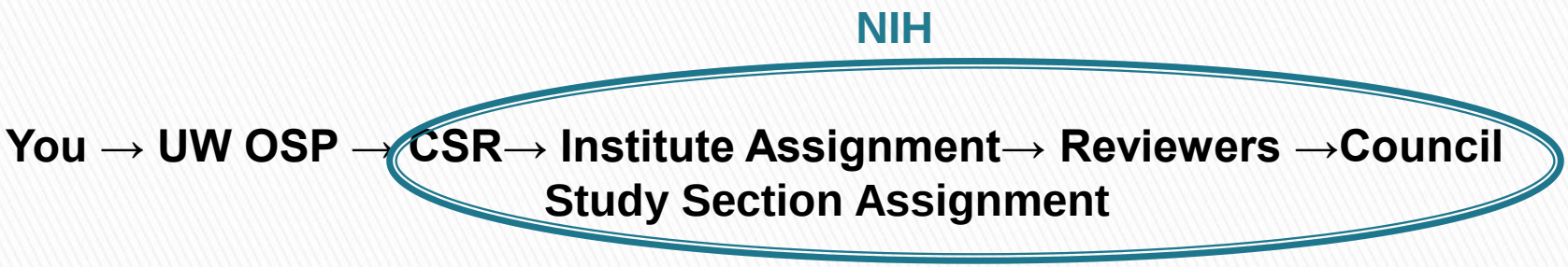
Research Career Development Awards: Success Rates



Data from NIH Databook

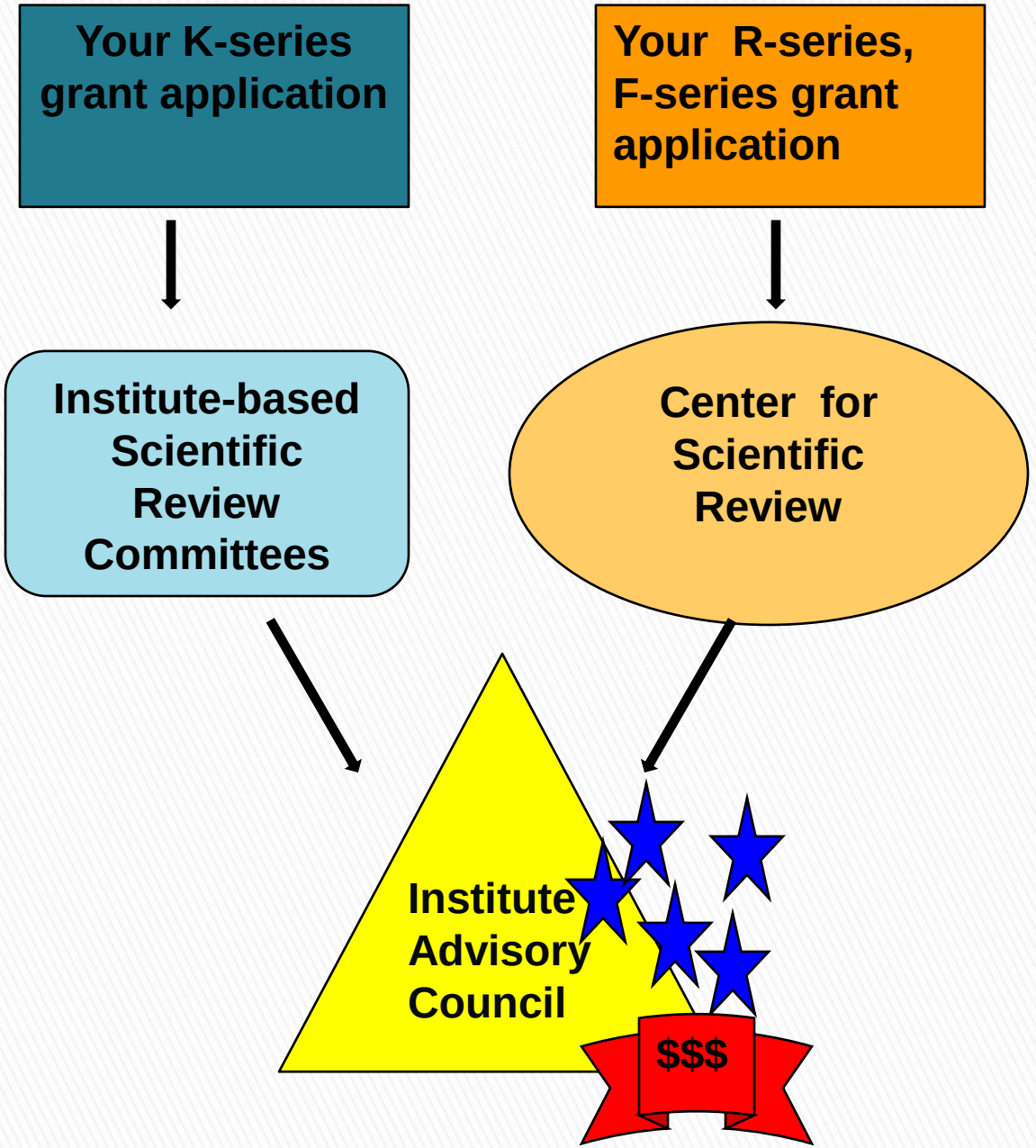
Your Application and the NIH Grant Review Process



