1.0 Why write a grant proposal?
Prior to performing research, an investigator must secure funding. Funding covers the cost of research associates (postdocs, graduate students, and undergraduate students), supplies, and all other necessary items. Generally, funding is secured through a grant application to one of many government agencies, such as the National Institutes of Health (NIH), National Science Foundation (NSF), or Department of Energy (DOE). Because funding has become increasingly competitive to secure, it is critical to learn excellent grantsmanship, which is the art of writing a grant. For new investigators, grantsmanship is often a foreign process, so practice is important.

1.1 URA proposal
The URA application process will teach you to write a one-page overview of an NIH-style grant. This overview is called an “aims” page. The aims page is the first page of an NIH grant and reviewers rely heavily on this page to decide if your project should be funded. Briefly, the aims page begins by outlining the current knowledge in a scientific area and an important “gap in knowledge” that if filled will significantly propel the scientific area. Next, the aims page succinctly states the proposed work and a central hypothesis with a rationale. Last, a list of specific aims is stated that directly test the central hypothesis.

By writing an aims page you will have created a clear roadmap for writing the rest of the grant. Although as an undergraduate you will not write a full grant proposal, writing an aims page will allow you to crystalize your research hypothesis, research goals, and construct a clear roadmap for performing research in the lab.

2.0 Brief guide for writing an aims page
Below you will find a short tutorial on writing each section of an aims page. You will be given more details at the workshop, but you should come with questions in order to make your aims page excellent and ready to be funded. Note that misuse of the sections (e.g., not writing an appropriate hypothesis, exceeding the sentence limits) is a common reason for proposals not being funded.

2.1 Lead first with an introductory sentence (1-2 sentences):
The aims page must begin with a sentence that gives a concise overview of the molecule/process/synthesis/reaction that you will be studying. This sentence must also give the reviewer an idea of why your project is important. Remember, you don’t get a second chance to leave a first impression!

Example: Superoxide Dismutase-1 (SOD1) is a homodimeric radical-scavenging enzyme that plays a central role in the protection of neurons and other tissues against oxidative stress.

2.2 Describe the current knowledge of the field related to your aims (4 sentences):
The current knowledge section must be brief but still provide enough key background information to set up the description of what is not known in your research area (i.e. gap in knowledge, section 2.3). Here you should describe state-of-the-art knowledge and/or older knowledge that is germane to your research proposal. This must be from accepted concepts based on published data. Generally, there are no citations, although citations are permissible if needed to give credibility to the idea.
Example: SOD1 mediates its tissue-protective effect by converting potentially toxic superoxides to molecular oxygen and hydrogen peroxide. Importantly, defects in SOD1 activity are known to underlie the neurodegeneration that causes amyotrophic lateral sclerosis (ALS). Published work has shown that defective SOD1 activity in a subset of ALS patients (comprising 22% of ALS patients overall) can be traced to increased acetylation of SOD1 at Lysine 120. Our recent data suggest that this acetylation blocks the dimerization of SOD1, which is necessary for its radical-scavenging activity.

2.3 Define the gap in current knowledge or unmet need (limit of 4 sentences):
The gap in current knowledge clearly defines what is not known in a research area. The gap in knowledge must not be vague and must be important enough that by filling in the gap you will significantly propel your research field forward. In addition, there must be an urgent need to fill the gap. Typically, after defining the knowledge gap, there is a bridging sentence that states why filling in this knowledge gap is important.

Example: While it is known that acetylation of SOD1 is upregulated in ALS and that acetylation inhibits its activity, what is not clear is how SOD1 acetylation is regulated. Specifically, the deacetylase enzyme that governs SOD1 acetylation is unknown. Furthermore, the environmental stimuli (e.g., metabolic stress) that modulate SOD1 acetylation are poorly understood. Lack of such knowledge is an important problem, because, without it, acquiring the ability to pharmacologically target SOD1 in ALS patients is highly unlikely.

2.4 State the long-term goal (2 sentences):
A long-term goal should summarize your research goals over the next 10-15 years. Therefore, you must give the big-picture here.

Example: Our long-term goal is to develop strategies to manipulate SOD1 for therapeutic purposes in neurodegenerative disease.

