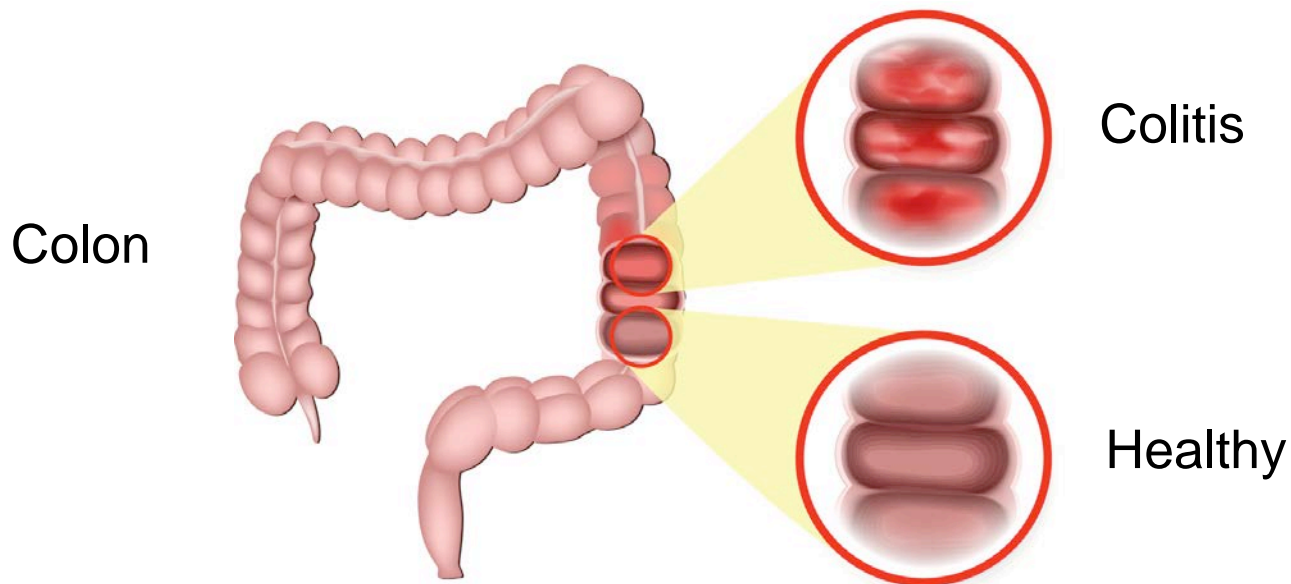


# STAR Talks 2016

## Mechanism of intestinal inflammation caused by antibiotics



Eric Velazquez  
Laboratory of Andreas Bäumler

# Factors Driving Gut Inflammation

Introduction

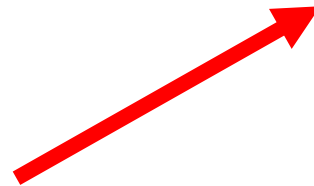
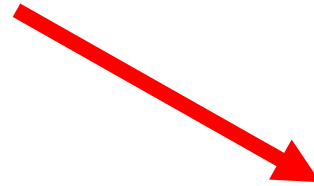
Hypothesis

Material & Methods

Results

Discussion

- Genetic Susceptibility
- Immune System
- Stress
- Surgery
- Food Sensitivity
- Enteric Bacteria