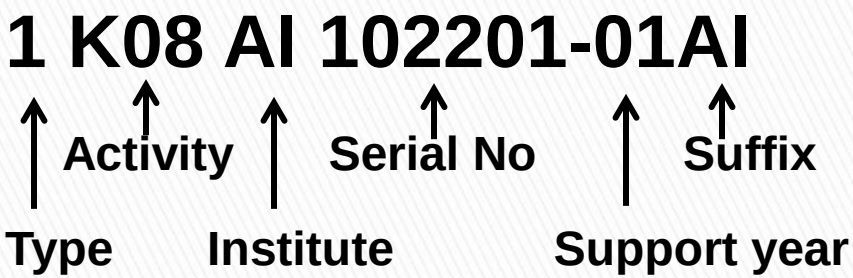
Cover letter

- Suggest Institute assignment
- Suggest study section
- Identify areas of needed expertise
- Identify conflicts
- *Do not recommend specific reviewers*

Application Pathway



Deciphering NIH Grant Numbers



- Type: 1 New, 2 Noncompeting renewal, 5 Competing renewal
- Activity: Type of grant
- Institute: Identifies parent Institute or Center
- Serial number: Unique 5-6 digit code, assigned by CSR
- Support year: Indicates current year of support, 01 is first year
- Suffix (optional): Indicates supplement, amended, etc

NIH Contacts

R or K series application

Program Officer

- Institute-based
- Before submission
- After study section review
- Has influence on funding
- Tracks progress

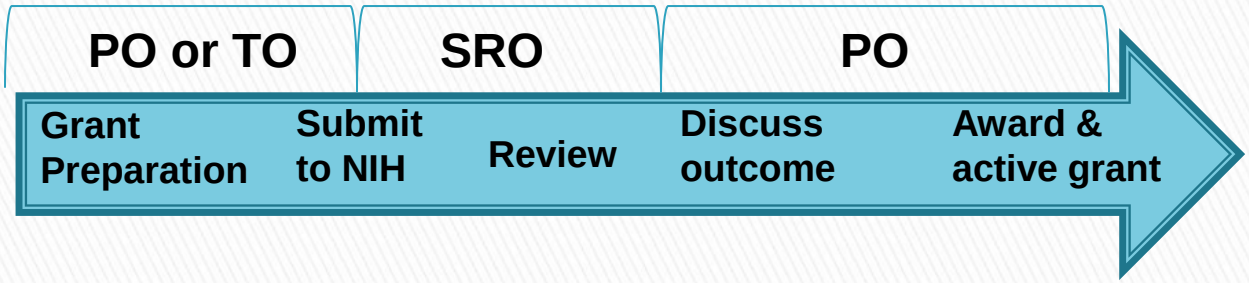
Scientific Review Officer (SRO)

- CSR- or Institute-based
- Before or during review stage
- Has no influence on funding

