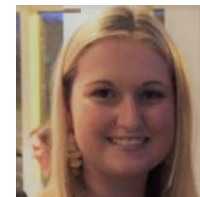


UNDERGRADUATE PERSPECTIVE : THE GRANT APPLICATION PROCESS



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SUMMATION

The requirement for monetary aid has been needed in scientific research since Galileo and prior. Grant writing is an art form that scientists use in order to move their research along, regardless of the size of the award. One of the largest struggles is the ability to write the technical piece, describing the research being performed, the need for money, and what it will be used for. Writing the piece in lay terminology can be one of the most challenging experiences new researchers face. I applied for a Ball State University internal grant through Sponsored Projects Administration office for funding to continue research in T-cell acute lymphoblastic leukemia. In this project, I analyze the process I went through, why I chose to write what I did, and what I would choose to do differently. My hope is that by explaining this process from an undergraduate perspective, others can learn from my challenges and experiences.

PROCESS ANALYSIS STATEMENT

In scientific research, as in many other areas of academia, it is imperative to receive grant funding in order to carry out the study to reach an end goal. As I am going into the research field, I thought it would be beneficial to study how to properly write a grant to aid in the research I am currently performing. The first step was finding the right grant program; for me, it was the Ball State University's Sponsored Projects Administration internal grant. This gave me experience in two distinct areas: first, in general grant writing, and secondly, in tailoring the grant to an audience who had little to no science background. This caused me to analyze my work further and determine how

to write what I was studying in a language the non-scientist could understand. This was a challenge, as I am accustomed to writing in a manner where scientists understand the complex terminology commonly used in research papers and presentations. Because of this, I had to complete numerous rewrites of the final draft. After advice from my mentors, I was able to complete the grant proposal and received funding for my research project. I will now share with you, the reader, my overall experience.

THE GRANT APPLICATION PROCESS

In order to identify which grant program is most relevant for your work, it is crucial to look into the types of grants available, the application requirements, and the audience who will be reviewing the proposed work. There are many types of external grants available from local, state, federal, private, and public agencies, as well as internal and organization-based grants. I chose an internal grant from the Ball State University (BSU) Sponsored Projects Administration, which gives students experience in grant writing without necessarily completing preliminary research. During the 2015–2016 fiscal year, the BSU Sponsored Projects Administration received 27 undergraduate applications and 135 graduate applications, funding 19 and 101 grant requests, respectively. In total, \$3,950 was awarded to fund 70% of the undergraduate applicants and \$269,819 was awarded to fund 75% of the graduate applications (Sponsored Projects Administration, 32). Other grants available to student researchers include the Ball State Chapter of Sigma Xi (local), the Indiana Academy of Science Senior Research Grant

(state), or the Sigma Xi Grant-In-Aid Grant (national), and the Federal Pell Grant, which needs to be applied for in conjunction with the primary investigator. However, the Federal Pell Grant is usually applied for as either a scientist who is a post-doc or lead researcher or as a secondary author on the grant. Most of these will require accompanying recommendation letters from your research mentor or others familiar with your work and leadership skills (more information on this in the next article "How to write a good recommendation letter," this issue of Fine Focus).

The requirements for the BSU internal application included a cover sheet, a budget, a project design, references, letter of support, and a curriculum vita. The cover letter is designed to give a brief summary of the research and gives readers a quick glance as to what the rest of the documents are about (Appendix I). Attached to the cover letter was the budget, which explained what the money would be spent on (Appendix I). It is common for granting organizations to have stipulations on how much can be funded. The BSU internal grant program limited undergraduate applicants to \$300 or less and graduate applicants to \$500 or less; it is important not to request more than the maximum allowable in the grant description. Other grants, such as the Indiana Academy of Science Grant, allows up to \$2500 to be requested by applicants. Although more uncommon, another potential decision factor for the amount requested includes matching policies, where a granting agency will match that raised from additional resources, with these latter sources usually stipulating their contributions and support in an ancillary letter that will comprise part of the overall grant application package.

