Grants 101 Part 1:
Training and Career Development Awards

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Grants 101

I. Training & Career Development Awards
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II. NIH Structure & Behind the Scenes at Study Section
   Tom Hawn

(Business aspects—Monica Fawthrop’s slides on line)
NIH and Career Development Awards

- Types of career development awards
- Getting information about K’s
- Components of a K application
- Tips on writing a great application
Types of Early Career Training Awards

- **US citizen, permanent resident**
  - K08: MD, DVM, DDS, other Clinical Doctorate
  - K23
  - K01
  - K22: MD or PhD
  - K25

- **US Citizen/PR or Non-citizen**
  - K99/R00 Pathway to Independence: MD or PhD
  - K99/R00 Physician/Scientist (NIAID only): MD only

Some institutes don’t offer all grant mechanisms
Overview of Relevant K Awards

- NIH Research Career Development Awards

https://researchtraining.nih.gov/programs/career-development
Mentored Career Development: K Awards

- **K08** Mentored Clinical Scientist Research Career Development Award
  - Laboratory focused research
  - May use human samples

- **K23** Mentored Patient-Oriented Research Career Development Award
  - Patient oriented research
    - Clinical trial not allowed
    - Clinical trial required
    - Independent basic experimental studies with humans required

Clinical doctoral degree: MD, DVM, PharmD
US citizen, permanent resident
Mentored Career Development: K Awards

- **K01** Mentored Research Scientist Development Award
  - Institute-specific purposes (e.g. NIAID limits to epidemiology, modeling techniques, and outcomes research)

- **K25** Mentored Quantitative Research Career Development Award
  - Quantitative or engineering degree moving to health-related topics

PhD or MD (or other doctorate)
US citizen, permanent resident
Mentored Career Development: K Awards

- Require 75% protected time for research and training
- 3-5 years duration
- Stipend ($50-100K per year)
- Very modest funds for research
K Awards: Transition to Independent Career

- **K99/R00** NIH Pathway to Independence Award
  - Mentored/Independent portions
- **K22** Career Transition Award
  - Not mentored

Participation varies by institute—check with your institute!!
K99/R00 Pathway to Independence

- Transition award for finishing postdoc and moving to Assistant Professor
- 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

*Eligibility extended by two cycles for JunJul 2020 – FebMar 2021 due dates

Uses and rules vary by institute—check with your institute
NIAID supports very few—for non US/PR
K99/R00 Pathway to Independence

K99 years

- Apply for K99 phase with specific postdoc career development and research plan, include broad description of independent phase
- Provides salary support ($50-100K) and benefits
- Modest research support ($20-50K/year)

Uses and rules vary by institute—check with your institute
NIAID supports very few—for non US/PR
K99/R00 Pathway to Independence

R00 years

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

*~$160 direct costs

Uses and rules vary by institute—check with your institute
NIAID supports very few—for non US/PR
K22 Career Transition Award

Two phases

1. Submit application while at postdoc institution
   - Scientific merit
   - No institution or $$ yet
2. Assistant Professor (2-3 years)
   - Protected research time (>75%)
   - $150K/$100K DC (NIAID)
   - $150K/year (NCI)
   - Limit of $50-100K per year for salary

Participation varies by institute—check with your institute
K22 Research Scholar Development

- Participation varies by institute

- Eligibility
  - Must not have >5 years* of postdoc training at time of application or resubmission (NIAID) OR
  - Have 2-8 years of postdoc training (NCI)
  - Must not have held an independent research position anywhere
  - Must not have been PI on another K award, R01 or equiv, or Project leader on P01 or U19.
  - PI of R03 (or R21) is OK if specific aims are the same as in K22 application
  - Must not have another K application pending

*Eligibility extended by two cycles for JunJul 2020 – Feb Mar 2021 due dates

Participation varies by institute—check with your institute
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......
Visual Appeal

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

Figures and flow charts to explain experimental approach

Structural predictions support the notion of surface exposure of 10 loop structures in those proteins. Eight of these loops contain regions (DR) in which the predicted AA sequence differs among strains and subspecies, and 2 contain conserved AA sequences. Preliminary data (Figure 6) demonstrate that antisera raised against shorter purified recombinant peptides from Nichols-TpC0D are able to opsonize the Nichols strain; these antisera are roughly equivalent to the antibodies to the amino-, central-, and carboxyl regions of TpC0D that will be prepared in Aim 2. Negative and positive controls include normal rabbit serum (NRS) and infection immune rabbit serum (IRS). Additional negative controls include rabbit antibodies to the encopiliferal sheath FlaA (Tp37) and the 47-kDa topoprotein antigen, both of which are abundant but are not surface exposed in the intact hepatocyte. Lack of opsonization by these antisera indicate the specificity of the assay for surface-exposed components and confirm that the treponemes in this assay are intact throughout the incubation period.

