LSU Health NEW ORLEANS

Writing Specific Aims

Nick Gilpin, Ph.D.
Director, Alcohol & Drug Abuse Center of Excellence
Vice Chair of Research, Physiology

“I know the score I am going to give a grant application after reading the Aims page.”

NIH Simplified Review Criteria

Reviewers only have to answer 3 questions about your proposal.

Factor 1 (1-9):

How important is the proposed work (NOT the disease you are studying)?

Factor 2 (1-9):

Can the work be done AND done well (i.e., rigor and feasibility)?

Factor 3 (Yes or No):

Does the team have the expertise and resources to do the work?

Help your advocate!

- Most study sections I serve on have 70-90 proposals. Only 10% of these will be funded, when you factor in A0 and A1 submissions.

- To be in the 10%, you need:
  - All 3 reviewers to “like” your grant AND
  - One reviewer to “love” your grant enough to fight for it. This is your advocate.

All 3 reviewers must understand the proposal, think it is very important, and believe you are the right team for the job.

NIH Impact Score

What next? Who cares?

- The overall score assigned to your proposal is called the Impact Score. NIH defines the impact score as a numerical score from 1 to 9 that represents the overall scientific merit and potential influence of a grant application.

- *Impact according to Gilpin: "If every experiment works exactly as predicted, what does that mean for the field or human health (i.e., the NIH mission)?*

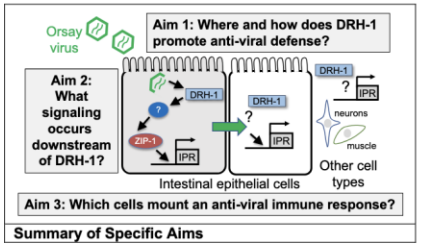
- *Impact according to Floyd Bloom: "Now that you know that, what do you know?"*

So, what is an Aims page?

Specific Aims – Innate immunity against viral infection in intestinal epithelial cells of *C. elegans*

Nearly, if not every, animal on the planet serves as host to some virus. Four out of five animals are nematodes, and the Nematoda phylum originated over 400 million years ago. However, relatively little is known about viral infection and anti-viral immunity in these hosts, in part because natural, full-cycle viral infections of the model nematode *C. elegans* were only discovered as recently as 2011, with the identification of an RNA virus infecting intestinal cells of wild-caught *C. elegans* from Orsay, France. *C. elegans* provides a powerful opportunity to examine the dynamics of anti-viral innate immune responses in a transparent whole-animal host, with extensive tools available for microscopy, genetics, genomics, transcriptomics, and proteomics.

Work from my lab has identified a novel *C. elegans* immune response induced by both the Orsay virus and by microsporidia, fungal pathogens that are the only other known obligate intracellular pathogens of the *C. elegans* intestine. We named this pathway the Intracellular Pathogen Response (IPR). The IPR involves transcriptional up-regulation of about 80 genes and regulates defense against both viral and microsporidia infection. Mutant screens have identified several regulators of the IPR, including "Dicer-Related Helicase" DRH-1, a homolog of RIG-I-like receptors (RLRs) in mammals. RLRs are cytosolic receptors that sense aberrant RNA species, such as viral products containing 5' triphosphates and double-stranded RNA (dsRNA). Our work indicates that the DRH-1 receptor senses Orsay virus replication products in *C. elegans* to trigger anti-viral defense. We found that DRH-1 triggers the IPR independently of RNA interference (RNAi) components such as Dicer, which have previously been shown to provide anti-viral defense in *C. elegans*. Several aspects of the IPR, including the upstream activation by DRH-1/RLR, have similarities with the Type-I Interferon (IFN-I) response in mammals. However, *C. elegans* lacks obvious homologs of the signaling factors that act downstream of RLRs in mammals, including MAVS, IRF3, NFkB and IFN-I itself. Therefore, here we will characterize how DRH-1 controls anti-viral IPR-regulated immunity in *C. elegans* with the following **Specific Aims**:



Summary of Specific Aims

Aim 1: Where and how does DRH-1/RLR promote anti-viral defense in *C. elegans*? Although work from my lab and others has demonstrated that DRH-1 is likely the receptor that triggers anti-viral defense in *C. elegans*, its endogenous expression pattern has not been described. It is also unknown where DRH-1 acts at either the tissue or subcellular level to regulate defense. Here we will determine endogenous expression of DRH-1 and use tissue-specific rescue and depletion to determine where it promotes defense. We will also build on our unpublished data that the DRH-1 protein forms puncta upon viral infection, and analyze DRH-1 subcellular co-localization with markers for Orsay virus, as well as organelles like the mitochondria, which serve as platforms for RLR signaling in mammals via MAVS. We will also examine which virus-induced IPR genes promote defense.

