School of Medicine
& Health Sciences
THE GEORGE WASHINGTON UNIVERSITY

**BMSC 8219**

# Overview
# The Qualifier and the NIH fellowship
# Intro to Specific Aims

Jan 11, 2021

# Course Design

The GW IBS grant-style qualifier

- specific aims page to committee by June 1 (starts clock)
  - draft specific aims (1 p)
  - draft research strategy (6 p)
- expect to revise
- expect to discuss with mentor

Additional materials for fellowship submission

- Always revise aims
- Always update candidate, sponsor training plan
- other required sections

What does *she* know?

- experience & assistance

# Course Design

Design of the course

- Writing outside class
  - use links and examples
  - persuasive writing, active tone
  - mimic good ideas, but don't copy…
- Discussion/ editing in class
  - rotate peer critiques
  - offer ideas in track changes
  - submit to Blackboard when due
- Think like a reviewer
  - use review criteria/ rubrics/ helpful feedback
- Periodic check-in with mentors
- Expect multiple opinions

# IBS Grant-Style Qualifier

*Students should be able to develop a novel line of research, propose a hypothesis, and develop a series of experiments to test that hypothesis…At the time of the oral defense, the student should also demonstrate knowledge of the larger field of the general area of the proposal and material covered in completed coursework…*

## Forms & Handbooks

- Application for IBS Membership
- Lab Rotation Mentor Guide
- IBS Program Handbook 2020-2021 updated 9.24.2020
- Lab Rotation Availability List 2020-2021 updated 12.10.2020
- Lab Rotation Student Guidelines
- Rotation Commitment Form
- Individual Development Plan (MyIDP)
- ORCID Identifiers
- Program Selection Form
- Graduation Guidelines - Fall 2020
- Dissertation Information
- IBS Qualifier Examination Form for the Advancement to PhD Candidacy
- Travel Award Application
- CNHS Special Volunteer Application instructions
- CNHS Special Volunteer Application
- Thesis Committee Meeting Summary Form

# IBS Handbook

*The student will submit the proposal title and specific aims to the advisor and committee members according to the timeline*

*The student's research advisor is expected to approve the topic, specific aims, and the final written proposal, but the advisor will not serve as a voting member of the examining committee.*

| DATE/DEADLINE | OBJECTIVE |
|---|---|
| January-February | Orientation of students to qualifier & discussion of hypothesis and aims with advisor |
| March-April | Selection and Approval of Qualifying Committee members |
| June 1 | Specific aims submitted to Qualifying Committee for rapid feedback/revision |
| June-July | Approved aims used to develop full proposal (5 week writing period) |
| July 20 (latest) | Student submits written proposal to Qualifying Committee |
| August 5 (latest) | Qualifying Committee returns any comments to student |
| September 15* (latest) | Oral defense of proposal |

# Qualifier aim criteria

The following are the criteria for evaluation and approval of the specific aims:

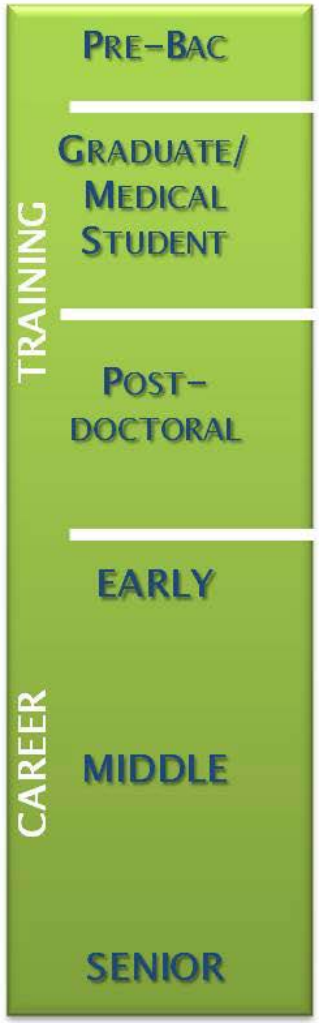
i) Is studying and writing about the topic of the proposal likely to be a sound educational experience for the student? The qualifying exam should enhance knowledge and understanding in fields related to the student's Ph.D. dissertation project.
ii) Do the aims address important questions in the field? In general, aims should be "hypothesis driven" rather than descriptive.
iii) Are the proposed methods reasonable and feasible using current technology? If not, has the student proposed new approaches that have a reasonable probability of succeeding?
iv) Can the proposed experiments be completed within the timeframe of a student's Ph.D. candidacy?
v) Is the style and level of detail of the specific aims appropriate for a doctoral fellowship application (e.g. NIH NRSA F31)?

