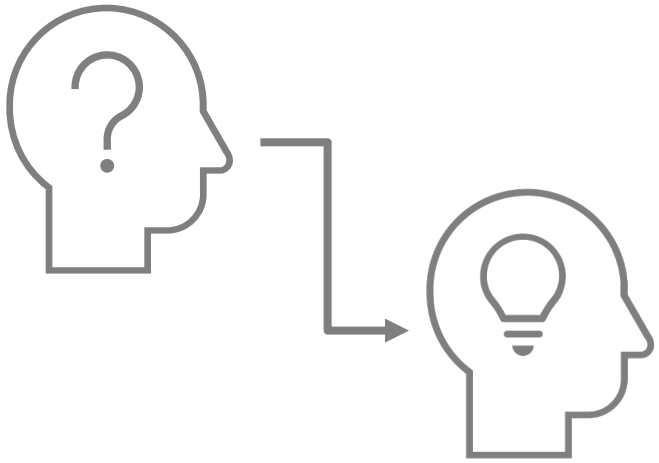
Say you have $1 million to give to someone's biological engineering project

What would you want to know from the person you're giving it to?

Research Proposals

20.109 Communication Workshop 6

Dr. Chiara Ricci-Tam



MIT BIOLOGICAL ENGINEERING
COMMUNICATION LAB

Helping you communicate effectively.
mitcommlab.mit.edu/be/

Today's agenda:

Key tips for research proposal presentations

Brief overview (more resources on wiki)

Work in teams to refine and get feedback on your chosen approach

Leave with a finalized research question/goal

Start to identify key experimental steps

Continue in lab section

Research proposal presentation: logistics

Team presentation of your idea
12min + Q/A

A few basic tactics will get you very far:

- Clear visuals with high signal to noise
- Strong title messages on slides
- Storytelling with clear messages and logic
- Hourglass structure to draw the audience in

A successful proposal must convince its audience that the proposed work is **significant** and **achievable**.

How might you get the audience on your side?

Include a slide that highlights the **impact** this work would have on society and science

> Why is this work important?
>
> Why should someone give you money to do this work?

Tell us the essential **why**, **what**, and **how**

Why Identify the gap/need or advance

What What is the clear idea you propose to try?
Impact?

How Key steps to accomplish goals ("aims")

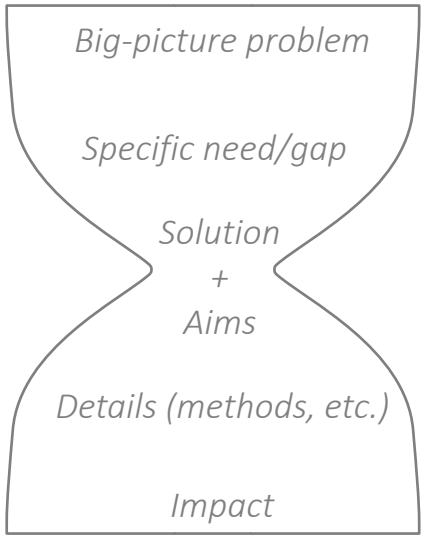
We care about the **methods**:
specify techniques, *in vitro*, *in vivo*, what system

Show us **expected data**
If things don't work, what will you do?
Have controls and work-arounds

Significant

Achievable

Use both slides & speech to convey main points



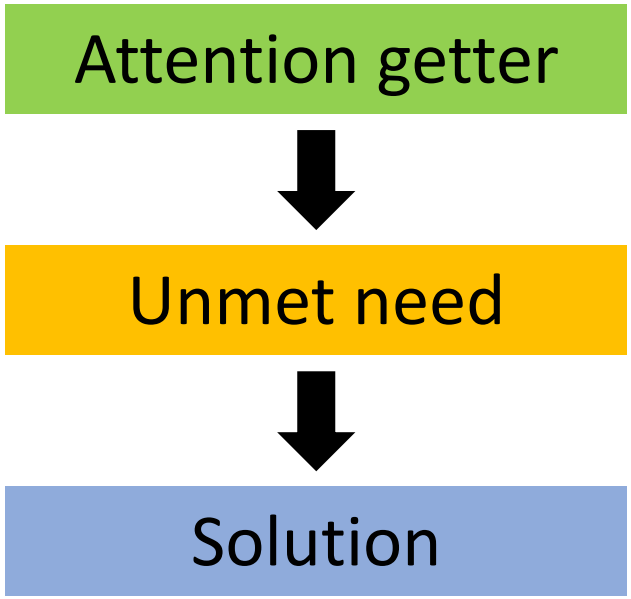
- Briefly introduce yourselves and the project
- Give minimally sufficient background to identify a clear **problem** and **approach**
- State the overall aim and goals ("specific aims")
- Describe each goal's **methods** and logic
- Show you've thought about predicted outcomes, alternate approaches, needed resources
- impact (scientific or societal) if all goes well

