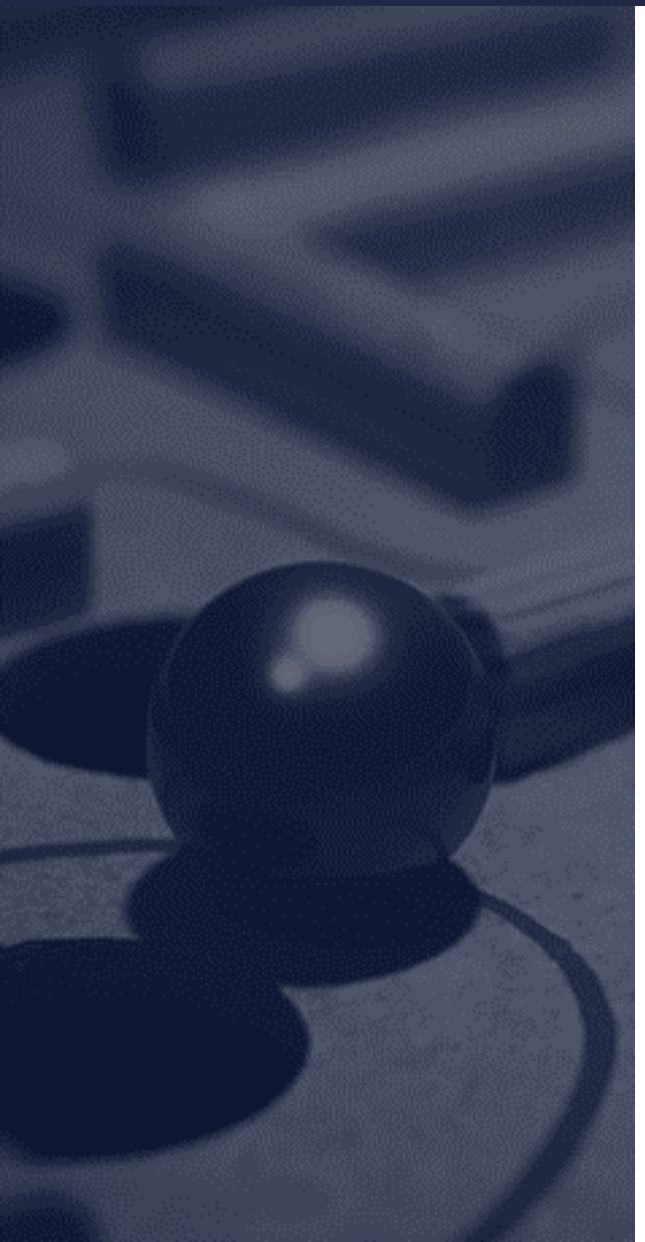
ANATOMY OF A COMPETITIVE SPECIFIC AIM

TODAY'S LOGISTICS



PRESENTATION LENGTH ~60 minutes

Q&A and WRAP-UP We will save time for questions at the end with a wrap-up discussion.

RECORDING & SLIDES All attendees can access the slides and corresponding recording following today's presentation.

SENIOR GRANTS CONSULTANT

Sarah Ott

SENIOR GRANTS CONSULTANT

TOTAL WINS

$100+

MILLION

More than $100 million in total grant funding for clients since 2007.

SPECIALIZES IN

- M.S. in Exercise Science and Health Promotion
- M.S. in Journalism
- Joined Hanover in 2013
- Supervises Hanover's NIH Team
- Started grant writing as a graduate student

On a Personal Note…

STRENGTH ATHLETE: Competes in strongwoman and powerlifting

CHILDHOOD DREAM: Be an Olympic gymnast

4 MOTHER OF FOUR: 2 kids, 1 cat, 1 dog

TODAY'S AGENDA

- Developing a strong hypothesis
- Developing good aims to support/refute your hypothesis
- Anatomy of an NIH Specific Aims Page

DEVELOP A TESTABLE HYPOTHESIS

- [x] **Start with a question**

  Does exercise influence chemotherapy side effects?

- [x] **Get specific**

  Do patients with cancer who exercise regularly experience fewer side effects from chemotherapy?

- [x] **Make it testable**

  If patients with cancer engage in moderate exercise for 15 min/day, they will have fewer side effects from chemotherapy.

