Differential Dendritic Cell Recruitment Induced by the Gut Microbiota in Cardiac Transplantation

UNIVERSITY of MARYLAND SCHOOL OF MEDICINE

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BACKGROUND

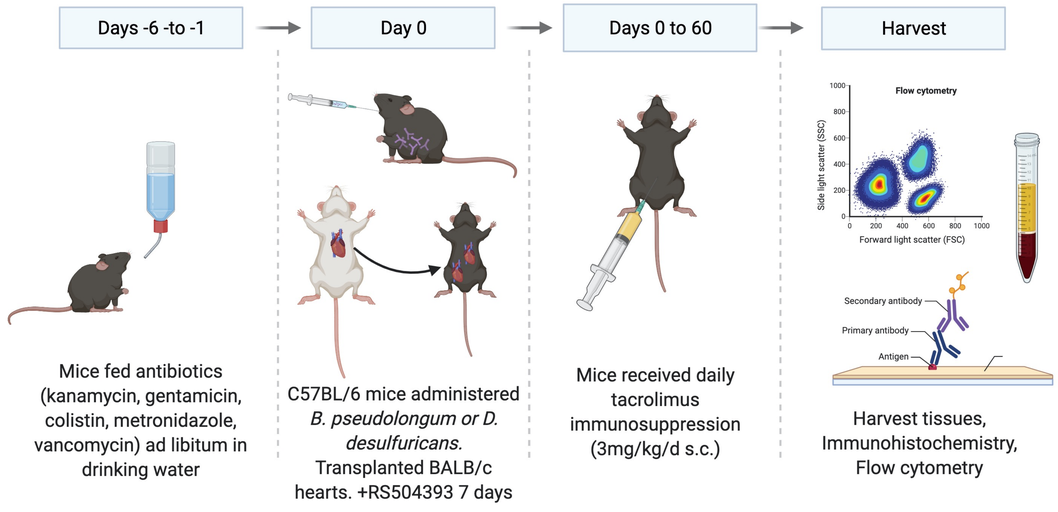
Bifidobacterium pseudolongum
- Identified from pregnant mouse fecal samples
- Significantly associated with an anti-inflammatory environment and a protective effect on transplant outcomes

Desulfovibrio desulfuricans
- Identified from colitic mouse fecal samples
- Significantly associated with a pro-inflammatory environment and a detrimental effect on transplant outcomes

OBJECTIVES

- To identify the mechanisms by which gut microbiota constituents *Bifidobacterium* and *Desulfovibrio* influence allograft survival
- To identify the effects of these microbiota constituents on innate immune cell recruitment

METHODS



- RS504393, a CCR2 antagonist that inhibits myeloid cell (primarily macrophage) migration, was administered for 7 days
- Statistical Analysis: Ordinary one-way ANOVA. P values < 0.05 shown
- Changes in CD11c+ dendritic cell (DC) content in intestine, lymph nodes (LNs), and spleen were analyzed by immunohistochemistry and flow cytometry
- N = 3 mice per group

