**Research at Children Hospital**

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**Major:** Chemistry ACS and Biological Sciences

**Title of Project:** OPA1 research

**Thematic Area:** Research

**Expected Project Start Date:** January 6th

**Expected Project End Date:** April 24th

**Abstract:**

 In this experience I will be doing research with Dr.Wang – one of the members of Dr.Huang’s group at the children hospital and we will work on a mitochondrial disease case. We will be working a on a gene called OPA1. One of our patient is having a point mutation on this gene and because of this the expression of OPA1 protein is really low. We are trying to fix this by adding the cell with normal genes and test to see if the extra cells can help to raise the expression of OPA1 protein in this patient or not. This gene product is a nuclear-encoded mitochondrial protein  and it is one of the component of mitochondrial network. Mutation in this gene has been associated with optic atrophy type 1 (OA1) which is a dominantly inherited optic neuropathy resulting in progressive loss of visual acuity, leading in many cases to legal blindness. The patient in our lab has a mutation in this gene and because of this the amount of OPA1 protein in his body is lower than normal. We are trying to see if adding new cells with normal OPA1 gene can help him reach the normal amount of OPA1 protein. Right now we are at our very first stage of this project. We have the plasmid that is designed from a company as we wanted and now we are confirming if the plasmid is exactly what we want it to be. My goal when decided to join this project is to learn more about genetics, one of the most important field nowadays and may be the next 20 years. Doing research in different fields is the best way for me to find my real passion. My role in this project is helping out our new post-doctoral member, Shadi, and follow her to learn as much skill as I can. I did some plasmid isolation and bacterial culture with Shadi. This project is really meaningful to me because it will help me to learn one of the most important aspects of the 21st century. After participated in the Summer Undergraduate Research Fellowship for honors students, I have gained a lot of knowledge and now I can read publications really easily. I can now start to do research on my own through reading papers. This is a huge improvement to me because before the SURF program, I cannot even complete one paper and I do not even know what research will be like. Now that I have experiences from SURF, I can now be confident when I do research with my mentor. As my goal in the future is to attend a graduate school to study about Biomedical this experience is exactly what I need. I will be doing this project from August 1st to December 14th. The time commitment will be 20 hours a week.

**Learning outcomes:**

**-I will possess a well-developed awareness of literature in the field.**

This research will help me to possess a well-developed awareness of literature in the field. For example, by reading a lot of papers and articles on this topic I will have a good view about the project that I am doing. With the help from my mentor, I will be able to completely understand her project and I will be able to conduct it on my own. Genetic diseases are really challenging and often does not have a simple way to treat so that why we are trying to study as much as to see if our method work or not before we bring it to clinical trial. Reading article will not only help me to pick up knowledge in a fast way but it also gives me an overview about the topic at the present too. This will eventually develop my awareness about the field. Great examples for this are the articles that I am reading right now:

[Mutation of OPA1 gene causes deafness by affecting function of auditory nerve terminals.](http://www.ncbi.nlm.nih.gov/pubmed/19733158)

Huang T, Santarelli R, Starr A.

[Heterozygous mutation of Drosophila Opa1 causes the development of multiple organ abnormalities in an age-dependent and organ-specific manner.](http://www.ncbi.nlm.nih.gov/pubmed/19718456)

Shahrestani P, Leung HT, Le PK, Pak WL, Tse S, Ocorr K, Huang T.

[The molecular mechanisms of OPA1-mediated optic atrophy in Drosophila model and prospects for antioxidant treatment.](http://www.ncbi.nlm.nih.gov/pubmed/18193945)

Yarosh W, Monserrate J, Tong JJ, Tse S, Le PK, Nguyen K, Brachmann CB, Wallace DC, Huang T.

These examples show that I am developing my awareness about newest issues in the field by following this project. I am learning things that will lead me to my goal in the future, to become a doctor in genetics field. This project is a great start for me in experiencing genetics subjects.

 Another example is the skills that I am going to pick up during the time I do the research. Cell culture is a skill that requires carefulness and patient because one wrong move you make can cause contamination to the cells. I read a lot about cell culture and I also did some cell culture during the time I joined SURF so I believe this study will strengthen my skills and help me learn more kind of cell culture. After we transfect the Hela cells with our plasmid we can use the to test whether the OPA1 is actually expressing like we want before we continue our research in stem cells.I will also be able to learn some other skills to get data for this research from my mentor so that someday, I will be able to conduct a research on my own. I will certainly develop my awareness of what to do and what to not do in the lab. This can be also consider as a great source of literature that I have to understand to make the most out of my research project.