Although our laboratory has conducted a very large number of opsonization experiments over the years, we have always used the Nichols strain as our target strain. In this proposal, we will examine the ability of antibodies directed toward TpC0D or TpD proteins from different subspecies and strains (or peptides derived from these)—each with distinct DR sequences—to opsonize homologous or heterologous strains. Because these DR sequences are fixed within a strain, and do not change within the course of infection, it is hypothesized that the DR confers a subspecies- or strain-specificity to opsonization and neutralization, and perhaps contribute to the lack of cross-immunity among strains and subspecies.

**EXPERIMENTAL APPROACH**

Antisera produced in Aim 2 will be tested in a checkerboard fashion with different T. pallidum strains in opsonization and neutralization assays (Figure 7), in the following order:

1. Antisera resulting from infection with each of the 7 strains
2. Antisera raised against each full-length recombinant TpC0D and TpD protein
3. Antisera raised against the sequences found in amino-, central, and carboxyl-regions of these proteins
4. Antisera raised against selected cyclic peptides

Experiments will first be conducted using the Nichols strain and Samoa D strain as the target strains. These two are chosen because they have least amount of similarity at the DR and throughout the central region of TpD. Comparison of results with these two strains should give us the most robust indication of the effect of the DR sequences on cross-reactivity in functional assays. Other strains will be tested based upon the initial findings, to determine the effects of specific amino acid differences on antibody function.

Opsonization assays will be conducted as previously described. After incubation of treponemes with control or test antisera plus macrophages, the uningested treponemes are washed off, and the cover slips containing macrophages are fixed and stained for T. pallidum (see color photo in Fig. 7). The percentage of macrophages containing ingested T. pallidum is determined on triplicate slices per condition. Past studies have indicated that counting the % of macrophages containing ingested T. pallidum is proportional to scoring the actual number of T. pallidum ingested (not shown). The choice to count macrophages, rather than individual treponemes, because it is significantly less labor-intensive. Importantly, the cover-slips are randomized on slides and coded so that the scorer is unaware of the experimental condition represented. Negative controls including incubation of treponemes + NRS + macrophages, and macrophages incubated without treponemes, the positive control will be infection-induced antibodies raised against the target strain. Each test antisera is tested in triplicate per macrophage donor, and with at least 3 macrophage donors.

Neutralization will be performed as described by Bishop and Miller. Treponemes will be incubated with heated control or test sera, with and without added active rabbit.
Components of K Applications

- Specific Aims (1 page)
- Candidate Section*
- Mentor’s statement, Co-Mentors (6 pages)
- Environment & Institutional Commitment to Candidate (1 page each)
- Research Plan*
- Human Subjects
- Vertebrate Animals

*combined 12 page limit
Components of K’s, continued

- Training in Responsible Conduct of Research (1 page)
- Authentication of Reagents
- Biohazards (in Facilities section)
- Select Agents
- Consortium/Contractual Arrangements
- Letters of Support (Collaborators)
- Resource Sharing Plan
“Extra” Required Components for K’s

- Biosketches for Mentor, Co-mentors
- Mentor’s Statement#
- Current & Pending Support for Mentor#
- Co-mentor statements#
- Letters of Reference
  - 3-5 letters from well-established scientists familiar with the candidate
  - May not be directly involved with the application

# Combined max 6 pages
Tips and Pet Peeves

• Keep the Personal Statement succinct
  • Make it clear when you joined the lab
• Honors—nothing from high school!!
  - Phi Beta Kappa
  - Summa cum laude
  - Poster or travel awards
• Contributions to Science—include publications
  - Up to 5 areas, with supporting pubs
  - Complete citations, all authors
  - Name changed? Make it clear!
  - List 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 preparation (clearly identify as such!!)
  - OK to add another heading for abstracts (e.g., Presentations)
Candidate Section

- Candidate’s Background
  - How did you get where you are?
  - Let the reviewers get to know you

- Career Goals and Objectives
  - Where do you want to be in 5, 10, 20 years?
Career Development/Training Activities
- How will this award fill your training gaps?
- Time plan
- Didactic coursework (req’d for 5 years)
- Technical training
- What will you be able to take with you to write an R01?
Candidate Section

- Career Development/Training Activities
  - Training in manuscript & grant writing, manuscript reviewing, budget management, lab/group management, directing staff/students
  - Attending scientific meetings, journal clubs
  - Presenting work orally, posters
Training in the Responsible Conduct of Research