A compelling way to present your idea is to connect the need to the solution

Hook audience attention with a summary of your proposal and its value

Keep it **concise** (~30 seconds), use **plain language**, and **set the stage** for your presentation

Communicate “so what” message of why we should care



For example:

Attention getter

↓

Unmet need

↓

Solution

Human papillomavirus (HPV) infections cause nearly all cases of cervical cancer worldwide. While there are over 150 genotypes of HPV, only a handful of genotypes cause cervical cancer and current diagnostics cannot provide same day results for which genotype is present.

That's why I am building a rapid diagnostic to genotype HPV and screen for cancer risk using programmable toehold switches and CRISPR enzymes to detect specific DNA or RNA sequences.

For example:

Attention getter

↓

Unmet need

↓

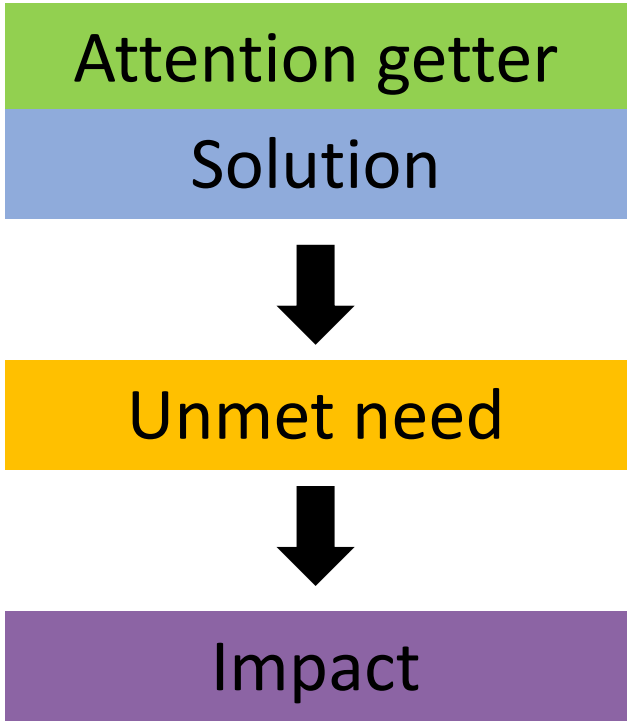
Solution

Human papillomavirus (HPV) infections cause nearly all cases of cervical cancer worldwide. While there are over 150 genotypes of HPV, only a handful of genotypes cause cervical cancer and current diagnostics cannot provide same day results for which genotype is present.

That's why I am building a rapid diagnostic to genotype HPV and screen for cancer risk using programmable toehold switches and CRISPR enzymes to detect specific DNA or RNA sequences.

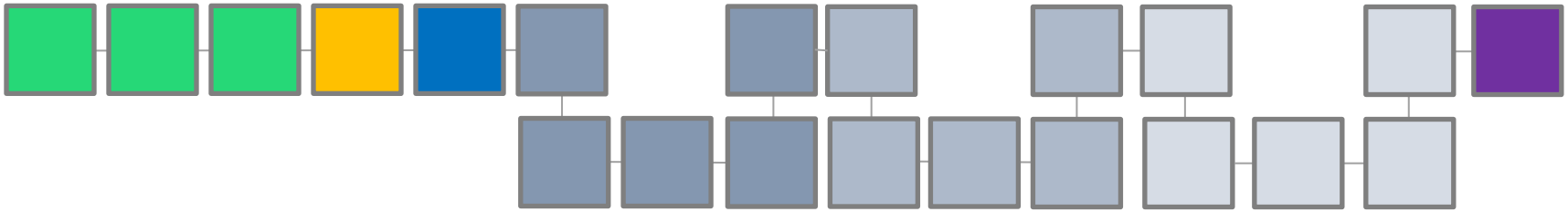
What is this potentially missing?