A GREAT HYPOTHESIS IS…

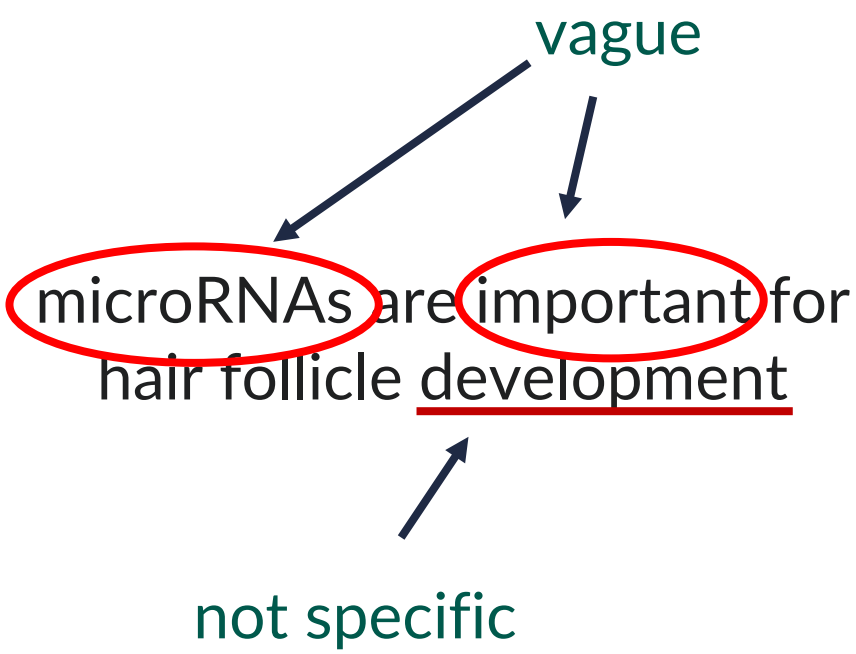
1. **Logical**
   Supported by a literature search and preliminary data
2. **Testable**
   With resources you have access to
3. **Focused**
   It addresses a specific unknown
4. **Simple**
   No great leap in logic

HYPOTHESIS EXAMPLE

microRNAs are important for hair follicle development

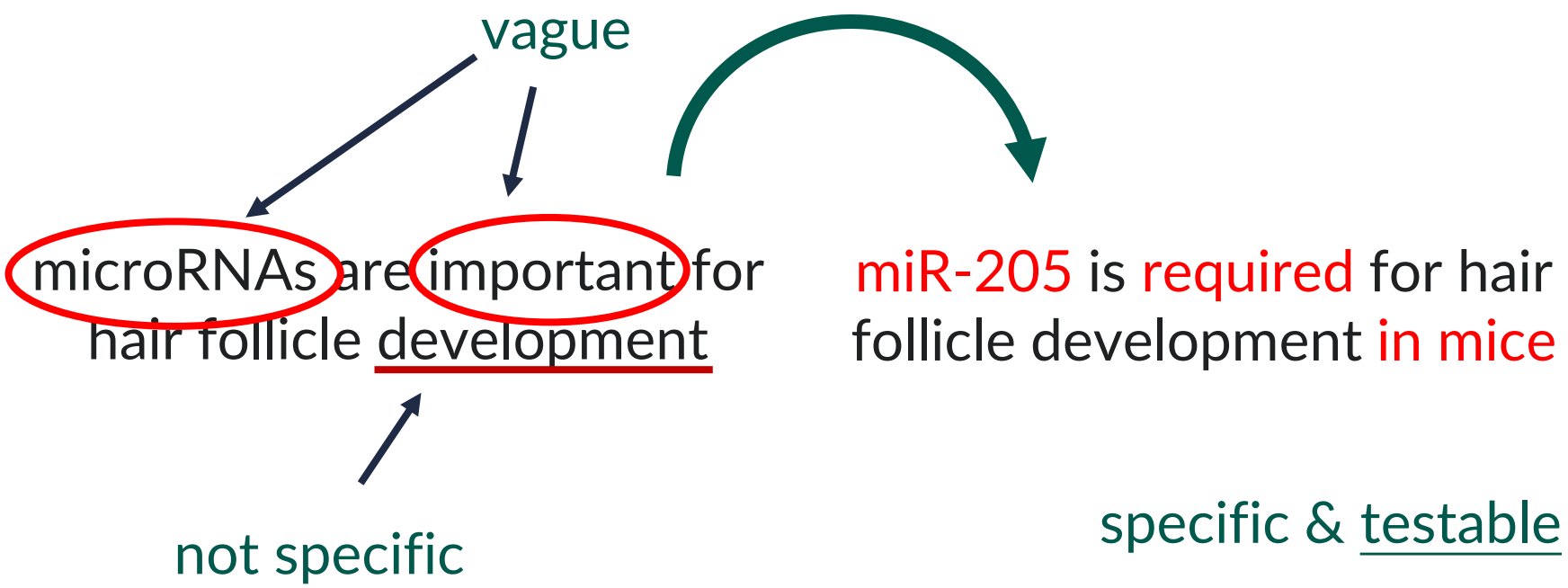
What do you notice about this hypothesis?
Is it strong or weak?
What makes it strong or weak?

