Alexandroupoli,29 October 2024

To the HIAS Board,

Following my return to Greece after my experience in Smirnakis Lab in Brigham and women's hospital/Harvard University, I am writing this letter to present everything I learned during my time there.

First of all, as my goal is to become a neurosurgeon, I was interested in doing research in the nervous system and its pathology, so I was introduced to Dr. Natalia Cordero, a post doc, and Dr. Amr Ellaithy, an epileptologist, to be involved in their epilepsy projects. More specifically, they are doing basic research using mouse models studying

i) neural network in a rare genetic form of epilepsy called Dravet syndrome
ii) epileptogenesis using a kainic acid model. In the next paragraphs I will explain both models.

However, before being able to start with these projects there was a lot to be done to be able to be added to the protocol and get trained to work with animals. I completed a lot of trainings, both online and in-person, as well as facility tours in the different buildings of Bringham and women's hospital before I was finally able to start working with animals and have access everywhere.

I. Regarding the Dravet Syndrome (DS) model, DS is a rare and devastating infantile-onset epilepsy, in which seizures are triggered by increases in body temperature and it is caused by loss of function of NaV1.1., which is a sodium channel that is found in inhibitory interneurons in the hippocampus and prefrontal cortex. This leads to increased excitation of pyramidal neurons, thus creating the epileptic phenotype. The goals of this study were to induce hyperthermia mechanically and understand how it contributes to seizure development via simultaneously recording the electrical activity of the brain with Electroencephalogram (EEG), and to test how effective is a novel drug in preventing those seizures. During my time in the lab, I learned the surgery technique, specifically how to implant the EEG electrodes in the epidural space, via holes drilled in mouse's head. We were testing 2 different setups, one in which the mouse is tethered, and one that the signal is amplified in the head of the mouse and then sent via Bluetooth to a data acquisition device and then to the computer. Therefore, I observed several different types of surgery and I was helping whenever it was possible (shaving the mouse, inducing anesthesia, performing different types of injections, etc).

II. Regarding the kainic acid model, kainic acid is a molecule that induces acute status epilepticus in mice, when it is injected in the hippocampus. Status epilepticus is then stopped using diazepam/pentobarbital and then mice develop chronic epilepsy, with a neuronal loss similar to that of mesial temporal sclerosis, which is observed in humans. So, the plan is to make the injection using accurate coordinates, record seizures with EEG and then monitor the mice for several weeks to monitor the development of epilepsy. After that, the plan is to harvest the brains of the mice and use transcriptomics to identify the differences in gene expression between healthy mice and those that underwent epileptogenesis. This way, we could potentially identify genes that are responsible for epileptogenesis. During my time there, I was able to inject kainic acid in the correct coordinates, using electronic coordinates, through a hole in the skull that was previously drilled. A headmount with screws and wires needs to be placed in mice's head, while the screws go inside the skull, in the epidural space, to allow for EEG recording. Then, the mice are being recorded long-term and at specific time points, after they heal from surgery and successfully undergo epileptogenesis, their brains are harvested and used for transcriptomics, using a library created by another lab member.

Apart from my work at the Lab, I tried to observe certain clinics when I had the time. First of all, I was going to rounds with Prof. Dr. Smirnakis when he was attending in the Neuro ICU unit. There, I saw patients with conditions like subarachnoid hemorrhage, intraparenchymal hemorrhage, ischemic stroke and subdural hemorrhage. I was able to see how these patients are managed, and I studied the pathophysiology, risk factors, management and treatment of these diseases. Apart from that, in the last few weeks, I was introduced to a functional neurosurgeon, Dr. Rees Cosgrove and I did an observership in the neurosurgery department of Bringham and women's hospital. I saw a lot of patients with essential tremor and Parkinson's disease, as well as their surgical management. I learned a lot about these diseases, as well as about other types of tremor, which I was trying to identify and grade in Dr. Cosgrove's clinic. Finally, I did some trainings in Massachusetts General Hospital, and got some experience in blood drawing, Electrocardiogram and vital signs.

Overall, it was a unique experience, I truly learned something different every day, I met a lot of great people and made memories that I will remember forever. My next plans are to get a good score in USMLE Step 2, be involved in clinical research with Prof. Dr. Smirnakis, as well as in other research opportunities and come back to the US to get some hands-on clinical experience before graduating.

Finally, I would like to thank Prof. Dr. Nicholas Ashford and the whole HIAS board for providing me with this once-in-a-lifetime opportunity and Prof. Dr. Kaxiras and Prof. Dr. Manoussaki for helping me through this whole process. I would like to thank Prof. Dr. Smirnakis for allowing me to work at his lab and always trying to help me with whatever I was asking for. I would also like to thank Dr. Cordero and Dr. Ellaithy for being excellent tutors and keeping me actively involved in their projects. Last but not least, I would like to thank Dr. Ioannis Mavridis and Prof. Dr. Kostas Fountas for the opportunities that they gave me and their mentorship, and my family for their endless support.

Sincerely Yours,

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