What is the NIH NRSA F31?

# NIH Fellowships and Career Stage

Mentored

Compare: Institutional or individual




← Institutional Training Grant (T34)

← Institutional Training Grant (T32)

← Individual NRSA Fellowship (F31, F30)

← Institutional Training Grant (T32)

← Individual NRSA Fellowship (F32)

← Pathway to Independence Award (K99/R00)

← Mentored Research Scientist Development Award (K01)

← Mentored Clinical Scientist Development Award (K08)

← Mentored Patient-Oriented RCDA (K23)

← Mentored Quantitative RCDA (K25)

Small Grant (R03)

Research Project Grant (R01)

Exploratory/ Developmental Grant (R21)

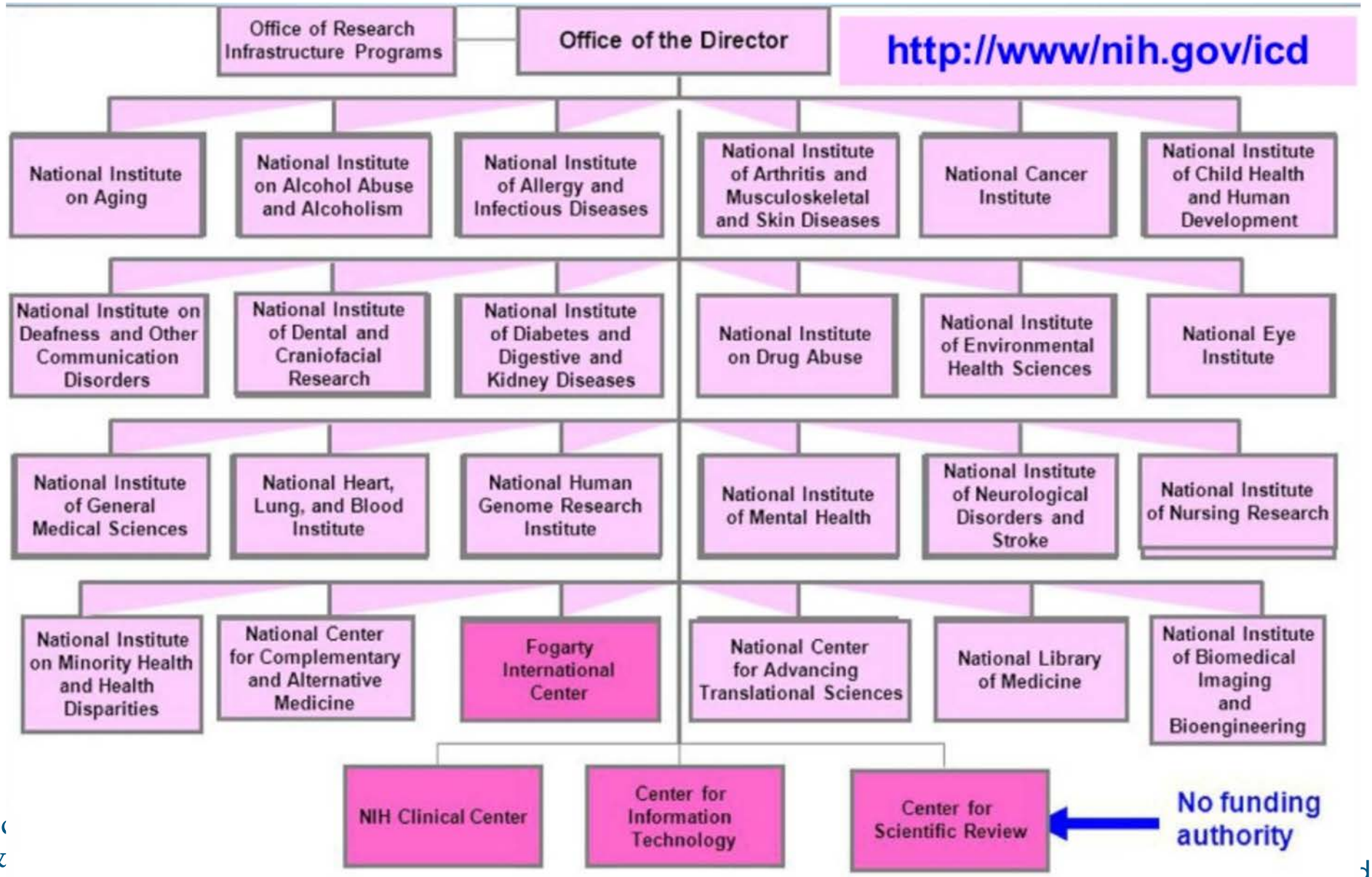
← Independent Scientist Award (K02)