K series application

Institute Training Officer

- Before submission



Center for Scientific Review

- Separate from Institutes
- Receives, assigns, and reviews
- 84,000 in FY2013
- 236 Scientific Review Officers
- ~17,000 reviewers/yr
- >220 Study Sections
- 1,500 review meetings/yr

Before electronic submission

Now

CSR Study Sections

- Organ-, disease, scientific-based expertise
  - 25 Integrated Review Groups
  - >220 Study Sections
- 12-24 members per SS, mostly from academia
  - Plus ~12+ ad hoc reviewers
- 60-100+ applications per meeting
  - ~12 per member
  - 3 reviewers per application
- CSR Website
  - Study section scope and policies
  - Roster of reviewers
  - Meeting schedules
- Study sections are advisory—they do not fund applications

Institute Review Committees

- Institute-related expertise
- 1-4 review committees per institute
- Focus on training awards: K's, T's
- 12-18 members per committee, mostly from academia
  - Plus ~6 ad hoc reviewers
- 30-50+ applications per meeting
  - ~6-8 per member
  - 3 reviewers per application
- Rosters are harder to find—look at each institute
- Review Committees are advisory—they do not fund applications

Who are the reviewers?

- Established Investigators
  - 50% Professors
  - 30% Associate Professors
  - 8% Assistant Professors
- Have active NIH funding
- Relevant expertise
- Reputation for unbiased approach
- Diversity
  - Racial & ethnic
  - Gender
  - Geographic

1946 First NIH Study Section

Today

Review Process

Before the meeting

- Applications are available via the internet
- Available to reviewers 6-8 weeks prior to the meeting
- 1°, 2°, 3° reviewers assigned

- Training Awards (K's, F's)
  - Reviewers typically review applications on a wide range of topics
  - May not be an expert in all applications assigned

Review Process

- Scores and critiques are uploaded 1 week before meeting
- Each criterion is given a score: 1,2,3….9 (1 is best!)
  - These scores are not discussed during the meeting, but are included in Summary Statement
- Each reviewer gives an overall Impact Score
  - Not the mean of the criterion scores; only score discussed at meeting
- Initial scores become available to all committee members
- Applications are ranked in order of initial mean Impact Scores
- Lower 40-60% are not discussed (Impact Score of ~4.0 and above)
  - Any such application can be “resurrected” at the meeting for discussion
  - Applicants receive the critiques and individual criteria scores
  - No summary of discussion is provided to applicant

Scored Review Criteria

Individual Training F-Series Grants

- Overall impact

Review Criteria

- Candidate
- Sponsor and training environment
- Research training proposal/plan
- Training potential

Career Development K-series Grants

- Overall impact

Review Criteria

- Candidate
- Career development plan
  Career goals and objectives
  Plan to provide mentoring
- Research Plan
- Mentor, consultants, collaborators
- Environment & Institutional commitment

Investigator-Initiated R-series Grants

- Overall impact

Review Criteria

- Significance
- Innovation
- Approach
- Investigator
- Environment

Human subjects, Vertebrate Animals, Inclusion Plans, Biohazards, Responsible Conduct of Research—all affect score

At the meeting

- Begin at 8 AM EST (i.e., 5 AM PST)
- Cramped room full of laptops, files, and jet-lagged reviewers
- Streamlining
- Review in groups
  - Grant type
  - Alphabetically
  - Best to worst
  - ESI separate
- 15-20 min per application
- Short lunch break, bad hotel food
- Work until 6 PM or later
- Eat, sleep (catch up on email)
- Repeat again the next day

Discussing an application at the meeting

- Conflicts identified
- All 3 reviewers announce their preliminary Impact Scores
- Primary reviewer briefly describes the application, and highlight strengths and weaknesses for each criterion
- Other assigned reviewers add only new items
- Additional review criteria (Humans, etc)
- Open for general discussion
- Reviewers restate scores
- Range, variation
- Each member scores in whole integers 1-9
- Final score is the mean of all scores, to the first decimal X 10 3.1 X 10 = 31
- Additional review considerations (Budget, Resource sharing)
- Do it again with next application

