NATIONAL INSTITUTES OF HEALTH (NIH) NATIONAL CANCER INSTITUTE (NCI)

F99/K00 FELLOWSHIP INFO SESSION

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F99/R00 Graduate Student to Postdoc Fellowship

Outline

- Introduction to the F99/R00 Fellowship
- Preparation Prior to Writing
- Overview of Application Components
- Applicant's Background and Goals
- Specific Aims Page
- Research Strategy
- Sponsors and Collaborators
- Question and Answer Session

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Introduction to the F99/K00

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NIH Awards Overview

Fellowships and Awards at Different Levels

- **F31: Predoctoral Fellowship**
- F32: Postdoctoral Fellowship – Apply your final year of your PhD or 1 – 2 years after starting a postdoc term
- **F99/K00: National Cancer Institute (NCI) Predoctoral to Postdoctoral Fellow Transition Award – one nomination for Purdue**
- K99/R00: Career Development Award given to experienced postdocs who have a year or two left as a postdoc and then will transition to a faculty position.

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NIH F99/K00 Fellowship Benefits

Graduate Years: Up to 2 years

- Tuition covered
- $25,836/year stipend
- $1,500 in the first year to defray the travel costs to attend a mandatory NCI-sponsored conference

Postdoc Years: Up to 4 years

- Stipend: $60,000 in the first year, $63,300 for the second year, $66,600 for the third year, and $69,900 for a fourth year
- $1500 in the first year to defray the travel costs to attend a mandatory NCI-sponsored conference, and up to $3000 annually to help defray other research training expenses

More than just the money!

→ Makes you stand-out to universities and employers
→ Fellowship recipients more likely to receive future NIH funding
→ Preparation for composing research grants

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F99/K00 Requirements

You are Eligible if:

- ❑ You must be in the start of your third or fourth year of your PhD or master-PhD program.
- ❑ You have US Citizenship, are a Permanent Resident, or have a Visa that allows you to legally work in the United States for 2 or more years after your PhD graduation.
- ❑ Your thesis defense will definitely occur after August 2023.
- ❑ Your current research relates to cancer, and/or your future postdoctoral research will relate to cancer.

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F99/K00 Nomination System

How the Process Works

- The NCI requires the university to nominate one student to be considered for the F99/K00 fellowship. The Fellowship Office will oversee the selection process and will file the nomination for the selected applicant.
- Students who wish to be considered for nomination will submit the following:
  - NIH Biosketch
  - Specific Aims Page
  - Research Strategy Document
  - List of the Sponsor (or co-sponsors), Collaborators, & Consultants with their names, department and university affiliations and 2-3 sentences about their role in your project.
  - A list of the 4 - 5 individuals whom you plan to ask for letters of recommendation if you are selected as Purdue's nominee: Please include their full names, positions, institutional or organizational affiliations, as well as one sentence that states when/how you worked/interacted with them.
- A panel of cancer researchers at Purdue will evaluate the nomination requests and select Purdue's one nominee.
- The nominee will then complete the full application documents, which will be submitted by the university.

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F99/K00 Nomination Timeline

Deadlines for Nomination Requests and Full Application Submission

- Nomination Submission Opens in early August
- Nomination Submission Closes in early September
- Early October: announcement of the F99/K00 nominee
- October November: nominee prepares full application, receives guidance from the Fellowship Office
- Mid-November: F99/K00 application submitted to NIH by the Purdue Office of Sponsored Program Services Pre-Award Specialist

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F99/K00 Project Timeline Planning

Timing from award receipt to project finish:

- The Review Process is estimated to take 6 – 7 months.
- F99/K00 awards are estimated to be announced in May or June 2023.
- Earliest Project Start Date: July 2023

Your earliest graduation date could be December 2023.
Your latest graduation date could be August 2025.

F99 Portion: Finishing PhD

- Year 1: July or August 2023 to July 2024
- Year 2: August 2024 – July 2025 or May 2025 if that is when you graduate

K00 Portion: Postdoc

- Year 3: June or August 2025 – July 2026
- Year 4: August 2025 – July 2027
- Year 5: August 2027 – July 2028
- Year 6: August 2029 – 2030

You do not have to request all four years of Postdoc funding.

→ Whichever graduation date you plan for and however many years of postdoc funding you request will be non-alterable once you win the award.

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Preparation Prior to Writing

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What NCI is looking for in the F99/K00 Fellowship

PhD research that is not exactly from your advisor's current grants:

"The F99 project can be within the overall scope of the sponsor's research awards. However, NCI expects the F99 candidate to make significant intellectual contributions to the project and write the Research Training Plan. There should be no text duplication or substantial duplication of the scientific aims, and the candidate 's application should propose a scientific research question or approach that is distinct from the specific aims of the sponsor's pending or active research grants."

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What NCI is looking for in the F99/K00 Fellowship

The "mentored research training experience" that you propose must provide:

- ❑ A strong foundation in **research design, methods, and analytic techniques**
- ❑ Experience **presenting and publishing the research findings as first author**
- ❑ The opportunity to interact with members of the scientific community at appropriate **scientific meetings and workshops**;
- ❑ **Skills needed to transition to the next stage** of the applicant's research career (technical and professional development)
- ❑ The opportunity to enhance the health-related sciences and the **relationship of the proposed research to health and disease**.

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First Steps: Read F31 Examples, Look at the F31 templates

NIH Page on the Grant Writing Resources Site

https://wiki.itap.purdue.edu/pages/viewpage.action?pageId=120723375

→ Login with your Purdue username and non-BoilerKey password

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First Steps: Read F31 Examples, Look at the F31 templates

