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Fecal Transplantation-Mediated Modulation of Neointimal Hyperplasia after Arterial Injury in Antibiotic-Treated Mice

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Background

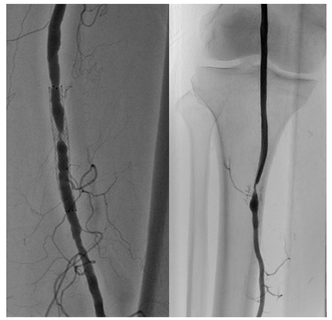


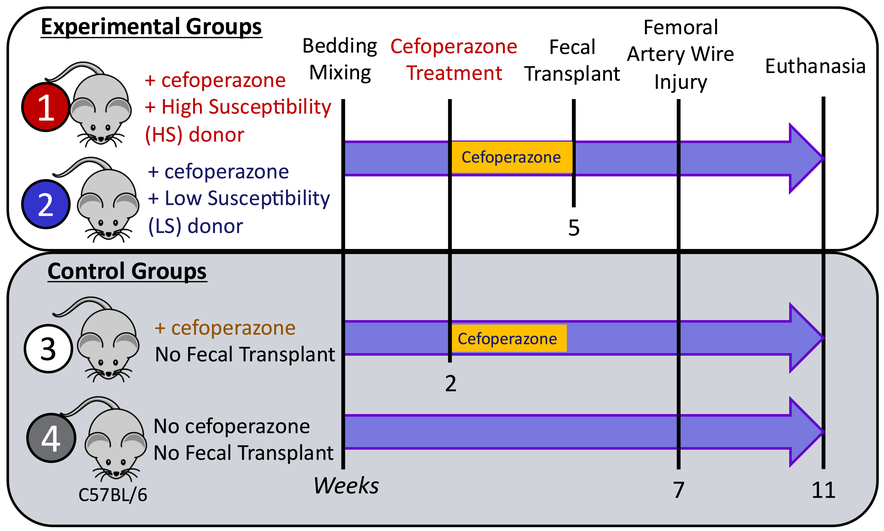
Figure 1: Examples of neointimal hyperplasia resulting in in-stent and bypass restenosis

- Neointimal hyperplasia is an inflammatory process that causes restenosis and failure of bypass surgery, angioplasty, and stenting for atherosclerosis
- In prior experiments, we demonstrated that the presence of gut microbiota increases susceptibility to neointimal hyperplasia in Germ Free (GF) mice
- Unfortunately, GF mice have abnormal immune development and responses, suggesting the utility of an alternative model
- Continued need to improve understanding of the environmental factors that influence susceptibility to neointimal hyperplasia

Objectives

- Use neointimal hyperplasia low susceptibility (LS) and high susceptibility (HS) rat donor based on prior experiments
- Determine whether neointimal hyperplasia phenotype (severity) can be transferred through fecal (microbial) transplant to antibiotic-treated conventional mice (CONV-R) as an alternative to Germ Free (GF) mice

Methods



Results

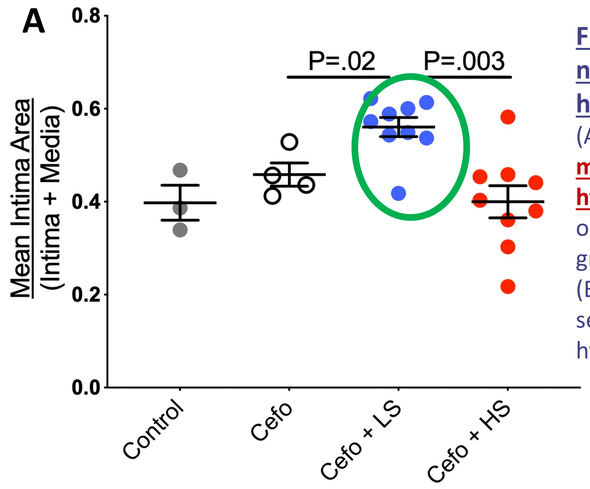
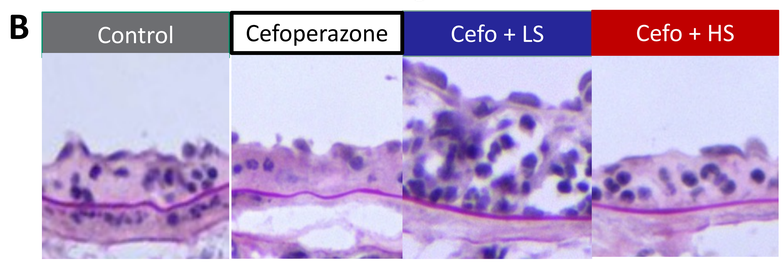


