M3D3:
Develop ideas for Research Proposal presentation

1. Draft aims that state the intended outcomes of your proposal

2. Brainstorm alternative approaches to key methods proposed in your aims

LOOK THE END IS NEAR

makeameme.org

12/1/22

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

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