There are five general categories for the BSU internal grant program: contractual,

supplies, travel, participant costs, and other. Contractual grants fund software licenses, such as needed statistical software to analyze data (or similar). Supplies include any reagents, materials, or small benchtop equipment needed by the researcher. In this case, the BSU program would fund \$300, while the remaining project costs would be funded by additional sources, such as the Biology Department and the Honors College. This is typical for most primarily undergraduate institutions (PUIs). Travel costs include travel to research sites or participation in research conferences. Participant costs, such as conference registration or abstract submission costs, go hand-in-hand with travel costs. Other costs include everything not described above, such as purchasing larger pieces of equipment. My advice would be to discuss the budget categories, needs, and spending timeline with your research mentor before drafting the budget, then carefully edit it together, including sources for each line item, quantity, and catalogue numbers.

Following the development of technical budget comes the budget narrative, where the applicant affirms why all of the costs described in the budget are necessary. In the budget narrative, it is important to describe why something has to be purchased, particularly items that seem conspicuously expensive, such as an antibody, enzyme, or unique reagent available from only a single source. These reasons should be clearly stipulated, and shipping costs (ex. dry ice shipping, hazardous material costs, and related) should be included and mentioned in the budget justification as well.

It is important to note that some research grants have caveats, such as the funding cannot be spent on compensation. This means the funding received could not be paid to myself or any other lab assistant

to compensate for work completed. Larger grants, such as those awarded by the National Institute of Health and National Science Foundation, have some additional funding categories, such as compensation and university costs. Smaller grants usually will not pay for compensation because of the additional resources that are required to pay employees, and would require tax forms, benefits, or other logistics usually out of the realm of smaller internal grant opportunities. Larger foundations have this resource and can go through the additional work to provide this benefit to researchers.

Another point worth mentioning would be indirect costs that go back to the applicant's university. At BSU, this can go as high as 23% of the grant awarded, some of which will go back to the Sponsored Projects Administration to fund student and faculty research, or to other administrative units. Other universities have a much higher indirect cost, which may deter funding organizations from approving and awarding a grant. However, most or all internal funding opportunities for undergraduate projects will not involve any discussion of indirect costs being factored into the budget.

When it comes to who applies for the grant, there is a distinct difference between the primary investigators and co-investigators. The primary investigator is the one who comes up with the initial idea for the research and applies for the larger grants. Typically, granting organizations want to hear from the person who had the idea for the overall project when granting large sums of money. However, for the BSU grant, the title of principal investigator was switched to the applicant and not the person who came up with the idea. In this instance, the student was the principal investigator instead of the professor. To decide what the idea for the project would be, my mentor, Dr.

James Olesen (BSU Biology) and I looked at previous work I had completed and decided to create a project that was a continuation of it.

The third section of a grant is the project design, which has many distinct parts: an overview, background, goals and significance, and the research method timeline, each approximately a paragraph in length (Appendix II). The overview of the project is similar to the introduction of an essay, in that it explains what will be attempted in the proposal and why the research is significant. Under background information, the information about the history of the project and the current status is explained. The writer lays out what is being studied in a way grant reviewers will understand. This is where it becomes imperative that one uses appropriate terminology. In terms of the BSU internal grant proposal, the audience included a panel of faculty from many different fields, such as history, math, english, and the sciences. Not all grants have a wide range of reviewers, as most are discipline specific. When they are discipline specific, grants can be more detailed as the readers will be more knowledgeable as to what the project is designed to accomplish, what the grant will be spent on, and why the project is important to society at large. Since the BSU grant proposal was open to a wide range of undergraduate majors, reviewers came from many different departments across campus to ensure a fair review of all proposals. Thus, the writing had to be simplified to a level where most people reading could understand. If technical terminology had to be used, a glossary of terms was added to help without taking away the professionalism of the application (Appendix III). Overall, this section should contain some level of detail, including any preliminary data, as it explains the concepts behind what is being studied or proposed.

Finally, appropriate references are included and formatted appropriately to the field in which the grant is being written (Appendix IV).