HYPOTHESIS EXAMPLE



What could you change about the wording to make this a stronger hypothesis?

HYPOTHESIS EXAMPLE



MIDWESTERN EXAMPLE

Our hypothesis is that BRG1 reduces nucleosome density at DSBs, thus allowing the recruitment of the DNA end resection nuclease CtIP and stimulating DNA end resection and HR, and that ARID1A and BRD7 are important for anchoring these complexes at DSBs.

What makes this hypothesis:

- Supported?
- Testable?
- Focused?

MIDWESTERN EXAMPLE

specific cause
FOCUSED

Our hypothesis is that BRG1 reduces nucleosome density at DSBs, thus allowing the recruitment of the DNA end resection nuclease CtIP and stimulating DNA end resection and HR, and that ARID1A and BRD7 are important for anchoring these complexes at DSBs.

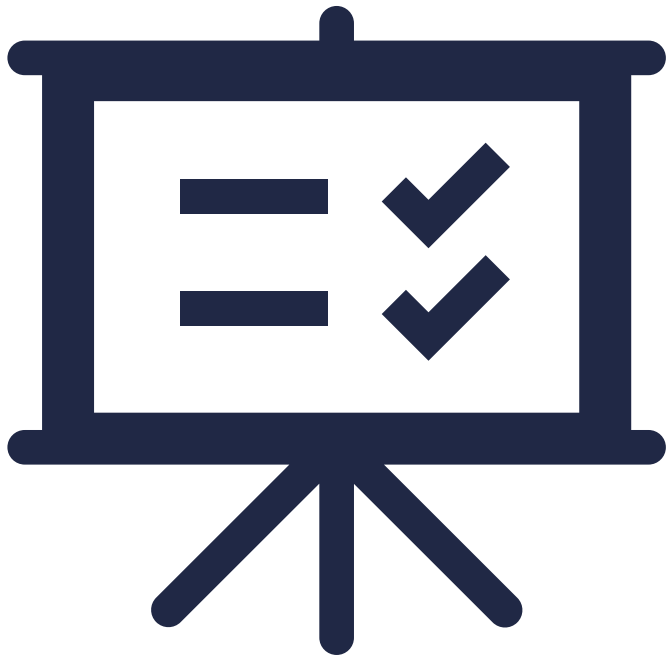
specific, testable effect
FOCUSED/TESTABLE

WHAT IS AN AIM?

A specific goal with a measurable outcome that can be accomplished in a reasonable amount of time

Good aims directly contribute to supporting or refuting your hypothesis or answering your research question

DEVELOPING AIMS



- Aims should be driven by your hypothesis or research question, not by methodology
- Keep your aims focused

AIMS "DO'S"

Aims are the actions to be taken to test the hypothesis or answer the question. They should

- Be a natural extension of the hypothesis or research question
- Be brief, informative, and attract the reviewer's attention
- Convey why each part of the research is being done
- Result in something measurable
- Be related but not interdependent

Sources: BioScience Writers (April 9, 2015); Dersbeck (2013); Giddings (n.d.); NIH (November 25, 2015); Univ. of Washington (n.d.)

AIMS "DON'TS"

Aims should not →

- Introduce new ideas that reviewers have not seen
- Be sequentially dependent
- Be unrealistic (the goal is to propose a project that is ambitious but attainable)

Sources: BioScience Writers (April 9, 2015); Dersbeck (2013); Giddings (n.d.); NIH (November 25, 2015); Univ. of Washington (n.d.)

WHAT'S WRONG?

