

# The Aims page: Paragraph 2

# The 2<sup>nd</sup> paragraph tells the reader what is going to be done by whom

1. Long-term goal
2. Objective for this proposal
3. Central hypothesis
4. Rationale
5. Competitive edge

# 1. Long-term goal:

Where will this research go in 10-20 years

“Our long-term goal is to elucidate the biological mechanisms of viral attenuation, fitness, and adaptation.”

- Long-term goal helps the reader understand the bigger picture of your work
- Can be different from or a subset of your personal long-term goals

## 2. Objective for this proposal: What exactly will be done in this project

“The objective for this proposal is to investigate viral attenuation and recovery in bacteriophage T7.”

- This needs to be realistic for the scope and duration of the project

### 3. Central hypothesis:

What is the overall idea/guiding principle?

“Our central hypothesis is that engineered transcriptional and translational de-optimization yields reliable, evolutionarily stable attenuation of viruses.”

- A good central hypothesis demonstrates that you have a reasonable angle of attack
- Scientists like hypotheses

## 4. Rationale:

# Why is your approach right for the problem?

“T7 provides a unique model system with which to probe generic principles of viral attenuation, because its genetic regulatory circuitry is well understood and a detailed, mechanistic computer model exists to interpret and predict transcription and [...] translation.”

- A good rationale distinguishes your project from others that might try to solve the same question

## 5. Competitive edge:

# Why are you uniquely qualified/positioned?

“We have assembled an experienced team of investigators to pursue this project ...”

- Many projects win on the competitive edge
- Competitive edge can comprise:
  - Existing expertise
  - Specific construct or measurement platform
  - Unique field site
  - Unique, established study system

# The actual Specific Aims



# Each Aim consists of Title, Hypothesis, Body

## **Aim 1: Assess fitness effects and recovery suppression in different genetic recodings of bacteriophage T7**

*Hypothesis: Various regulatory modifications [...] reduce fitness to varying degrees; the more that fitness reduction is caused by genetically irreversible modifications, the more resistant these recodings are to recovery.*

Our prior work has shown that fitness in bacteriophage T7 can be reduced by several engineered designs, and that fitness recovery is often suppressed during even 1000 generations of subsequent adaptation. Here, we will extend those approaches, measuring the fitness effects of non-preferred codons throughout the genome ...

# Use conceptual Aims, not descriptive ones

- Conceptual:  
“Aim 2: Dissect molecular mechanisms of fitness reduction and recovery”
- Descriptive:  
“Aim 2: Measure RNA and protein abundances in recoded T7 via RNAseq and MassSpec proteomics”