Put your punchline up front and end on impact



I am building a diagnostic to genotype HPV and screen for cancer risk by rapidly identifying the handful of HPV strains that cause cervical cancer out of over 150 genotypes that exist. This will allow us to provide a rapid, same-day diagnostic for Human Papillomavirus, an infection that cause nearly all cases of cervical cancer worldwide. Using this diagnostic we can accurately treat patients in a timely manner.

The introductory pitch can guide the storyline of your overall presentation



Human papillomavirus (HPV) infections cause nearly all cases of cervical cancer worldwide. While there are over 150 genotypes of HPV, only a handful of genotypes cause cervical cancer and current diagnostics cannot provide same day results for which genotype is present.

That's why I am building a rapid diagnostic to genotype HPV and screen for cancer risk using programmable toehold switches and CRISPR enzymes to detect specific DNA or RNA sequences.

Using this diagnostic we can accurately treat patients in a timely manner.

Tell us the essential **why**, **what**, and **how**

Why Identify the gap/need or advance

What What is the clear idea you propose to try?
Impact?

How Key steps to accomplish goals ("aims")

We care about the **methods**:
specify techniques, *in vitro*, *in vivo*, what system

Show us **expected data**
If things don't work, what will you do?
Have controls and work-arounds

Significant

Achievable

Example: successful NIH R03 research proposal (2-year project scope)

Title: Forward genetics-based discovery of *Histoplasma* virulence genes

Public Health Relevance Statement

Histoplasmosis, a respiratory and systemic disease caused by infections with the fungal pathogen, *Histoplasma capsulatum* afflicts thousands each year in the United States regardless of the host's immune status. The mechanisms that enable *Histoplasma* to subvert immune defenses are poorly understood. This proposal will identify new virulence factors through a genetics approach to improve our understanding of *Histoplasma* pathogenesis. Identification of these processes essential to virulence will aid in the development of improved therapeutic options to treat histoplasmosis.

https://www.niaid.nih.gov/grants-contracts/sample-applications#r03

Chad A. Rappleye, Ph.D., of Ohio State University

Example: successful NIH R03 research proposal (2-year project scope)

Title: Forward genetics-based discovery of *Histoplasma* virulence genes

Abstract, excerpt:

"... In this proposal, we will use a forward genetics approach to discover the virulence factors that enable *Histoplasma* to subvert the defenses of the macrophage, *Histoplasma*'s primary host cell. Random mutants of *Histoplasma* yeasts will be created using insertional mutagenesis. Mutants will be screened for decreased virulence in macrophages using.... Mutants will be classified according to...The virulence genes represented by each attenuated mutant will be identified by mapping of the mutation. The final collection of virulence-defective mutants will be ranked according to....These rankings will be used to prioritize further characterization of the discovered virulence factors in future studies to define their roles in facilitating *Histoplasma* survival and growth in host macrophages."

https://www.niaid.nih.gov/grants-contracts/sample-applications#r03

Chad A. Rappleye, Ph.D., of Ohio State University

ACTIVITY – 25 minutes

Finalize your research question / goal

Define problem *5min*

Define solution *10min*

Describe goal and how it advances field *15min*

What is the clear idea you propose to try?
Impact?

As you revise your approach, consider:

- what problem / unmet need is being addressed?
- how does your solution incorporate both biology and engineering?
- how will it advance the field / build on what is already known?

Example: successful NIH R03 research proposal (2-year project scope)

Title: Forward genetics-based discovery of *Histoplasma* virulence genes

Specific Aims, excerpt:

Aim 1: Screen *Histoplasma* T-DNA insertion mutants for attenuated virulence in macrophages.

- Aim 1A. Generate a library of T-DNA insertion mutants in Histoplasma yeast.
- Aim 1B. Identification of mutants deficient in survival and replication within macrophages.