Overall Impact or Criterion Strength	Score	Descriptor
High	1	Exceptional
	2	Outstanding
	3	Excellent
Medium	4	Very Good
	5	Good
	6	Satisfactory
Low	7	Fair
	8	Marginal
	9	Poor
Other Designations for Final Outcome		
AB	Abstention	
CF	Conflict of Interest	
DF	Deferred	
ND	Not Discussed	
NP	Not Present	
NR	Not Recommended for Further Consideration	

Vagaries of Peer Review

- Reviewers are humans
- Assigned reviewers have the most influence on scoring
- A passionate reviewer (pro or con) can influence the group
- New reviewers tend to be the toughest
- Any committee member can vote outside the “range”
- Final Impact Score is usually (85%) close to the initial Impact Score

Mock Study Section Video

http://public.csr.nih.gov/aboutcsr/contactcsr/pages/contactorvisitcsrpages/nih-grant-review-process-youtube-videos.aspx

Will you get funding?

- Funding decisions are made by Councils
- Paylines are published—go to institute web site
- Percentiles vs. Impact Scores
- Vary among institutes (~10%)
- Paylines shift during the FY
- You may be funded beyond the payline

Inside the Reviewer's Head

- Understand what reviewers go through

- Make it as easy for them as possible

- Put your best foot forward!!

Where and When are Applications Reviewed?

- At home, on a plane, on vacation…..
- At the last minute—thus many at once
- Reviewers get tired, frustrated, stressed, less than optimally sympathetic

SO…….

- Do not make the reviewers read papers or go to the internet—they won't do it!
- Do not make the reviewer think!
- Do not tick off the reviewers!

Optimize Your Chances: Don't Make the Reviewers Think

- Use simple, clear, concise language
- Emphasize (bold, underline, box) the important points
- Repeat key pieces of information, hypotheses, etc.
- Flow logically between sentences, paragraphs
- A figure is worth 1000 words!

Read successful applications

Optimize your Chances:
Put Your Best Foot Forward

- Use correct font and margins
- Observe page length restrictions
- Use proper English, grammar, punctuation
- Avoid jargon, too many abbreviations
- No typographical errors!
- Visually appealing

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 subcellular 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 hemolysinIII 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
- Figures and flow charts to explain experimental design

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]

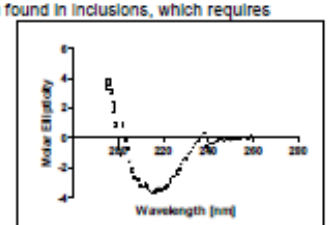


Figure 5. CD spectrum for purified refolded recombinant TprK, another likely OM protein of *T. pallidum*. The spectrum indicates abundant β-sheet composition.

