

## **ABSTRACT TITLE**

**TITLE:** HLA-B27 affects the gut microbiome of transgenic rats

## **PROGRAM # (Final ID)**

**ABSTRACT FINAL ID:** 353

**SESSION TYPE:** Paper Session

## **POSTER BOARD # (DOI)**

**DIGITAL OBJECT IDENTIFIER (DOI):**

## **PRESENTATION START/END**

**SESSION ABSTRACT START TIME:** 10:30 AM

**SESSION ABSTRACT END TIME:** 10:45 AM

## **SESSION # (Abbreviation)**

**SESSION ABBREVIATION:** 116

**SESSION TITLE:** CNS and Ocular Inflammation and Infection

**SESSION DAY & DATE:** Sunday, May 5, 2013

**SESSION START TIME:** 10:30 AM

**SESSION END TIME:** 12:15 PM

**AUTHORS (LAST NAME, FIRST NAME):** Lin, Phoebe<sup>1</sup>; Bach, Mary<sup>2</sup>; Lee, Aaron Y.<sup>5</sup>; Akileswaran, Lakshmi<sup>3</sup>; Taurog, Joel D.<sup>6</sup>; Rosenbaum, James T.<sup>1,4</sup>; Van Gelder, Russell N.<sup>3</sup>

**INSTITUTIONS (ALL):** 1. Ophthalmology, Oregon Health and Science University, Portland, OR, United States.  
2. Rheumatology, University of Washington, Seattle, WA, United States.  
3. Ophthalmology, University of Washington, Seattle, WA, United States.  
4. Ophthalmology, Devers Eye Institute, Portland, OR, United States.  
5. Ophthalmology, Washington University, St. Louis, MO, United States.  
6. Rheumatic Diseases and Internal Medicine, UT Southwestern, Dallas, TX, United States.

## **Study Group:**

### **ABSTRACT BODY:**

**Purpose:** The HLA-B27 gene is a major risk factor for acute anterior uveitis, but its mechanism of risk enhancement is not completely understood. The gut microbiome has been shown to be important in the development of HLA-B27-mediated arthritis in transgenic rats as demonstrated by abrogating clinical disease by rearing animals in a germ-free environment. However, the role of HLA-B27 in shaping the gut microbiome has not been elucidated. In this study, we characterize the differences in the gut microflora mediated by the presence of the HLA-B27 gene.

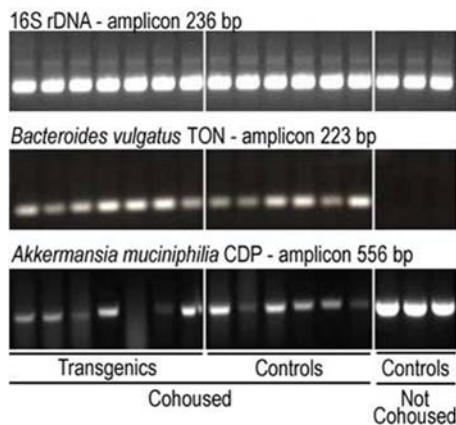
**Methods:** We identified differences between the cecal microbiome in 45 day-old co-transgenic HLA-B27/beta2-microglobulin Lewis rats (n=7) compared with wild-type Lewis rats (n=6 co-housed, n=3 non-co-housed) using biome representational in situ karyotyping (BRISK). Co-housed rats are housed in the same cages as their transgenic littermates, which is expected to minimize microbiome differences since rats are coprophagic. We confirmed differences by quantitative PCR (qPCR) with normalization based on amplification of 16S ribosomal DNA.

**Results:** Of 909 species of bacteria identified by BRISK, 30 species showed statistically significant differences in HLA-B27/beta2microglobulin transgenic rats compared to wild-type controls as determined by iterative Monte Carlo analysis of the dataset. The three organisms showing the most difference were *Faecalibacterium prausnitzii*, *Bacteroides vulgatus*, and *Akkermansia muciniphila*. A difference in *F. prausnitzii* could not be confirmed by qPCR. However, there were higher levels of *B. vulgatus* and lower

levels of Akkermansia in transgenic rats compared to non-co-housed control rats (Figure 1). Co-housed control rats did not demonstrate as large a difference in these two organisms compared to their transgenic cage mates. Both *B. vulgatus* and Akkermansia have been implicated in other immune-mediated diseases.

Figure 1. Relative abundance of *B. vulgatus* and Akkermansia muciniphila from cecal flora of B27/beta2microglobulin rats compared to control rats. 16S rDNA served as amplification controls.

**Conclusions:** The presence of HLA-B27 alters the gut microflora by increasing *B. vulgatus* and decreasing Akkermansia. While a causal role cannot be proven, a protective effect of Akkermansia and a disease-producing effect of *B. vulgatus* are plausible.



**Commercial Relationship(s) Disclosure:**

Phoebe Lin: Commercial Relationship: Code N (No Commercial Relationship)

Mary Bach: Commercial Relationship: Code N (No Commercial Relationship)

Aaron Lee: Commercial Relationship(s);Cogent 14 Productions LLC (threeplus.org):Code P (Patent)

Lakshmi Akileswaran: Commercial Relationship: Code N (No Commercial Relationship)

Joel Taurog: Commercial Relationship: Code N (No Commercial Relationship)

James Rosenbaum: Commercial Relationship(s);Genentech:Code C (Consultant);Abbott:Code F (Financial Support);Xoma:Code C (Consultant);Eyegate:Code F (Financial Support);Bristol Myers:Code F (Financial Support);Lux:Code C (Consultant);Novartis:Code C (Consultant);Regeneron:Code C (Consultant);Teva:Code C (Consultant);Therakine:Code F (Financial Support);Mitotech:Code F (Financial Support);Aquinox:Code F (Financial Support);Allergan:Code C (Consultant);Santen:Code C (Consultant)

Russell Van Gelder: Commercial Relationship(s);Novartis:Code F (Financial Support)

**Grant Support:** Yes

**Support Detail:** NEI grant 1K08EY022948; Burroughs-Wellcome Translational Science Award, Research to Prevent Blindness, and NIH CORE grant EY001730

**Clinical Trial Registration:** No

**Other Registry Site:**

**Registration Number:**