Candida albicans and Candida tropicalis are both commensal and opportunistic pathogens of the gut that are of increasing medical significance and that have been implicated in human Crohn’s Disease [2,3]. We were interested in understanding how the gut-associated lymphoid tissues (GALT) sample these two fungi, and what the consequences of this might be for the intestinal mucosa. Peyers Patches (PPs) are responsible for sampling of microbes that pass through the gut. Our research utilized three approaches.

i) Our first question was, are fungi sample by PPs? To answer this question, BALB/c mice were gavaged with fungi, and the PPs were cryosectioned and immunofluorescently stained at 24 hours. To quantify the sampling of fungi, BALB/c mice were infected by gavage with C. albicans and C. tropicalis, respectively, and the PPs were cryosectioned and immunofluorescently stained at 24 hours. Our results revealed significantly higher CFU of C. albicans from PP compared to C. tropicalis within PP. However, fungal undetectable in spleen and MLN. In contrast, fluorescent microscopy showed that C. tropicalis was more abundant in PPs. Therefore, it appears that PP do sample fungi, but in a rather selective way. The reason for this is not yet entirely unknown. There may be a different dynamic with C. tropicalis because it is a commensal organism to mice, while C. albicans is not.

ii) To determine whether trafficking of fungi from PP depended on DCs, an additional mouse model was employed. In BALB/c mice, a subset of DC cells (CD11b-CD8α-), but positive for Langerin+.

iii) To determine whether these two fungi compromise the immune system, five groups of five BALB/c mice each were gavaged with cholera toxin alone (a strong adjuvant), C. albicans or C. tropicalis plus cholera toxin, cholera toxin plus cyclophosphamide (positive control for immune suppression), or PBS only (negative control). We used an indirect ELISA to measure fungal antibodies in the serum and feces, mice were examined on days 7, 14, and 21. Both serum and fecal data clearly showed that mice gavaged with fungi have significantly reduced antibody (Ab) titers, IgG, IgA, IgM titers when compared with cholera toxin alone.

Using these three approaches, we now have a better understanding of how fungal pathogens interact with the gut mucosa. This may help determine new leads for better treatments of human intestinal disease.

Questions to be Addressed

1. Are fungal organisms sampled by Peyers patches?
2. Is trafficking of fungal dependent on dendritic cells?
3. Do the fungi weaken an immune response?

Candida albicans and Candida tropicalis

Results

First, the uptake of live fungi was analyzed by cryosectioning and immunostaining. As expected, the fungi were only taken up by the subset of PP DCs which are CD8α-CD11b-, but Langerin+. The DCs in mice gavaged with C. tropicalis had a larger volume of fungi taken up, compared to mice gavaged with C. albicans. From the CFU experiment it is important to see that the abundance of C. tropicalis cells that are taken up are not viable, compared to smaller volume of C. albicans taken up, as shown by cross-sections. Also, it is important to see that no detectable level of fungi was present in the CFU experiment, even though C. tropicalis is a commensal organism to mice. When using the CCR7 knockout mice, the fate of fungi after uptake was tested. The CCR7- mice were gavaged with fungi, and at the twenty-four hour time point the DCs are significantly more gorged.

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C. albicans and C. tropicalis

Conclusions

i) Is trafficking of fungi dependent on dendritic cells?
ii) Is fungal infection upregulated by exposure to both fungi?
iii) To determine whether these two fungi compromise the immune system, five groups of five BALB/c mice each were gavaged with cholera toxin alone (a strong adjuvant), C. albicans or C. tropicalis plus cholera toxin, cholera toxin plus cyclophosphamide (positive control for immune suppression), or PBS only (negative control). We used an indirect ELISA to measure fungal antibodies in the serum and feces, mice were examined on days 7, 14, and 21. Both serum and fecal data clearly showed that mice gavaged with fungi have significantly reduced antibody (Ab) titers, IgG, IgA, IgM titers when compared with cholera toxin alone.

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Introduction

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