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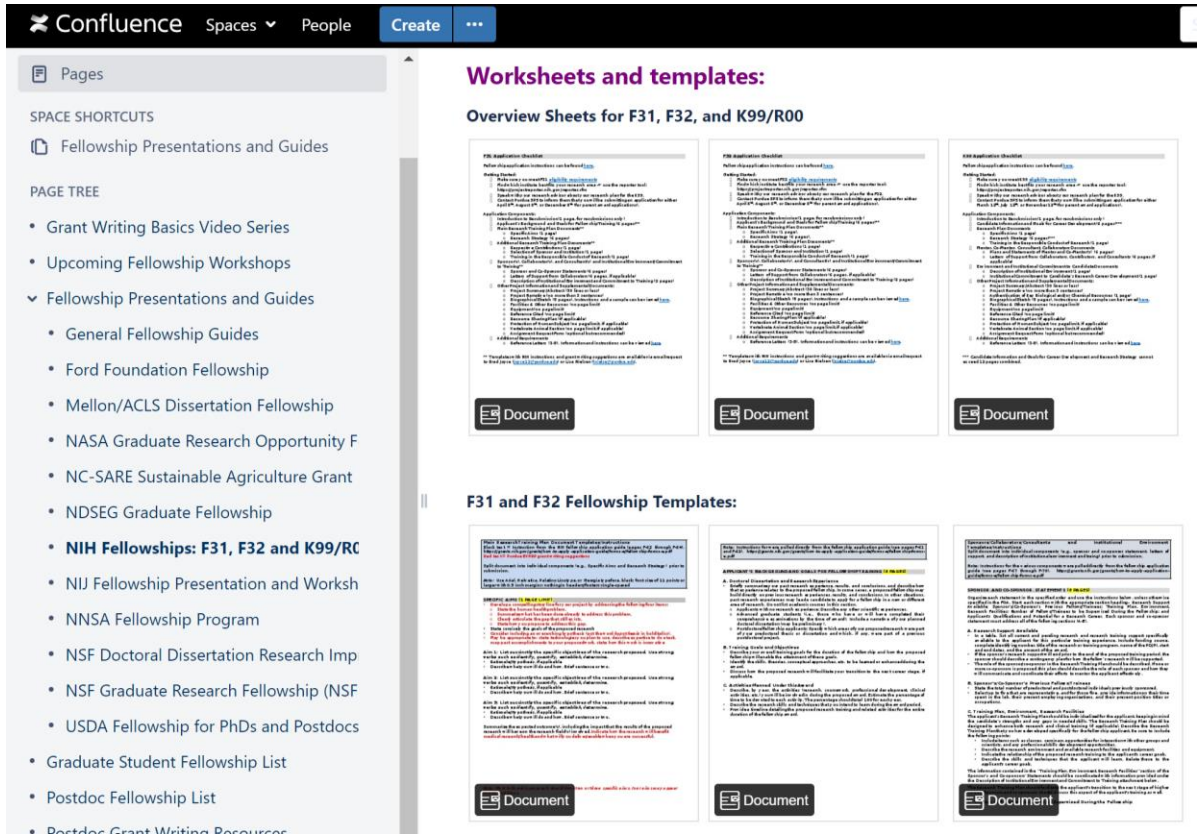

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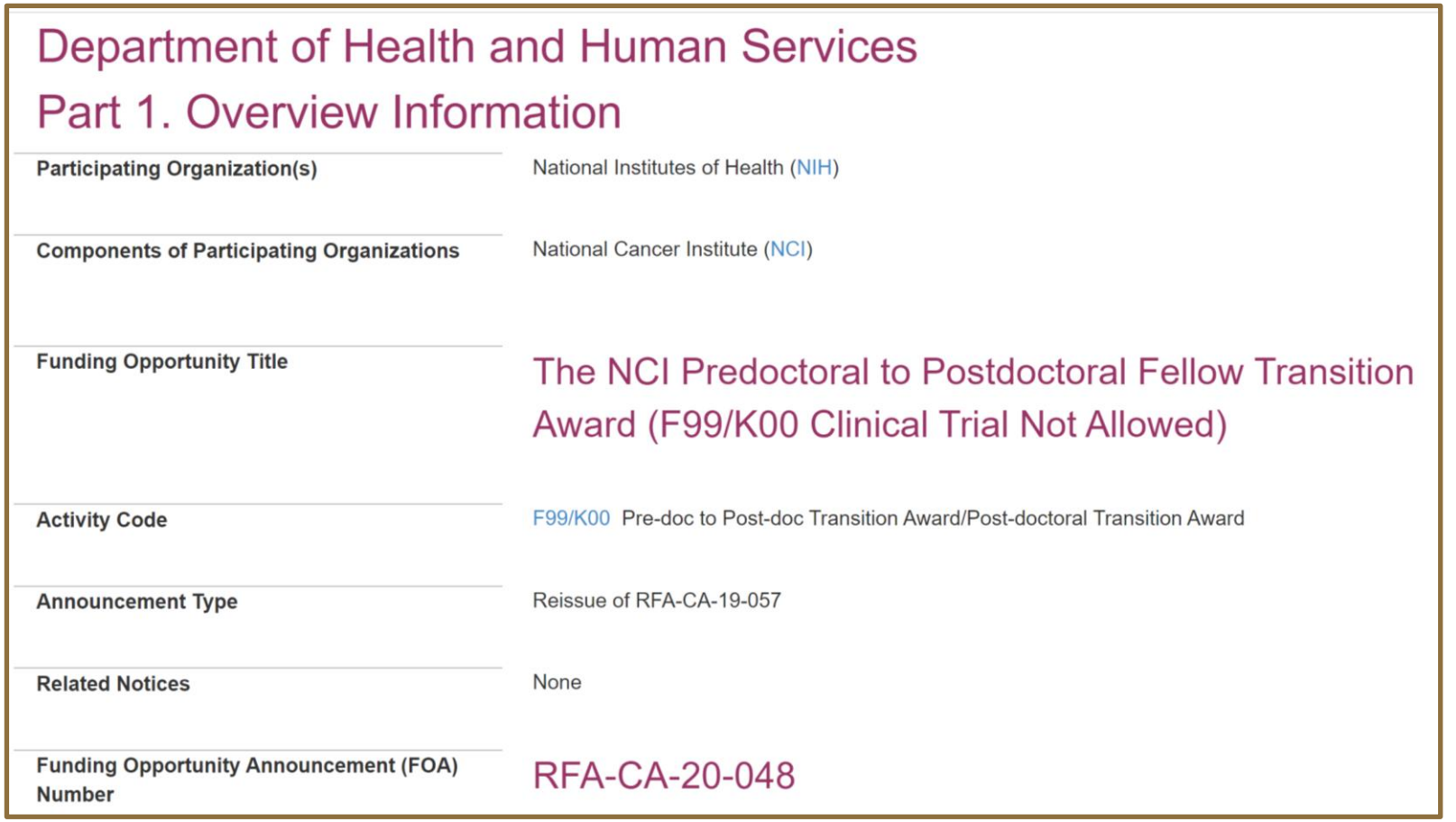
First Steps: Check out the Solicitation

https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-20-048.html



Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)	National Institutes of Health (NIH)
Components of Participating Organizations	National Cancer Institute (NCI)
Funding Opportunity Title	The NCI Predoctoral to Postdoctoral Fellow Transition Award (F99/K00 Clinical Trial Not Allowed)
Activity Code	F99/K00 Pre-doc to Post-doc Transition Award/Post-doctoral Transition Award
Announcement Type	Reissue of RFA-CA-19-057
Related Notices	None
Funding Opportunity Announcement (FOA) Number	RFA-CA-20-048

- → This page contains grant writing jargon and tons of information that is not pertinent to you directly.
- → Look over these pages, but do not try to read it all!