Aim 2: What signaling pathway is activated downstream of DRH-1/RLR in *C. elegans*?
We have found that expression of the N-terminal domain (NTD) alone of DRH-1 will trigger the IPR in the absence of infection (unpublished data), similar to RIG-I NTD overexpression triggering IFN-I expression in mammals. Here we will characterize the effects of DRH-1 NTD overexpression on downstream signaling. We will perform a suppressor screen in a DRH-1 NTD strain to look for loss of IPR reporter expression to identify signaling factors. As an orthogonal method to identify these factors, we will perform proteomic analysis to identify binding partners of DRH-1, and examine candidates we identify for regulation of the IPR.

Aim 3: Which host cells mount an anti-viral immune response in *C. elegans*?
The major cell type infected by Orsay virus is the *C. elegans* intestinal cell, which has structural and functional similarity to human intestinal epithelial cells. The *C. elegans* intestine comprises 20 non-renewable cells, and it is unknown whether immune responses are restricted to infected intestinal cells, or if bystander cells participate in defense. Here we will use a combination of GFP reporters, Fluorescence In Situ Hybridization (FISH) and scRNAseq to determine whether bystander intestinal cells, or any other cells types in *C. elegans*, mount an immune response to viral infection, indicating there is intercellular and/or inter-tissue anti-viral signaling.

Overview: Through our analysis of responses in *C. elegans*, from the whole-animal to the molecular level, we will determine how this simple animal fights off natural viral infection of intestinal epithelial cells. Factors and mechanisms we identify may provide insight into anti-viral defense in humans, as well as inflammatory diseases.

What similarities do you see between these Aims pages?

SPECIFIC AIMS

Adeno-associated virus (AAV) vector has been successfully applied to target the liver in clinical trials with hemophilia patients[1,2]. These trials have suggested that the AAV capsid specific cytotoxic T lymphocytes (CTLs) eliminate AAV vector targeted liver cells, following AAV2 or AAV8 transduction, and result in therapeutic failure. Our studies and others have demonstrated that both classical antigen presentation and cross-presentation pathways are involved in mounting an AAV capsid specific CTL response[3-7]. In clinical trials, ion exchange chromatography has been used to purify AAV vectors. Unlike CsCl purification approach, the chromatographic method cannot currently separate genome-containing AAV capsids (full particles) from empty particles. The contamination of empty virions potentially increases the AAV capsid antigen load in transduced cells and it has been demonstrated that empty virion contamination in vector preparations induces liver damage, which potentially enhances capsid antigen presentation from full virion transduction[8,9]. Although we have observed a lower capsid antigen presentation from AAV empty virion infection compared to full particles *in vitro*[10], our *in vivo* preliminary result demonstrated that AAV empty capsids still elicit capsid antigen presentation. In this proposal we will investigate the kinetics of capsid antigen presentation from empty virions and the effect of empty particles on antigen presentation from full particle transduction (**Aim 1a and 1b**). We have demonstrated that AAV capsid cross-presentation is dependent on virion endosomal escape and proteasome-mediated capsid degradation in AAV transduced cells *in vitro*[10]. However, the mechanistic insights of the work were largely elucidated *in vitro*, and over a limited time period (24 to 48 hrs), and therefore it remains unclear which aspects of our discoveries translate *in vivo* regarding long-term antigen processing and presentation. The mechanism of capsid antigen presentation from empty virions and full particles *in vivo* will be performed using mouse models deficient in the genes responsible for classical class-I antigen presentation (TAP -/- mice) or classical class-II antigen presentation (Cat S -/- mice) (**Aim 1c**).

Our data have shown that capsid antigen presentation is dose-dependent and requires capsid ubiquitination for proteasome mediated degradation[11,12]. To decrease antigen presentation on AAV transduced cells for avoiding capsid specific CTL-mediated elimination, it has been proposed to modify the AAV capsid surface in order to enhance AAV transduction while lowering the effective dose, or to escape capsid ubiquitination[13,14]. It is unclear whether the enhancement of liver transduction with AAV mutants or a decrease in capsid ubiquitination influences capsid antigen presentation *in vivo* (**Aim 2a**). Proteasome inhibitors have been shown to enhance AAV transduction and inhibit antigen presentation[12,15]. However, our further *in vitro* study demonstrated varying effects of the proteasome inhibitor on capsid antigen cross-presentation in a dose related manner. A high dose of the proteasome inhibitor bortezomib blocks capsid antigen presentation, while a lower dose of bortezomib increases capsid antigen presentation without enhanced transduction. We hypothesize that proteasome inhibitor treatment will change the profile of AAV antigen presentation *in vivo* and the combination of AAV mutants and proteasome inhibitors will further increase AAV transduction while inhibiting capsid antigen presentation (**Aim 2b and 2c**).

