

The Art of the Aim

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CAIRIBU U-RIG Summer Workshop

July 17, 2026

Learning Objective

- Distinguish between a project goal and a specific aim
- Identify common weaknesses in aims
- Write a hypothesis-driven NIH-style specific aim for a grant proposal.
- Give constructive feedback on scientific aims

Agenda

- Introductions
- What is a specific aim?
- Breakout groups: Review aims in small groups
- Work on your own: Students each develop one aim on their own
- Breakout groups: Students review and provide feedback on each others' aims
- Whole group debrief
- CAIRIBU conclusion

Introductions

- Name
- University
- Stage in training (undergrad, grad student, postdoc, other?)
- Research area (if known)
- Have you ever written any kind of grant or fellowship proposal? If so, briefly detail.

What is a specific aim?

- Imagine NIH gives you \$2 million.
- What exactly are you promising to discover?
 - I will study UTIs ✗
 - I will perform RNA-seq ✗
 - I will determine whether intracellular bacterial communities promote recurrent urinary tract infections. ✓

What is a specific (scientific) aim?

- A specific aim is **not**
 - a task
 - a method
 - a to-do list
 - a milestone
- A specific aim is:
 - **A question that will be answered by a defined set of experiments.**
 - One aim = one biological question

Why do we need to write aims?

- Grants
- Fellowship applications
- Candidacy exams / proposals
- To clarify our own scientific logic and experimental plan

Guidelines for NIH Aims

- **Is the aim important?**
- **Is the aim testable?**
- **Can the proposed experiments actually answer the question?**
- Every NIH aim should answer:
 - If I complete this aim successfully, what will I know that I don't know today?
 - NOT: What experiments will I have done?

Parts of a Scientific Proposal

- **Project Goal:** Long term vision
- **Hypothesis:** WHY do you think this is true?
- **Specific Aim:** What question will you answer?
- **Experiment (Approach):** How you answer the question?
- **Expected Outcome:** What will I know if the Aim succeeds?
- **Impact:** Why should the NIH care? (How those findings will advance the field, improve future studies, or ultimately benefit health.)

Example 1

- **Project Goal**

- Reduce recurrent urinary tract infections

- **Aim**

- Determine whether intracellular bacterial communities contribute to recurrent urinary tract infection by protecting bacteria from antibiotic treatment.

- **Hypothesis**

- Intracellular bacterial communities protect uropathogenic *E. coli* from antibiotics, promoting recurrence.

- **Experiments**

- Mouse infection model, microscopy, bacterial counts before and after antibiotics.

Example 2

- **Project Goal**

- Improve treatment of catheter-associated urinary tract infections.

- **Aim**

- Determine whether catheter-associated biofilms increase antibiotic tolerance of uropathogenic *E. coli*.

- **Hypothesis**

- Catheters promote biofilm formation that reduces antibiotic susceptibility.

- **Experiments**

- Grow catheter biofilms
 - Antibiotic challenge
 - Quantify surviving bacteria

Reviewing Aims and Giving Feedback

- **Is the aim important?**
- **Is the aim testable?**
- **Can the proposed experiments actually answer the question?**
- Evaluate the logic
- Be respectful, specific (NOT: “Bad aim”)
- What could improve this aim?
- In your breakout groups, identify
 - Strengths
 - Weaknesses
 - Recommendations

Breakout Groups

- Each group will be assigned 4 aims. As a group review and discuss the aims. (10 min)
 - **Group 1 (and 4): Aim 3, 6, 9, 12**
 - **Group 2 (and 5): Aims 4, 7, 10, 13**
 - **Group 3 (and 6): Aims 5, 8, 11, 14**

Example 3

- **Aim 1:** Study urinary tract infections.
- Problems
 - Not a question
 - Too broad
 - No hypothesis
 - Impossible to review

Example 4

- **Aim 1:** Perform RNA-seq on bladder tissue after UTI.
- Problem
 - RNA-seq is a method.
 - What scientific question is being answered?

Example 5

- **Aim 1:** Investigate all host-pathogen interactions during urinary tract infection.
- Problem
 - Impossible scope.

