Higher IL-6 Concentration Correlates with Higher HIV-1 Infection Rate in Resting CD4+ T Cells

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Abstract

CD4+ resting T cells are highly resistant to HIV infection in vitro. When they are exposed to endothelial cells the infection rate significantly increases. Previous research suggests that there is a correlation between IL-6, a cytokine secreted by endothelial cells, and HIV-1 infection rate in CD4+ resting T cells. Using ELISA techniques, we found higher infection occurs most commonly with a higher IL-6 final concentration within the supernatant. Memory T cells secrete more IL-6 than naïve T cells and also produce a higher infection rate. Additionally, the endothelial cells with which the T-cells are cultured seem to secrete a variable amount of IL-6. Human Umbilical Vein Endothelial Cells (HUVECs) secrete a significantly higher concentration of IL-6 than Lymphatic Endothelial Cells (LECs). This affirms previous research showing that HUVECs induce higher infection than LECs. While IL-6 appears to be strongly correlated with infection rate, we also showed that while IL-6 was completely blocked using antibodies, infection still occurred, albeit at a lower rate. This suggests that there are additional mechanisms used to induce infection.

Introduction

HIV-1, the virus that leads to AIDS, is a worldwide problem affecting nearly 40 million people worldwide. It selectively infects CD4+ T cells and forms latent vectors which makes the virus particularly difficult to treat. (1) To make matters more complicated, HIV can infect a limited amount of Resting CD4+ T cells without prior activation. More recently Choi et el demonstrated that endothelial cells, the cells that line human blood vessels and have frequent contact with Resting CD4+ T Cells, seem to have a positive effect on the infection of Resting CD4+ T Cells. (2,3) Shen et el further demonstrated that ECs have the ability to increase both productive and latent infection rates. (4) IL-6 was determined to be a key cytokine in this process.

Figures

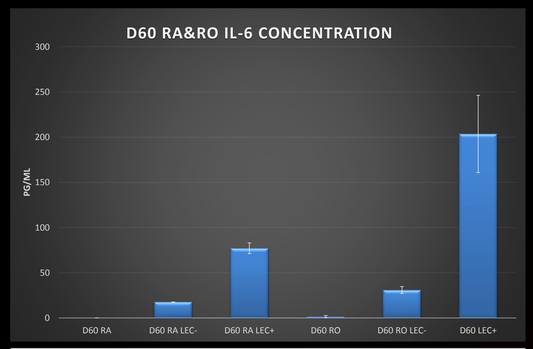

Figure 1. CD4+ Resting Memory T Cells secrete a higher concentration of IL-6 than CD4+ Resting Naïve T Cells When CD4+ Resting T Cells are cultured with Lymphatic Endothelial Cells (LECs), the concentration of IL-6 secreted appears to correlate with whether the cell is categorized as a memory CD4+ T cell (those displaying the RO cell surface marker) or a naïve CD4+ T cell (those displaying the RA cell surface marker.) According to the data collected, memory cells of this type secrete a higher concentration of IL-6 than that of naïve cells. This also correlates with a higher infection rate of memory cells than naïve cells (refer to Figure 2.)

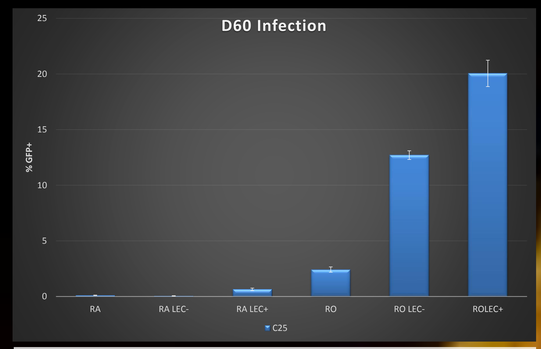

Figure 2. CD4+ Resting Memory T Cells display a higher infection rate with HIV than CD4+ Resting Naïve T Cells When CD4+ Resting T Cells are cultured with Lymphatic Endothelial Cells (LECs), the infection rate correlates with whether the cell is categorized as a memory CD4+ T cell (those displaying the RO cell surface marker) or a naïve CD4+ T cell (those displaying the RA cell surface marker.) This correlates with data from Figure 1 which suggests that the a higher IL-6 secretion, typically seen with memory cells, is correlated with a higher infection rate, measured using Green Fluorescent Protein (GFP).