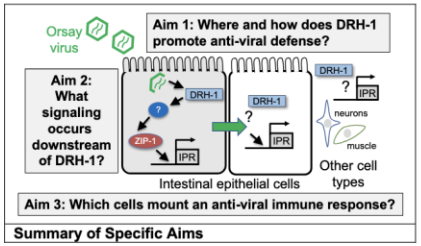
It is well-known that the transduction of AAV vectors in mouse models does not always translate into the human host. To address this, a mouse model xenografted with human hepatocytes has been used to develop AAV vectors for human liver targeting gene therapy[16]. In this proposal we will explore the directed evolution approach combined with a rational design strategy to isolate AAV vectors with human hepatocyte specific tropism and the ability to evade a capsid specific CTL response in humanized mice (**Aim 3**). Elucidation of AAV empty capsid antigen presentation *in vivo* and the development of an AAV vector with enhanced *human* liver transduction and CTL immune-evasion, will allow us to design safer and more effective strategies that address the current clinical complications for human liver gene therapy using AAV. To address these issues, we will execute the following specific aims:

1. **Study the effect of AAV empty particles on AAV capsid antigen cross-presentation *in vivo*.**
   - **a**. The kinetics and dose-response of AAV capsid antigen presentation from AAV empty virions *in vivo*.
   - **b**. The effect of empty particles on capsid antigen presentation from full-particle AAV transduction *in vivo*.
   - **c**. AAV capsid antigen presentation in TAP-/- and in Cat S-/- mice.
2. **Investigate AAV capsid antigen presentation following administration of AAV mutants and/or proteasome inhibitors for enhanced liver transduction *in vivo*.**
   - **a**. Capsid antigen presentation from AAV mutants with enhanced liver transduction in mice.
   - **b**. The effect of proteasome inhibitors (high vs low dose) on natural AAV capsid antigen presentation *in vivo*.
   - **c**. The effect of a combination of AAV mutants with proteasome inhibitors on antigen presentation *in vivo*.
3. **Isolate AAV chimeric capsids with human hepatocyte tropism and the capacity for CTL evasion.**
   - **a**. Verify AAV human liver transduction efficiency in xenograft mice.
   - **b**. Characterization of AAV mutants recovered from human liver xenografted mice.
   - **c**. Investigation of capsid CTL evasion from humanized AAV mutants.

Specific Aims – Innate immunity against viral infection in intestinal epithelial cells of *C. elegans*

Nearly, if not every, animal on the planet serves as host to some virus. Four out of five animals are nematodes, and the Nematoda phylum originated over 400 million years ago. However, relatively little is known about viral infection and anti-viral immunity in these hosts, in part because natural, full-cycle viral infections of the model nematode *C. elegans* were only discovered as recently as 2011, with the identification of an RNA virus infecting intestinal cells of wild-caught *C. elegans* from Orsay, France. *C. elegans* provides a powerful opportunity to examine the dynamics of anti-viral innate immune responses in a transparent whole-animal host, with extensive tools available for microscopy, genetics, genomics, transcriptomics, and proteomics.

Work from my lab has identified a novel *C. elegans* immune response induced by both the Orsay virus and by microsporidia, fungal pathogens that are the only other known obligate intracellular pathogens of the *C. elegans* intestine. We named this pathway the Intracellular Pathogen Response (IPR). The IPR involves transcriptional up-regulation of about 80 genes and regulates defense against both viral and microsporidia infection. Mutant screens have identified several regulators of the IPR, including "Dicer-Related Helicase" DRH-1, a homolog of RIG-I-like receptors (RLRs) in mammals. RLRs are cytosolic receptors that sense aberrant RNA species, such as viral products containing 5' triphosphates and double-stranded RNA (dsRNA). Our work indicates that the DRH-1 receptor senses Orsay virus replication products in *C. elegans* to trigger anti-viral defense. We found that DRH-1 triggers the IPR independently of RNA interference (RNAi) components such as Dicer, which have previously been shown to provide anti-viral defense in *C. elegans*. Several aspects of the IPR, including the upstream activation by DRH-1/RLR, have similarities with the Type-I Interferon (IFN-I) response in mammals. However, *C. elegans* lacks obvious homologs of the signaling factors that act downstream of RLRs in mammals, including MAVS, IRF3, NFkB and IFN-I itself. Therefore, here we will characterize how DRH-1 controls anti-viral IPR-regulated immunity in *C. elegans* with the following **Specific Aims**:



