

M3D3:

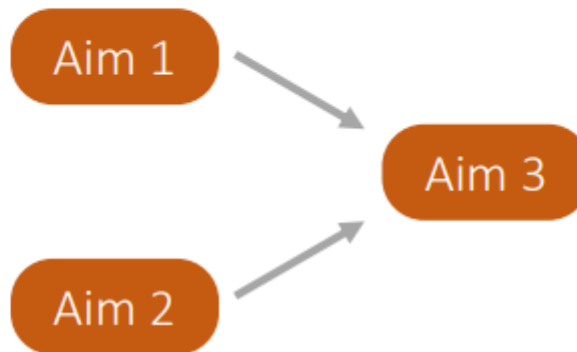
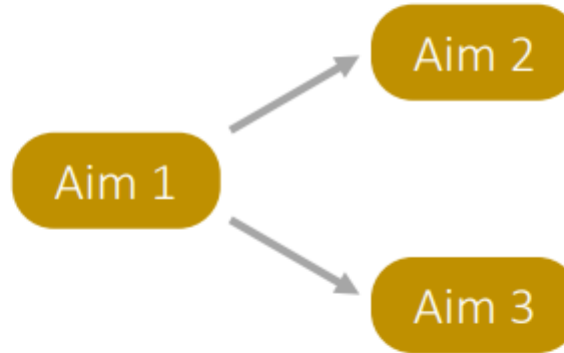
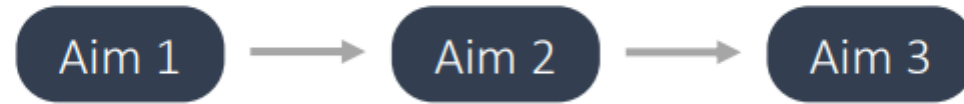
Develop ideas for Research Proposal presentation

1. Draft aims for your Research proposal
2. Brainstorm alternative approaches for the key methods in your aims

How to organize and present your proposal

- Research goal = **what you intend to accomplish**
 - What problem do you intend to solve?
 - What tool do you intend to engineer?
- Specific aim = **objective that will allow you to progress toward reaching your research goal**
 - Develop 2-3 specific aims that are complementary, but independent
 - Should provide step-by-step progression to solution / tool
 - Ensure that something is gained even if aim doesn't yield expected outcome

Your aims may be connected to each other in different ways



Example: New antifungal treatment #1

Research Goal: To engineer a new topical ointment for the treatment of *Fakeomyces notrealia*

Aim 1: Test the efficacy of rationally designed compound X on fungal culture survival

Aim 2: Test efficacy of rationally designed compound X in an organ-on-a-chip model

Aim 3: Test compound X in an animal model

Example: New antifungal treatment #2

Research Goal: To engineer a new topical ointment for the treatment of *Fusarium solani*

Aim 1: Test the efficacy of rationally designed compound X on fungal culture survival

Aim 2: Develop method to coat nanoparticles with compound X

Aim 3: Test compound X in an animal model

EXAMPLE FROM NIH FUNDED PROPOSAL:

- Research goal: 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
- 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.

Helpful places to start!

- Review the following resources for constructing specific aims:

<https://www.niaid.nih.gov/grants-contracts/draft-specific-aims>

<https://morganonscience.com/communication/how-to-write-a-specific-aim/>

<https://writingcenter.catalyst.harvard.edu/write-your-specific-aims-page>

For today...

- Draft specific aims and research which methods will enable you to address the aims
- Identify alternative approaches / methods

For M3D4...

- Prepare a brief write-up of your proposal

EXAMPLE FROM REAL LIFE:

- Research goal: Find my wedding ring that was dropped of my back patio using the help of my husband, which will ensure that I remain happily married
- Specific aims:
 1. Recruit husband to help in search
 2. Retrieve flashlight for better visibility
 3. Find wedding ring!
 - a. Search stone patio in grid-by-grid pattern
 - b. Search grass / hay around patio by lifting and shaking



Aims should be independent

- Research goal: Find my wedding ring that was dropped of my back patio using the help of my husband, which will ensure that I remain happily married

- Specific aims:

1. Recruit husband to help in search
2. Retrieve flashlight for better visibility
3. Find wedding ring!
 - a. Search stone patio in grid-by-grid pattern
 - b. Search grass / hay around patio by lifting and shaking

Retrieving a flashlight is not dependent on recruiting my husband as both can be accomplished independently to find the wedding ring

Alternatively...

1. Recruit husband to help search
2. Tell husband to retrieve flashlight

Here, retrieving a flashlight is dependent on recruiting my husband

Methods should be based on literature

- Research goal: Find my wedding ring that was dropped of my back patio using the help of my husband, which will ensure that I remain happily married

- Specific aims.

1. Recruit husband to help in search
2. Retrieve flashlight for better visibility
3. Find wedding ring!
 - a. Search stone patio in grid-by-grid pattern
 - b. Search grass / hay around patio by lifting and shaking

In previously reported research, my husband was recruited to find my engagement ring after I dropped it down the drain of the bathroom sink

Husband is a valid method because...

1. previously found a similar, but closely related, item
2. previously used techniques that can be applied to a new, but closely related, aim

Alternative approaches needed for key aims

- Research goal: Find my wedding ring that was dropped of my back patio using the help of my husband, which will ensure that I remain happily married

- Specific aims:

1. Recruit husband to help in search
2. Retrieve flashlight for better visibility
3. Find wedding ring!
 - a. Search stone patio in grid-by-grid pattern
 - b. Search grass / hay around patio by lifting and shaking

Because I am unable to see in the dark, having a light source is a critical step in achieving my research goal

Another approach would be to wait until day light to find my wedding ring or to use another light source

Experiments should be explained

- Research goal: Find my wedding ring that was dropped of my back patio using the help of my husband, which will ensure that I remain happily married

- Specific aims:

1. Recruit husband to help in search
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3. Find wedding ring!
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How will the proposed experiment(s) be used to accomplish the aim?

For Aim 2b...

Because my wedding ring is heavier than hay, I lifted small scoops of the hay and applied shaking to allow heavier objects to drop to the ground