The third section of the project design includes explaining the overall goals or specific objectives of the research as well as the significance of the research. In research proposals, there may be two or three major goals that are presented. In this section, the applicant explains those goals to the reader and describes what they will do to attain them. In my lab, the ultimate end goal is to determine how the transcription factor TAL-1 impacts leukemic T-cells and prevents cell death. The specific objectives are what the independent researcher is attempting to accomplish, such as what each lab tech is trying to accomplish to help reach the main goals. In Dr. Olesen's lab at Ball State, there are three other students all working on different projects, so my specific objectives are different from theirs. My goal is to understand if TAL-1 influences caspase-10, thus preventing cell death. The significance of research is being able to take the knowledge outside of the laboratory and apply it to the real world. For this specific project, the significance is to be able to explain why the leukemic T-cells do not undergo death when treated with a chemotherapeutic drug and then use what we learn to help develop therapeutic treatments that may be able to treat T-cell Acute Lymphoblastic Leukemia.

The final section of the project design includes the research methods and timeline of the project. The methods section includes a description of what experiments and protocols will be utilized and are written in a way that others could follow. When detailing the protocols, not every step is included for sake of brevity, but other grants require that level of detail. Typically, the

larger the grant, the more detail the granting agency will require. This description of the methods shows reviewers the applicant has thought through the project, including what protocols will be best to run, and any additional experiments if the project does not go as planned (contingency plan). The timeline gives the granting agency an expected deadline as to when the project will be completed. This gives the reviewer a sense of how long the research will take and whether the timeline is feasible.

After the project design is completed, at least one letter of recommendation is needed. In the case of the BSU internal grant, a letter of recommendation was required from the faculty mentor of the student who submitted the application (Appendix V). The letter of support must include the viability of the project, a description of how the project will contribute to society, how the project fits with the aspirations of the student, and what role the student plays in the research of the faculty member. This letter of recommendation gives credibility to the student or applicant as to why the funding is needed and verifies the importance of the project.

Finally, a curriculum vita (CV) is required as documentation of the applicant's abilities; the CV is generally required for all grant programs, regardless of the funding level or source (Appendix VI). A CV is required to provide support as to the applicant's background and to chronicle other work they have done in the chosen field of research. For the BSU grant, the CV included education, research experience, and awards and honors sections. Under education, the university attended, majors, grade point average, and expected date of graduation is listed. Additionally, examples of relevant coursework that have contributed to the skills or experience of the student may

be included in this section. The research experience section is where all of the applicant's previous professional research is explained. The professional title, lab, location, and dates are listed for each professional lab in which the applicant has worked. This also includes a brief description of the research completed and the job responsibilities. Responsibilities can range from skills, such as running specific experiments, to training new lab assistants. Furthermore, attendance at conferences should be listed. By attending conferences, either local, regional, or national, this shows the applicant is capable of explaining his or her research to a group and is invested in the dissemination of the research. For some of the conferences, a peer-review of the applicant is done in order to determine if a presentation should be accepted. For example, our annual Ball State University Student Symposium only accepted 100 presentations out of many more applications. By being accepted into a conference, the applicant has shown the significance of the work they are doing and the ability to communicate that significance to others. Finally, many granting organizations want to see if the investigators have been publishing their work and how frequently prior to granting larger sums.

Finally, the last component of a grant is a final report that is submitted to the granting organization. After a designated amount of time, perhaps 12 months following the award, the recipient of the grant is required to submit a report describing how the project went, what was discovered, and where the project will go in the future. For the BSU internal grant, this gives the administration an opportunity to make sure the research was completed, while also validating the faculty mentor is worth funding in the future, should other students apply for a grant from his or her lab.

If funding is denied, the hope is that the review panel would provide a ranking and/or a thorough overview of reasons on what aspects of the proposal were lacking or poorly written, in order to improve for a resubmission during the next cycle. Occasionally, different reviewers may generate comments that contradict one another, or that seem out of place. However, a good review process will minimize the frequency of superficial or incorrect criticisms, which should be resolved during the panel's deliberation and ranking discussion, in order to allow the submitter to learn how to make the proposal stronger and more clearly written after revisions. Your research mentor will assist you with this phase as well, and offer encouragement along the way so that you are not hopelessly frustrated.