Summary of Specific Aims

Aim 1: Where and how does DRH-1/RLR promote anti-viral defense in *C. elegans*? Although work from my lab and others has demonstrated that DRH-1 is likely the receptor that triggers anti-viral defense in *C. elegans*, its endogenous expression pattern has not been described. It is also unknown where DRH-1 acts at either the tissue or subcellular level to regulate defense. Here we will determine endogenous expression of DRH-1 and use tissue-specific rescue and depletion to determine where it promotes defense. We will also build on our unpublished data that the DRH-1 protein forms puncta upon viral infection, and analyze DRH-1 subcellular co-localization with markers for Orsay virus, as well as organelles like the mitochondria, which serve as platforms for RLR signaling in mammals via MAVS. We will also examine which virus-induced IPR genes promote defense.

Aim 2: What signaling pathway is activated downstream of DRH-1/RLR in *C. elegans*?
We have found that expression of the N-terminal domain (NTD) alone of DRH-1 will trigger the IPR in the absence of infection (unpublished data), similar to RIG-I NTD overexpression triggering IFN-I expression in mammals. Here we will characterize the effects of DRH-1 NTD overexpression on downstream signaling. We will perform a suppressor screen in a DRH-1 NTD strain to look for loss of IPR reporter expression to identify signaling factors. As an orthogonal method to identify these factors, we will perform proteomic analysis to identify binding partners of DRH-1, and examine candidates we identify for regulation of the IPR.

Aim 3: Which host cells mount an anti-viral immune response in *C. elegans*?
The major cell type infected by Orsay virus is the *C. elegans* intestinal cell, which has structural and functional similarity to human intestinal epithelial cells. The *C. elegans* intestine comprises 20 non-renewable cells, and it is unknown whether immune responses are restricted to infected intestinal cells, or if bystander cells participate in defense. Here we will use a combination of GFP reporters, Fluorescence In Situ Hybridization (FISH) and scRNAseq to determine whether bystander intestinal cells, or any other cells types in *C. elegans*, mount an immune response to viral infection, indicating there is intercellular and/or inter-tissue anti-viral signaling.

Overview: Through our analysis of responses in *C. elegans*, from the whole-animal to the molecular level, we will determine how this simple animal fights off natural viral infection of intestinal epithelial cells. Factors and mechanisms we identify may provide insight into anti-viral defense in humans, as well as inflammatory diseases.

What differences do you see between these Aims pages?

SPECIFIC AIMS

Adeno-associated virus (AAV) vector has been successfully applied to target the liver in clinical trials with hemophilia patients[1,2]. These trials have suggested that the AAV capsid specific cytotoxic T lymphocytes (CTLs) eliminate AAV vector targeted liver cells, following AAV2 or AAV8 transduction, and result in therapeutic failure. Our studies and others have demonstrated that both classical antigen presentation and cross-presentation pathways are involved in mounting an AAV capsid specific CTL response[3-7]. In clinical trials, ion exchange chromatography has been used to purify AAV vectors. Unlike CsCl purification approach, the chromatographic method cannot currently separate genome-containing AAV capsids (full particles) from empty particles. The contamination of empty virions potentially increases the AAV capsid antigen load in transduced cells and it has been demonstrated that empty virion contamination in vector preparations induces liver damage, which potentially enhances capsid antigen presentation from full virion transduction[8,9]. Although we have observed a lower capsid antigen presentation from AAV empty virion infection compared to full particles *in vitro*[10], our *in vivo* preliminary result demonstrated that AAV empty capsids still elicit capsid antigen presentation. In this proposal we will investigate the kinetics of capsid antigen presentation from empty virions and the effect of empty particles on antigen presentation from full particle transduction (**Aim 1a and 1b**). We have demonstrated that AAV capsid cross-presentation is dependent on virion endosomal escape and proteasome-mediated capsid degradation in AAV transduced cells *in vitro*[10]. However, the mechanistic insights of the work were largely elucidated *in vitro*, and over a limited time period (24 to 48 hrs), and therefore it remains unclear which aspects of our discoveries translate *in vivo* regarding long-term antigen processing and presentation. The mechanism of capsid antigen presentation from empty virions and full particles *in vivo* will be performed using mouse models deficient in the genes responsible for classical class-I antigen presentation (TAP -/- mice) or classical class-II antigen presentation (Cat S -/- mice) (**Aim 1c**).

