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| **Client:** | Xiaoling Chen | **File:** 24-134 |
| **Dept:** | Medicinal Chemistry and Molecular Pharmacology | **Faculty:**  **Student:** |
| **Date:** | 11/5/24 | **Initial Meeting:**  **Follow-up:** |
| **Consultant and Attendees:** Sumeeth Guda, Dr. Xiaoling Chen, Dr. Bruce Craig | | |
| **Statement of Problem:**  To determine if there is a difference in the neuronal activity (e.g., firing rate) between the control (WT) and mutant (HET) organoids. | | |
| **Goal of this Project:** Journal Publication, Grant application | | |
| **Background:**  The client is a post-doctoral researcher in the MCMP department who is investigating and deciphering the role of SCN2A deficiency in autism-associated impairments through advanced human brain organoid models. The client submitted a grant proposal to get funding for the project, however it was not grants with reviews stating there is insufficient power. The client came to the SCS seeking help with the power analysis, as well as a review of the application to make sure that all of the statistical methods were valid and reasonable. | | |
| **Progress of project at this time:** Design (No data collected) | | |
| **Relevant information presented at the meeting:**  At the start of the meeting Dr. Craig asked if the client’s project is similar to any previous projects that the advisor’s lab brought to the SCS. The client confirmed this. Additionally, since the client had a hard deadline for submitting the grant application, Dr. Craig wanted to know if she needed a letter of support from the SCS. The remainder of the meeting was spent discussing the various experiments being performed in the grant.  The client is planning 10 separate experiments within this study. Experiments 1 to 3 are all focused on neurons sampled from wild type (WT) and mutated (HET) organoids, which are a small collection of brain cells. Experiments 4 to 7 are all focused on assembloids which are like groups of connected organoids. The experiments in 4 to 7 are similar to the first three experiments. Experiments 8 to 10 are all focused on mouse behavior. The client wants all the experiments to have a power of 0.8 for an effect size of 0.5 and a significance level of 0.05. The client went into the details of each experiment so we could understand the process and outcomes  The client talked about each of their experiments, which are described in the document “24-134 Experiment Notes”. But generally, the client will collect responses from either neurons or organoids from each group (WT, HET). In some cases, there was some clustering, such as several neurons from the same organoid, it was proposed that an two-sample t test would be the likely analysis approach.  There is one exception to the general approach where one of the experiments has each neuron being tested over a range of current intensities. This experiment would be analyzed using GLMMs to account for the repeated measurements. | | |
| **Recommendations for Design and/or Analysis:**  Given the quick timeline, we focused on the issue of effect size and power. Dr. Craig pointed out that the various experiments proposed different sample sizes, which doesn’t jibe with the fact that sample size was determined using effect size. We recommended the client use the same sample size for all the experiments.  Because there are three aims, Dr Craig suggested using an overall significance level of 0.05 for each aim but consider using a 0.01 significance level for each study within an aim to address the concerns of multiplicity raised by the reviewers. We will provide sample size numbers for various effect sizes ranging from 0.5 to 1.0 so the client can assess power versus cost. Finally, we requested pilot data from some of the studies performed so we can see what sort of effect sizes they are currently seeing in their experiments. | | |
| **Who will carry out these actions?**  Client:   * Provide the SCS with the pilot study data. * Provide the SCS with the grant application containing the methods and initial findings.   Consultant:   * Do power analysis computations and give guidance to the client if they need help verifying if the sample size is appropriate for the effect size. * Help review and edit the grant proposal to see if the methods are statistically sound, and if the effect size, power, and significance is appropriate.   Dr. Craig:   * Provide the client with a letter of support for their grant application. | | |
| **Status:** Follow up needed. | | |

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