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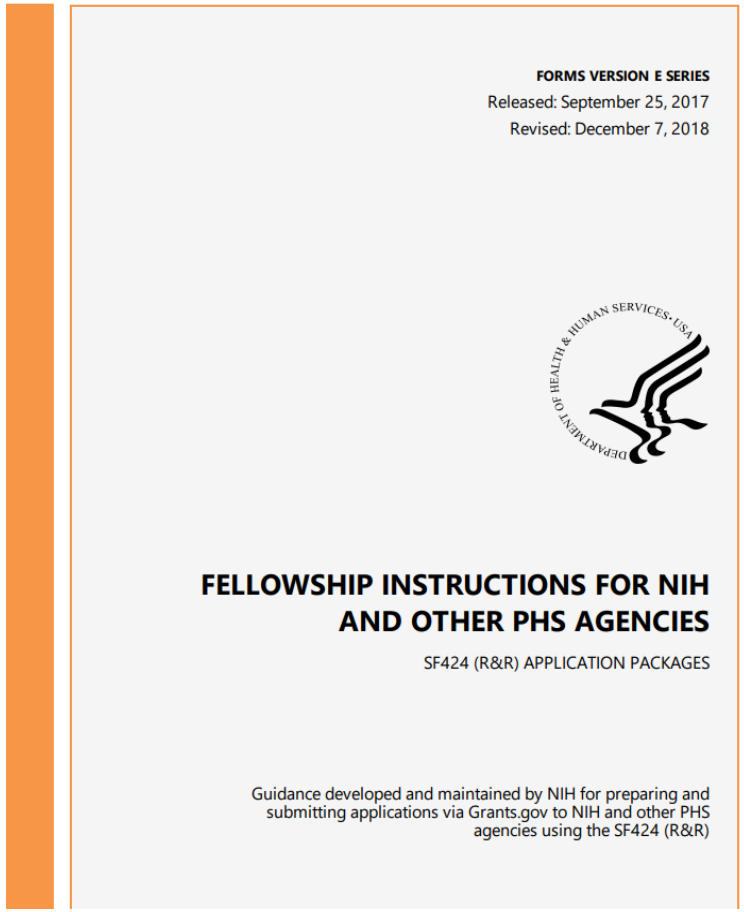
First Steps: Check out the Fellowships Guide

Download application guide and read the advice for the written components

https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/fellowship-forms-e.pdf



FORMS VERSION E SERIES
Released: September 25, 2017
Revised: December 7, 2018

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

FELLOWSHIP INSTRUCTIONS FOR NIH AND OTHER PHS AGENCIES

SF424 (R&R) APPLICATION PACKAGES

Guidance developed and maintained by NIH for preparing and submitting applications via Grants.gov to NIH and other PHS agencies using the SF424 (R&R)

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Form your F99/K00 Mentoring Team

Sponsor, Co-Sponsor, Collaborators, and Consultants

Either one should have prior NIH funding.

- **Sponsor:** your research advisor or supervisor
- **Co-Sponsor (optional):** an additional advisor or supervisor, may or may not be a second advisor but serves as a second advisor for your F31 research
- **Collaborators (2- 6):** Faculty or staff at Purdue or another institute who provide you with training, advice, and/or will help complete parts of the project.
- **Consultants (optional):** “An individual who provides professional advice or services for a fee, but normally not as an employee of the engaging party”

→ Each person needs to know what role they serve for your project and be listed as that role in the application.

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Checklist: Getting Started

- ❑ View the F31 examples and templates on the Grant Writing Resources Page: https://wiki.itap.purdue.edu/pages/viewpage.action?pageId=120723375 (login with your Purdue username and non-BoilerKey password)
- ❑ Look over the F99/K00 information on the NCI website (https://www.cancer.gov/grants-training/training/funding)
- ❑ Look over the Fellowships Guide from NIH (https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/fellowship-forms-e.pdf)
- ❑ Decide how many years of funding you need to request for both the F99 and the K00 sections of the funding.
- ❑ Figure out who will serve on your mentor committee for the research project.

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Overview of Nomination Request Components

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F99/K00 Nomination Request Components

Nomination Request Components - Submit as a single PDF in this order:

1. Your NIH-formatted Biosketch

2. Specific Aims Page (follow the F99-specific instructions)

3. Outline for the Research Strategy Document (follow the F99-specific instructions)

4. List of the Sponsor (or co-sponsors), Collaborators, & Consultants with their names, department and university affiliations and 2-3 sentences about their role in your project.

5. A list of the 4 - 5 individuals whom you plan to ask for letters of recommendation if you are selected as Purdue's nominee: Please include their full names, positions, institutional or organizational affiliations, as well as one sentence that states when/how you worked/interacted with them.

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F99/K00 Full Application Components

- **Nomination Letter from the Institution**
- **Applicant's Background and Goals for Fellowship Training (6 pages)****
- **Main Research Training Plan Documents**
  - **Specific Aims (1 page)**
  - **Research Strategy (6 pages)**
- **Additional Research Training Plan Documents**
  - Respective Contributions (1 page)
  - Selection of Sponsor and Institution (1 page)
  - Training in the Responsible Conduct of Research (1 page)
- **Sponsor(s), Collaborator(s), and Consultant(s) and Institutional Environment/Commitment to Training****
  - Sponsor and Co-Sponsor Statements (6 pages)
  - **Letters of Support from Collaborators** (6 pages, if applicable)
  - Description of Institutional Environment an Commitment to Training (2 pages)
- **Other Project Information and Supplemental Documents:**
  - Project Summary/Abstract (30 lines or less)
  - Project Narrative (no more than 3 sentences)
  - **Biographical Sketch (5 pages)**
  - Facilities & Other Resources (no page limit)
  - Equipment (no page limit)
  - Reference Cited (no page limit)
  - Resource Sharing Plan (if applicable)
  - Protection of Human Subject (no page limit, if applicable)
  - Vertebrate Animal Section (no page limit, if applicable)
  - Assignment Request Form (optional but recommended)
- **Additional Requirements**
  - **Reference Letters (3-5)**