Our data have shown that capsid antigen presentation is dose-dependent and requires capsid ubiquitination for proteasome mediated degradation[11,12]. To decrease antigen presentation on AAV transduced cells for avoiding capsid specific CTL-mediated elimination, it has been proposed to modify the AAV capsid surface in order to enhance AAV transduction while lowering the effective dose, or to escape capsid ubiquitination[13,14]. It is unclear whether the enhancement of liver transduction with AAV mutants or a decrease in capsid ubiquitination influences capsid antigen presentation *in vivo* (**Aim 2a**). Proteasome inhibitors have been shown to enhance AAV transduction and inhibit antigen presentation[12,15]. However, our further *in vitro* study demonstrated varying effects of the proteasome inhibitor on capsid antigen cross-presentation in a dose related manner. A high dose of the proteasome inhibitor bortezomib blocks capsid antigen presentation, while a lower dose of bortezomib increases capsid antigen presentation without enhanced transduction. We hypothesize that proteasome inhibitor treatment will change the profile of AAV antigen presentation *in vivo* and the combination of AAV mutants and proteasome inhibitors will further increase AAV transduction while inhibiting capsid antigen presentation (**Aim 2b and 2c**).

It is well-known that the transduction of AAV vectors in mouse models does not always translate into the human host. To address this, a mouse model xenografted with human hepatocytes has been used to develop AAV vectors for human liver targeting gene therapy[16]. In this proposal we will explore the directed evolution approach combined with a rational design strategy to isolate AAV vectors with human hepatocyte specific tropism and the ability to evade a capsid specific CTL response in humanized mice (**Aim 3**). Elucidation of AAV empty capsid antigen presentation *in vivo* and the development of an AAV vector with enhanced *human* liver transduction and CTL immune-evasion, will allow us to design safer and more effective strategies that address the current clinical complications for human liver gene therapy using AAV. To address these issues, we will execute the following specific aims:

1. **Study the effect of AAV empty particles on AAV capsid antigen cross-presentation *in vivo*.**
   - **a**. The kinetics and dose-response of AAV capsid antigen presentation from AAV empty virions *in vivo*.
   - **b**. The effect of empty particles on capsid antigen presentation from full-particle AAV transduction *in vivo*.
   - **c**. AAV capsid antigen presentation in TAP-/- and in Cat S-/- mice.
2. **Investigate AAV capsid antigen presentation following administration of AAV mutants and/or proteasome inhibitors for enhanced liver transduction *in vivo*.**
   - **a**. Capsid antigen presentation from AAV mutants with enhanced liver transduction in mice.
   - **b**. The effect of proteasome inhibitors (high vs low dose) on natural AAV capsid antigen presentation *in vivo*.
   - **c**. The effect of a combination of AAV mutants with proteasome inhibitors on antigen presentation *in vivo*.
3. **Isolate AAV chimeric capsids with human hepatocyte tropism and the capacity for CTL evasion.**
   - **a**. Verify AAV human liver transduction efficiency in xenograft mice.
   - **b**. Characterization of AAV mutants recovered from human liver xenografted mice.
   - **c**. Investigation of capsid CTL evasion from humanized AAV mutants.

NIH Specific Aims Page

according to AI

Strategies for Success

- Lead with public-health impact & NIH alignment
- Be concise, clear, and visually scannable
- Choose independent, feasible aims
- Highlight innovation and feasibility explicitly
- End with strong, confident impact statement

Pitfalls to Avoid (“loose threads”)

- Overambitious aims
- Inter-dependent aims
- Vague gap/hypothesis (Who cares?)
- Excessive methods detail … this is not the place for it
- Misalignment with NIH institute priorities … talk to your PO!!

Design Essentials

- Use short paragraphs and clear aim titles
- Avoid jargon and define key terms
- Quantify outcomes where possible
- Use bold/italics **sparingly** for emphasis

Content essentials

- Clearly state the critical knowledge gap (first).
- Define what you aim to accomplish and why it is important (Factor 1)
- Convince the reviewer you can do the experiments (Factor 2)

NIH Specific Aims Page

some reasonably useful pointers from (someone at) NIH

Specific Aims Page: Critical Elements (NINDS)

1. Identify a research gap. Will your research move the field forward?
2. Determine the significance of the problem and impact of the work. Is the work important—will progress make a difference to our understanding of science and/or human health?
3. Determine if your team is experienced and able to carry out the work.