- Hypothesis: A causes B
- Aim 1: Determine that A causes B
- Aim 2: Determine how A causes B

WHAT'S WRONG?

only relevant to one aim

- Hypothesis: A causes B

implies that you already know A causes B

- Aim 1: Determine that A causes B
- Aim 2: Determine how A causes B

what if A doesn't cause B?

COMMON EXPECTATIONS

- If you have a strong, focused concept, it is common (and acceptable) to propose a separate hypothesis for each aim, rather than an overarching hypothesis
- This is also typical for mixed-methods research
- As you navigate the process from concept to proposal, it can still be very helpful to start with a broad central hypothesis, and get more specific from there

GOOD VS. BAD AIMS: QUANTITATIVE

Aim: To compare outcomes associated with clinical decision support for glycemic control.

We hypothesize that the use of our tool will reduce adverse events. We will activate and deactivate the tool in phases. We predict that the tool will be effective.

Aim: To compare glycemic, clinical, and economic outcomes associated with clinical decision support for glycemic control in academic and community hospitals. We hypothesize that the use of our tool in both academic and community hospitals will improve glycemic control and reduce rates of medical and surgical complications, length of hospital stay, hospital disposition for extended care, readmissions rates, hospital-related costs, and inpatient mortality. Our prospective intervention will involve repeatedly activating or deactivating the tool over 24 months across eight alternating phases lasting three months each. We predict that the tool will be similarly effective in both hospital settings at improving glycemic, clinical, and economic outcomes.

GOOD VS. BAD AIMS: QUALITATIVE

Aim: To understand the perspectives of users of clinical decision support.

We will use a sample to conduct interviews to understand factors leading to the adoption of our tool. We will conduct thematic analysis to better understand reasons for adoption.

Aim: To understand the perspectives of users of clinical decision support through a qualitative analysis. We will use a purposeful sample to conduct semi-structured, open-ended, one-on-one interviews of key stakeholders to understand factors leading to the adoption of our tool. We will conduct a rigorous thematic analysis to better understand topics pertaining to quality of care, hospital benefits, providers' workflow, and system barriers.

THE NIH SPECIFIC AIMS PAGE

The *Specific Aims* section is arguably the **most important** part of the application. Most federal funders and national foundations follow the NIH standard for Specific Aims pages, but some funders will have unique requirements. Always read the application guidance and speak to a program contact when guidance is unclear.

Multiple revisions are required and input from colleagues and team members can be helpful.

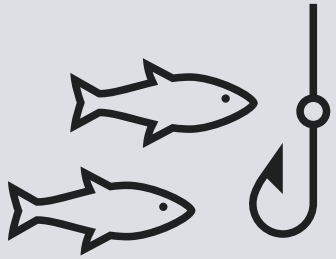
- Different sources describe *Specific Aims* as an overview of project, the template or master plan for the rest of your Research Plan, or central element of proposal.
- Due to its nature and significance, experts frequently recommend that this be the initial section that is generated (for an NIH proposal).
- It is often noted that producing a clear, precise, concise statement of specific aims is a challenge.

Sources: BioScience Writers (April 9, 2015); Dresbeck (2013); Giddings (n.d.); NIH (November 25, 2015); Univ. of Washington (n.d.)

FIRST PARAGRAPH: THE HOOK

Here, you want to *introduce your research subject* to reviewers and capture their attention.

- Hook
- What is known
- Gap in knowledge/Critical need

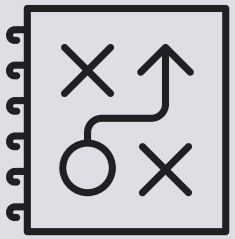


Kidney stones (KS) are painful mineral deposits that affect 1 in 11 people in the United States. Lifestyle factors, genetics, and diet may contribute to the development of KS. The most common type of KS is composed of calcium oxalate (CaOx) crystals which form when urine becomes supersaturated with these constituents. Meals containing high amounts of oxalate can increase urinary oxalate excretion and promote crystal formation. Accumulation of crystals within the kidney can lead to stone formation. Unfortunately, treatment options to prevent stone formation/recurrence are limited, and this contributes to increased healthcare costs and diminished quality of life.

THE AIMS: THEN

Briefly describe each of the aims. Some PIs prefer a simple, single-sentence explanation, and others go into more detail.