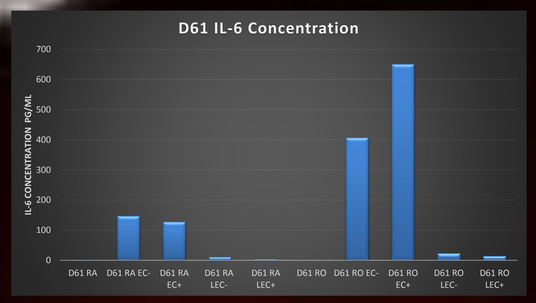

Figure 3. When cultured with Human Resting CD4+ T Cells, Human Umbilical Cord Endothelial Cells secrete a higher concentration of IL-6 than do Lymphatic Endothelial Cells in vitro Human Umbilical Cord Endothelial Cells (HUVECs,) here portrayed as EC- and EC+ depending on whether they were exposed to interferon gamma, have been shown to induce a higher HIV infection rate among Resting CD4+ T Cells than do Lymphatic Endothelial Cells (LECs) (Refer to Figure 4). This data shows that the HUVECs also secrete a higher concentration of IL-6 than do LECs. This supports our hypothesis that higher IL-6 concentration correlates with a higher infection rate.

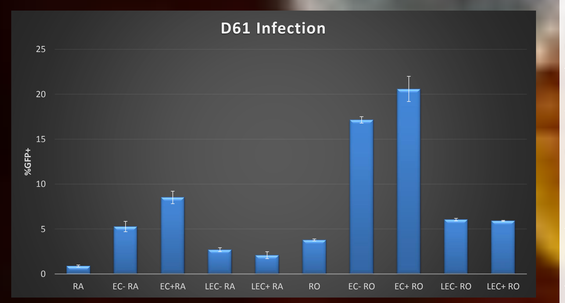

Figure 4: When cultured with Human Resting CD4+ T Cells, Human Umbilical Cord Endothelial Cells induce a higher HIV infection rate than do Lymphatic Endothelial Cells. This data supports previous research suggesting that HUVECs induce a higher HIV infection rate, measured by Green Fluorescent Protein (GFP) than do Lymphatic Endothelial Cells.

Results

The results from the data can be summarized into two main points:

- CD4+ Resting Memory T Cells secrete a higher concentration of IL-6 than do Naïve cells and also display a higher infection rate.
- HUVECs secrete a higher concentration of IL-6 than do LECs and also induce a higher infection rate in Resting CD4+ T Cells

Conclusions

Through these experiments, we were able to further understand the effects IL-6 has on Resting CD4+ T cells in vitro. Previously, studies had shown IL-6 was positively correlated with a higher infection rate. Here, we were able to show that certain categories of T cells tend to secrete higher concentrations of IL-6 and this correlates with their higher infection rates. Additionally, we were able to show that HUVECs and LECs secrete different concentrations of IL-6 and this correlates with previous research demonstrating higher infection rates when cells are cultured with HUVECs.

Future Directions

Although ELISA has been very helpful in determining correlations between secretions of IL-6 and infection rates in Resting CD4+ T Cells, this research is fairly new and there is still much to be discovered and understood. We have reason to believe that there are other cytokines assisting in the role of infection. Determining what these cytokines are, and their role in the infection process is crucial for future ELISA studies. Additionally, we have found that endothelial cells (both HUVECs and LECs) seem to secrete a variable amount of base IL-6 that can change the way the cells interact with the T-cells. We have yet to understand the mechanism behind this variance.

References + Acknowledgements

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