Implantable Light Source Development for Optogenetic Alteration of Immune Response

BME 400 Design

Client: Matyas Sandor, PhD

Advisor: Justin Williams, PhD

Team members: Ruochen Wang, Jacky Tian, Lisa Xiong, Hanna Rainiero

Function:

The discovery of microbial opsin genes, which is a group of genes that was first studied in neurons, makes it possible to selectively control activation or silencing of neurons or other cells by light. Optogenetics is the study that combines optics with tissue genetically modified to express light-sensitive channels in the cell membrane. Our client aims to study immune trafficking in tuberculosis and inflammation of the brain by using optogenetics [1]. Our group's product will be safe to be implanted in mice and should emit light within certain wavelength requirement. The light source can also be switched on and off easily by operator for research use. The light's intensity is able to trigger all of the light sensitive channels inside the mouse tissue.

Client requirements:

The goal of our client is to use optogenetic activation or blocking of neurons to alter immune cell functions in mice to understand inflammatory responses in brain and lung diseases [1]. In vivo light delivery is key to this project and our client needs a solution for 480nm and possible 405nm light that can deliver light to a larger area, which is about one square centimeter, and can be switched on and off for specific increments in the mice. The heat produced by the light should neither be harmful nor kill the cells and tissues near implantation site. The light should be delivered deep enough to stimulate the lung tissue of the mice without causing harmful phototoxicity. The light should also be reusable if it is expensive to fabricate.

Design requirements:

1. Physical and Operational Characteristics

a. Performance requirements:

The device will be turned on for the complete duration of the experiment which will last for two hours. Not only does the device need to be powered for the duration of the experiment, it must continue to be functional and biocompatible under physiological conditions within the mouse's subcutaneous tissue (wet, temp: 36.9 °C, pH: 6-8) [2].

Light must have a size of approximately one square centimeter with a broad light source range able to penetrate deep into the organs of the mice. It also needs to have a wavelength of 405nm and/or 480nm without producing UV rays that may damage the tissue.

Light source must be able to be switched on and off for 15-30 second intervals over each 2-hour experiment. The light source must be flexible and able to be inserted subcutaneously to the mice's skull.

b. Safety:

The heat generated by light should be minimal and not be harmful to neighboring cells and tissues. The thermal tolerance for implantable devices is approximately 1 degree celsius. During the duration of the experiment, the device should be able to diffuse the heat from the light emitting diode to prevent thermal damage. In addition, the team should make sure the UV light is not produced by the light source as the UV light would cause harm to the cells. The device should also be designed to limit phototoxicity of the living tissue. The material should also be biocompatible so that it will not cause an inflammatory response in the tissue. Electronic components of the device will be coated in a biocompatible and implantable material (example parylene C or PDMS) to prevent voltages and currents from harming the mice.

c. Accuracy and Reliability:

The light needs to be durable and biocompatible so that it is able to withstand the environment inside the blood vessels of mice. Also, the light source developed should be broad enough to cover enough areas on the organs of the mice to make sure the light-sensitive genes can be triggered and monitored. The light emitting diodes should emit wavelengths of 405nm and 480nm.

d. Life in Service:

Ideally the electrical components of the device will be reusable while the coating biomaterial would be covering the light and could be sterilized by ethanol. The light source should also work continuously and consistently without unpredicted damage in the hardware. The heat sink would also aid performance in maintaining the energy from dissipating in the form of heat to maintain light intensity for the time during use.

e. Operating Environment:

The device will be exposed to physiological conditions in the subcutaneous tissue of the mice in the chest and cranium. The device will be exposed to the body temperature and pH of the mice which is approximately 36.9 °C and pH 6-7, respectively [2]. Since the device is in an aqueous, saline environment, there is risk of corrosion and/or electric shock. The individuals at risk are the mouse itself or the person carrying out the experiment and this risk must be mitigated.

f. Ergonomics:

The device should be readily and easily picked up using tweezers. Once the device is in the mouse, it will not be handled by a human until it needs to be removed - a microcontroller will simply need to be turned on to operate the device.

g. Aesthetics, Appearance, and Finish:

The design needs to be small, compact, and streamlined. Since the design will be used *in vivo*, wires are acceptable but not preferred. The materials used need to be durable and able to function when in the subcutaneous environment of the mice. The device needs to be biocompatible and prevent any form of liquid from seeping into the device.

2. Production Characteristics

a. Target Product Cost:

The client did not specify the budget as long as we make reasonable use of the money provided by our client. Our team will try to minimize the amount we might spend and try to make our device reusable and reliable.

3. Miscellaneous

a. Standards and Specifications: FDA Regulation of Implantable Medical Devices

Our device to be built will be implanted subcutaneously in the mouse. According to the FDA the ambient temperature must not increase by more than 1°C or brain damage may occur [3].

b. Customer:

For a preliminary design specification in regard to customer, the device should be user-friendly (easy to handle, will not fall apart easily when mishandled, etc). This device will not be available to the commercial consumer - it will be used for research purposes at the client's research lab.

c. Patient-related concerns:

Our design will not be applied to patients directly even though the ultimate goal might be to alter immune response of humans. For our research subjects, mice, the use of light source must not be detrimental to the research projects and the device should be safe to mice when being implanted.

d. Competition:

1. Biocompatible optical fiber-based nerve cuff can be used for light delivery that wraps around the target neuron. The research mainly considers light delivery to peripheral axons [3].
2. Epidural fiber-optic implants:

Epidural fiber is used in light delivery for spinal cords. The system [4] enables sufficient light intensity and different light wavelength to be delivered.

References:

[1] Fabry, Z., Chreiber, HS., Harris, MG., Sandor, M. (2008). Sensing the microenvironment of the central nervous system: immune cells in the central nervous system and their pharmacological manipulation. *Curr Opin Pharm.* doi: 10.1016/j.coph.2008.07.009.

[2] The Staff of the Jackson Laboratory. Biology of the Laboratory Mouse. New York: *Dover Publications INC*., 1966.

[3] Reichert, W. (2008). Indwelling Neural Implants: Strategies for Contending With the in Vivo Environment (Frontiers in neuroengineering). CRC Press, Chapter 3.

[4] Towne, C., Montgomery, K. L., Iyer, S. M., Deisseroth, K., & Delp, S. L. (2013). Optogenetic Control of Targeted Peripheral Axons in Freely Moving Animals. *PLoS ONE,8*(8). doi:10.1371/journal.pone.0072691

[5] Bonin, R. P., Wang, F., Desrochers-Couture, M., Ga¸secka, A., Boulanger, M., Côté, D. C., & Koninck, Y. D. (2016). Epidural optogenetics for controlled analgesia. *Molecular Pain,12*, 174480691662905. doi:10.1177/1744806916629051