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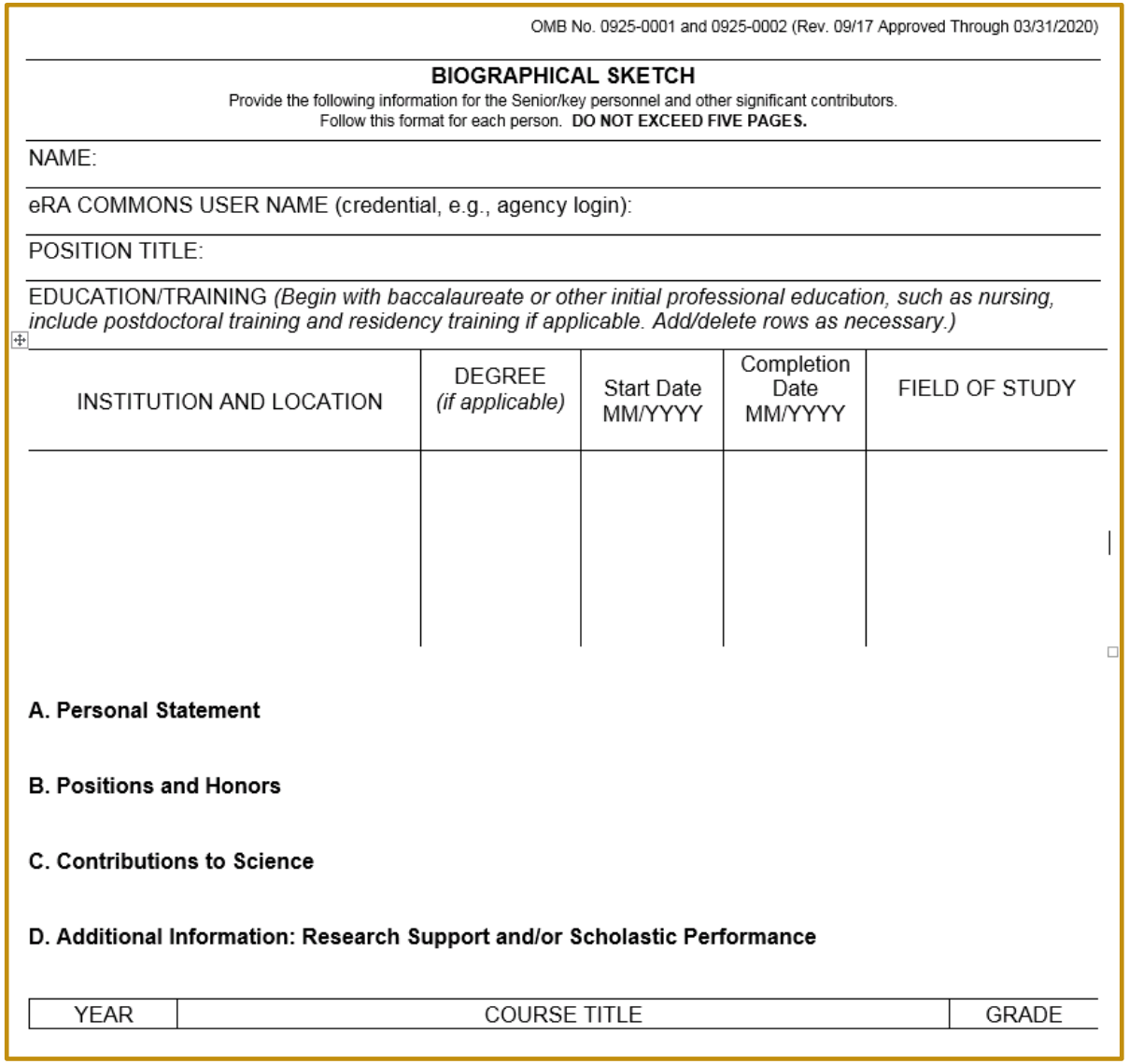
Biographical Sketch ("Biosketch")

Use up to four pages:

- If gaps in work, explain in personal statement, e.g. illness
- Include teaching and mentoring
- State what you hope to gain from fellowship and your motivation for your career
- Emphasize how your postdoc research will be different from your PhD research and how the postdoc research experience will help prepare you for a faculty role.

Access the Biosketch Templates and Samples: https://grants.nih.gov/grants/forms/biosketch.htm



OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

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)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY

A. Personal Statement

B. Positions and Honors

C. Contributions to Science

D. Additional Information: Research Support and/or Scholastic Performance

YEAR	COURSE TITLE	GRADE

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Specific Aims Page

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F99/K00 Specific Aims Page

The Most Critical Part of your Application

- Problem-based, can have a hypothesis or objective
- Aims not dependent on each other
- Rationale for that aim and how it helps meet the overall project goal

Required to have Two Aims:

- **Specific Aim 1:** The Dissertation Research Project: Provide a detailed description of the research to be completed in the F99 phase.

- **Specific Aim 2:** The Postdoctoral Research Direction: Identify the research direction to be pursued for the K00 phase.

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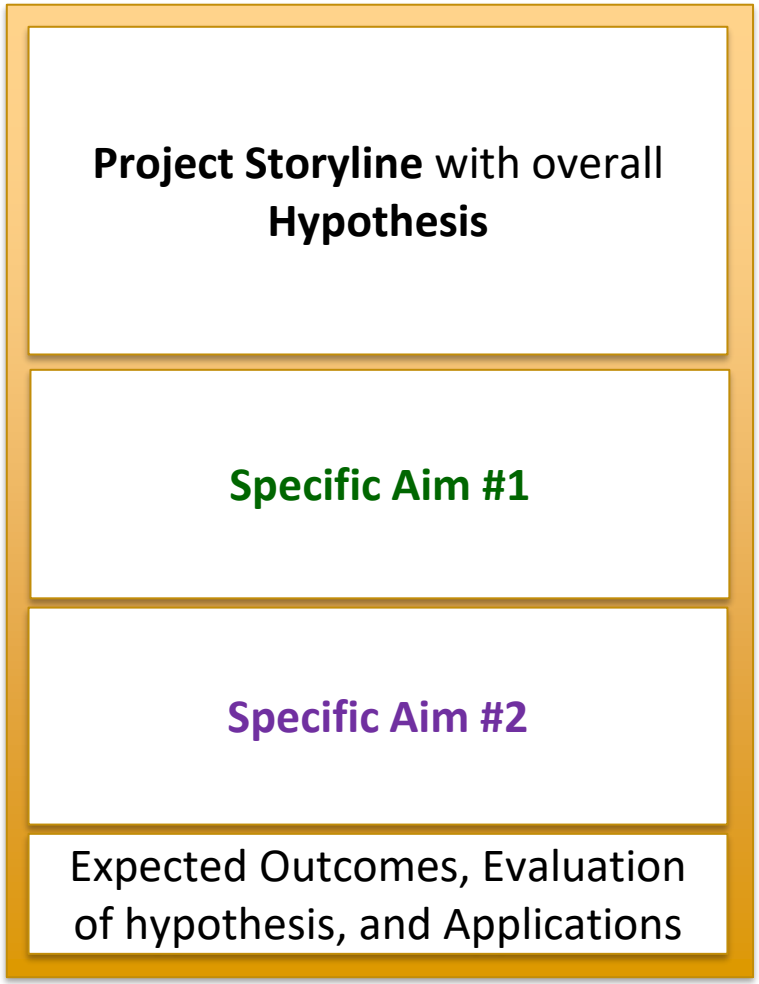
Formatting your F99/K00 Specific Aims (1 page)

Example Layout



Must Include:

- ❑ The human health problem
- ❑ What has been done already to address this problem
- ❑ Explanation of the gap that still exists
- ❑ Method for how you propose to address this gap

→ Put "Hypothesis" as its own header!