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

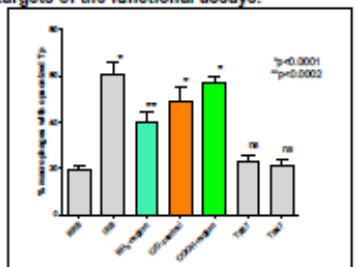
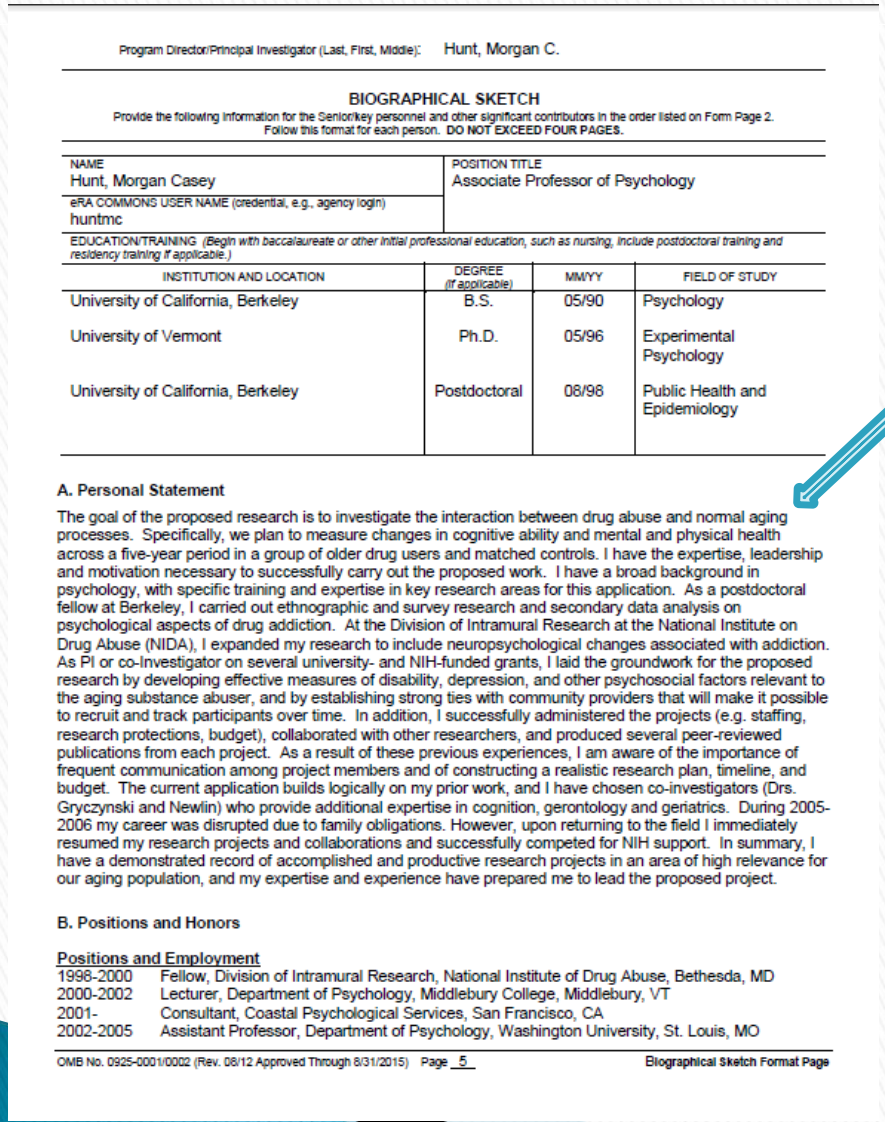


Fig. 6. Opsonization of *T. pallidum* Nichols strain by antisera directed to recombinant peptides of TprC/D.

Biosketch



Program Director/Principal Investigator (Last, First, Middle): Hunt, Morgan C.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Hunt, Morgan Casey	Associate Professor of Psychology
eRA COMMONS USER NAME (credential, e.g., agency login) huntmc	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of California, Berkeley	B.S.	05/90	Psychology
University of Vermont	Ph.D.	05/96	Experimental Psychology
University of California, Berkeley	Postdoctoral	08/98	Public Health and Epidemiology

A. Personal Statement

The goal of the proposed research is to investigate the interaction between drug abuse and normal aging processes. Specifically, we plan to measure changes in cognitive ability and mental and physical health across a five-year period in a group of older drug users and matched controls. I have the expertise, leadership and motivation necessary to successfully carry out the proposed work. I have a broad background in psychology, with specific training and expertise in key research areas for this application. As a postdoctoral fellow at Berkeley, I carried out ethnographic and survey research and secondary data analysis on psychological aspects of drug addiction. At the Division of Intramural Research at the National Institute on Drug Abuse (NIDA), I expanded my research to include neuropsychological changes associated with addiction. As PI or co-Investigator on several university- and NIH-funded grants, I laid the groundwork for the proposed research by developing effective measures of disability, depression, and other psychosocial factors relevant to the aging substance abuser, and by establishing strong ties with community providers that will make it possible to recruit and track participants over time. In addition, I successfully administered the projects (e.g. staffing, research protections, budget), collaborated with other researchers, and produced several peer-reviewed publications from each project. As a result of these previous experiences, I am aware of the importance of frequent communication among project members and of constructing a realistic research plan, timeline, and budget. The current application builds logically on my prior work, and I have chosen co-investigators (Drs. Gryczynski and Newlin) who provide additional expertise in cognition, gerontology and geriatrics. During 2005-2006 my career was disrupted due to family obligations. However, upon returning to the field I immediately resumed my research projects and collaborations and successfully competed for NIH support. In summary, I have a demonstrated record of accomplished and productive research projects in an area of high relevance for our aging population, and my expertise and experience have prepared me to lead the proposed project.