Aim 2: Determine the identify of genes required for *Histoplasma* virulence in macrophages.

- Aim 2A. Map the disrupted loci in attenuated mutants.
- Aim 2B. Classify and prioritize virulence mutants.

https://www.niaid.nih.gov/grants-contracts/sample-applications#r03

Chad A. Rappleye, Ph.D., of Ohio State University

ACTIVITY – 5 minutes

Begin brainstorming experiments/steps needed to accomplish your ideas

What critical experiments are needed for your solution?

What statements (claims) must be true for your solution to work?

Reviewing this list, you can then identify the critical questions that will need to be answered to provide evidence for those claims

Appendix

Additional tips and resources

Remember the fundamental tips for good slide design

- **Maximize signal to noise**
- One message per slide
- Slide title is a message
- Use visuals/schematics when you can
- Minimally sufficient information

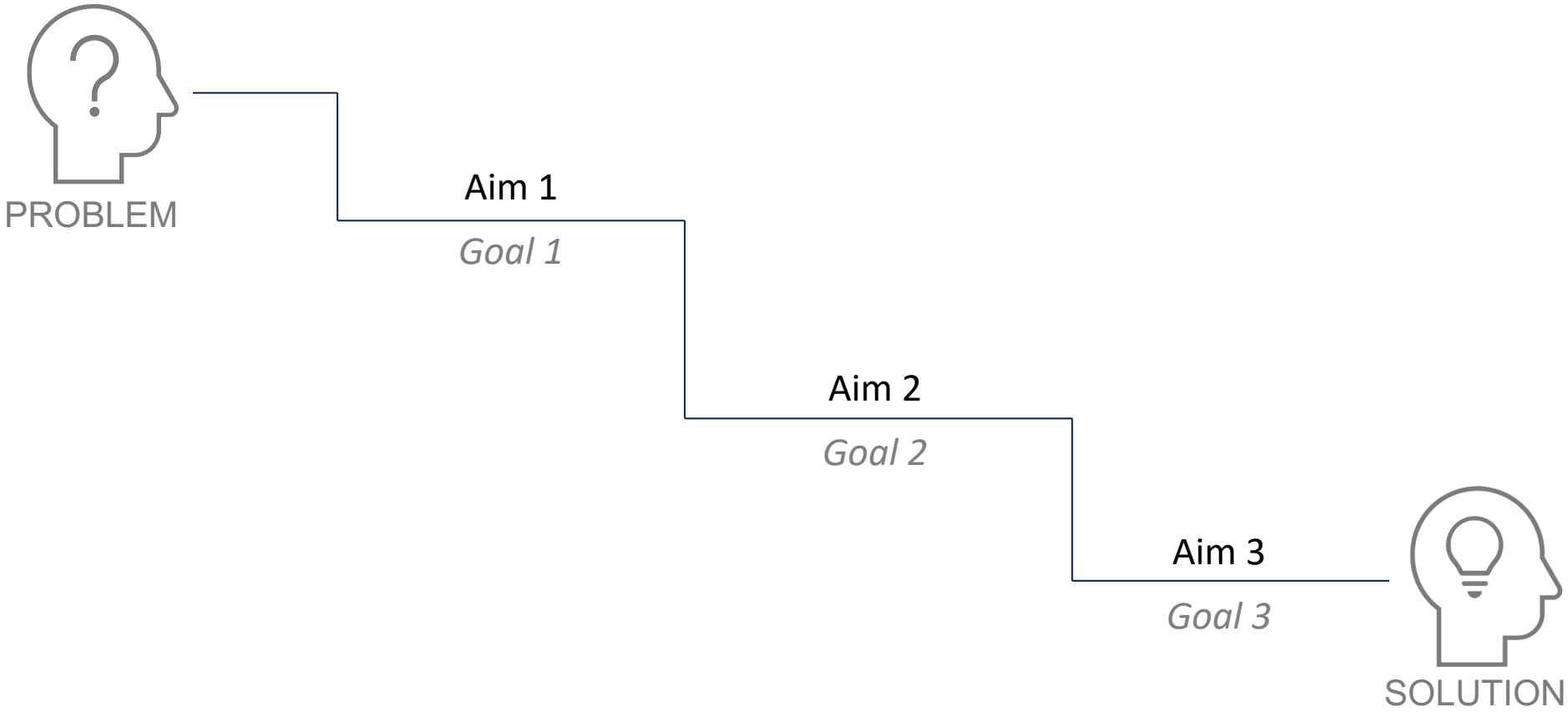
Adapt to presenting as a team

- Decide who will say what
- Can announce organization + transitions

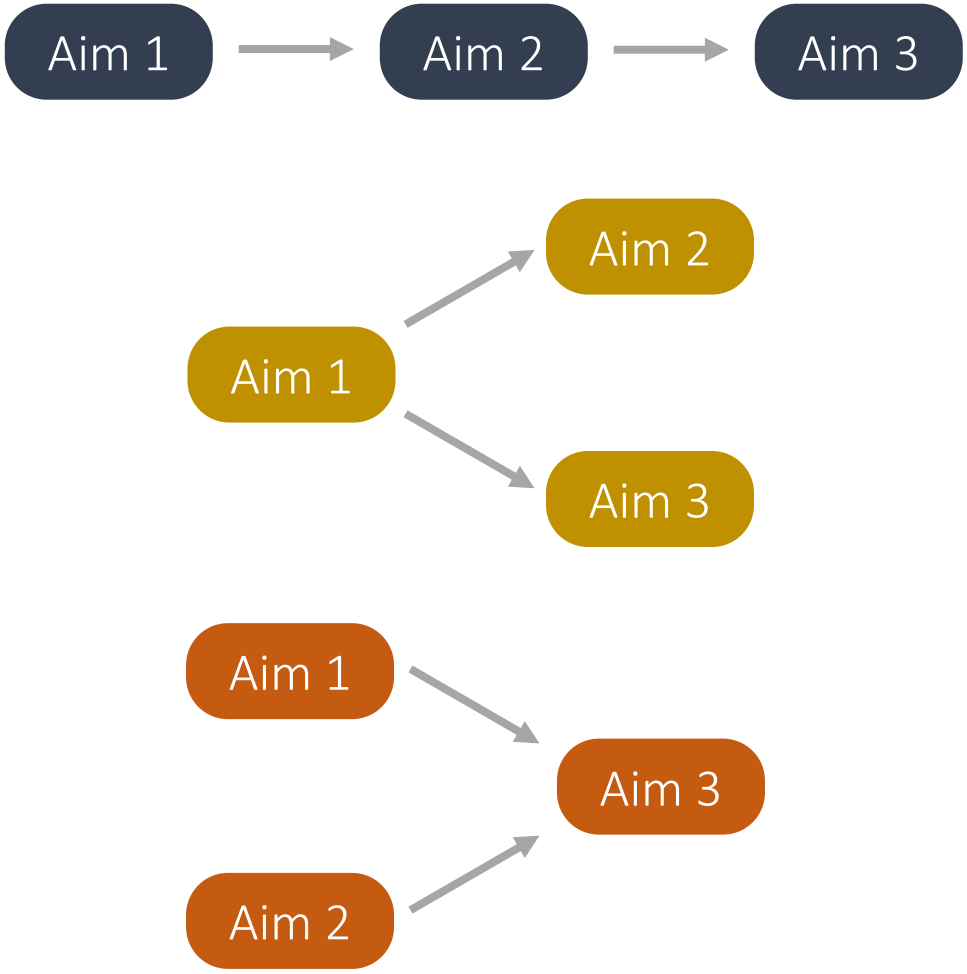
  "I'll introduce our Question and Aims, and Chiara will talk about the Methods we'll use…"
- Stay visually quiet when you're not speaking
- Q&A: Share answers
- If worked on parts separately, do a final revision to ensure consistency between your individual sections

PRACTICE PRACTICE PRACTICE

Your specific aims should address critical steps needed to achieve your larger project



Your aims may be connected to each other in different ways



Your aims *can* be interdependent, but only if you can demonstrate that they will not fail

"What would it look like for this Aim to be successful?"