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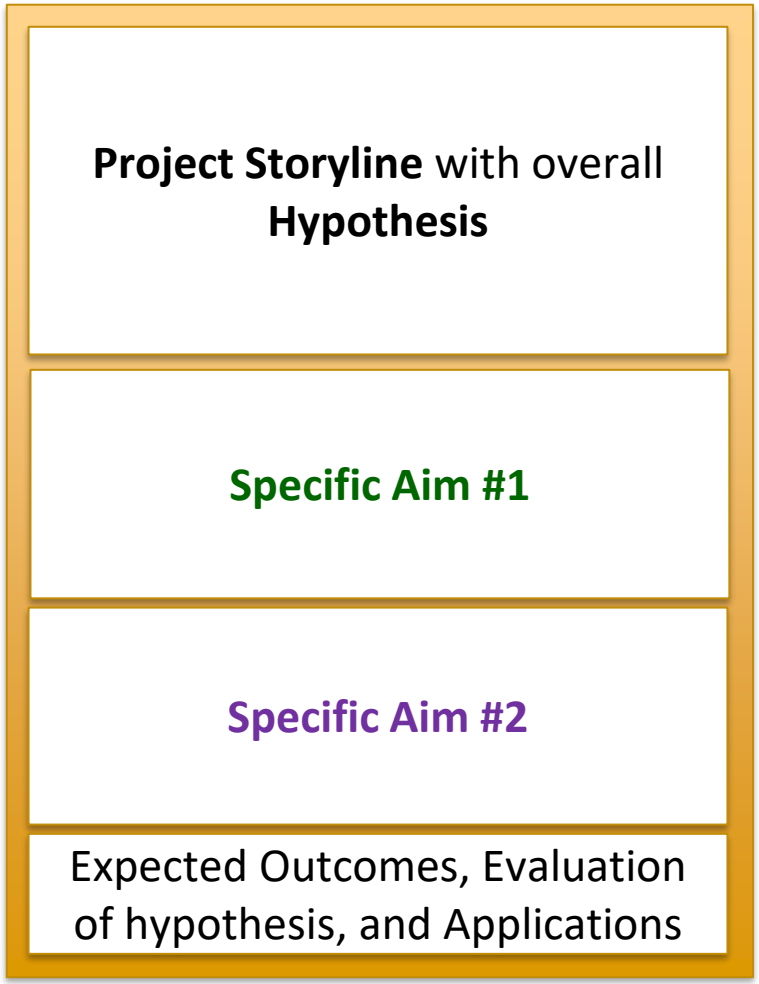
Formatting your F99/K00 Specific Aims (1 page)

Example Layout



For Specific Aim 1:

- ❑ Give the specific hypothesis or rationale for what you have left to do to finish your PhD project.
- ❑ Describe what you will do and how. Focus on what you have yet to do, not what you have already done.
- ❑ Keep Aim 1 feasible within the amount of time you have till graduation.
- ❑ Use strong verbs such as identify, quantify, establish, determine.

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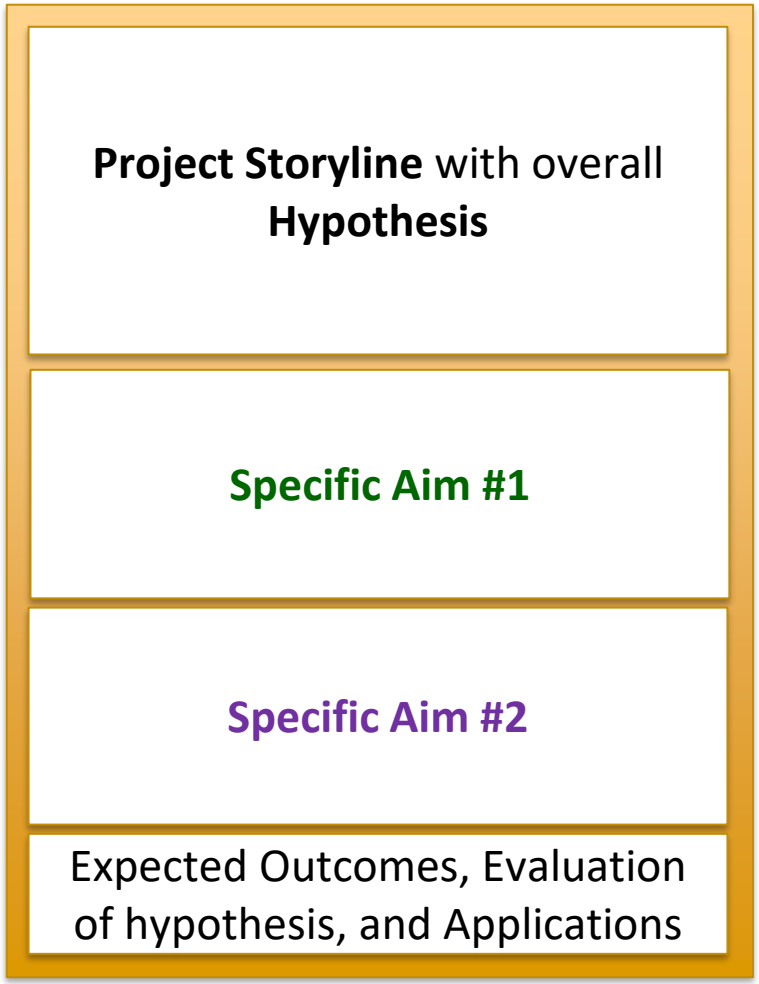
Formatting your F99/K00 Specific Aims (1 page)

Example Layout



For Specific Aim 2:

- ❑ Discuss the main focus of your future postdoc research.
- ❑ You do not yet know which university or mentor you will work under, but identify the research objective and skills you plan to gain.
- ❑ Make sure to distinguish how your postdoc work will be different from your PhD project.
- ❑ Use strong verbs such as identify, quantify, establish, determine.

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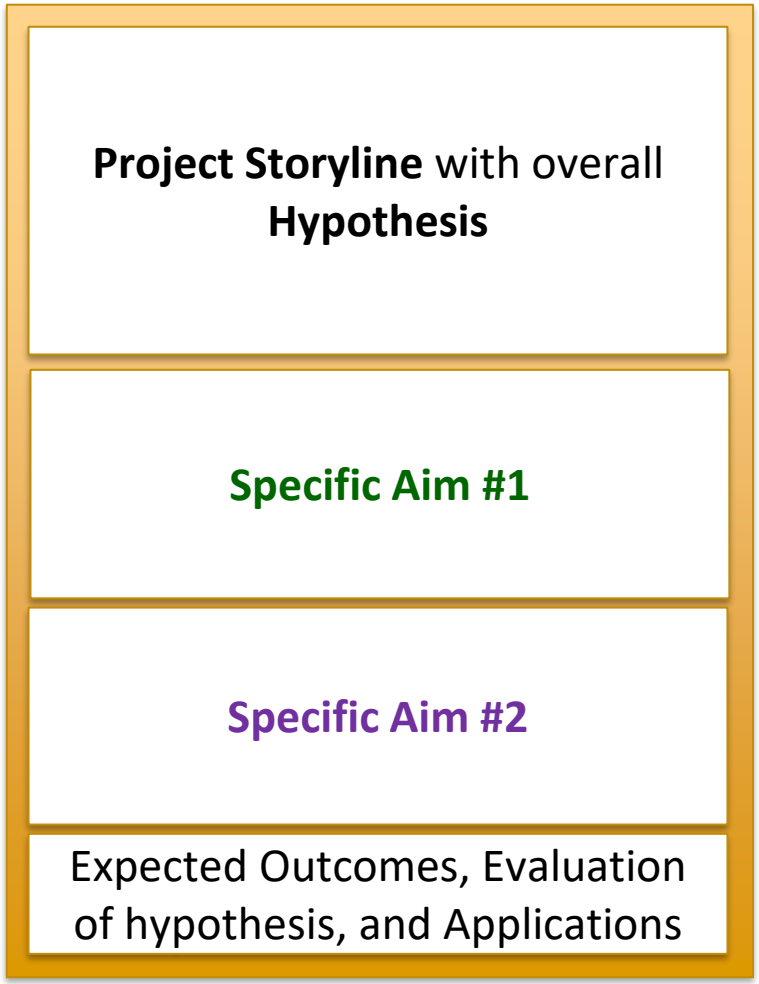
Formatting your F99/K00 Specific Aims (1 page)

Example Layout



For Concluding Paragraph:

- ❑ Expected outcomes
- ❑ How the research will benefit medical research and/or human health
- ❑ What you will deliver/enable when you are successful

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Research Strategy Document

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Begin with Significance :
Pages 1 & 2 of the Research Strategy

Introduction/Storyboarding in specific aims serves as a preview for the Research Strategy.