← Midcareer Investigator Award in Patient-Oriented Research (K24)

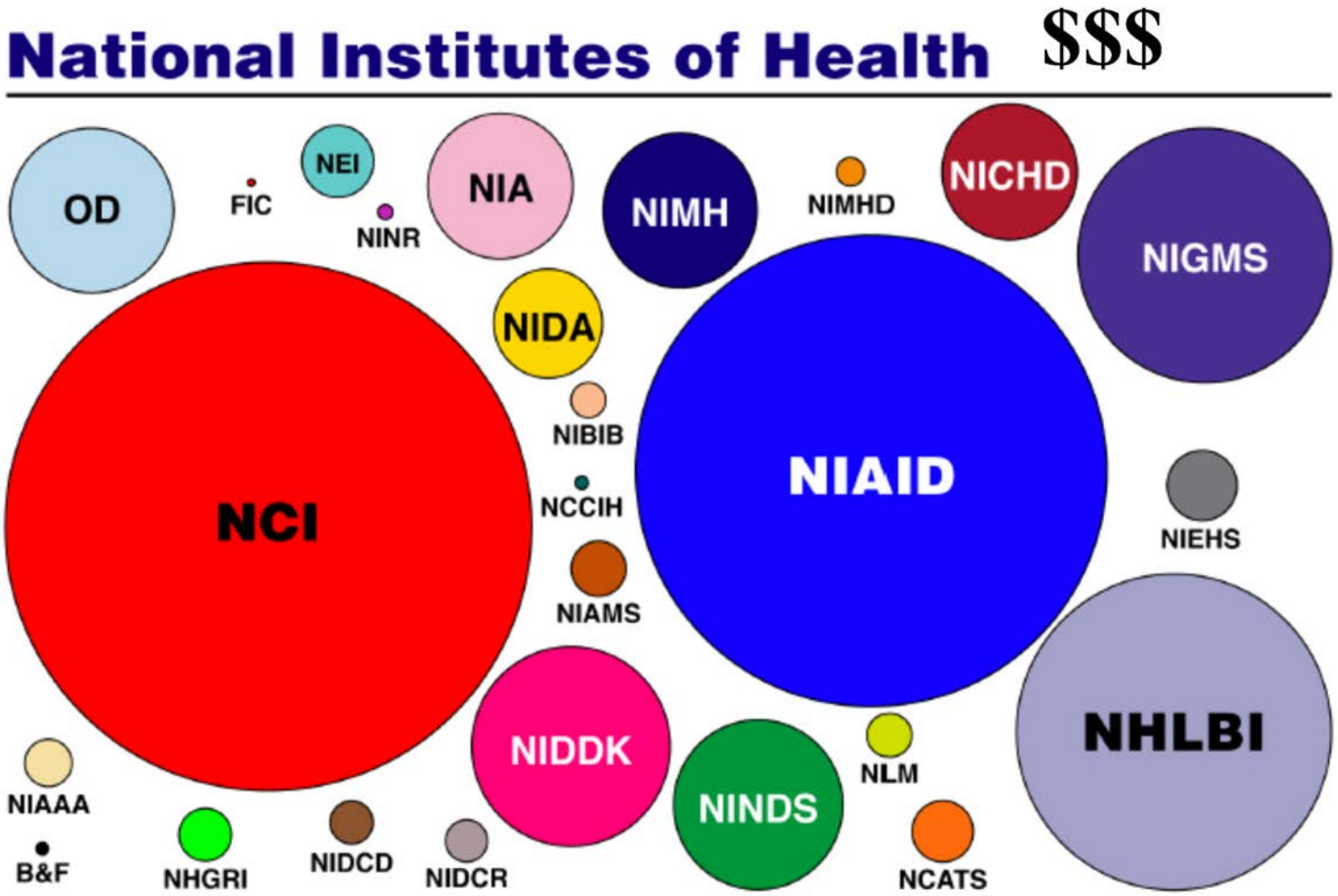
← Senior Scientist Award (K05)

# An aside about the NIH…

# Research of interest to NIH institutes



# NIH institute extramural $ differs




From Hahn, UCSF 2018

# NIH F31 Funding Announcement

Funding Opportunity Announcement (FOA)
Parent Announcement (PA)
Request for Application (RFA)

