Intellectual Merit Criterion

Overall Assessment of Intellectual Merit
Excellent

Explanation to Applicant
The applicant graduated from [redacted] and is now enrolled in a PhD program at [redacted]. She has an outstanding academic record at both universities. She has research experience from an REU at the [redacted], at [redacted] and also spent two years as a technician at the [redacted] which has led to a publication. All of these research experiences have prepared her well for her proposed research study on the role of glycosylation defects on rhodopsin trafficking and eye development in zebrafish. The aims are clear and well-articulated. One question I wished had been addressed is whether an experiment could be done to test whether Rho is hypo-glycosylated in the dpagt1 mutant. Letters from research advisors at three different institutions all attest to the applicant's strong potential as a researcher and mentor.

Broader Impacts Criterion

Overall Assessment of Broader Impacts
Very Good

Explanation to Applicant
The applicant has a strong interest in educating others, and served as a tutor in the Mathematics Learning Center, as well as a tutor and TA for the biology department at [redacted]. At [redacted], she is participating in the [redacted], where she travels to area middle schools to teach and perform science experiments. She also plans to participate in [redacted] to educate area school children about brain development and function.

Summary Comments
This is a strong application with excellent intellectual merit and very good broader impacts. The applicant has strong academic and research preparation for her proposed work, which is well described. She has already become involved in community outreach as a graduate student and plans to continue these activities in the future.

Intellectual Merit Criterion

Overall Assessment of Intellectual Merit
Excellent

Explanation to Applicant
Intellectual Merit: 1. What is the potential for the proposed activity to advance knowledge and understanding within its own field or across different fields (Intellectual Merit)? The main objective of this application is to understand how changes in rhodopsin (Rho) glycosylation of affect trafficking of rod photoreceptors in zebrafish. Dolichyl-phosphate N-acetyglucosamine phosphotransferase 1 (DPAGT1) is the initial enzyme of the N-glycosylation pathway, and reduced presence decreases enzymatic activity to reduce global glycolysis. The applicant's lab has demonstrated DPAGT1 knockout zebrafish mutants have smaller, misshapen eyes with thinner photoreceptor cell layer. Rho has two glycosylation sites that are highly conserved in vertebrates. Changes in either Rho expression or glycosylation results in decreased outer disc size and defective disc assembly. In aim 1 DPAGT1 mutants will be examined using transmission electron microscopy to determine defects in Rho trafficking from the ER. In aim 2 a CRISPR/Cas9 will be used to alter Rho glycosylation sites to observe temporal changes in eye

development. In aim 3 optokinetic response assays will be performed to track eye movement in DPAGT1 mutants and CRISPR zebrafish. Strengths: Understanding the importance of glycosylation and how disruptions in glycosylation effect organ development is critical in developmental biology. Andersen's disease is one of the most documented of glycosylation congenital disorders. Due to the rarity of the disease and lack of reproducible model systems, little research or understanding of the disease has been undertaken regarding this disorder. Weaknesses: Translatability to higher vertebrate diseases will always be a concern in a zebrafish model; however, the importance of a basic cellular processes such as protein trafficking and organ assembly is critical to understand. 2. To what extent do the proposed activities suggest and explore creative, original, or potentially transformative concepts? The overall hypothesis of the project was well-developed, creative, and original. Testing alteration in glycosylation in a conserved phenomenon can be extrapolated to eye development in multiple species. The use of cutting-edge techniques will expose the applicant to a number of educational opportunities. 3. Is the plan for carrying out the proposed activities well-reasoned, well-organized, and based on a sound rationale? Does the plan incorporate a mechanism to assess success? The applicant appears to be enthusiastic and well prepared for the proposed tasks. The application presented and developed a sound rationale, but the importance of work and broader intellectual merit was not fully explored. The elegance of the studies are appreciated and extremely exciting. It would have been nice to see a more comprehensive mechanism to assess success as this did detract from the overall research plan. Inclusion of these details is critical to gauge the applicant's deep understanding and critical thinking ability regarding the subject and techniques of proposed work. 4. How well qualified is the individual, team, or institution to conduct the proposed activities? 5. Are there adequate resources available to the PI (either at the home institution or through collaborations) to carry out the proposed activities? The applicant has an outstanding academic record with evidence of undergraduate and graduate research fellowships, presentations, and publications as this strengthens the applicant's potential for success. Partnering with the mentoring team is outstanding. The institution(s) will provide an outstanding environment to conduct the proposed studies and foster graduate training.

Broader Impacts Criterion

Overall Assessment of Broader Impacts

Very Good

Explanation to Applicant

Broader Impacts: What is the potential for the proposed activity to benefit society or advance desired societal outcomes (Broader Impacts)? The applicant has had prior commitment to community service and advancement of women in the STEM fields, and a history of promoting STEM awareness with high school students. It is evident the applicant is both a team player as well as a budding scientific leader. These examples were well-documented in both the personal statement and recommendation letters. The applicant did not present a very clear plan to increase outreach and mentoring opportunities to advance societal and global outcomes regarding the experimental design and educational plans. The plan for the future training and education is clear. As a whole, the broader impacts are very good for the application. Additionally, the model system used has the potential to draw a number of undergraduates and high school students into the STEM field. Not capitalizing on it dampened enthusiasm for broader impacts.

Summary Comments

Summary Statement The applicant is very good and is enthusiastic about the proposed research, which is an outstanding trait to possess. Please continue along this trajectory in your career. The depth of the proposal concerning research design, originality, and expected outcomes are excellent. There are no concerns regarding the potential training. Overall, the intellectual merit is excellent, and broader impacts are very good.

Intellectual Merit Criterion

Overall Assessment of Intellectual Merit

Excellent

Explanation to Applicant

This applicant has an excellent academic record, including honors. She has an impressive array of work and research experience that resulted in several local and regional presentations, a second author publication, and a possible book chapter. References attest to her drive, maturity, high academic potential, and ability to think critically. The research plan is well-written and proposes to investigate the depagt1 mutation in zebrafish and its rhodopsin trafficking and eye development, which should be no problem given her experiences and knowledge.

Broader Impacts Criterion

Overall Assessment of Broader Impacts

Very Good

Explanation to Applicant

The applicant appears to be committed to broader impacts, as evidenced by mentoring (e.g. tutoring math at MLC) outreach (e.g. volunteering at the VSVS with middle school students). The scientific broader impacts of the proposed research are well-written and describe how the project will advance our understanding of the development of organ systems. In addition, the applicant points out that the results can be used at community events such as the Brain Blast, which will hopefully help to inspire future generations of scientists.

Summary Comments

The applicant aims to study rhodopsin trafficking and eye development in zebrafish and how these processes are altered in depagt1 mutants compared to WT. The application as a whole is very well-written and compelling and implies that the applicant has as extremely bright future in her chosen field.