Both of these examples are pointing out my plan to develop my awareness about genetics field. They also help me to realize that my project will contribute greatly to this field too.

**-I will demonstrate awareness of key weakness/limitations of the research and provide guidance on the most important and fruitful directions for future research on this topic.**

 There is no doubt that individual performance is my main goal in this project. Having joined Dr.Huang’s lab since the beginning of summer 2013 I have learned so much about genetics and stem cell research. Since I have never had any formal training for medical research skills, reading and watching my mentors doing their job is really essential for my learning process. Last semester I have been able to do cell culture on my own and it was a really meaningful experience to me. This time, I will get to do plasmid isolation, transformation and possibly doing some stem cell work on my own. This is a really important stage of my learning project because I have to do well to proof to my PI that I will be ready to take on a project in the future. My performance in this project will be really essential for my future work in this lab. Having done some of the work in this project, the limitations of this this research is that it will take a really long time. It has taken us 4 weeks already to confirm the plasmid that we receive from the company. We have to test its structure, functions before we move on to the next stage so it take us a really long time to do experiments. The reason why it took us a long time to test is because we have to first do bacterial culture to get more plasmid. Then we do plasmid isolation to see if we can get the right concentration of the DNA using the nanodrop machine. Then we test it structure using enzyme digestion and run it on agarose gel. Now that we confirmed the structure, we move on to confirm if the OPA1 promoter is working fine. We design another plasmid by ourselves and this plasmid contain OPA1 promoter linked with a special sequent.

Through these examples I believe that I will be able to demonstrate awareness of key weakness/limitations of the research and provide guidance on the most important and fruitful directions for future research on this topic.

**-I will have the ability to think beyond the just completed research and articulate how my world of view has been impacted by the experience.**

I believe after I finish this project my knowledge about genetics will be strengthened and I will have the ability to think about a new project that I can work on in the genetics field. I will also be able to know what I have to read so that I can have the sense of the important topics to find an idea of what to do for my future career. I believe after I finish this project this srping semester, I will have quite good amount of techniques to use.

This topic is very interesting because it requires me to read about a lot of things. A lot of scientist is interested in OPA1 because it is one of the components in mitochondrial activity. Because of this, mutation in OPA1 can lead to a lot of mitochondrial diseases. This is why there are a lot of paper out there writing about OPA1 research. I also have to a lot of protocol to learn more technique. Right now, to me, technique is really important because without a proper set of techniques I can not do research on my own. My plan is to try to read as much as I can about these topics so that I can at least understand in detail everything that I am doing in the lab. This will not just help me to improve my knowledge but also help me to understand more about the field that my mentor is interested in. What I am about to do research on is just a small part of a big picture that my mentor is trying to paint. I hope in the future I can understand completely that big goal of my mentor to see what it is like to be a real scientist.

I will be able to think beyond the research that I am about to conduct. This topic opens a lot of door for me in the future. I can go ahead and do research more mitochondrial diseases in the future just like my mentor or I can do research more on stem cell. Right now my idea after this project is to use the skills that I pick up to do research my own. I believe I am slowly but firmly reaching my goal as an undergraduate student. I hope I can do a presentation about my research at UC poster presentation to share my work with other students. I will also be able to receive ideas form experts so that I can develop my research better.

**Connection to Goals and Academic Theories:**

My future goal is to attend graduate school for further learning. After the stem cell experience, I decided to try to do research on genetics field because I realize that as a doctor you have to have knowledge in a lot of aspects, not just stem cell or genetics. Therefore, this project is really suitable for my goal and it is really great to have Dr.Wang as my guidance because she has already had in-depth knowledge in this field. This project connects well with my previous project so I believe this is a great chance for me to develop a systematic learning. Genetics is one of the most important fields of 21st century so I am really happy to be able to work on genetics subjects. I am really glad to be involved in another field that I am interested in doing. I believe in the future, when I apply for graduate school I will be able to have different options for my career. With a great preparation from college I am having a strong background in General Chemistry, Organic Chemistry, Analytical Chemistry and Biology I think that this project suited me well. This is the place for me to actually use my knowledge in college to apply it on a real project. Also I read a lot of paper on this field and some specific papers are listed below:

[The dynamin GTPase **OPA1**: more than mitochondria?](http://www.ncbi.nlm.nih.gov/pubmed/22902477)

Belenguer P, Pellegrini L.