Overall, this exercise has helped me become a better researcher by providing me with experience in how to fund a research project. I now know how hard scientists have to work to come up with hypotheses and perform research. They have to continuously publish their work and make sure the significance of the work is known. However, most people do not realize the importance of grant funding and how it is the foundation of any research. By starting grant writing in my undergraduate years, I have been able to learn how to apply for grants, what is required, and why it is important. With this understanding of the process of applying for grants, I hope to be able to better fund the research of my future employers based on the knowledge I gained from writing the BSU grant.

Overall, grant writing is an art form that helps progress all areas of research, whether it is in the arts or in the sciences. This project has shown the importance of reworking different pieces of writing to cater to all

those who may read the application and all the necessities that go into grant writing. It is not an easy feat for one to obtain funding for their research and should be a celebrated moment in the applicant's life when he or

she finally does receive funding.

WORKS CITED

Sponsored Projects Administration. (2016, November 17). Ball State Research 2016. https://issuu.com/ballstatespo/docs/research_2016_1116

APPENDIX I

Budget	ASPIRE Request	College/Dept Support	Other Support
Contractual (incl. software licenses)			
Supplies, Materials, Minor Equipment	\$300.00	\$134.00	
Travel			
Participant Costs			
Other			
Totals	\$300.00	\$134.00	

Budget Narrative: Please explain & detail all costs requested in the table above in the space provided below.

The cost to purchase the inactive form of Caspase-10 is \$434 from Abcam, a company that sells high-quality antibodies that aid in the analysis of protein expression in various cell types. The \$300 provided by the Aspire grant will be used to purchase the antibody, with the remaining \$134 being paid from Dr. Oleesen's research fund in the Department of Biology. All other supplies and reagents needed to carry out the planned experiments are in place. By being able to understand how this protein is being regulated, we will be able to better understand the characteristics of T-ALL and why natural cell death is not occurring.

APPENDIX II

EXECUTIVE SUMMARY:

T-cell acute lymphoblastic leukemia (T-ALL) accounts for 15–25% of all acute lymphoblastic cases in children and adults. Characterized by a resistance to chemotherapy, this cancer originates from white blood cells (T-lymphocytes) in the bone marrow. After becoming malignant, these cells continue to over-proliferate in the blood stream and upset the balance of the immune system. The development of new treatments for T-ALL has been stalled due to the complexity of the molecular signaling pathways involved (1). T-ALL is thought to occur from the ectopic expression of a transcription factor, known as TAL-1, which has the ability to bind to DNA and influence the expression of additional genes (2). It is thought that TAL-1 may impact the expression of genes, especially those influencing the apoptotic or death cascade, thus allowing a cell to avoid death induced by chemotherapeutic treatments. Thus, the influence of TAL-1 needs to be further characterized, which is what this study is meant to accomplish.

Background Information:

Further examination of important proteins that are potentially targeted by TAL-1 is necessary. If the apoptotic-signaling pathway in a malignant T-cell is understood, this could serve as vital information for the development of a treatment therapy for T-ALL. In normal cells, the apoptotic pathway is key in removing unwanted or abnormal cells through a well-defined series of events. One protein that has shown to be critically important in the apoptotic cascade, which may be influenced by TAL-1, is caspase-10. Found in the cytoplasm of the cell (outside the nucleus), caspase-10 acts as an initiator of the apoptotic pathway. If activated, this protein can go on to activate other caspases responsible for the destruction of the cell (3). Thus, caspase-10 has the ability to activate apoptosis in the cell. By determining expression changes in caspase-10, the characteristics of the apoptotic signaling pathway involved in T-ALL can be further determined. These insights are crucial to the development of better, more targeted drug treatments for this rapidly spreading cancer.

GOALS, OBJECTIVES, AND SIGNIFICANCE:

Previous research from our lab suggests that TAL-1 may negatively influence the induction of apoptosis, but further investigation is needed to understand the exact mechanism of this inhibition. The goal of this research proposal is to determine if TAL-1 influences the expression of an important initiator caspase known as caspase-10, thus promoting survival after etoposide drug treatment. The Jurkat T-cell line will be used to mimic T-ALL and inhibition of apoptosis will be assessed through examination of protein expression levels. In the end, a better understanding of the proteins and molecular interactions influenced by TAL-1 may be realized.

