IMPACT OF TREATMENT ON THE ESOPHAGEAL MICROBIOTA AND BACTERIAL RECEPTOR EXPRESSION IN EOSINOPHILIC ESOPHAGITIS

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Disclosure

none

Eosinophilic Esophagitis (EoE)

- Environmental triggers: food allergy
- Th2 mediated chronic inflammation
- Esophageal mucosal eosinophilia
- Treatment: steroids and/or diet
- Proton pump inhibitor (PPI) therapy before formal diagnosis of EoE

Rationale

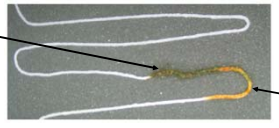
Early life exposures associated with increased odds of developing pediatric-onset of eosinophilic esophagitis EoE

- **Antibiotic use in infancy (6 times odds)**
- **Cesarean delivery**
- **Preterm birth**
- **Formula-only or mixed feeding**

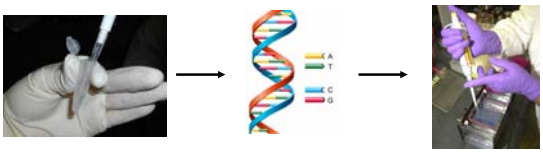
Jensen et al. JPGN 2013

What is the esophageal bacterial composition in EoE?

Esophageal string (EST)

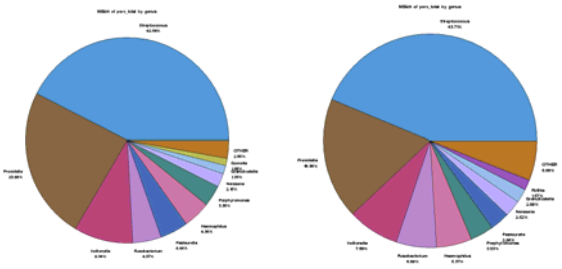


Methods



- DNA purification
- 16S amplification
- Bacteria sequencing by 454 pyrosequencing and Mi Seq illumina

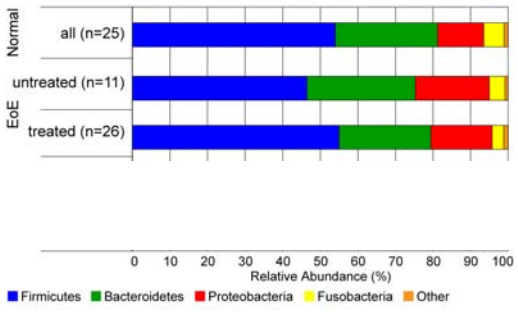
Microbiota on string and biopsy match



String N=15 normal Biopsy

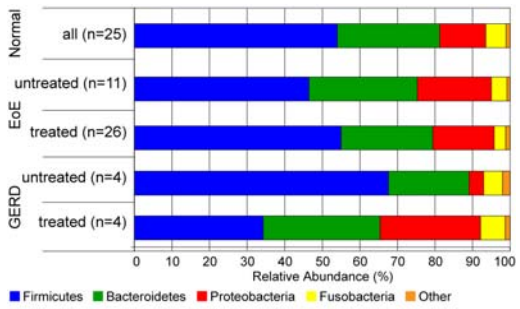
Fillon SA. et al. Plos One Sept 2012

Proteobacteria enrichment in active EoE



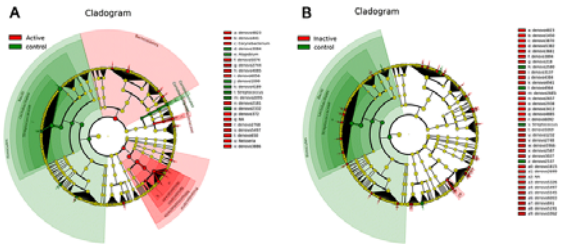
Harris JK et al. and Fillon SA. Plos One May 2015

Proteobacteria enrichment in active EoE



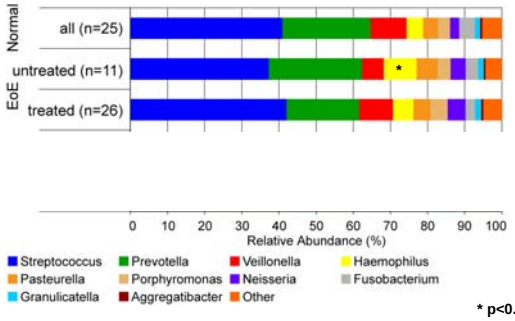
Harris JK et al. and Fillon SA. Plos One May 2015