Read and decode NIH funding announcement
Read IC-specific links
Read *instructions* (Fellowships Forms F here, pp58)

NIH guidelines similar to foundation guidelines
(e.g. American Heart Association)
…see other opportunities at SMHS Research\Funding

# About the NIH F31

The NIH invests in support for research training and education These grants include all NRSAs (T32; F31, F32)

## Ruth L. Kirschstein National Research Service Award (NRSA)

PA-20-251 -diversity

National Center for Complementary and Integrative Health (NCCIH)
National Cancer Institute (NCI)
National Eye Institute (NEI)
National Human Genome Research Institute (NHGRI)
National Heart, Lung, and Blood Institute (NHLBI)
National Institute on Aging (NIA)
National Institute on Alcohol Abuse and Alcoholism (NIAAA)
National Institute of Allergy and Infectious Diseases (NIAID)
National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
National Institute of Biomedical Imaging and Bioengineering (NIBIB)
Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
National Institute on Drug Abuse ( NIDA )
National Institute on Deafness and Other Communication Disorders (NIDCD)
National Institute of Dental and Craniofacial Research (NIDCR)
National Institute of Diabetes and Digestive and Kidney Diseases ( NIDDK )
National Institute of Environmental Health Sciences (NIEHS)
National Institute of General Medical Sciences (NIGMS)
National Institute of Mental Health (NIMH)
National Institute on Minority Health and Health Disparities (NIMHD)
National Institute of Neurological Disorders and Stroke (NINDS)
National Library of Medicine (NLM)
National Institute of Nursing Research (NINR)
Division of Program Coordination, Planning and Strategic Initiatives, Office of Research Infrast

PA-21-051

National Center for Complementary and Integrative Health (NCCIH)
National Cancer Institute (NCI)
National Eye Institute (NEI)
National Human Genome Research Institute (NHGRI)
National Heart, Lung, and Blood Institute (NHLBI)
National Institute on Aging (NIA)
National Institute on Alcohol Abuse and Alcoholism (NIAAA)
National Institute of Allergy and Infectious Diseases (NIAID)
National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
Eunice Kennedy Shriver National Institute of Child Health and Human Development (NI
National Institute on Deafness and Other Communication Disorders (NIDCD)
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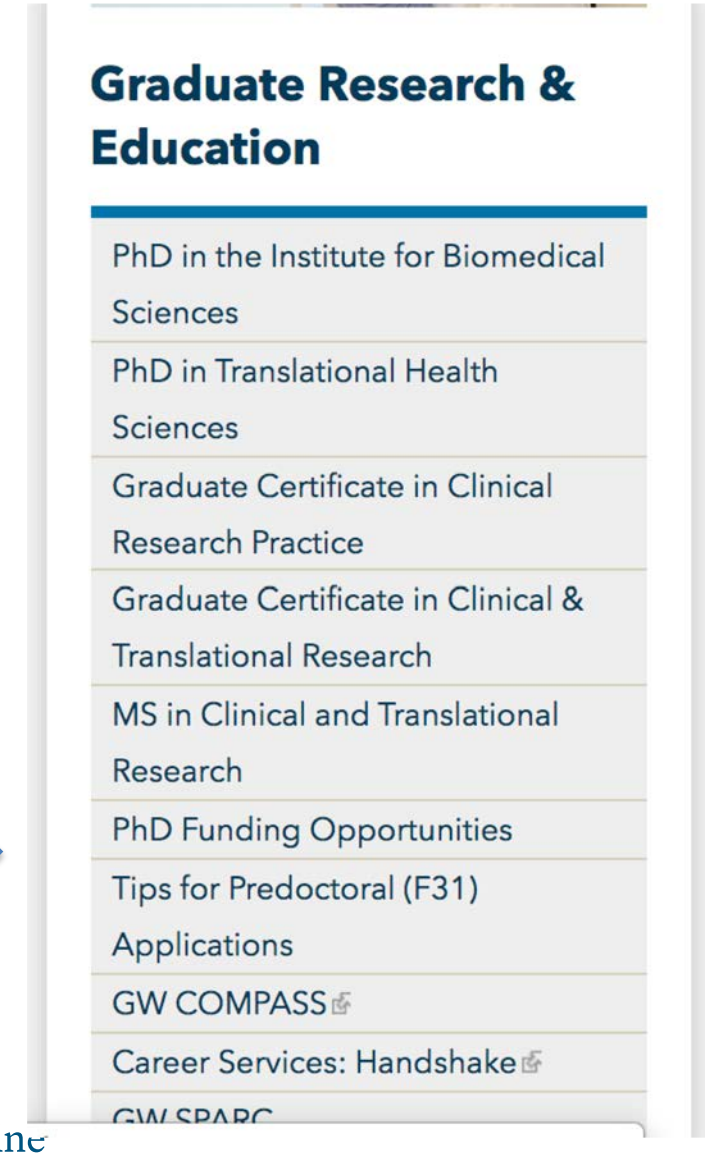
National Institute of Environmental Health Sciences (NIEHS)
National Institute of Mental Health (NIMH)
National Institute on Minority Health and Health Disparities (NIMHD)
National Institute of Nursing Research (NINR)
National Institute of Neurological Disorders and Stroke (NINDS)
National Library of Medicine (NLM)
Office of Research Infrastructure Programs (ORIP)
National Institute on Drug Abuse ( NIDA )

