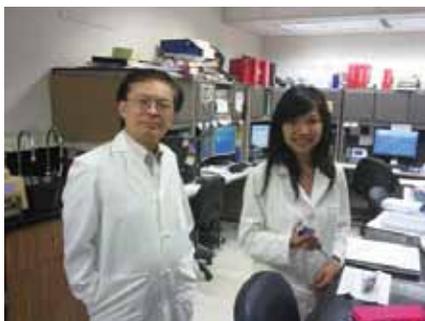


Lan La

Sophomore

Mentor: Dr. Edward K.L. Chan, (Oral Biology)

Personal Statement Before Starting Science For Life Award



I believe that my participation in the Science for Life HHMI Undergraduate Research Program will greatly enhance my understanding of science and the field of research. It will open a door to many great opportunities beyond what I can gain from my biochemistry undergraduate degree. With my strong passion and intellectual aspiration, I hope to contribute to the scientific field a deeper understanding of the science around us and within us. I hope to learn the constantly improving knowledge and continuously advancing techniques in the field of science and to use that knowledge to apply to my career and to contribute to the scientific community.

My passion for science is my greatest motivation to pursue an experience and a career in research. I am always inspired when I learn about DNAs, RNAs, and proteins since I knew about their important role in every living organism. Many synthesizing processes such as transcription and translation intrigue me and the details of these processes on the molecular level amaze me. I believe by deeply understanding this field of science, many of the diseases that humans suffer today such as cancer can be prevented, diagnosed early, and possibly cured. I'm glad that I found a mentor, Dr. Chan, who is working in my area of interest. I kindly contacted him after I read about his research focus on the University of Florida dental research website. After my visit to his lab, I learned that his research has the potential and the futuristic approach to treat autoimmune diseases such as cancer, systemic lupus erythematosus and arthritis. By enhancing our knowledge of miRNAs and RNA interferences, replacement therapy for diagnosis and treatment of these autoimmune diseases can be made possible which will save many lives and increase our overall quality of living.

I plan to work in Dr. Chan's research lab this summer and the upcoming two years, and hope to acquire more science knowledge through working on my project. I hope to attend a professional school and possibly earn a research-oriented PhD. I hope to continue to excel in various areas including research in the near future. As a highly motivated and passionate person, intellectual challenge will push me to become the best of who I am.

I believe this research will bring me countless professional development experience which includes presenting my research findings to knowledgeable professionals who are experts in the field, participating in regional and national meetings such as the Undergraduate Research Forum and many professional conferences that

become available to me, writing as a co-author on a peer-reviewed scientific publication such as in the field of miRNA which I hope to become an expert in, and possibly joining HHMI Extramural Research Award Program and Provost Scholar Program. The opportunities that the HHMI Undergraduate Research Program provides are endless. Researching in the field of interest will further my undergraduate studies and provide me a hand-on laboratory understanding of the science that I learned from textbooks. Within this research, I can see how science comes to life and the futuristic screenings and treatments for autoimmune diseases.

Abstract

The role of GW motifs in the functioning of GW182 protein in miRNA-induced translational repression

La L, Chan EKL, Yao B

MicroRNAs (miRNAs) are 21-nucleotide-long RNAs that regulate gene expression in many living organisms (1). At least a thousand miRNAs are predicted to play an important role in regulating gene expression in humans. MicroRNAs are transcribed endogenously from their encoded genes and further incorporated into the RNA-induced silencing complex (RISC) in the cytoplasm. Based on the sequence complementarily, miRNA guides the RISC complex to the target mRNAs to affect translational repression or RNA degradation (2). The Argonaute protein family, a highly conserved key component of the RISC complex (3), is represented by four proteins (Ago1-Ago4) in mammals, and is involved in miRNA-mediated translational repression.

GW182 was first identified and characterized by Professor Chan's laboratory in 2002 as a novel protein recognized by an autoimmune serum from a patient with motor and sensory neuropathy (4). It is an 182 kDa protein characterized by multiple glycine (G) and tryptophan (W) motifs and is an essential component of GW bodies (also known as mammalian processing bodies, or P bodies), since knockdown of this protein leads to the disassembly of these cytoplasmic foci (5). To date, GW182 is known to play a critical role in the repression of translation of the miRNA-targeted mRNAs (6-8). Two non-overlapping regions, the middle region $\Delta 12$ (aa896-1219) and the C-terminal region $\Delta 5$ (aa1670-1962) were demonstrated to induce silencing in a tethering reporter assay. Transfection of $\Delta 12$, but not $\Delta 5$, released miRNA reporter repression regulated by endogenous miRNA. Alanine substitution showed that GW/WG motifs in $\Delta 12a$ (aa896-1045) were important for repression activity and endogenous miRNA function.

To further fine map the functional significance of GW/WG repeat in $\Delta 12a$ region, individual mutations from GW/WG to AA will be generated to evaluate their specific role in silencing tethered reporter or interfering endogenous miRNA function. To achieve this goal, mutagenesis will be performed, confirmed by direct sequencing and analyzed in i) luciferase reporter tethering assay for the effect on repression activity and ii) "20 bulge" reporter miRNA interfering assay.

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Personal Statement After Starting Science for Life Award

Participating in the HHMI science for life intramural research program is an invaluable experience that allows me to grow both academically and intellectually. I'm learning a vast amount of scientific knowledge that possibly opens up a new direction for my future career. Most important of all, I'm participating in the ongoing scientific findings that help make a difference in people's life. To me, science is interesting and intriguing. Thus, participating in research brings it to another level which I want to be a part of, learning and contributing. It is within the research laboratory where I see my scientific knowledge from textbooks and lecture halls comes to life. Being able to make the connection and apply the knowledge increases my critical thinking ability, creativity as well as memorization of established facts and details.

Aside from the academic and intellectual side, participating in research also challenged my physical ability. I became much more proficient at minute hand and eye coordination and muscle's endurance from techniques as simple as pipetting, which personally will benefit my future dental career. Aside from that, I become more careful and competent at staying well focus on my work because I know a small error can cost as little as a week of time and efforts.

Participating in research was the highlight of my summer and I fully enjoyed it. With research, I could manage to balance my time well to achieve success academically with extracurricular activities on the side. In the near future, I hope to participate in the DMD-PhD combined degree program to continue pursuing my research interest as well as obtaining a dental degree.