Specific Aims Page: Step by Step (NINDS)

- **Step 1:** Determine whether your research questions are exploratory (hypothesis-generating) or confirmatory (hypothesis-testing). If confirmatory, make sure the hypotheses are focused, testable, built on a solid scientific foundation, and important.

- **Step 2:** Draft aims to generate and/or test the hypotheses feasibly within the grant period.
  - The aims should be focused and easy to assess by reviewers.
  - Avoid interdependent aims.
  - In drafting the specific aims, it can be informative to:
    - Outline experiments and outcomes.
    - Determine approximate personnel, resources, and timeline.
    - Identify a potential funding institute and funding mechanism.
    - Consider potential study sections and expertise of reviewers.
    - Assess feasibility of proposed work and fit for funding mechanism.

- **Step 3:** Revise aims as needed.

Specific Aims Page: Composition (NINDS)

- Part 1 – Narrative:
  - Describe the rationale, significance and goals of your planned research
  - State your hypothesis and describe how aims build on rigorous prior work.
  - State the technologies you plan to use.
  - Note the expertise to do a specific task or that of collaborators.
  - Describe past accomplishments related to the project.
  - Describe preliminary studies and new and highly relevant findings in the field.
  - Explain the area's biology.
  - Show how the aims relate to one another.
  - Use **bold** or *italics* to emphasize items they want to bring to the reviewers' attention.

- Part 2 - Aims:
  - State your plans using strong verbs like *identify, define, quantify, establish, determine*.
  - Describe each aim in one to three sentences.
  - Add bullets under each aim to refine your objectives.
  - Describe expected outcomes for each aim.
  - Explain how you plan to interpret data from the aim’s efforts.
  - Describe how to address potential pitfalls with contingency plans.

- Part 3 – Closing Statement:
  - Emphasize the significance of the work, collaborators, or any other points of focus.

NIH Specific Aims Page

according to Your LSU Health Colleagues

As a reviewer, what are the most important fundamental elements of an NIH Specific Aims page?

I want to be convinced that the question is important, answerable, and and that the team is appropriate.

Core Ingredients:

1. Clear & compelling hypothesis: Testable, bold, and the anchor of all aims
2. Strong rationale & significance: Explains why this matters and what gap it fills
3. Feasible, independent aims: Integrated but not interdependent
4. Grounded in science: Logical foundation with preliminary support
5. Explicit outcomes: What new knowledge or impact will result

Make it Readable, memorable and convincing:

1. Clear, accessible language: Avoid jargon and long technical sentences
2. Logical, easy-to-follow structure: Paragraph breaks, short sections, flow
3. Eye-catching summary figure: Conveys the big picture at a glance
4. Professional polish: Typo-free, authentic tone
5. Concise, focused writing: Only essential ideas, not details
6. Reviewers skim first: Design for clarity, white space, and visual flow

As an applicant, how do you generally go about structuring an Aims page and what are your main goals on this page?

I want my Aims page to excite, assure, and inspire confidence in my science and my team.

Main goals of the NIH specific aims page:

1. Engage and persuade the reviewer immediately — make them care!!!
2. Convey a logical and cohesive flow from rationale to outcomes
3. Demonstrate feasibility and innovation — ambitious yet credible
4. Show clear linkage between aims and central hypothesis
5. Leave the reviewer thinking: “This is important, feasible, and impactful.”

Structural elements of a strong Specific Aims page:

1. Start with the big picture and rationale: Engage the reader and frame significance
2. Define the specific gap in knowledge your work will fill
3. Present the central hypothesis or overall objective clearly
4. Lay out 2–4 clear, non-overlapping aims that test the hypothesis
5. End with expected outcomes and impact tied to the big picture
6. Summarize preliminary data or expertise showing feasibility
7. Include a concise overview of approach (models, design, key methods)
8. Use a simple summary figure to orient reviewers

NIH Specific Aims Page

according to Gilpin

NIH Specific Aims Page
according to Gilpin

Five Aims Page rules to live by:

1. Who cares??? EXCITE reviewers.
2. Write the Aims page for reviewers that are NOT in your field.
3. Write the reviewers' critiques for them!
4. Reviewers should not be surprised by anything after the Aims.
5. A graphic that truly represents all aims and experiments, and how they fit together, is worth its weight in gold.