*Different institutes participate*

# Explore Additional Fellowships




SMHS Research

Federal and foundation

- Research mission
- Career level
- Citizenship
- Application deadlines

Plan to apply to several…

# Major sections of the Application

| | |
|---|---|
| Project Summary/Abstract | 30 lines of text |
| Project Narrative | 3 sentences |
| Applicant's Background and Goals | 6 pages |
| Fellowship Biosketch | 4 pages |
| Specific Aims | 1 page |
| Research Strategy | 6 pages |
| Respective Contribution | 1 page |
| Selection of Sponsor and Institution | 1 page |
| Responsible Conduct of Research | 1 page |
| Sponsor/ Co-Sponsor Statements | 6 page |
| Letters of support from collaborators | 6 page |
| Inst Environment; Comm. to Training | 2 page |

Letters of recommendation

# Proposal Worksheet

What is the goal of your project?
What is the specific gap in knowledge you will address?
Why is it important to address this?
Hypothesis to be tested?
Major scientific approaches/methods you plan to use?
Particular strengths to address this question now?
Aim #1
Aim #2
If you fully succeeded, what would the new info lead to?

*Due next class meeting*

# Pose Complex Aims

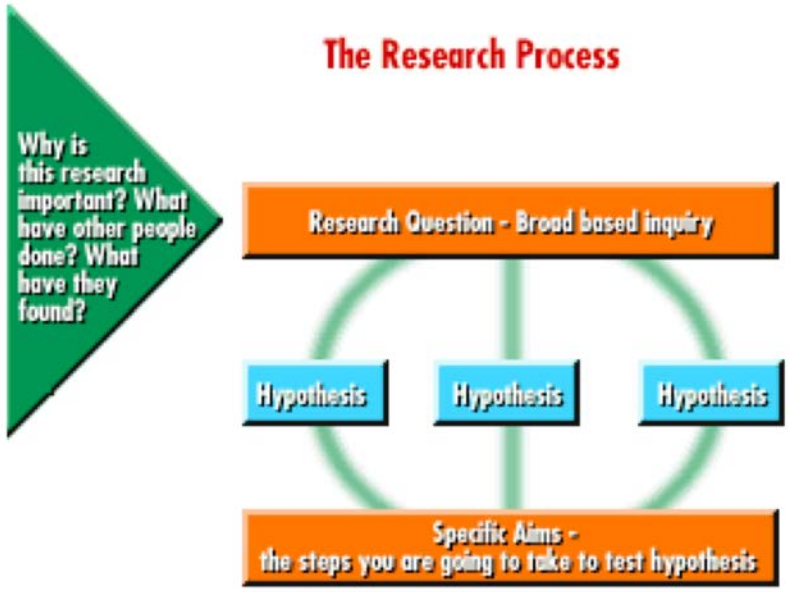
**Table 25.1** Verbs for Use in Writing Learning Objectives