B. Positions and Honors

Positions and Employment

1998-2000 Fellow, Division of Intramural Research, National Institute of Drug Abuse, Bethesda, MD
2000-2002 Lecturer, Department of Psychology, Middlebury College, Middlebury, VT
2001- Consultant, Coastal Psychological Services, San Francisco, CA
2002-2005 Assistant Professor, Department of Psychology, Washington University, St. Louis, MO

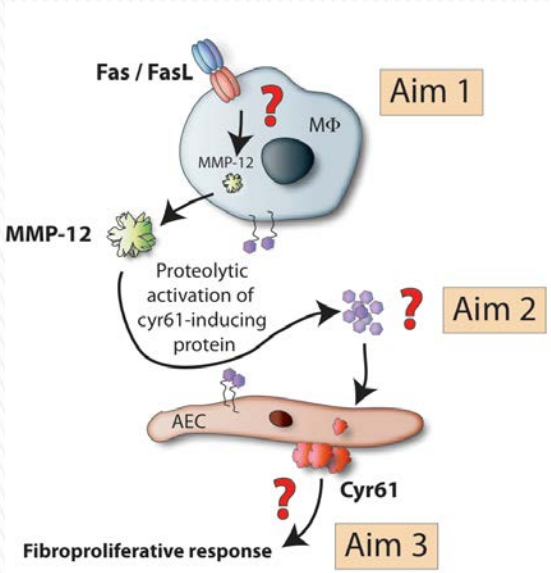
OMB No. 0925-0001/0002 (Rev. 08/12 Approved Through 8/31/2015) Page 5 Biographical Sketch Format Page

Tips and Pet Peeves

- **Keep the Personal Statement succinct**
  - **Make clear when you started your time in the lab**
  - **Do not follow the NIH example**
- **Honors—nothing from high school!!**
- **Publications**
  - **Up-to-date (no "In press… for 2005")**
  - **Complete citations, all authors**
  - **Name changed? Let us know.**
  - **Must match what we see online**
- **Some leeway is OK for new investigators**
  - **OK to include manuscripts submitted and in preparation (separate section?)**
  - **OK to add another heading for abstracts (e.g., Presentations)**
- **Important to show what you have done**

Specific Aims

- The most critical page in the application
- The first line(s) must be compelling!!
- It is a one page summary of the application
  - Why is this problem significant?
  - What is the hypothesis(es), 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?
- Summary diagram is good



Significance (+Background)

- ~1 page
- Why does this research matter?
- Critically review the literature
- Cite original, timely papers, not reviews
- Identify gaps in knowledge; state how you will fill those gaps
- Tie the background to each Specific Aim
- Don’t be afraid to disagree with something, but say why
- Stay focused on issues that you will study
- Graphics (cartoons, model, pathways, etc) are helpful
- Show tempered enthusiasm
- Assume you are writing for a non- expert

Pet Peeves

- Too long
- Strays from focus
- Not timely or scholarly
- Selective citation of literature
- Unfettered exuberance

Innovation

- What is new about your idea?
- How will it change the way people think about your topic?
- How will your results affect the future of research in your field?
- How will your results affect research in other fields?

