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UNDERGRADUATE RESEARCH JOURNAL

Prevention of Hypoglycemia-Induced Neuron Damage: A Personal Review

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Nearly three years ago, I started my journey as an undergraduate researcher by going to the office of undergraduate research at the University of Utah, in Salt Lake City. They were extremely helpful as they were able to tell me who was doing research at the University and they were able to narrow down the list to what pertained to my degree as there were probably a couple thousand researchers located on or near campus. They printed off a list of thirty or forty Principle Investigators (PIs) with brief descriptions of their research to contact on my own. Contacting a PI in itself was a daunting task for me as it was hard for me to believe that a PI with a lab full of post-doctorates and Ph.D. students would want a sophomore who just finished anatomy and physiology in their laboratory. Yet, if they said they want undergrads by posting an application in UROP then just maybe they would want me. So, I emailed three PIs and waited to hear back.

Dr. Fisher was the quickest to respond by emailing me back the next day and after a quick series of emails, I had an interview on Friday. I wanted to be well prepared so I did some online searching for his publications on diabetes mellitus. Unfortunately, it was only during the interview that I realized that it had been a few years since his lab studied changes in fat metabolism changes associated with diabetes, but they are currently researching the physiologic changes that occur during insulin-induced hypoglycemia. I felt quite embarrassed as I should've checked the dates of when those papers were published. Nevertheless, he seemed to like me and took me on a brief tour of his laboratory where I met the people with whom I would spend the next three years. Then near the end of the tour, he asked me several questions about glucose metabolism and why might the brain be particularly vulnerable to hypoglycemia. It was only later I realized how much I did not know. After the interview, he asked me to stay while he talked to the people in the lab. When he came back he asked me when I could start, I said Monday.

For the first month or so I was to shadow the post-doctorates and see what projects were already underway. My training included injecting live animals subcutaneous, and intraperitoneal, along with starting to learn how to perform surgeries on rats and mice. Along with training, there was still much to learn about why particular things were being researched, why the researchers designed their experiments in a certain way, and what were the expected results and implications of those results. Simply said there was much to learn, but it was all worth it looking back.

Following the first month, Dr. Fisher brought me and another undergraduate student, who started working there at the same time as me, into his office to give us a general review of diabetes and asked us what project we wanted to work on. He also gave us another option, to lead our own project. To this point, the only people we thought would get to lead a project would be a post-doctoral researcher or Ph.D. students. It would be an opportunity to investigate a concern in the medical community, design our own protocols, learn from our own

failures, and maybe given enough effort, and sheer luck, the opportunity to write a manuscript for publication as an undergraduate. The new project involved designing a protocol to screen for pharmaceuticals to be given following an acute episode of insulin-induced severe hypoglycemia for the prevention of brain damage.

We decided to seize the opportunity and the next day I had to reload the printer probably two or three times because of all the papers we were printing off to better understand what we would be doing. After a few months of trial and error of combining previously published protocols we finally found a protocol that maximized the distance between our negative control group, euglycemic animals with normal blood sugar, and a positive control group, who would experience hypoglycemia without treatment. The next step then was finding a drug to test. We found one that showed promising results in a seizure model, it wasn't terribly expensive, so we decided to test it. It completely backfired on us, if anything it increased brain damage fivefold and to this day I still don't understand why. Yet, that didn't stop us from continuing to look into other potential drugs. In addition to looking into seizure models, we decided to study more about the mechanism of neuron apoptosis and necrosis pathways to screen drugs not only on their ability to work in other models but also if they made sense based off the known metabolic pathways.

After testing a few other drugs, we came across one that seemed to work in our model of brain damage. So, we tested it again a few more times and it reached statistical significance in reducing the number of dying neurons in the hippocampus and cortex a week following severe hypoglycemia compared to our positive (non-treated) group. Then we had to ask the question, is it actually protecting the neurons and preventing brain damage or is it accelerating the dying process thereby masking its pro-apoptotic abilities? After searching for a method for testing the drugs prognostic abilities, we tested the animals in a Morris water maze to test the capacity for the animal to learn where a hidden platform is located using only external visual cues. As expected the group with severe hypoglycemia without treatment had significantly reduced the animal's ability to find the platform compared to the euglycemic control group. The drug we chose was shown to retain the learning abilities lost in severe hypoglycemia, we were ecstatic.

It has been a few months since we finished our testing, and since then I wrote a manuscript and submitted it to be published in a scientific journal. We are still waiting to hear back from the reviewers on their concerns and changes they wish to make before it can be published. I hope that this reflection has encouraged you to also pursue undergraduate research as there is so much opportunity to learn and help to further the field of your interest. I wish you the best of luck in your research. Just remember a trip to the undergraduate research office may change your life.