| Knowledge | Comprehension | Application | Analysis | Synthesis | Evaluation |
|---|---|---|---|---|---|
| cite | associate | administer | analyze | adapt | appraise |
| collect | classify | apply | arrange | assemble | argue |
| copy | convert | calculate | breakdown | collaborate | assess |
| define | describe | change | categorize | combine | conclude |
| describe | differentiate | chart | classify | compile | convince |
| duplicate | discuss | choose | compare | compose | criticize |
| enumerate | distinguish | collect | connect | concoct | decide |
| identify | estimate | compute | contrast | construct | deduce |
| label | explain | construct | correlate | contrive | defend |
| list | express | demonstrate | detect | create | determine |
| match | extend | determine | diagram | design | discriminate |
| memorize | group | develop | differentiate | develop | infer |
| name | identify | discover | discriminate | devise | interpret |
| order | indicate | employ | dissect | formulate | judge |
| quote | order | establish | distinguish | generalize | justify |
| recall | paraphrase | examine | divide | generate | persuade |
| recognize | predict | exhibit | examine | hypothesize | prioritize |
| record | report | illustrate | experiment | imagine | rate |
| recount | restate | interview | group | incorporate | rank |
| relate | retell | manipulate | identify | integrate | recommend |
| repeat | review | modify | illustrate | invent | relate |
| reproduce | select | operate | inspect | modify | revise |
| show | summarize | practice | interpret | organize | score |
| specify | translate | predicts | investigate | originate | support |
| state | understand | prepare | order | plan | value |
| tabulate | | produce | organize | predict | validate |
| tell | | relate | outline | produce | |
| when | | report | probe | propose | |
| what | | schedule | question | reconstruct | |
| where | | show | relate | reorganize | |
| who | | sketch | select | revise | |
| | | solve | separate | speculate | |
| | | transfer | survey | systematize | |
| | | use | test | | |

Low complexity

Higher complexity

# Strong research Idea




*A strong research idea should pass the "so what" test.*

What is the benefit of answering your question?

What is the purpose of your research?

Why you chose the approach?

Anticipated results, alternative approaches

How will the proposed studies move the field forward?

# Specific Aims-Main components

Overall problem (eg disease, # people, costly etc)
Specific problem that needs solution (eg poor diagnostics)
What is known about how to solve the problem
What is knowledge gap?
How YOU propose to take steps to solve the problem

Aims-main things you will accomplish
- knowledge to be gained
- hypothesis and rationale
- research design

Final paragraph
- innovation, expected impact
- what new research this will lead to

# Include Research Design

How will you test your hypothesis?

What is experimental approach?

Is it feasible in the lab or collaborator?

Are there preliminary data (eg feasible?)

What is premise of the study (strong findings in field)?

*Always* include

- Sample size, blinding, statistics, controls, replication
- Cite papers, but do not expect reviewer to read
- Anticipated outcome and alternative approaches

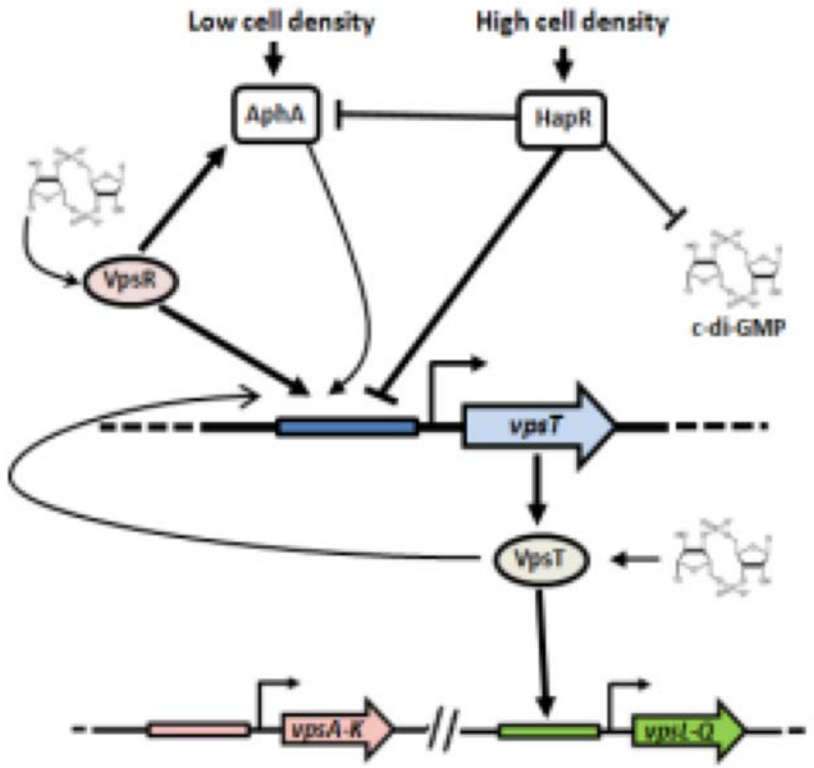
# Tips for Specific Aims Page

- Provide 2 or at most 3 aims
- Define the question you will answer
- Address a hypothesis that is logical, testable, focused, informative, simple