Example 6

- **Hypothesis:** Inflammation influences recurrent UTI.
- **Aim:** Determine the role of inflammation in recurrent urinary tract infections.
- Problems
 - Which inflammatory pathway?
 - Which cells?
 - Which outcome?
 - Too vague.

Example 7

- **Hypothesis:** Antibiotics alter the microbiome.
- **Aim:** Determine whether antibiotics alter the gut microbiome, urinary microbiome, immune response, epithelial repair, bacterial persistence, and recurrence
- Problems
 - How many aims is this really?
 - Five or six.

Example 8

- **Hypothesis:** Uropathogenic *E. coli* survives antibiotics inside bladder cells.
- **Aim:** Determine whether intracellular bacterial communities promote recurrent infection.
- **Approach:** 16S sequencing
- Problem:
 - Does the experiment actually test the hypothesis?
 - No.

Example 9

- **Hypothesis:** Urinary dysbiosis causes recurrent UTI.
- **Aim:** Determine whether urinary dysbiosis causes recurrent UTI.
- **Approach:** Compare microbiomes of healthy women and women with recurrent UTI.
- Problem
 - Can an observational study demonstrate causation?

Example 10

- **Hypothesis:** Neutrophils promote recurrent UTI by damaging the bladder epithelium.
- **Aim:** Determine whether neutrophil infiltration promotes recurrent UTI.
- **Approach:** Measure neutrophil numbers.
- Problem
 - Correlation is not mechanism.

Example 11

- **Hypothesis:** Biofilms protect bacteria from antibiotics.
- **Aim:** Determine whether catheter biofilms increase treatment failure.
- **Approach:** Confocal microscopy.
- Problems
 - Microscopy alone cannot demonstrate treatment failure.
 - Need bacterial survival data.

Example 12

- **Hypothesis:** The urinary microbiome influences susceptibility to recurrent infection.
- **Aim:** Determine whether the urinary microbiome regulates susceptibility to recurrent UTI.
- **Approach:** Treat mice with antibiotics.
- Problems
 - What is missing?
 - No microbiome measurements
 - No recolonization
 - No mechanistic link

Example 13

- **Hypothesis:** Commensal bladder bacteria suppress uropathogenic *E. coli* colonization by competing for iron.
- **Aim:** Determine whether commensal bladder bacteria limit UPEC colonization through iron competition.
- **Approach**
 - Competition assays
 - Iron supplementation
 - Mouse infections
- **Problem / concerns**
 - Only one commensal strain?
 - Alternative mechanisms?
 - Is iron competition actually measured?

Example 14 (Strong)

- **Aim 1:** Determine whether intracellular bacterial communities promote recurrent urinary tract infection by protecting uropathogenic *E. coli* from antibiotic treatment.
- **Hypothesis:** Intracellular bacterial communities act as protected reservoirs that survive antibiotic exposure and seed recurrent infection.
- **Approach:** Using a mouse model of recurrent UTI, we will quantify intracellular bacterial communities before and after antibiotic treatment using confocal microscopy and bacterial culture. Pharmacologic disruption of intracellular invasion will determine whether eliminating these reservoirs reduces recurrence.
- **Expected Outcome:** These studies will establish whether intracellular bacterial communities represent a mechanistic driver of recurrent UTI.
- **Impact:** This work could identify new therapeutic strategies to prevent recurrent urinary tract infections.

Write your own NIH-style Aim

- Considering a topic that you are or may be interested in studying, develop your own NIH-style (5 min):
 - **Aim**
 - **Hypothesis** (optional)
 - **Approach** (optional)

In breakout groups

- Is the aim important? (Yes/No)
- Is the aim testable? (Yes/No)
- Is the biological question (aim) clear? (Yes/No)
- If an approach is provided, can the approach answer the question? (Yes/No)

Debrief

- What patterns did everyone notice

NIH Aim Checklist

- Can I explain the biological question in one sentence?
- Is there one central hypothesis?
 - Reviewers ask: Is the hypothesis logical and supported?
- Do the experiments directly test that hypothesis?
- If successful, what new knowledge will be gained?
- Is the scope realistic for one aim and the proposed budget/period?
 - Reviewers ask: If the aim fails, does the project fall apart?
- Would a reviewer know exactly what success looks like?
 - Reviewers ask: Does the investigator have a realistic path to success?

Happy Aim Writing! 😊