Specific Aims

Microscopy has emerged as one of the most powerful and informative ways to analyze cell-based hi… throughput screening (HTS) samples in experiments designed to uncover novel drugs and drug ta… However, many diseases and biological pathways can be better studied in whole animals–partic… diseases that involve organ systems and multicellular interactions, such as metabolism and infection. Th… m Caenorhabditis elegans is a well-established and effective model organism that can be robotic… repared and imaged, but existing image-analysis methods are insufficient for most assays. We propos… evelop algorithms for the analysis of high-throughput C. elegans images, validating them in three spe… experiments to identify chemicals to cure human infections and genetic regulators of host response to pathogens and fat metabolism. Novel computational tools for automated image analysis of C. elegans assays will make whole animal screening possible for a variety of biological questions not approachable by cell-based assays. Building on our expertise in developing image processing and machine learning algorithms for high-throughput screening, and on our established collaborations with leaders in C. elegans research, we will:

Research Strategy

A Significance

The NIH is committed to translating basic biomedical research into clinical practice and thereby impacting global human health[1], and Francis Collins identifies high-throughput technology as … of five areas of focus for the NIH's research agenda[2]. For many diseases, researchers have …ified successful novel therapeutics or research probes by applying technical advances in … nation to high-throughput screening (HTS) using either biochemical or cell-based assays[3–6]. R… archers are using genetic perturbations such as RNA interference or gene overexpression … based HTS assays to identify genetic regulators of disease processes as potential drug targets[7–9]. However, the molecular mechanisms of many diseases that deeply impact human health worldwide are not well-understood and thus cannot yet be reduced to biochemical or cell-based assays.

Ideally, researchers could approach disease from a phenotypic direction, in addition to the traditional molecular approach, by searching for chemical or genetic regulators of disease processes in whole model organisms rather than isolated cells or proteins. Moving HTS towards more intact, physiological systems also improves the likelihood that the findings from such experiments accurately translate into the context of the human body (e.g., in terms of toxicity and bioavailability), simplifying the path to clinical trials and reducing the failure of potential therapeutics at later stages of testing. In fact, for some diseases, a whole organism screen may actually be necessary to break new therapeutic ground; in the search for novel therapeutics for infectious agents, for example, it is widely speculated that the traditional approach of screening for chemicals that directly kill bacteria in vitro has been largely exhausted[10]. Our work recently identified six novel classes of chemicals that cure model organisms from infection by the important human pathogen E. faecalis through mechanisms distinct from directly killing the bacterium itself[11]. Anti-infectives with new mechanisms of action are urgently needed to combat widespread antibiotic resistance in pathogens.

Enabling HTS in whole organisms is therefore recognized as a high priority (NIH PAR-08-024)[12,13]. C. elegans is a natural choice. Manually-analyzed RNAi and chemical screens are well-proven in this organism, with dozens completed[14–16]. Many existing assays can be adapted to HTS; instrumentation exists to handle and culture C. elegans in HTS-compatible multi-well. Its organ systems have high physiologic similarity and genetic conservation with humans[17,18]. C. elegans is particularly suited to assays involving visual phenotypes: physiologic abnormalities and fluorescent markers are easily observed because the worm is mostly transparent. The worms follow a stereotypic development pattern that yields identically-appearing adults[19,20], such that deviations from wild-type are more readily apparent.

The bottleneck that remains for tackling important human health problems using C. elegans HTS is image analysis (NIH PA-07-320)[21,22]. It has been recently stated, "Currently, one of the biggest technical limitations for large-scale RNAi-based screens in C. elegans is the lack of efficient high-throughput methods to quantitate lethality, growth rates, and other morphological phenotypes"[23]. **Our proposal to develop image analysis algorithms to identify regulators of infection and metabolism in high-throughput C. elegans assays would bring image-based HTS to whole organisms, and have the following impact:**

The Research Strategy document should be divided into Aim 1 and Aim 2. **Each aim will have its own significance section and its own approach section.**

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Begin with Significance :
Pages 1 & 2 of the Research Strategy

Introduction/Storyboarding in specific aims serves as a preview for the Significance section in your research strategy.

RESEARCH STRATEGY (6 PAGES TOTAL)

SIGNIFICANCE (~1 PAGE)

- Expand storyline from the specific aims page:
  - What is the problem?
  - What has been done to address the problem?
  - What is the gap that remains?
  - How do you propose to address the gap?
- Explain how the proposed project will improve scientific knowledge, technical capability, and/or clinical practice in one or more broad fields.
- Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be changed if the proposed aims are achieved.

Specific Aim 1: Significance

Provide an overview of the dissertation research, including the scientific question being addressed and its potential impact on the dissertation research field.

Specific Aim 2: Significance

Explain the significance of the K00 research direction. Describe a specific scientific question or observation that will be investigated. Explain how this question or observation is related to the applicant's research interests and how this work will help advance this research direction.

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Begin with Significance :
Pages 1 & 2 of the Research Strategy

Preliminary Data may be included in the Significance section.

Preliminary Studies

- For new applications, include information on preliminary studies (including data collected by others in the lab), if any.
- Discuss the applicant's preliminary studies, data, and/or experience pertinent to this application.

These figures are schematics the applicant made to show the biological mechanism that they have already investigated.

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RESEARCH STRATEGY

A. SIGNIFICANCE

2'-5'-oligoadenylate synthetase 1 (OAS1) is an important component of the innate immune system that provides a critical first line of defense against viral infection. OAS1 is a sensor of cytosolic double-stranded RNA (dsRNA) (1-3), a potent pathogen-associated molecular pattern (PAMP), present in some viral genomes or produced as a consequence of viral gene expression or replication (4). Viral dsRNA-promoted OAS1 activation leads to subsequent activation of the latent endoribonuclease L (RNase L) via dsRNA-dependent production of 2'-5'-oligoadenylate secondary messengers. RNase L activation effectively halts viral replication through the degradation of target viral and cellular RNAs (**Fig. 1A**) (5-8). The goal of this project is to reveal novel insight into the importance of RNA sequence, structure, and context to dsRNA regulation of OAS1 activity. These details will aid in our understanding of host-pathogen interactions and, for example, how viruses might circumvent the OAS1/RNase L pathway.