Research Methods and Timeline:

The Jurkat T-cell line will be cultured in an RPMI/10% bovine growth serum media and maintained at 37°C and 5% CO₂ to promote cell growth and division. Drug treatments with etoposide will be performed over a 24 hour period at concentrations of 0 μM (control), 1 μM, and 5 μM and whole cell lysate protein extracts will be

created from all three cell populations. A Bradford Assay will determine the protein concentration of each extract. The extent of apoptotic induction will then be assessed using Western blot analysis, immunofluorescence, and flow cytometry. For Western blot analysis, polyacrylamide gels will be loaded with the extracts and proteins will be separated by electrophoresis. The separated proteins will be transferred to a nitrocellulose membrane using a semi-dry transfer apparatus. After transfer, the membrane will be exposed to a primary antibody against caspase-10. Expression levels of caspase-10 will be analyzed and quantified using a Li-Cor imager system. Furthermore, immunofluorescence will be performed where cells will be fixed with paraformaldehyde, air-dried onto slides, and incubated with the caspase-10 primary antibody. Next, cells will be incubated with a secondary antibody containing a fluorescent tag, which will bind to the primary antibody. A Zeiss fluorescence microscope, fitted with a UV light source, will be used to excite the fluorochrome, allowing for the visualization of caspase-10. Finally, flow cytometry will be used where cells will be washed in PBS and then exposed to permeabilization buffer to disrupt the plasma membrane so the caspase-10 antibody will enter cells. A secondary antibody containing a fluorochrome tag will be added and will join to the primary antibody so caspase-10 can be visualized in cells. This research project will be completed during Spring Semester of 2017 and presented at the upcoming Ball State Student Symposium and also at the 132nd Indiana Academy of Science meeting in March 2017.

APPENDIX III

GLOSSARY OF TERMS:

Apoptosis: the highly ordered and timely process of programmed cell death, which can be beneficial to an organism in the removal of unwanted or damaged cells.

Caspase-10: a protein that activates/cleaves other proteins (protease) in the apoptotic cascade.

Concentration: the amount of a protein, in μg, that is present in 1 μl of whole cell lysate

Electrophoresis: a technique used to separate proteins through migration in an electronegative field

Ectopic: the expression of a biological molecule in an abnormal location in an organism or its cells.

Etoposide: a chemotherapeutic drug that stops cell growth and division, while also moving the cell into apoptosis.

Flow Cytometry: a laser-based technology used in cell counting, sorting, and the detection

of proteins.

Immunofluorescence: a technique used to determine the presence of a protein or antigen biomarker inside of a cell through antibody binding.

T-ALL: T-cell acute lymphoblastic leukemia is a rapidly spreading malignant cancer of the blood cells and bone marrow.

TAL-1: a transcription factor involved in blood cell development. Abnormal expression may result in various cancers such as T-ALL.

Transcription Factor: a protein that binds to DNA sequences and controls the expression of other genes.

Western Blot Analysis (protein immunoblot): an analytical technique that can detect the presence of specific proteins isolated from cells.

Whole Cell Lysates: protein extracts created from cells, which can be used as samples in Western blot analysis.

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APPENDIX IV

RESOURCES:

- 1) Chiaretti S, Foá R. T-cell acute lymphoblastic leukemia. *Haematologica*. 2009;94(2):160-162. doi:0.3324/haematol.2008.004150.
 - 2) Soumyadeep, D., Curtis, D., Jane, S., & Brandy, S. (2010, May). American Society for Microbiology. Retrieved April 06, 2016.
 - 3) Overview of Apoptosis (2016). Cell Signaling Technology, Inc.
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APPENDIX V



COLLEGE OF SCIENCES AND HUMANITIES
DEPARTMENT OF BIOLOGY

Muncie, Indiana 47306-0440
Phone: 765-285-8820

Chairperson
Aspire Undergraduate Student Grant
Ball State University

November 4, 2016

To Chairperson of Review Committee,

I am writing this letter of recommendation in support of Amanda Baskfield, who is applying for an Aspire Undergraduate Student Grant. I have known Amanda for approximately two years and first met her when she approached me about research opportunities in my lab. She started in my lab during Spring Semester 2015 and has been exposed to many experimental techniques and has been a part of several ongoing projects. The proposed project represents an important part of her overall research plan that she needs to complete. This project will also give Amanda additional research experience that should prove useful as she builds on her skills to help in future endeavors. Over the last year, she has completed preliminary research that will be presented at the Sigma Xi Undergraduate Research Conference in November 2016. This is commendable for an undergraduate student.

