Roles of Endothelial Cells on HIV-1 Infection and Latency in Resting CD4+ T Cells

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The World Health Organization estimates that around 40 million individuals worldwide are infected by HIV. For these 40 million people, their diagnosis is a life sentence. Even though much progress has been made since the initial outbreak of the virus, the best that modern medicine can do is manage the symptoms of HIV via highly active antiretroviral therapy (HAART). While this enables those who have access to treatment to enjoy a relatively high quality of life, the virus will rebound if medication is discontinued. The viral rebound of HIV is made possible by a latent reservoir of cells harboring the virus in an inactive form. CD4+ T cells, immune system cells which can be infected by HIV, comprise a significant stable reservoir of the virus in the body. Previous research has shown that interactions between CD4+ and other cell types via both direct contact and cytokine secretion increase the infectivity of the CD4+ T cells. In our lab this summer we studied the interactions between resting CD4+ T cells and endothelial cells, the cells which line the blood vessels, in order to better understand the mechanisms by which the interactions increase HIV infection rates in the T cells.

Throughout the history of this project, the resting CD4+ T cells that we use have been isolated from volunteer blood donors on-site and the endothelial cells have been from a cell line known as HUVEC (Human Umbilical Vein Endothelial Cells). Recently, we have begun to use a different endothelial cell line derived of lymphoid tissue in order to better emulate in vivo conditions. My research focus has been comparing the relationship between resting CD4+ T cells and HUVEC to the relationship between resting CD4+ T cells and lymphatic endothelial cells (LEC). To study these relationships, we first collect blood from a donor and isolate peripheral blood mononuclear cells via a Ficoll procedure. Next, we use a process known as bead depletion to isolate the specific T cell type we are looking at (either resting CD4+, naïve, or memory) and plate the T cells in wells together with endothelial cells. The next day, the wells are infected with a pseudotyped strain of HIV infection that is tagged with Green Fluorescent Protein (GFP). After a designated incubation time (3-10 days), infection rates are measured using flow cytometry.

Our results have enabled us to make some interesting conclusions thus far this summer. During time course experiments, in which infection rates are measured over the course of 3-10 days at various intervals, we found that T cells cocultured with LEC showed a later peak of infectivity than T cells cocultured with HUVEC. We also theorized that varying infection patterns in different trials were due to the proportion of the T cell population that was naïve vs. memory and also corresponded to the passage numbers of the endothelial cells.

Researching in the Shen lab has been an invaluable experience for me this summer. I have loved seeing the concepts I learn about in class unfold in real life and be utilized in an attempt to renew God’s world by helping others. Due to my interest in the field of immunology, being able to work on this project was incredibly exciting. I have learned so much from Dr. Shen and I cannot thank her, my lab mates, and the National Institute of Health enough for making my research experience this summer so meaningful.