2.5 State the proposal’s overall objective (2 sentences):
Here you state the proposal’s overall objective. Generally, it is important to add a sentence indicating how the proposal’s objective is linked to your long-term goal.

Example: The objective of this proposal, which is the next step in the pursuit of our long-term goal, is to determine how acetylation of SOD1 is regulated.

2.6 State the central hypothesis (2 sentences) and its rationale (3 sentences):
The central hypothesis is often the next most important point after the gap in knowledge. It is critical to have a well written hypothesis that can be tested through experiment or theory. Most important, the hypothesis must stem from a solid and logical rationale. This means that you must provide an explanation of how your central hypothesis was formulated.

Example: Our central hypothesis is that increased acetylation of SOD1 at Lysine 120 in ALS is induced by glucose deprivation, which leads to the aberrant loss of activity of an unidentified deacetylase. This hypothesis has been formulated on the basis of our preliminary data acquired by analyzing tissue homogenates from ALS and healthy patient samples. The rationale for the
proposed research is that, once it is known how acetylation of Lysine 120 is regulated, SOD1 activity can likely be modulated pharmacologically. This would result in new and innovative approaches for the prevention and treatment of ALS.

2.7 State the specific aims (2 sentences per aim), starting with a lead-in sentence:
Provide a single sentence that gives enough, but not overwhelming, detail of what you specifically aim to do. Aims are generally given in bold print. Each aim relates back to testing your central hypothesis. After the specific aim sentence, you should provide one more sentences that provide a slightly more detailed working hypothesis about why the specific aim is being pursued.

Example: We plan to test our central hypothesis and thereby accomplish the objective of this proposal by pursuing the following two specific aims:

1. **Identify the deacetylase that governs SOD1 acetylation.**
   Based on preliminary data referred to above, our working hypothesis is that a metabolically regulated deacetylase, which is inactivated in ALS tissue, deacetylates SOD1 at Lysine 120.

2. **Determine how SOD1 acetylation is modulated by different stimuli.**
   We postulate, based on our preliminary data, that SOD1 acetylation is triggered by glucose deprivation stress, which is commonly observed in ALS-affected brain tissue.

2.8 State the expected outcomes (limit of 4 sentences):
This set of sentences spells out how your project will advance your research field. This will be somewhat redundant what you have already written. However, this paragraph allows you to describe the benefit to your research filed in a little more detail.

Example: The work proposed in aims 1 and 2 is expected to characterize the cellular and environmental factors that govern SOD1 acetylation and thereby account for the loss of SOD1 activity in ALS patients. These results are expected to have a positive impact because the identified components are very likely to be new targets for therapeutic interventions in ALS. In addition, the completion of these aims will significantly advance the fields of acetylation biology and neurodegenerative disease.

2.9 Ancillary points
**Remember, the most important part of a grant is the idea/hypothesis.** No amount of grantsmanship will make up for a poor research idea. However, poor grantsmanship can sink a great idea! So make sure to start with a great idea.

2.9.1 Figures
*You are encouraged, but not required, to make and refer to one figure in your aims page.* The key is to make sure figures are concise, easily understandable, and not vague. Every inch of space on an NIH aim page is critical, so a figure must significantly enhance understanding or portray an idea.

2.9.2 References
Citations are generally not found in an aims page, but they are permissible if needed. They should be embedded in your text.
2.9.3 How long can the aims page be?
*You are limited to one page! Use it wisely.* Below you will see an example of the final product.

3.0 How should I save my file?
Save the file as a .pdf for submission with filename: YourName URARenewal Term Year.pdf
Term should be F, W, S for Fall, Winter, Spring/Summer, and you can just put the last two digits for the year, like F19.pdf

You should be able to fill one page, but do not exceed one page. Keep the formatting, font, and text size from this template. You can, but you do not need to include references in this proposal.

4.0 URA expectations
After you have written a rough draft of your aims page and attended the URA workshop, it is expected that you will get help from your mentor to refine your proposal. Without the help of your mentor it is unlikely that your URA proposal will achieve a score high enough to be funded.

If your proposal is funded, you are committing to ~10 hrs of research per week during the semester and you will present your research at the Student Research Conference (SRC).