Amanda's project is based on previous research from my lab that indicated Jurkat cells, which ectopically express Tal-1 (a transcription factor), do resist apoptotic induction when treated by the chemotherapeutic drug called etoposide. She now needs to assess how this apoptotic resistance is mediated and how Tal-1 is potentially involved. There is not much information in the primary literature suggesting how Tal-1 negatively impacts cell death, thus it is important to perform experiments such as what she is proposing. We need to continue to look for the molecular targets of this transcription factor to better understand how gene expression patterns change in T-cell acute lymphoblastic leukemia. With an increase in our understanding, this can lead to more insights into how Tal-1 contributes to the over-proliferation of cells and the resistance to death. Overall, the viability of the project is great and any information gained could prove useful in future cancer therapies.

The proposed research that Amanda will complete represents an area of ongoing research in my lab. My last several students laid the groundwork for what she is working on now and I envision this work to continue for the foreseeable future. Thus, it is crucial that this project be completed to give us a better idea of what is happening at the cellular level. She is asking for support to purchase a caspase-10 antibody to be used for Western

blotting, immunofluorescence and flow cytometry experiments. By purchasing this antibody, she can assess an important initiator caspase that triggers the apoptotic cascade. Since Jurkat cells resist apoptotic induction, there may be a change in the expression level of this protein due to the presence of Tal-1. Other miscellaneous reagents/supplies will be provided to Amanda through research support provided to me by the Department of Biology. Support through this grant will afford her, and in turn, my lab, the ability to assess if/how Tal-1 affects important proteins involved in the control of apoptosis.

I also want to mention that another undergraduate working with me, Mallori Wisuri, is submitting an Aspire Grant at the same time. While my letter and the overall grant proposals are similar, they truly are different, albeit, related projects. Both of these students are looking for potential target proteins whose expression might be changed in Jurkat cells treated with etoposide. Both projects are equally important and significant in their own right.

In conclusion, I feel Amanda can successfully complete this portion of her research and it will provide key data to be used by my lab in future projects. I hope your committee will look favorably on her proposal and if you need additional information or clarification, please feel free to contact me.

Sincerely,
James B. Olesen
Dr. James B. Olesen
Department of Biology
Ball State University
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APPENDIX VI

Amanda N. Baskfield

3015 North Oakwood Avenue, Apt 439,
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Phone: 317.478.0841
Email: andingman@bsu.edu

Education

Ball State University, Muncie, IN
Majors: Biology and Finance
Grade Point Average: 3.67
Graduation (Expected): May 2017

Selected Examples of Coursework: Molecular Biology, Cancer Biology, Undergraduate Research, Cell Biology, Microbiology, and Genetics

Research Experience

Research Assistant
Dr. James Olesen, Muncie, IN January 2014 – Present

- Run protocols, such as Western Blot Analysis, Immunofluorescence, and Flow Cytometry, in order to demonstrate protein expression in T-cell Acute Lymphoblastic Leukemia.
- Alter protocols to fit within the dimensions of the study, in order to obtain the best possible results.
- Train new lab assistants in the protocols and the expectations of the lab, while reporting to Dr. Olesen about their skills.
- Determine proper techniques to fit within the yearly budget of the lab.
- Present findings at local and national conferences, including National Collegiate Honors Council, Sigma Xi Annual Meeting, Indiana Academy of Science Annual Meeting, and Ball State Research Symposium.

Awards and Honors

Honors College Undergraduate Fellowship, Sigma Xi Scientific Research Society Member, Dean's List, Honors College, Golden Key Society Member, Society for Collegiate Leadership and Achievement, Miller College of Business Honors Program, Receiver the Scholarship from the *Estate of Wally Miller*, Flanner and Buchanan Volunteer of the Month, and Circle K International Board Member of the Month for the State of Indiana