<u>Sample structure:</u>

- First sentence: *hook to capture attention*
- 1st paragraph: what's known, the gap you will address
- 2nd Paragraph: *your solution* to fill the gap
- 3rd paragraph: why your idea, your place, your lab
- Each Aim: A short paragraph to each aim: what/how
- Summary Paragraph: What new things we will know, why the application should be supported
- Consider: *Model*s/Charts/Diagrams

# Working Model for your study




F31 Ayala-Figueredo

Example to show how aims addressed? Introduce terms

# Begin to think about aims…

The best aims are designed not to “prove” a point, or ask “does A cause B.” Best aims where different outcomes are of interest.

- Define the role of X in Y mediated perturbation of function
- Elucidate the role of X signaling on function in disorder
- Evaluate tissue as reservoir for virus
- Determine response of cells during infection
- Define RNA features that lead to process
- Determine mechanism by which X and Y differ in effects on activity

# Reviewers read the Aims

NIH Study Section (of faculty reviewers)

- Read grants in advance, submit initial scores before meeting
- Score 1 (great) to 9 (not great); don't discuss higher than 5
- Primary, secondary, third reviewers
- Your application gets about 15 minutes discussion
- Whole group then scores in whole numbers
- Get summary and strengths/weaknesses

# Schwartz F31 Summary Statement

**RESUME AND SUMMARY OF DISCUSSION:** An excellent predoctoral applicant, in this application, seeks training in virus – host interactions with a project that focuses on studying the regulation of the 2'-5'-oligoadenylate synthetase (OAS) by cytosolic double-stranded RNA (dsRNA). The applicant is a first-generation college student who achieved a very good undergraduate academic record and gained undergraduate research experience that resulted in one first-author and several co-author publications. She is now a graduate student in the Biochemistry, Cell & Developmental Biology (BCDB) program at Emory. She is viewed as very strong. The sponsor and co-sponsor are reviewed as very strong with complementary research expertise and experience in mentoring graduate students. The research training plan is well articulated, although some review it as somewhat risky (high risk, high reward). The applicant will need to learn new techniques such as x-ray crystallography and mass spectrometry. Some reviewers view this as a potential weakness, whereas others view it as a strength of an overall excellent training plan. The institutional environment is excellent. Overall, there is high enthusiasm for the applicant, outstanding sponsors, excellent institutional environment, and important potential impact on advancing our understanding of host-pathogen interactions.

SCHWARTZ,SAMANTHA
Emory University
[redacted]

**DESCRIPTION (provided by applicant):** The innate immune system is a broad set of critical intracellular and extracellular processes that limit viral infectivity. In order to provide its essential first

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*Review Group:* ZRG1 F13-C (20)
Center for Scientific Review Special Emphasis Panel
Fellowship: Infectious Diseases and Microbiology
*Meeting Date:* 03/16/2017
*Council:* MAY 2017 *PCC:* I5A
*Requested Start:* 07/01/2017

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*Project Title:* Regulation of 2'-5'-oligoadenylate synthetase 1 (OAS1) by dsRNA
*Requested:* 3 Years
*Sponsor:* Conn, Graeme L
*Department:* GRS: GDBBS BCDB
*Organization:* EMORY UNIVERSITY
*City, State:* ATLANTA GEORGIA

*SRG Action:* Impact Score:17

NIAID has many samples
From successful applicants
That serve as very useful guides
here

# Examples -Look at aims

**Aim 1: Define the role of TLRs and IL-1R in *S. aureus*-mediated perturbation of osteoclastogenesis.**

Based on preliminary studies that suggest a MyD88-mediated mechanism of OC perturbation by bacterial components *in vitro*, I hypothesize that *S. aureus* modulates pre-OC cell biology through TLR recognition or IL-1R signaling upstream of MyD88. To test this hypothesis, we will perform osteoclastogenesis assays on bone marrow (BM) cultures from wild-type and immune-deficient mouse strains, including TLR2, TLR9, and IL-1R-deficient mice, with and without RANKL stimulation, components of *S. aureus*, TLR agonists, or recombinant IL-1 to (i) identify changes in expression of TLRs and factors known to modulate osteoclastogenesis, (ii) define the activation status of intracellular signaling cascades and transcription factors, and (iii) investigate the functionality of OCs induced by bacterial components with bone resorption assays. Taken together, these data will detail how bacterial stimulation modulates OC differentiation and function through TLR and IL-1 signaling.