Some of the URA awards are funded from the college of physical and mathematical sciences (CPMS) as well as other private donors. If your URA proposal is funded you may be asked by CPMS or the chemistry and biochemistry department to write a short letter describing your mentored experience that will be shared with donors. If you are asked you are required to write this short personal letter in a timely fashion.

4.1 How is the URA proposal reviewed?
A review panel of faculty from the Department of Chemistry and Biochemistry will score each URA proposal based on the following criteria:

- Logical flow leading to hypothesis
- How well the specific aims address the hypothesis
- Overall quality

4.2 When will you find out if your proposal is funded?
If your proposal is funded, you will receive an email approximately one week after the proposal submission deadline.
Mechanism of SOD1 Regulation in ALS

Superoxide Dismutase-1 (SOD1) is a homodimeric radical-scavenging enzyme that plays a central role in the protection of neurons and other tissues against oxidative stress. SOD1 mediates its tissue-protective effect by converting potentially toxic superoxides to molecular oxygen and hydrogen peroxide. Importantly, defects in SOD1 activity are known to underlie the neurodegeneration that causes amyotrophic lateral sclerosis (ALS). Published work has shown that defective SOD1 activity in a subset of ALS patients (comprising 22% of ALS patients overall) can be traced to increased acetylation of SOD1 at Lysine 120. Our recent data suggest that this acetylation blocks the dimerization of SOD1, which is necessary for its radical-scavenging activity.

While it is known that acetylation of SOD1 is upregulated in ALS and that acetylation inhibits its activity, what is not clear is how SOD1 acetylation is regulated. Specifically, the deacetylase enzyme that governs SOD1 acetylation is unknown. Furthermore, the environmental stimuli (e.g., metabolic stress) that modulate SOD1 acetylation are poorly understood. Lack of such knowledge is an important problem, because, without it, acquiring the ability to pharmacologically target SOD1 in ALS patients is highly unlikely.

Our long-term goal is to develop strategies to manipulate SOD1 for therapeutic purposes in neurodegenerative disease. The objective of this proposal, which is the next step in the pursuit of our long-term goal, is to determine how acetylation of SOD1 is regulated. Our central hypothesis is that increased acetylation of SOD1 at Lysine 120 in ALS is induced by glucose deprivation, which leads to the loss of activity of an unidentified deacetylase. This hypothesis has been formulated on the basis of our preliminary data acquired by analyzing tissue homogenates from ALS and healthy patient samples. The rationale for the proposed research is that, once it is known how acetylation of Lysine 120 is regulated, SOD1 activity can likely be modulated pharmacologically. This would result in new and innovative approaches for the prevention and treatment of ALS.

We plan to test our central hypothesis and thereby accomplish the objective of this proposal by pursuing the following two specific aims:

1. **Identify the deacetylase that governs SOD1 acetylation.**
   Based on preliminary data referred to above, our working hypothesis is that a metabolically regulated deacetylase, which is inactivated in ALS tissue, deacetylates SOD1 at Lysine 120.

2. **Determine whether SOD1 acetylation is induced by glucose starvation.**
   We postulate, based on our preliminary data, that SOD1 acetylation is triggered by glucose deprivation stress, which is commonly observed in ALS-affected brain tissue.

The work proposed in aims 1 and 2 is expected to characterize the cellular and environmental factors that govern SOD1 acetylation and thereby account for the loss of SOD1 activity in ALS patients. These results are expected to have a positive impact because the identified components are very likely to be new targets for therapeutic interventions in ALS. In addition, the completion of these aims will significantly advance the fields of acetylation biology and neurodegenerative disease.
Template

Title:

Introductory sentence(s) (1-2 sentences):

Current knowledge (4 sentences):

Define the gap in current knowledge or unmet need (2 sentences):

Long-term goal (2 sentences):

Proposals overall objective (2 sentences):

Central hypothesis (2 sentences):

Rationale for hypothesis and proposed research (3 sentences):

We plan to test our central hypothesis and, thereby, accomplish the objective by pursuing two specific aims:

1. (2 sentence):

2. (2 sentence):

The expected outcomes, (significance and impact), of the specific aims are (limit of 4 sentences).