[Dominant optic atrophy.](http://www.ncbi.nlm.nih.gov/pubmed/22776096)

Lenaers G, Hamel C, Delettre C, Amati-Bonneau P, Procaccio V, Bonneau D, Reynier P, Milea D.

[Mitochondria and neuroplasticity.](http://www.ncbi.nlm.nih.gov/pubmed/20957078)

Cheng A, Hou Y, Mattson MP.

These are papers that have topic related to my research. The first one is an article about OPA1 and its role in cell processes. The second one is about optic atrophy in general and the third one is about mitochondria and its role in neuronlogy. Reading these article help me to have a clinical view about how OPA1 can affect a human when there is a mutation happen and how serious it is in the world. In these paper they talk about research procedure really carefully. They show every single step they did and how they construct a research plan. Reading these paper help me to learn how to build up a plan to do research In the future. To be able to write papers like these, they have to read a lot and the materials they read are usually put down as reference at the end of their paper. I usually use this as the source to find more useful paper for my project.

**Initiative, Independence and creativity:**

In this project I will work independently but Shadi will be looking after me every time I do an experiment. She will be the one who teach me techniques and help me to analyze data. I will be helping her with Hela cell culture and some experiments that are needed for our project like plasmid isolation, gel electrophoresis, bacterial culture and maybe some stem cell work in the future. I will also be the one who prepare materials for our work like medium, antibiotic and pyruvate. Because it is my first and also Shadi’s first time working with the tools that we have in the lab so creativity and independence performance is really important. If something does not work we have to make know why it does not work and figure out the solution so that we can finish our project in time. We also have to read a lot of protocol to know which is the best one to use and try to do it as careful as possible so that we can get the best result. It will take a long time because we are both learning and making new knowledge at the same time but I feel really confident because I have been trained really well by Dr.Wang. I am also feel really excited because although this is not my individual project, I have the chance to actually follow it from the beginning to the end so I am sure that this will be a really valuable experience.

**Reflection:**

I was given a notebook on the first day I came to lab so my plan right now is to write down everything I am going to do into this notebook. Also I will write briefly things that I read in different paper that might be helpful for our project into this notebook too. By doing this I will be able to have a detail reflection at the end of my experience. It is also a good way to keep track of my work and review every time I need to figure out anything new. I will also create a blog on a word file to tell about my personal thought during this project. It will be like a file where I keep new ideas and special stuffs that I think might be helpful for my future career. I will write down my feeling for this project and my own personal development for it in the future. It will also be a place where I list difficulties that I have during the time I work in the lab. I will try to clearly reflect my relationship with people in the lab and how I develop them into my future connection. These connections can help me later on when I am trying to apply for graduate school or any research program that I am interested in. I come here mainly to learn and I am not trying to just narrow myself down into 1 small project. I will try to learn different things in the lab and figure out my options for the future. For example I can come and talk to other mentors in the lab to know about their project and ask them to show me some basic information about their projects. I can reach out to different fields and to understand them a bit at a time. These small information is not too detail but they do give me a good look into different fields so that I reduce my options. I will keep my mind open to receive knowledge from anyone that is willing to talk to me. All these things will be written down into the word file for my future.

**Dissemination:**

I am planning on using it as my poster for the poster session this spring semester if possible. The poster session in spring semester is a great way to show people what I did and let them know the potential of our project. My further plan is to find and contact researchers that are doing in the same field to let them know that I am interested in develop this project. I am applying to some SURF programs to continue to learn genetics in a different environment. I understand that to do great things we have to do it together so I will try to let people understand my project and inspired other students so that they can have an option for their future just like I did.

**Project Advisor:**

**Taosheng Huang, MD, PhD**

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**Budget:**

20 hours a week.

The work time is going to be between 1:30 p.m to 6:00p.m every day.