Viruses have evolved ways of circumventing the innate immune system. As obligate parasites, viruses depend on the host cell to complete their life cycle. In particular, all viruses require the cellular translation machinery for expression of their proteins. Viruses must also avoid detection by innate antiviral factors that can potently restrict viral replication, often by interfering with cellular translation. Attesting to the specific importance of the OAS1/RNase L pathway in this process, many viruses have developed ways to evade detection by directly inhibiting OAS1, sequestering dsRNA produced as a result of viral infection, or producing 2'-5'-analogs (1,9-17). Therefore, *determining the molecular mechanisms of dsRNA-mediated OAS1 regulation is a vital component of understanding how the OAS1/RNase L pathway contributes to the control of viral infection.*

OAS1 shuts down host translation through the OAS/RNase L pathway. OAS1 is an important innate immune sensor that detects cytosolic dsRNA produced as a consequence of viral replication (1-3). Previous structural studies revealed that dsRNA binding allosterically induces the conformational changes necessary in OAS1 to form its active site and thus drive polymerization of ATP into 2'-5'-linked oligoadenylates (18). These 2'-5'-oligoadenylate secondary messengers promote the dimerization and subsequent activation of RNase L (**Fig. 1A**) (7,8). Activated RNase L degrades both viral and cellular RNA to halt viral replication and limit the spread of infection (19-22). RNase L targets specific messenger (m)RNA transcripts encoding proteins known to regulate cell adhesion and proliferation (23) as well as ribosomal (r)RNA to prevent translation and viral spread to neighboring cells (24).

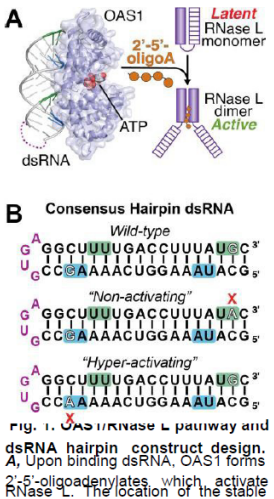

Fig. 1. OAS1/RNase L pathway and dsRNA hairpin construct design. *A*, Upon binding dsRNA, OAS1 forms 2'-5'-oligoadenylates, which activate RNase L. The location of the stable

OAS1 is activated upon binding viral dsRNA. OAS1 lacks an RNA-binding motif and instead interacts with dsRNA through patches of positive residues on the protein's surface (18). RNA binding to OAS1 requires double stranded regions with a minimum length of 18 base pairs (bp) (25). However, while OAS1 can be activated by dsRNA that meets this 18 bp requirement, activation is strongly potentiated by activating consensus sequences and the 3'-end single-stranded pyrimidine (3'-ssPy) motif that our lab recently identified (26-28). *However, how these molecular signatures in dsRNA affect the level of OAS1 activity, and thus the potency of its antiviral effect, is not well understood.*

The dsRNA used in previous structural studies (18) contained two overlapping and antiparallel copies of a known OAS1 activation consensus sequence WWN_9WG, where W is A or U, and N is any nucleotide (26). Although one consensus sequence was present on each strand of the helix, the dsRNA bound OAS1 in a single, unique orientation (18). Our preliminary data indicate

Approach: Pages 2 – 6 of the Research Strategy

Example Layout

Specific Aim 1: Approach

Provide an overview of the dissertation research, including the background, goal, rationale and hypotheses of the research project(s). The Approach for this Aim should be organized into **two sections**:

- **A progress report** on the dissertation research project thus far, including the approaches used, research outcomes obtained, and important methodologies learned;

- **A detailed research proposal** for the work to be completed in the F99 phase, including experimental design, anticipated results, potential problems, alternative strategies, and potential follow-up studies.

Specific Aim 2: Approach

Provide a general description of how the research will be conducted, including approaches and methodologies to be used, anticipated results, challenges that might arise and how to address them.

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Approach: Pages 2 – 6 of the Research Strategy

Each specific aim should include this information:

If space allows, you can insert a “Future Work” section or “Contingency Plan” section after the aims.

“If the applicant is proposing to gain experience in a clinical trial as a part of their research training, describe the relationship of the proposed research project to the clinical trial.”

Title of Specific Aim #1 (verbatim from your specific aims page)

Justification and Feasibility

- Provide overview sentence and review of relevant literature (as necessary/appropriate)
- If the project is in the early stages of development, describe any strategy to establish feasibility, and address the management of any high risk aspects of the proposed work.

Research Design

- Describe the overall strategy and methodology.
- Consider breaking aim up into multiple tasks or subaims
- For trials that randomize groups or deliver interventions to groups, describe how your methods for analysis and sample size are appropriate for your plans for participant assignment and intervention delivery. These methods can include a group- or clusterrandomized trial or an individually randomized group-treatment trial.
- Summarize your rigorous experimental design for robust and unbiased results (e.g., blinding samples, statistical analysis, etc.)
- Summarize considerations of relevant biological variables (e.g., age, sex, etc.)

Data Analysis and Interpretation

- Describe how the data will be analyzed and interpreted.

Potential Problems and Alternative Strategies

- Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims.

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Approach: Pages 2 – 6 of the Research Strategy

Preliminary Data should be included.

Preliminary Studies

- For new applications, include information on preliminary studies (including data collected by others in the lab), if any.
- Discuss the applicant's preliminary studies, data, and/or experience pertinent to this application.

intersection of bone biology and immunology.

C. APPROACH

C1. Preliminary Studies

C1A. *S. aureus* supernatants modulate OC differentiation.

Our preliminary data demonstrate that *S. aureus* supernatants modulate differentiation of OCs with and without the canonical OC differentiation factor RANKL, in cultures of whole bone marrow (WBM), containing myeloid, lymphoid, and stromal cells, and in bone marrow macrophages (BMMs). BM cultures were stimulated with *psm*-deficient *S. aureus* supernatants to prevent cytotoxicity resulting from the α-PSMs in *S. aureus* wild-type supernatants. We observed that *S. aureus* supernatants drive BMM differentiation to OC-like cells without the addition of exogenous RANKL **(Figure 3A).** These cells are TRAP-positive, but differ in size and cell fusion from RANKL-treated BMMs. Alternatively, *S. aureus* supernatants inhibit osteoclastogenesis from BMMs following RANKL treatment by limiting the size (data not shown). These data support the notion that in pre-OC cultures, *S. aureus* induces RANKL-independent osteoclastogenesis and inhibits RANKL-induced osteoclastogenesis.

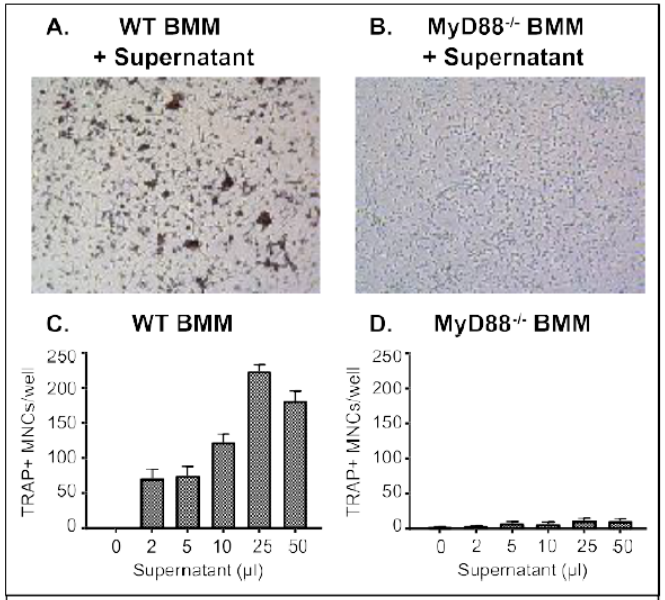

Figure 3. *S. aureus* supernatants are able to induce OCs from WT, but not MyD88-deficient BMMs. BMMs were stimulated for 7 days with M-CSF and concentrated *S. aureus* supernatants (50µl). WT (A) and MyD88 (B) are shown following fixation, TRAP stain, and 20X imaging. TRAP-positive multinucleated cells were quantified manually in triplicate from WT (A) and MyD88-deficient (B) BMM cultures with varying amounts of supernatants.