Aim titles should be concrete

Each aim should have a clear goal that is easily defined.

Use wording that assures success.

Use verbs that convey a clear endpoint.

Specific: isolate, determine, identify, define, discover, elucidate, ascertain
Vague: examine, explore, evaluate, study, investigate

Focus on the outcome rather than the method.

Vague (for hypothesis-driven aims): perform, measure, characterize, describe, compare, catalog, correlate

Use parallel grammatical structure.

Make the aim statements clear and concise.

https://www3.mdanderson.org/library/education/pdf/crafting-strong-specific-aims-handout.pdf

“What would it look like for this Aim to be successful?”

Aim titles should be concrete

Each aim should have a clear goal that is easily defined.

The feasibility of each aim should be justified.

Make it clear **how** and **which** data would be gathered, and how they would be **interpreted**.

For each **aim**, we want to know:

a) Experimental Rationale
b) Experimental Plan
c) Expected Results
d) Potential Challenges and Solutions

- Why you are doing this
- What you will do
- What you will learn
- What happens if this doesn't work as expected
- How this will further your project

Explain **why** you picked a specific approach

a) Experimental Rationale
b) Experimental Plan
c) Expected Results
d) Potential Challenges and Solutions

Why did you choose this approach and not another one to answer your question?

What evidence exists that supports its feasibility?

Tell us what you plan to do

a) Experimental Rationale
b) Experimental Plan
c) Expected Results
d) Potential Challenges and Solutions

Outline major methods, experiments, tests.

How do you obtain the data needed to dis/prove your hypothesis?

Tell us what you expect to see

a) Experimental Rationale
b) Experimental Plan
c) Expected Results
d) Potential Challenges and Solutions

Use schematics and other visuals to help us imagine outcomes.

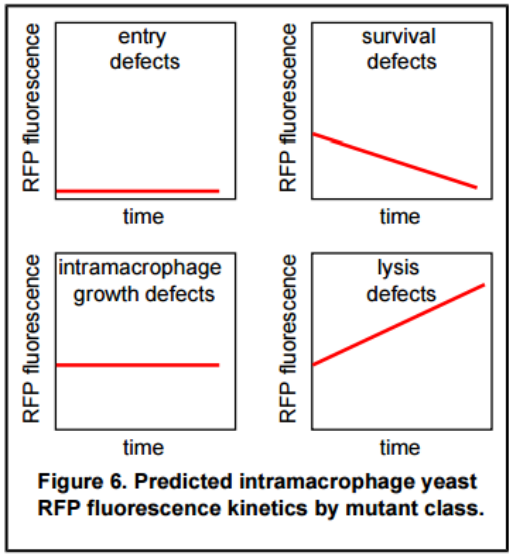


Figure 6. Predicted intramacrophage yeast RFP fluorescence kinetics by mutant class.