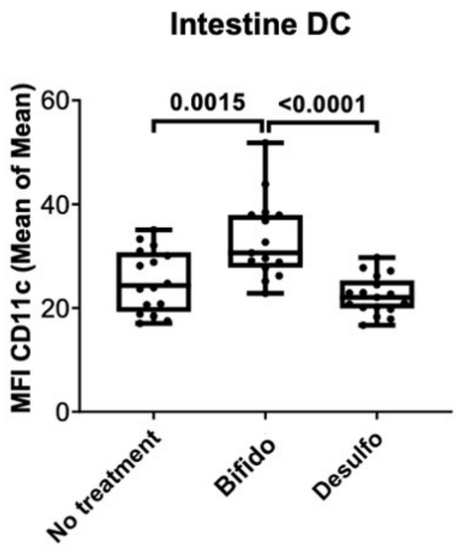


Figure 1: CD11c+ DC Recruitment to Intestines

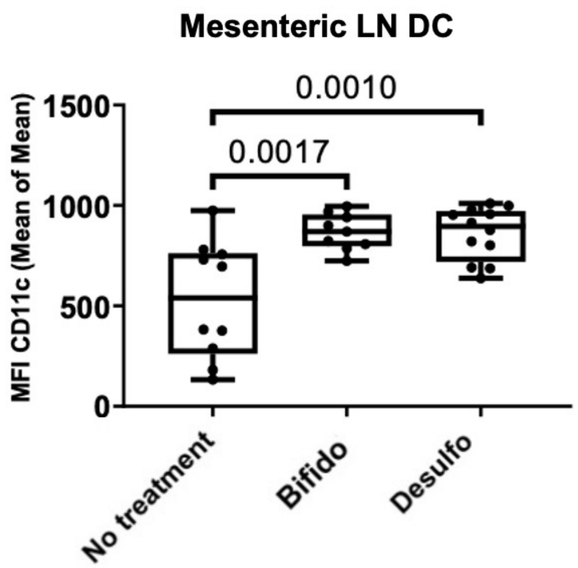


Figure 2: CD11c+ DC Recruitment to Local Mesenteric Lymph Nodes

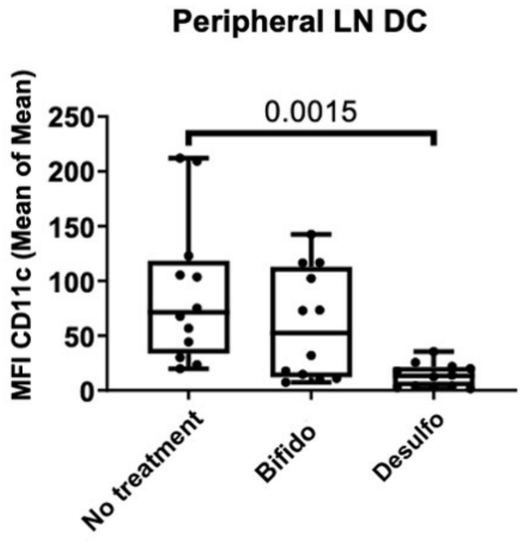


Figure 3: CD11c+ DC Recruitment to Systemic Peripheral Lymph Nodes

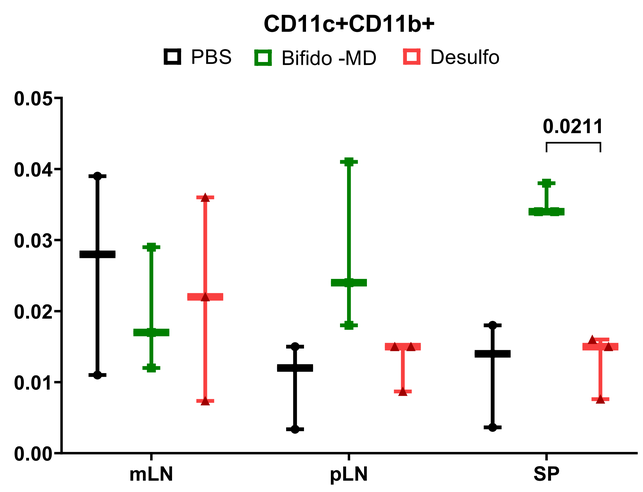


Figure 4: Tolerogenic CD11c+CD11b+ DC Subset Recruitment to Lymph Nodes and Spleen

RESULTS

- The *Bifidobacterium* group had significantly more DC in the intestine compared to *Desulfovibrio* and control
- Both *Bifidobacterium* and *Desulfovibrio* groups had increased DC in downstream mesenteric LNs
- In systemic peripheral LNs, only the *Desulfovibrio* group showed decreased DC compared to *Bifidobacterium* and control
- The *Bifidobacterium* group induced increased tolerogenic CD11c+CD11b+ DC subset content in the spleen

CONCLUSIONS

- Gut microbiota constituents differentially regulate DC migration to and retention in intestines as well as regional and systemic LNs
- This subsequently can lead to downstream differences in immune cell recruitment in the lymphoid organs, ultimately affecting long-term allograft survival

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Funded by the ASTS Presidential Student Mentor Grant

ASTS American Society of Transplant Surgeons