Aaron “Ari” received his Bachelor of Science degree in Chemical Engineering from California State University, Long Beach. He is now a 4th year graduate student in the UC Berkeley Bioengineering Program and working in Professor Daniel Fletcher’s lab. He is researching the biophysics of protein organization and signaling at immune cell interfaces with other cells and pathogen.

Fellowship Proposal

Parasitic worm infections account for the most prevalent neglected disease group in the world, with nearly one third of the world’s population being infected. One reason for the high prevalence is that infection with worms often does not lead to easily identifiable sickness and death. While individuals infected with parasitic worms can display lethargy, anemia, malnourishment, and other symptoms they are usually able to partake in normal daily life. This fact may be explained by the ability of parasitic worms to appear invisible to their host’s immune system or promote an immunosuppressive environment around them. The molecular mechanisms by which worms are able to evade the immune system remain unknown, but understanding how they do so could have far-reaching implications for eliminating filarial infections, as well as healthcare applications where suppression of the immune system is desired.

Multiple studies have shown that parasitic worms are able to modulate the immune response of their host by inducing an immunosuppressive environment characterized by Tregulatory cells and regulatory cytokines. It is hypothesized that secretion of immune inhibiting molecules may be involved, but little is known about their identity and the extent to which immunosuppression is mediated independently by the worm in response to its tissue environment. Furthermore, the immune response to the surface of a parasitic worm, which is largely composed of the polysaccharides chitin and chitosan, has not been well characterized, as previous studies have found conflicting results on whether it is inflammatory or suppressive.

In this project, Ari proposes to adapt the in vitro tools that he has developed to understand macrophage target recognition in cancer to address basic questions about how filarial parasites regulate the immune system. The first aim of the project will be to study the effect of worm secretions on innate immune cells in vitro to determine the importance of soluble factors on immunosuppression. In the second aim, Ari will test whether filarial surface polysaccharides are sufficient to activate macrophage effector function.

This will be the first study directly probing interactions between parasitic worms and innate immune cells in vitro that will provide insight into the mechanisms of immune evasion employed by worms. Elucidation of this mechanism will be directly useful in two ways: (i) it can be used to find new ways to overcome immune evasion and redirect the immune system to clear worm infections and (ii) it can be engineered into therapies and procedures where immune evasion is a desired outcome, such as in implantable devices.