The CD5 Coreceptor's Effect on T Cell Proliferation in Periodontal Disease

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Introduction

Periodontal Disease: Periodontal disease (gun disease) is a preventable yet common oral inflammatory disease caused by prolonged exposure of the oral epithelium to bacteria. With prolonged exposure to pathogens, inflammation begins and T cells are recruited to the infection site. In particular, helper T cells are recruited and exacerbate bone destruction and resorption by increasing inflammation and recruiting more immune cells to the site of infection.

T cell Interactions: T cell function is regulated via signaling of the T cell receptor (TCR) and co-receptors expressed on the surface of the cell, which can stimulate or inhibit T cell function. CD5 is a T cell co-receptor that regulates T cell development and function. Our study investigates the role of CD5 in helper T cell activation and its effect in oral inflammation. We will compare the differences in proliferation of stimulated T cells with and without CD5. Cell proliferation is an indication of T cell activation. If CD5 regulates helper T cell activation it could be a target for treatments of periodontal disease.

Purpose

To investigate the relationship helper T cell activation in response to stimuli associated with periodontal disease

Hypothesis

We hypothesize that T cells lacking CD5 (CD5 KO) will have increased proliferation compared to T cells expressing CD5 (CD5 WT).

Materials and Methods

Cell lines used: Oral mucosa epithelial cells, and Gingiva epithelial cells from mice (C57BL/6 background). Cell lines were exposed to LPS from *P.gingivalis* (LPS-PG) and LPS from *E.coli* (LPS-EC) for 24 hrs.

Splenocytes from CD5KO and CD5WT mice (C57BL/6 background), were isolated and co-cultured as follows:

1. Each of the oral epithelial cells and their supernatant for 48 and 72 hours.
2. Observed differences in T cell proliferation by comparing intensities of intracellular staining (CFSE) using flow cytometry.

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Preliminary Results

CD4+ T cells exposed to Mucosal epithelial cells treated with LPS from *P. gingivalis* for 48 and 72 hours

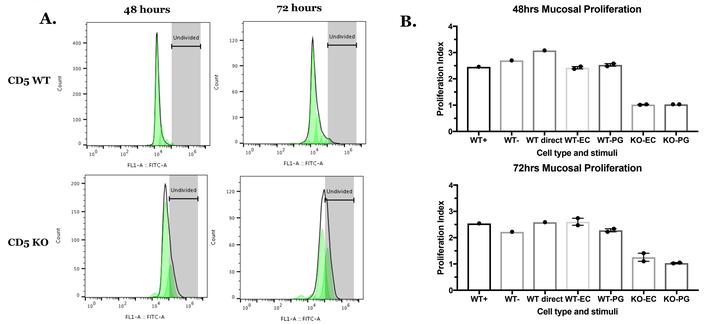

Figure 1. CD5KO CD4 T cells appear to proliferate less than CD5WT CD4 T cells. A. CD5WT CD4 T cells have more cells present in later generations showing more proliferation. Green peaks represent the proliferation model fit to the data, which is shown on the graph as a solid black line. **B.** Proliferation indexes of CD5WT and CD5KO CD4 T cells were compared with WT controls after 48 and 72 hours. The bars for the CD5KO CD4 T cells are significantly less than the CD5WT.

CD4+ T treated with CD3/28 Dynabeads as Positive Control or R10 Media Only as Negative Control

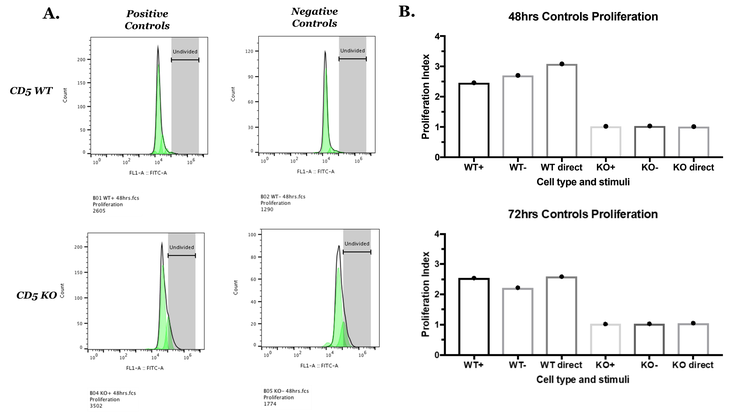

Figure 2. Positive and negative controls do not show distinct differences. A. CD4 T cells from both CD5WT and CD5KO stimulated with CD3/28 beads showed no significant difference in proliferation after 48 hours. Green peaks represent the proliferation model fit to the data, which is shown on the graph as a solid black line. **B.** Proliferation indexes of all controls were compared at 48 and 72 hours. Columns labeled as "direct" represent CD4 T cells stimulated with LPS from *E. coli.*

Conclusions and Future Directions

It is hard to say if our preliminary data is starting to suggest that our hypothesis is correct because our controls have not been reliable. We have not been able to show a clear distinction between a positive and negative control. There are certainly some interesting trends in our data but no conclusions can be drawn without clear positive and negative controls.

Previous studies conducted in our lab have suggested that our hypotheses are correct. Some of our research showed significant differences between CD5 WT and CD5 KO CD4 T cells surface markers commonly associated with early and late activation (CD69 and CD25). Because of these results we would suspect that proliferation would also be inhibited in cells with CD5 present.

We are still in the process of optimizing this experiment and hope to have more convincing results in the future to draw conclusions about the role of CD5 in T cell proliferation associated with periodontal disease.

Clinical Implications of Research

Some of the most detrimental consequences of severe periodontitis (bone and tooth loss) result directly from the body's immune inflammatory response to bacterial infection in the gingiva. Our research aims to deepen our understanding of the immune response to infection in the oral cavity.

This relevant in the dental field since an understanding in oral immunology response could help to comprehend clinical associations between periodontal disease and systemic diseases, which might result in the improvement of patient management, as well as the creation of new avenues for periodontal disease treatment. Our main aim is to understand how managing CD5 expression in the oral cavity could dampen the body's immune response, and mitigate the negative consequences of periodontal disease.

Acknowledgements

Study conducted with funding from **Roseman University of Health and Brigham Young University** BYU undergraduate research award (CURA).

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