Tell us what you will do if you don't get expected results

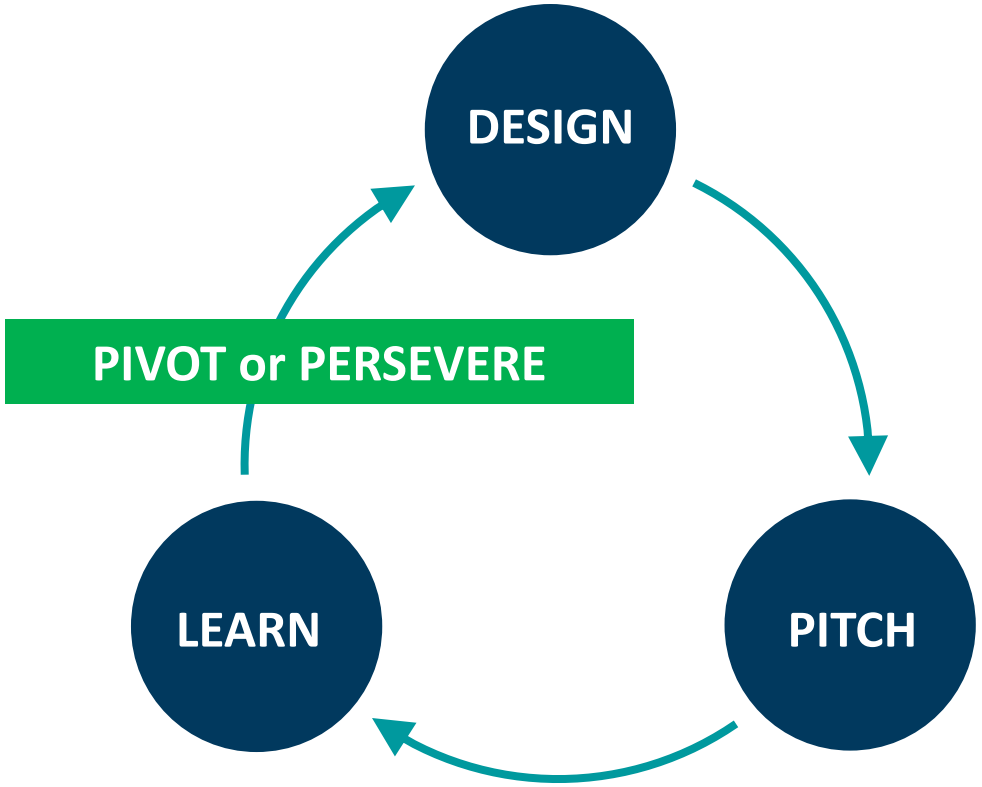
a) Experimental Rationale
b) Experimental Plan
c) Expected Results
d) Potential Challenges and Solutions

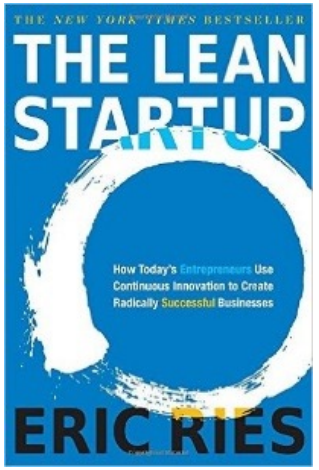
Every method has shortcomings. Reviewers will predict many: anticipate their concerns.

Suggest alternative approaches.

Demonstrate both the robustness of your plan, and the depth of your knowledge of the field.

Going through feedback loops improves your design





Stay **open to feedback**—it is how you learn and grow!

Be nimble and **pivot** or build support for your **intuition**

Example: successful NIH R03 research proposal (2-year project scope)

Title: In vitro source of human extracellular matrix to support tissue repair and regeneration

Public Health Relevance Statement

Tissue and organ failure from diseases or trauma pose substantial health issues and expense to society, and there exists an acute shortage of transplantable organs and available tissue material for organ repair. Here, we propose to develop therapeutic human tissue material from lab-grown three-dimensional (3D) human tissues that is unique from other existing laboratory methods of culturing 3D human tissues, because our system is superior in mimicking cells in healthy human tissues. We believe by better mimicking healthy tissue conditions, we can generate 3D tissues with tissue material that have enhanced efficacy for tissue repair.

https://reporter.nih.gov/project-details/9929626

Also see "Other resources" slide for more links to NIH grant examples

Example: successful NIH R03 research proposal (2-year project scope)

Title: In vitro source of human extracellular matrix to support tissue repair and regeneration

Abstract, excerpt:

"... In this R03, we will utilize our patented micro-mold technology to generate stable 3D scaffold-free human cardiac tissue with human cardiac fibroblasts, cardiomyocytes and cardiac microvascular endothelial cells and evaluate three decellularized protocols to generate optimal quality decellularized ECM in Aim 1. We will then develop, optimize and execute three complementary methods to evaluate protein composition between the different ECM, as well as to examine the quantity and injectability of the ECM in Aim 2. We envision these technologies can have other bioengineering applications to enhance human biomimicry, including microfluidic devices to study disease progression such as tumor invasion."

https://reporter.nih.gov/project-details/9929626

Also see "Other resources" slide for more links to NIH grant examples

Example: successful NIH R03 research proposal (2-year project scope)

Title: Deciphering the effect of human microbiota on Alzheimer's disease using C. elegans models of protein conformational diseases