Pet Peeves

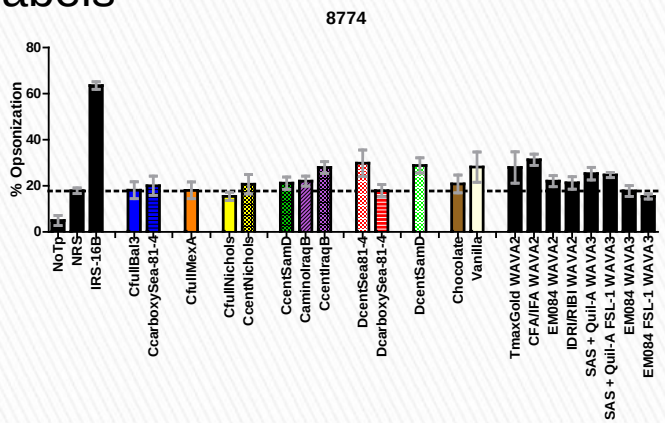
- Thinking that being the first to apply an already trendy technique to your field is innovative
- Looking at new strain, cell line, etc. unless there is a compelling biological reason to do so

Preliminary Studies

- Summarize relevant experience and contributions
- Relate preliminary data to each aim (highlight your data)
- Critically interpret your data
- *Thus, these data indicate….* Draw conclusions for the reviewer!
- About 5-8 readable figures or tables (fewer for K's)
- Embed figures near text
- Figures should be self-explanatory. Use legend to reinforce conclusions
- Do not rely on published papers, websites, or appendix material

Pet Peeves

- No (or incorrect) figure or table numbers
- Not crediting work of others
- No link to the Aims
- Having to look for the figures being discussed in the text
- Figures too small to see or read labels



Research Plan

- This is the meat of the science
- More narrative than technical
- Organize by Specific Aim
  - Rationale
  - Approach (brief summary of strategy)
  - Experiments
  - Expected results & interpretation
  - Potential Pitfalls and Alternative Approaches
  - Future Directions (short)
- Quantification and statistics
- Methods
  - Justify why, not how, you are doing something
  - Give priority to new or difficult methods

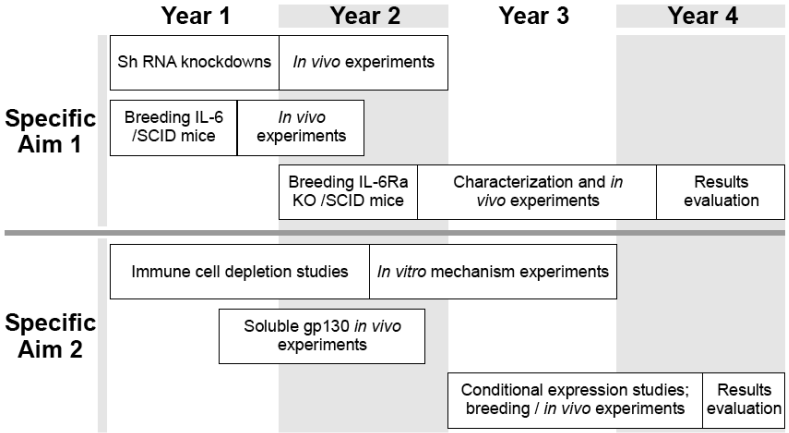
Pet Peeves

- No logical flow from aim to aim
- Everything dependent on Aim 1
- No link to the Aims
- Having to look for the figures being discussed in the text
- Figures too small to see or read labels
- Overly ambitious
- Too much methodological detail
- No interpretation of expected findings

More Tips: Reviews like

- Strong detailed letters from collaborators and consultants
- Priorities and timelines

Table IV. Timetable



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 Sections

- Answer all categories
  - Biohazards
  - Humans subjects
  - Vertebrate animals
  - Letters of support
- Address or state “NA”
  - Select agents, Resource Sharing, etc
- Bibliography
  - Correct format

Pet Peeves

- All sections not addressed
- Incomplete references
- Misnumbered or incorrect references
- Lack of detail in Human or Animal sections
- No Biohazard section

Sections Specific to Training Awards

- Candidate
  - Reviewers want to feel as if they know you—obstacles, inspiration, pathway
- Career Goals & Objectives
  - Strengths & weaknesses of your training/preparation; where you see yourself in 10 years; what you need to get there
- Career Development Plan
  - Courses, specific training, teaching, lab/project management skills, paper and grant-writing, mentoring students, timeline to independence

Pet Peeves

- Science-focused, ignoring other aspects of career development
- No sense of what motivates the applicant
- No self-reflection about weaknesses in preparation
- No detailed timeline for career development activities

Good Luck!!!!