If you prefer the paragraph approach, address the **hypothesis** as appropriate, **experimental approach**, and the **expected outcome or impact**.



Aim 1: Test the hypothesis that oxalate stimulates reverse electron transport (RET) through mitochondrial complex I in monocytes from healthy subjects.

- Healthy subjects will consume a previously optimized low oxalate or oxalate-enriched controlled diet over 14 days. A novel approach to quantify urinary nanocrystals will be evaluated using NanoSight technology.
- Monocyte cellular energetics and mitochondrial complex activity will be evaluated using a Seahorse XF Analyzer.
- Flow cytometry and molecular biology approaches will be used to evaluate monocyte and macrophage subtype characteristics by RNA sequencing, RET, mitochondrial properties, oxidative stress, synthesis of inflammatory cytokine/chemokine levels, and macrophage phagocytosis.

Aim 2: Test the hypothesis that oxalate mediated crystalluria induces ROS and disrupts macrophage immunometabolism in rat kidneys.

- Sprague-Dawley rats (male and female) will be fed either low (1%) or high (5%) HLP for 28 days. Urinary crystals will be confirmed using NanoSight technology and crystal deposition will be assessed via histology.
- Flow cytometry and molecular biology approaches will be used to assess mitochondrial properties, oxidative stress, RET, and inflammatory proteins in monocyte or macrophage populations from the circulation and kidney. Additionally, the cellular transcriptome of macrophages isolated from the kidney will be examined.

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FINAL PARAGRAPH: THE BIG PICTURE

In the final paragraph, briefly summarize your project. Depending on the opportunity, address:

- Innovation
- Expected Outcomes
- Impact

These aims complement the ongoing experiments in my K01 award. Successful completion of these aims will reveal mechanisms regarding the role of dietary oxalate on crystalluria and monocyte and macrophage responses during CaOx KS disease. The impact of this research may identify: 1) tools to assess stone risk and immune status, and 2) therapeutic targets to alter monocyte and macrophage immunometabolism in KS disease. The data generated from this proposal will advance our knowledge about the role of dietary oxalate and innate immunity in KS disease and serve as a key foundation for subsequent R01 funding.

REVIEW THE SAMPLES PROVIDED

1. .Circle and label the components we highlighted in the last few slides:

- Hook
- What is known
- Gap in knowledge
- Critical need
- What do you want to do?
- Why are you doing it?
- How do you want to do it?
- Aims
- Innovation
- Expected Outcomes
- Impact

2.. Examine each component

- Is the problem clearly defined?
- Is the hypothesis clear?
- Are the aims brief and specific?

3. How could you use more explicit language or improve formatting and language to help reviewers find your key information?

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INCLUDING FIGURES

Specific Aims CAN include figures

Best to include clear and simple figures

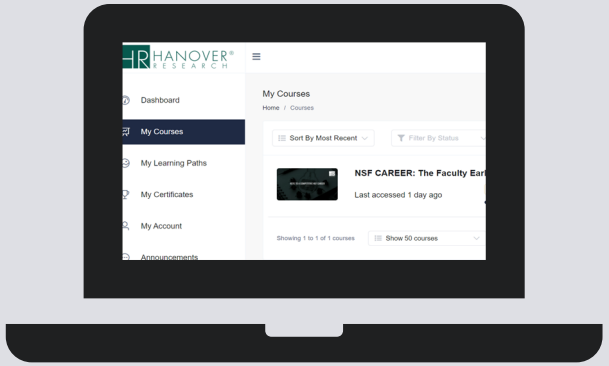
A model showing your aims and how they are connected to a central hypothesis.

A NOTE ON PERSUASIVE WR

- Much of what goes into creating a competitive Specific Aims page includes crucial elements of persuasive writing.
- You want to be strategic in your argument to the funder that you are worth funding.
- Giving reviewers reasons why is critical.
- We humans don't usually like to be told to accept something with no explanation– a study showed that people are more likely to agree with a request if you give them a reason why, even if it doesn't make sense.*

*Langer, E., Blank, A., & Chanowitz, B. (1978). The mindlessness of Ostensibly Thoughtful Action: The Role of "Placebic" Information in Interpersonal Interaction. Journal of Personality and Social Psychology, 36(6), 635-642.

GRANTS LEARNING CENTER



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QUESTIONS?

Hanover's **Grant Rant** podcast will supplement our webinar series, addressing outstanding questions from attendees.

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