Figure 2: Severity of neointimal hyperplasia by group
(A) Cefo + LS group has more severe neointimal hyperplasia than Cefo only and Cefo + HS groups
(B) Example histological sections of neointimal hyperplasia per group



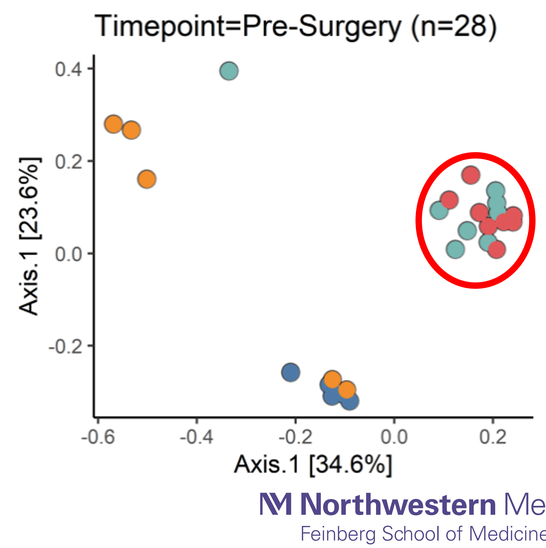


Figure 3: Microbial β-Diversity using 16S sequencing of fecal samples and principal components analysis
The transplanted groups cluster together, separately from the control groups. (Red Circle)

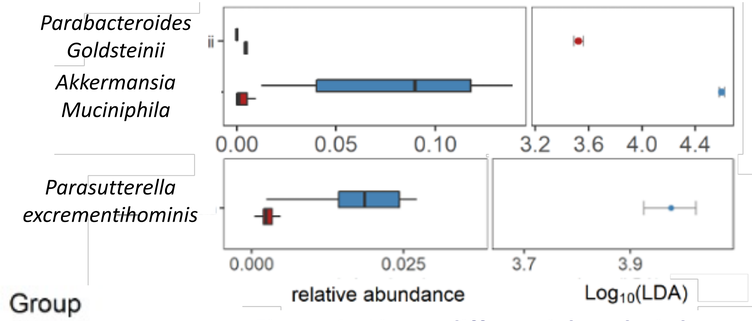


Figure 4: Linear differential analysis between Cefo + LS and Cefo + HS microbiota
Three bacterial species had significant differences in relative abundance

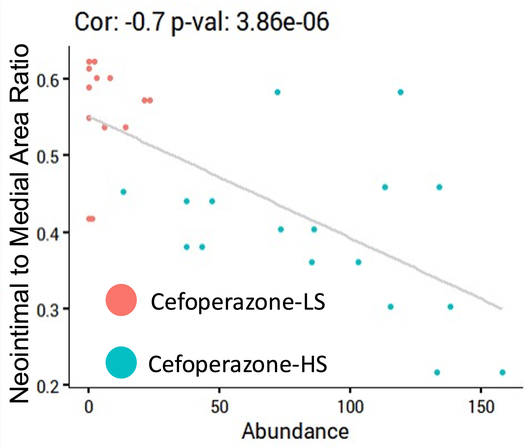


Figure 5: Correlation between relative abundance of *Akkermansia* and neointimal hyperplasia
Akkermansia was highly correlated with severity of neointimal hyperplasia. It plays a key role in modulating the gut mucin barrier

Conclusions

- Fecal transplant after antibiotic treatment in CONV-R mice impacts susceptibility to neointimal hyperplasia through modulation of key members of the gut microbiota
- Relative abundance of *Akkermansia mucinophila* is correlated with decreased neointimal hyperplasia
- Ongoing shotgun metagenomics have revealed key associated pathways in complex microbial sugar and metal metabolism
- This new knowledge can be potentially used for adjunctive synbiotic, pre-biotic, or pro-biotic therapies for patients undergoing cardiovascular procedures

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