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Approach: Pages 2 – 6 of the Research Strategy

Example Layout

Reviewers Look for:

- ❑ Is the proposed research project of high scientific quality, and is it well **integrated with the proposed research training plan?**
- ❑ Based on the sponsor's description of his/her active research program, is the applicant's proposed research project sufficiently distinct from the sponsor's funded research for the applicant's career stage?
- ❑ **Is the research project consistent with the applicant's stage of research development?**
- ❑ **Is the proposed time frame feasible to accomplish the proposed training?**
- ❑ If proposed, will the clinical trial experience contribute to the proposed project and/or the applicant's research training?

Sponsors and Collaborators

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For the nomination request:

Names, Department and University Affiliations and 2-3 sentences about their role in your project

Either one should have prior NIH funding.

- **Sponsor:** your research advisor or supervisor
- **Co-Sponsor (optional):** an additional advisor or supervisor, may or may not be a second advisor but serves as a second advisor for your F31 research
- **Collaborators (2- 6):** Faculty or staff at Purdue or another institute who provide you with training, advice, and/or will help complete parts of the project.
- **Consultants (optional):** “An individual who provides professional advice or services for a fee, but normally not as an employee of the engaging party”

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Selection of Sponsor and Institution (1 page)

Sponsor and Co-Sponsor Expertise, Funding, and Competencies

One page document where you describe:

- Why your advisor is the best advisor for your project and for you
- Your advisor's technical expertise, availability to train and mentor you
- The laboratory space and research resources available from your advisor, your department, and Purdue overall
- Why your institution is the best place for you to conduct this research

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Sponsor and Co-Sponsor Statements: Written by your advisor

Research Support Available and Previous Fellows/Trainees

- Need to demonstrate that your sponsor(s) have adequate resources to support your research training during the proposed funding period.
  - Current or prior NIH funding helps but is not required.
  - Consider having a Co-Sponsor if your Sponsor's research support is limiting.
  - Describe a contingency plan if the Sponsor's funding will end before the conclusion of the training period.

- Describe the role of the Sponsor/Co-Sponsor(s) in your research training and career development goals.
- Sponsor should provide 5 examples of successful trainees they have mentored.

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Letters of Support – NOT letters of recommendation

Do the following:

- ❑ Work with your research advisor to identify who would be good **collaborators** for your project
- ❑ Provide letter writers with a polished copy of your specific aims page
- ❑ Compose a **draft letter** for them that clearly states what form of guidance/help they will provide and what their role will be in the project.

Letters should include:

- ❑ How the individual will help with the project – **specific expertise given**, guidance for experimental design and analyses
- ❑ The **resources the individual has access to** that you may not have access to
- ❑ The individual's **record of mentorship and funding history**

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Applicant’s Background and Goals

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A. Doctoral Dissertation and Research Experience First 2 pages of the 6 page document

What Research Experiences Prepared you for taking on your proposed project?

- Undergrad
- Grad
- Industrial (optional)

- ❑ Main goal of the project
- ❑ Your role in the project
- ❑ Skills you gained from the project
- ❑ Outcomes of the project
- ❑ Motivation that lead you to your current work

The two pages of the "Doctoral Dissertation and Research Experience" are something you can work on at the start of the application writing.

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B. Training Goals and Objectives
Pages 3 & 4 of the 6-page document

Be specific:

- Define a common **technical research theme** between your career goals and your previous research experience
- Explain what you have already received training on and what you will do to gain the skills needed for your F99/K00 research.

Training Goals should include:

→Technical training for equipment and sample handling
→Technical training for statistics and data analyses
→Professional Development Training
→Writing and presentation practice
→ Classes or seminars you will take to gain the knowledge you need
→ Who on your mentoring team will guide or teach you those skills

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C. Activities Planned Under this Award
Pages 5 & 6 of the 6-page document

Give details on how you will Undertake your Proposed Research Project

C. Activities Planned Under this Award

- Describe, by year, the activities (research, coursework, professional development, clinical activities, etc.) you will be involved in during the proposed award. Estimate the percentage of time to be devoted to each activity. The percentage should total 100 for each year.
- Describe the research skills and techniques that you intend to learn during the award period.
- Provide a timeline detailing the proposed research training and related activities for the entire duration of the fellowship award.

- Timeline of how you will implement each aim of your specific aims
- Specific tasks, both technical and non-technical, that correspond to each semester
- Demonstrate that the project can be undertaken in the time you have till graduation for Aim 1 and that Aim 2 fits within the number of years requested for your postdoc position.

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C. Activities Planned Under this Award
Pages 5 & 6 of the 6-page document

Give details on how you will Undertake your Proposed Research Project

- Timeline of how you will implement each aim of your specific aims
- Specific tasks, both technical and non-technical, that correspond to each semester
- Demonstrate that the project can be undertaken in the time you have till graduation

Activities Planned Under this Award

I have applied for two years of NRSA support. I will dedicate 100% of my effort to research, training, and career development activities detailed below.

CALENDAR YEAR	2017	2018	2019
F31 AWARD YEAR	YEAR 1	YEAR 2	
AIM 1A			
AIM 1B			
AIM 1C			
AIM 2A			
AIM 2B			

Year 1: July 2017-June 2018

Research: 80%

- Meetings with Dr. Cassat (weekly)
- Meetings with Thesis Committee (bi-annually)
- Submit first lead-author publication, detailing the impact of staphylococcal coagulases and *S. aureus* strain differences in osteomyelitis
- Submit second first-author publication, detailing findings in Aim 1

Seminars and Presentations: 10%

- Present research and participate at events at Vanderbilt University Medical Center (VUMC):
  - Pathology, Microbiology, and Immunology seminar (weekly)
  - Microbiology and Immunology Research in Progress seminar (weekly)
  - Microbial-Host Interaction seminar (bi-monthly)
  - Host-Pathogen Interaction journal club (bi-monthly)
  - Infection, Inflammation & Immunity Frontiers seminar (monthly)
  - Vanderbilt Symposium of Infection and Immunity (annually)
  - Bone Center Seminar Series (weekly)
- Organize/Attend Southeastern Immunology Symposium 2017
- Attend St. Jude's Invited Graduate Student Symposium 2017

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Questions and Answers

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THANK YOU!

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