Proteobacteria enrichment in active EoE



Benitez AJ et al. and Wang ML. Microbiome June 2015

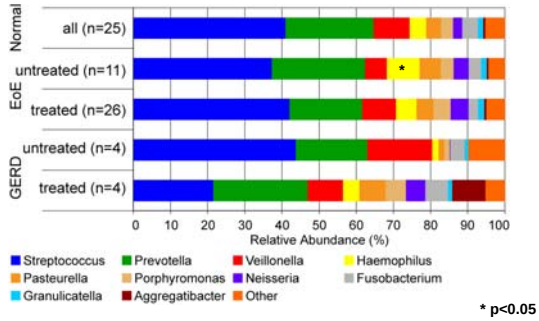
EST genera with diagnosis and treatment



* p<0.05

Harris JK et al. Plos One May 2015

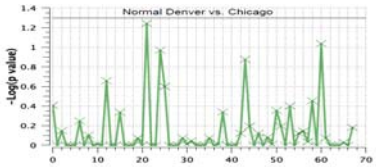
EST genera with diagnosis and treatment



* p<0.05

Harris JK et al. Plos One May 2015

Significant difference between locations in EoE



Harris JK et al. Plos One May 2015

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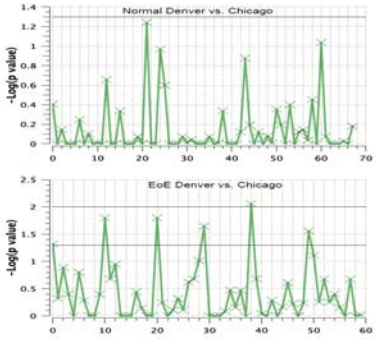
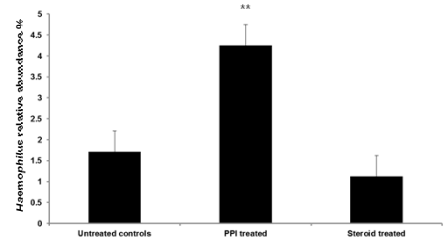


Harris JK et al. Plos One May 2015

Does treatment alter the esophageal microbiota in EoE ?

Impact of proton pump inhibitor and steroid on *Haemophilus* relative abundance

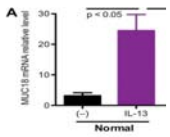


N=	15	42	23

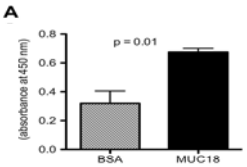
** p<0.01

Does treatment alter expression of bacterial receptor for *Haemophilus* in esophageal epithelial cells?

Effects of IL-13 on MUC18 expression of bronchial epithelial cells



MUC18 interactions with nontypeable *Haemophilus influenzae* (NTHi)



Simon GC et al. Am J of Respiratory Cell and Molecular Biology May 2011

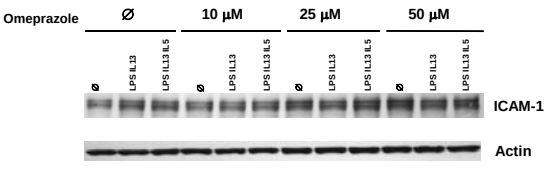
Intercellular Adhesion Molecule 1 (ICAM-1)

Outer Membrane Protein (OMP) P5-homologous adhesin (P5 fimbriae)

from Nontypeable *Haemophilus influenzae* (NTHI) binds ICAM-1

Avadhanula V. et al. Infection Immun. 2006

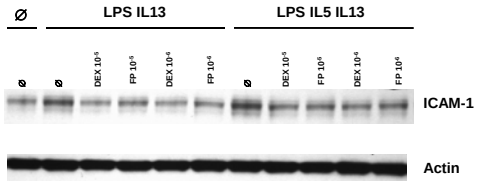
Effect of proton pump inhibitor (PPI) on ICAM-1 expression in esophageal epithelial cells (EPC2-hTERT)



LPS (1 µg/ml)

IL-13 and IL-5 (50 ng/ml)

Effect of steroids on ICAM-1 expression in esophageal epithelial cells (EPC2-hTERT)



Dexamethasone 1 µM: Dex 10^{-6}
Fluticasone Propionate 1 µM: FP 10^{-6}

Dexamethasone 10 µM: Dex 10^{-5}
Fluticasone propionate 10 µM: FP 10^{-5}

LPS (1 µg/ml)

IL-13 and IL-5 (50 ng/ml)

Summary

- Gram negative Phyla Proteobacteria particularly the genus *Haemophilus* is significantly increased in the esophagus of EoE subjects
- Proton pump inhibitor treatment increases the relative abundance of *Haemophilus* in the esophagus by 50%
- Th2 environment and LPS increases the expression of bacterial receptor for *Haemophilus* (ICAM-1) in esophageal epithelial cells
- Omeprazole treatment increases the expression of *Haemophilus* bacterial receptor ICAM-1 in esophageal epithelial cells

Summary

- Steroid treatment in EoE decreases the relative abundance of *Haemophilus* in the esophagus by 25%
- Steroid treatment decreases the expression of *Haemophilus* bacterial receptor ICAM-1 in esophageal epithelial cells

Conclusions

- Subjects with active EoE have a dysbiotic esophageal microbiota
- The bacterial composition and bacterial receptor expression in esophageal epithelium are altered by PPI and steroid treatment

Clinical relevance and impact on patient care

Reconsider the impact of long term use of PPI on the microbiota in EoE

Acknowledgments

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