Comparing Effects of Atmospheric Oxygen Levels vs. Physiological Oxygen Levels on HIV Infection of T Cells

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Introduction and Background

HIV, (human immunodeficiency virus) is the retrovirus that causes AIDS. It infects T cells, which are part of the body’s immune system and found throughout the bloodstream. These T cells may be resting when they are not needed to fight infection, or may become activated if needed. Under previous understanding, only activated T cells could become infected by the HIV virus, and latency (virus DNA “hiding” inside resting cells) would develop when the virus entered during the activated-to-resting transition. Findings in recent years revealed, however, that contact with endothelial cells (which line the body’s blood vessels) plays a role in facilitating resting T cell infection. This year’s research included several sub-projects attempting to better describe this interaction, including experiments set in oxygen levels more similar to those encountered physiologically. This has been a significant issue in experiments with T cells, as recent investigations have shown there to be a difference in cell behavior when cultured at atmospheric oxygen levels (~21%) vs. physiological levels (~5%).

Research Methods

At the beginning of the summer, we were given a list of some 65 procedures which we would be drawing from as part of our research. While we didn’t encounter many of these protocols regularly, the difference of how much each student researcher could do at the beginning and end of the 10-week program was stark. I in particular became the default person to “ficoll,” a procedure which involved separating the desired peripheral blood mononuclear cells from the rest of the blood. These cells were then often isolated to contain only CD4+ T cells by labeling with magnetic antibodies and running them through a magnetic column. Cells would then be plated for various experiments, such as time courses to test infection and viability rates. Analysis was done by counting cells and by flow cytometry, which allowed us to sort cells based on expression of green fluorescent proteins (GFP).

Results

Activated cells cultured in lower, more physiologically representative oxygen levels typically showed lower infection rates and thus, not surprisingly, better rates of survival. Other resting cells showed mixed results, suggesting that these cells are not as affected by oxygen levels. There was also a pattern noticed in the percentage of cells that became activated when cultured in atmospheric vs. physiological oxygen levels: more cells became activated at lower oxygen levels than in unregulated levels. This percent activation contrasts what we called “density” of activation markers on each cell, which was higher in unregulated oxygen. This observation may or may not have significance.

Personal Experience

Working in Professor Shen’s lab has been a great experience. As a pre-med student, I wanted to do something this summer that would both build on the skills I had learned through my coursework, but also strengthen my résumé. Its amazing to think that I and the other undergrads that I work with are taking part in such innovative research! My time here has done so, as well as allowed me to get to know Professor Shen outside the classroom. Her instruction has been very beneficial, and hopefully will be beneficial in both her immunology class and my future in medicine.