- Provide details for each section: format, topics, faculty participation, duration, frequency

- Future plans for RCR training

- 1 page (not counted in limit)
Mentor Statements (6 pages total)

- Mentor’s statement should include
  - Evidence of successful training history
  - Evidence of active productive research
  - Evidence of support for proposed research
  - Details about mentoring—e.g. frequency of meetings
  - Topic areas in which mentoring will occur
  - Plan for transitioning candidate to independence

- Co-Mentors’ statements should be specific about the expertise that they bring to the mentoring team
Environment & Institutional Commitment to the Candidate

› Description of Institutional Environment (1 page)
  - Intellectual environment
  - Facilities, resources

› Institutional Commitment to Candidate’s Research Career Development (1 page)
  - Is usually letter from Chair/Division Head
  - Guarantees >75% protected time for research training
  - Lab space, office, academic appointment
The Science: Last, But Certainly Not Least!

- Schedule uninterrupted time to sit and think—days of time
- Think about the unknowns in the topic that you are studying
- Read the latest papers in your field as well as some well-written review articles
- Begin to see 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 critical page in the application
- Start with an intriguing statement
- One page summary of the application
  - What is the hypothesis(es), and what data support it?
  - What are the exciting new preliminary data that support your aims? Which data are YOURS?
  - What are you going to do?
  - What will your results mean for the field?
Specific Aims—1 page!!

- List your aims simply
  - 2-4 Specific Aims are sufficient
- Don’t be too ambitious!!
- Everything should not be dependent upon Aim 1
- Aims serve as the backbone of Research Plan
Significance (Background)

- Assume you are not writing for an expert
- Identify gaps in knowledge; state how you will fill those gaps
- Tie the background to each Specific Aim
- Avoid selective citation of the literature
Innovation

- 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
Approach: Research Design and Methods

- Organize by Specific Aim
  - Rationale and Hypothesis
  - Experimental Approach
  - Expected Results & Interpretation
    - Statistical analysis, sample size
    - Potential Pitfalls and Alternative Approaches

- Other Important Sections
  - Future Directions
  - Timeline
Approach: Preliminary Studies

- Show preliminary data relevant to each aim and clearly tie the data to the aim (highlight your data)
- Include control data
- About 3-5 readable figures or tables (K award)
Approach: Preliminary Studies

- Put figures on relevant pages
- Number figures; refer to figure number in the text in bold (Fig. 1)
- Figures should be self-explanatory—legends, labeled axes, etc.
Approach: Research Design & Methods

- Describe experimental design
- Details of methods are unimportant (boring)
- Get collaborators and consultants- strong letters
- Timeline

<table>
<thead>
<tr>
<th>Aim</th>
<th>Description</th>
<th>YR 1</th>
<th>YR 2</th>
<th>YR 3</th>
<th>YR 4</th>
<th>YR 5</th>
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<tbody>
<tr>
<td>1A</td>
<td>Role of matrilysin in ischemia-reperfusion repair</td>
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<td>1B</td>
<td>Neutrophil activation <em>in vivo</em></td>
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<td>2A</td>
<td>Neutrophil binding to KC/syndecan-1 complexes</td>
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<td>2B</td>
<td>Requirement of syndecan-1 shedding</td>
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<td>2C</td>
<td>Syndecan-1 association with integrins</td>
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<td>3A</td>
<td>Binding sites of KC syndecan-1 interaction</td>
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<td>3B</td>
<td>Neutrophil activation with disrupted KC/syndecan-1</td>
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<tr>
<td>3C</td>
<td>Inhibit KC/syndecan-1 interaction <em>in vivo</em></td>
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Other Considerations

- Be thorough in addressing or stating “Not applicable” for **all sections**
  - Humans subjects
  - Vertebrate Animals
  - Biohazards
  - Authentication of reagents
  - Select agents, Resource Sharing, etc

- Bibliography
  - Correct format
Scored Review Criteria-K Award

- Overall Impact
- Candidate
- Career Development Plan
- Research Plan
- Mentor(s), Consultants, Collaborators
- Environment & Institutional Commitment
Additional Review Criteria*

- Training in Responsible Conduct of Research
- Protection for Human Subjects
- Inclusion of Women, Minorities & Children
- Vertebrate Animals
- Biohazards

* These criteria DO affect the score
Will your Application be Funded?

- Priority score will be posted on NIH Commons within a few days of the review meeting
- Summary Statement will appear 4-6 weeks later
- Paylines are posted by most institutes
- Final funding decisions are made by institute’s Council
The Rewards!

- Discovery!
- Help to understand, control, prevent, or cure a disease
- Opportunity to develop the next generation of outstanding scientists