Presenter Disclosure Information

Monica M. Santisteban, PhD
Intestinal permeability and dysbiosis are linked to hypertension

FINANCIAL DISCLOSURE:
None

UNLABELED/UNAPPROVED USES DISCLOSURE:
None
Intestinal permeability and dysbiosis are linked to hypertension

Mónica M. Santisteban,
Rubiano A, Steward D, Yang T, Cole-Jeffrey CT, Zingler MB, Lobaton GO,
Shenoy V, Zubcevic Z, Simmons C, Raizada MK

Department of Physiology and Functional Genomics
College of Medicine
University of Florida, Gainesville, FL

Sept. 17, 2015
Gut microbiota: health and disease

• 10 microbial cells for every 1 human cell

• Human gut microbiota is made up of *trillions of microorganisms*, dominated by:
  - Firmicutes
  - Bacteroidetes
  - Actinobacteria
  - Proteobacteria
  - Verrucomicrobia

• These *adapt* and *modify* based on:
  - Environment
  - Age
  - Diet
  - Lifestyle modifications
  - Disease states
  - Medications

Fu J et al. Circ Res. 2015 Sep 10
Gut microbiota: health and disease

• Gut dysbiosis is linked to chronic diseases associated with the cardiovascular system:
  • Diabetes
  • Obesity
  • Cardiac dysfunctions
  • Cardiovascular disease

*Diet-independent and –dependent microbial effects on host metabolism*

Introduction

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Conclusions

• Short chain fatty acids (SCFAs) produced by gut microbiota influence BP regulation\(^1\)

• Significant decrease in SBP and DBP in patients who consumed a daily dose of \(\geq 10^9\) CFU of probiotics (meta-analysis of 9 randomized trials)\(^2\)

• Link between gut microbial content and BP regulation in the Dahl rat genetic model of hypertension\(^3\)

• Gut dysbiosis is associated with animal (\textit{SHR and Ang II-induced model}) and human hypertension\(^4\)

**Aim**: Examine the role of the gut microbiota and intestinal pathology in hypertension

**Methods**: SHR and Ang II-induced rat models of hypertension

- Fecal microbial analysis
- Intestinal barrier permeability
  - FITC-dextran translocation
  - qPCR: tight junction components
  - Ex vivo atomic force microscopy
- Autonomic nerve function in the gut
  - In situ electrophysiology: lesser splanchnic nerve
- Intestinal inflammation
  - IHC: CD3, CD68, and HMGB1
  - qPCR: IL1b, TNFa, HMGB1, CD3, and CD68
Gut dysbiosis is associated with hypertension in SHR

Introduction

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Gut dysbiosis is associated with Ang II-induced hypertension


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**Introduction**

**Hypothesis**

**Experimental Data**

**Conclusions**
Increased intestinal barrier permeability in the SHR

**mRNA**

*Small Intestine*

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<th>Gene</th>
<th>Fold Increase</th>
<th>WKY</th>
<th>SHR</th>
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*Proximal Colon*

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**Introduction**

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**Conclusions**

Unpublished
Increased stiffness of SHR intestinal tissue is associated with permeability

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Increased splanchnic sympathetic nerve activity in SHR

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Unpublished
Dr. Jasenka Zubcevic lab
Increased intestinal inflammation in the SHR

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Unpublished

### Experimental Data

#### CD68

- **mRNA**
  - Small Intestine: 
    - WKY: 1.0
    - SHR: 2.0
  - Proximal Colon: 
    - WKY: 1.0
    - SHR: 2.0

#### CD3

- **Fold Increase**
  - Small Intestine: 
    - WKY: 1.0
    - SHR: 6.0
  - Proximal Colon: 
    - WKY: 1.0
    - SHR: 9.0

* * * 

**Note:** The data and images are unpublished.
Increased intestinal inflammation in the SHR

**Small Intestine**

**mRNA**

**Proximal Colon**

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*Increased intestinal inflammation in the SHR mRNA*
Summary

- Extensive gut pathology in HTN includes:
  - Microbial dysbiosis
  - Increased gut barrier permeability
  - Decreased expression of tight junction components
  - Increased splanchnic sympathetic nerve activity
  - Increased intestinal proinflammatory cytokines and immune cell infiltration
Conclusions


Oral Presentation 029
Now
Oral Presentation 075
Tomorrow 9:30am
Poster 057
Today 1:00-2:30pm
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