**Aim 2: Elucidate the role of skeletal cell-specific MyD88 signaling on pathogen clearance and bone remodeling during *S. aureus* osteomyelitis.**

Aim 1 will identify *in vitro* changes caused by *S. aureus* during osteoclast differentiation, including alterations in OC signaling and function. Our *in vitro* assays demonstrate that MyD88 in skeletal cell precursors could be responsible for downstream changes following *S. aureus* stimulation. Interestingly, preliminary data obtained in our *S. aureus* osteomyelitis model shows that MyD88 is also necessary to limit bacterial replication and dissemination to other organs. Based on these data, I hypothesize that innate sensing of *S. aureus* by skeletal cells *in vivo* impacts
hypothesis we will induce ost

Expt does itself: To test this hypothesis, XX assays on bone marrow cultures will be performed on XX cells, and XX changes identified.

# Hauser Specific Aims

## Specific Aims

The goal of this study is to identify the roles SpxB and $H_2O_2$ play in the aeration-dependent reduction of capsule production in *Streptococcus pneumoniae*. The specific aims are to:

1. **Determine effects of $H_2O_2$ and *spxB* mutations on capsule production.** My data demonstrate that aeration-dependent reduction of capsule in *S. pneumoniae* serotype 2 is due in part to $H_2O_2$ produced as a byproduct of the SpxB-mediated conversion of pyruvate to acetyl-phosphate. In this aim, I will determine whether capsule production in other serotypes is similarly affected by exogenous $H_2O_2$. For serotypes that respond to $H_2O_2$, *spxB* mutations will be generated to investigate the dependence on the pyruvate oxidase. For those serotypes that do not respond to $H_2O_2$, I will use capsule switching experiments to determine whether the failure to respond is due to capsule-specific enzymes or elements outside the capsule genetic locus. Lastly, I will construct strains in which $H_2O_2$ levels are altered as a result of specific point mutations in *spxB*.
2. **Determine effects of *spxB* mutations and $H_2O_2$ on enzyme activities and oxidation states.** Specific enzymes involved in serotype 2 capsule biosynthesis, such as the initial glycosyltransferase Cps2E, have been shown to respond to aerated/oxidized and non-aerated/reduced environments. In this aim, I will determine the effects of mutations in *spxB* on the enzymatic activities of proteins involved in capsule production, and will determine *in vivo* oxidation states using thiol-trapping methods. I will also initiate studies to examine the global effects of $H_2O_2$ on cellular proteins by identifying redox-sensitive proteins using thiol-trapping and Isotope Coded Affinity Tag technology coupled with mass spectrometry
3. **Determine effects of the *spxB* mutations on virulence *in vivo*.** In this Aim, I will use mutants constructed in Aim 1 to examine the effects of alterations in SpxB and $H_2O_2$ on colonization and pneumonia in mice. Two parent strains, their *spxB* deletion derivatives, and derivatives containing *spxB* point mutations that alter the levels of $H_2O_2$ will be examined. For mutants that retain the ability to colonize or cause pneumonia, I will examine capsule production and gene expression using recovered bacteria.

# Stay in Style

All assignments (and NIH) *require*:

- Arial 11 font, single spaced throughout
- 0.5 margins (“narrow”)
- Prefer left margin justified

- A direct tone and active verbs
- Limited use of "I" or “we”
- Declarative topic sentences to express the main idea

Check yourself:

- Reduce commas and parentheses
- Watch for –ing
- Experiment ”does itself”

# More Style Mechanics

Use “insert text box” and put figures and legends in same box so they edit together. Arrange/ wrap tight so text fills in around it.

Love Biorender!

Watch font size in figure legends—both the text (Fig. 7 description might be Arial 9 or 10)

Watch font in figures—when reduced, they may be too small to read—this is a common reviewer complaint!!

# Examine other applications

NIAID examples
https://www.niaid.nih.gov/grants-contracts/sample-applications

University of Alabama Grants Library
https://www.uab.edu/ccts/research-commons/grant-help/proposal-development/grant-library

Learn how to use NIH Reporter to find out who else has this kind of grant (can only see abstract of funded awards)

Refer to Hollenbach AD (2014) A practical guide…NRSA Grant (available online at Science Direct)

# For Next class (2 weeks)

Look up & review successful examples

Read the reviewer criteria in IBS qualifier
and your funding announcement

Look up resource materials

Complete proposal worksheet

Draft 2 experimental aim statements

Think about your working model…