Public Health Relevance Statement

There is no cure or effective treatment for Alzheimer's disease, primarily because its contributing factors have yet to be fully identified. Recently, it was discovered that bacteria may play a role in the onset and progression of Alzheimer's disease and other protein conformational diseases, suggesting a direct influence on host proteostasis. We propose to decipher the role of the human microbiome on host proteostasis using C. elegans models of protein conformational diseases.

https://reporter.nih.gov/project-details/10341111

Also see "Other resources" slide for more links to NIH grant examples

Example: successful NIH R03 research proposal (2-year project scope)

Title: Deciphering the effect of human microbiota on Alzheimer's disease using C. elegans models of protein conformational diseases

Abstract, excerpt:

> "... we propose to further investigate the effect of bacteria on proteostasis using C. elegans models by: (I) determining the impact of intestinal colonization by all human microbiome bacterial isolates on host proteostasis and pathogenesis of AD, and (II) observing the effect of exogenous and endogenous butyrate on bacteria that enhance protein aggregation. Deciphering the effect that bacteria have on host proteostasis will ultimately provide a basis for the development of prophylactics, therapeutics, and biomarkers."

https://reporter.nih.gov/project-details/10341111

Also see "Other resources" slide for more links to NIH grant examples

Example: successful NIH R01 research proposal (4-year project scope)

Title: Synthetic toolkit for precision gene expression control and signal processing in mammalian cells

Public Health Relevance Statement

Methods that allow scientists to turn on and off genes in living cells are fundamental to biomedical research, and in particular to advancing the development of new therapies for many diseases, such as cancer and autoimmunity. However, tools for controlling gene expression in mammalian cells have significant limitations: they do not allow multiple genes to be controlled at once, cannot be triggered by many chemical and biological stimuli of interest, and do not provide precise control over how genes are expressed. To address this, we will develop a new toolkit that enables scientists to flexibly and rapidly create gene expression programs to precisely control mammalian cell behavior in response to diverse chemical and biological stimuli.

https://reporter.nih.gov/project-details/10584605

Also see "Other resources" slide for more links to NIH grant examples

Example: successful NIH R01 research proposal (4-year project scope)

Title: Synthetic toolkit for precision gene expression control and signal processing in mammalian cells

Abstract, excerpt:

"... Here we will develop and characterize mammalian self-assembling [synthetic transcription factors] that have superior properties for installation into human cells relative to existing tools. We will use these tools to develop three classes of gene expression controllers...(1) Inducible controllers regulated by orthogonal, FDA-approved drugs. (2) Cell-autonomous controllers that sense and process biological stimuli....(3) Signal integration controllers that can perceive and integrate multiple biological signals...We anticipate that this toolkit will be broadly used by researchers to enable precision gene expression control across mammalian systems, including in biomedical applications of synthetic biology, cell reprogramming, and cell-based therapeutics."

https://reporter.nih.gov/project-details/10584605

Also see "Other resources" slide for more links to NIH grant examples

Other resources

- From Prof. Jen Heemstra's blog: Research ideas, part 1: It's not magic (also parts 2-4 on the side)
- NIH Small Grant Program (R03): appropriate scale
  - Example applications via NIH NIAID (includes alternate approaches, summary statement of grant reviewer comments)
  - Database of funded NIH grants (lists abstract and public health relevance statements; can search by keywords, grant categories, etc.)
- "NIH Grant Applications: The Anatomy of a Specific Aims Page"
- "Introduction to the Specific Aims Page of a Grant Proposal"
- BE Research Guide: (email Howard Silver hsilver with questions or suggestions!)
- Previous workshops on wiki, BECL website

Be sure your presentation includes:

- ❑ Sufficient background to orient the audience to the problem and current state of the field
- ❑ A strong problem statement/knowledge gap
- ❑ A clear proposal statement/hypothesis
- ❑ Clear aims/goals that follow a logic leading to the end goal
- ❑ Succinct methods highlighting what you will do
- ❑ Alternate approaches
- ❑ Strong impact statement

Your slides and presentation should:

- ❑ Convey a single message per slide
- ❑ Have titles that are messages
- ❑ Only contain relevant material (reduce noise)
- ❑ Include schematics to help your audience
- ❑ Be organized to share the speaking between presenters