# Experimental Colitis in Mice

Introduction

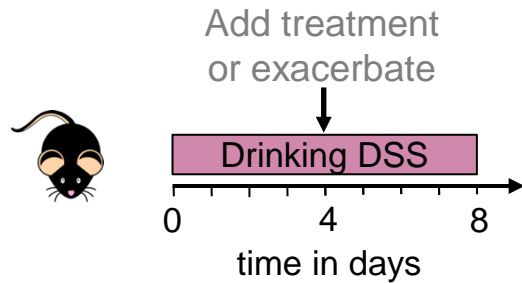
Hypothesis

Material & Methods

Results

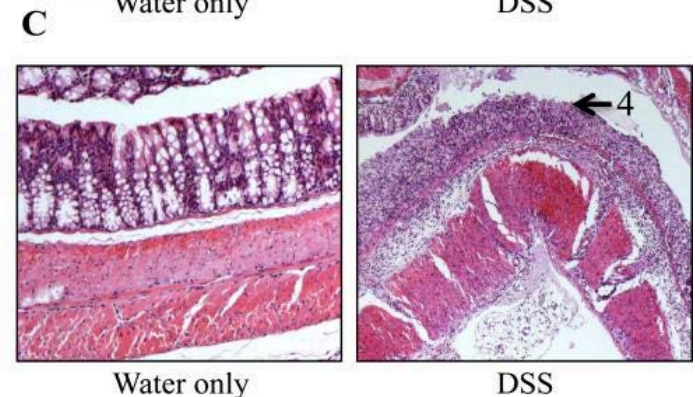
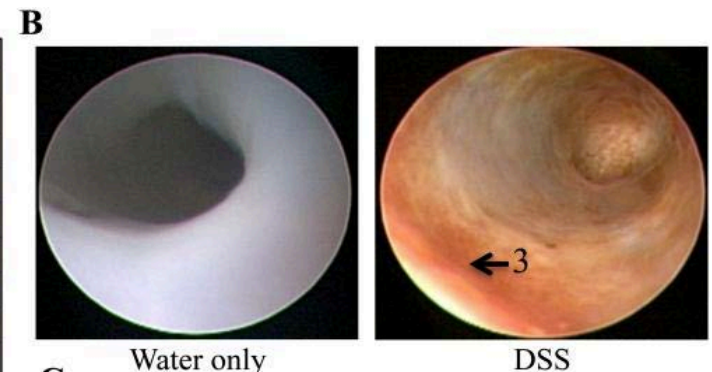
Discussion

Chemically-induced using **Dextran Sodium Sulfate (DSS)**



## Pathophysiology:

- Localized to distal colon
- Direct mucosal damage
- Activation of inflammatory signaling pathways
- Infiltration of immune cells
- Erosion of epithelial layer
- Dissemination of bacteria



# Preliminary Findings

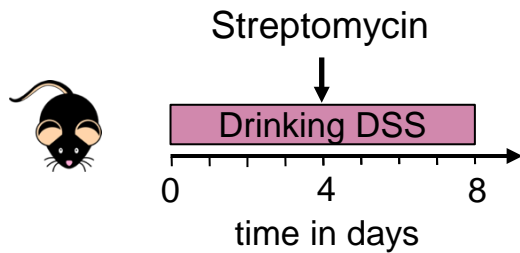
Introduction

Hypothesis

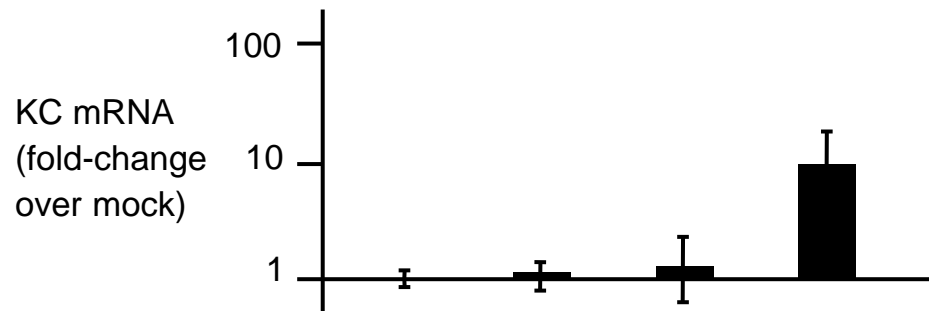
Material & Methods

Results

Discussion



## Antibiotics exacerbate sub-pathological colitis



20mg Streptomycin gavage:

- - + +

1% DSS in drinking water:

- + - +

# Possible Mechanisms

Introduction

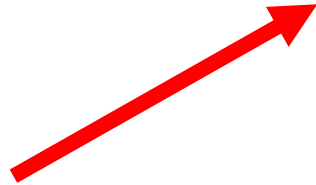
Hypothesis

Material & Methods

Results

Discussion

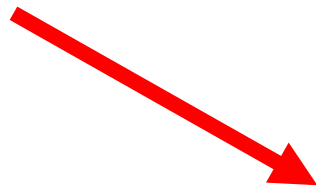
- How streptomycin worsens DSS?



- Direct toxicity to epithelial cells.



- Bacteria normally degrade DSS.



- Expansion of pro-inflammatory microbes.
- Loss of anti-inflammatory microbes.

# Proposed Mechanism

Introduction

Hypothesis

Material & Methods

Results

Discussion

Antibiotics make the bowel more irritable by depleting anti-inflammatory signals from bacteria that help maintain immune homeostasis.

# Experimental Model

Introduction

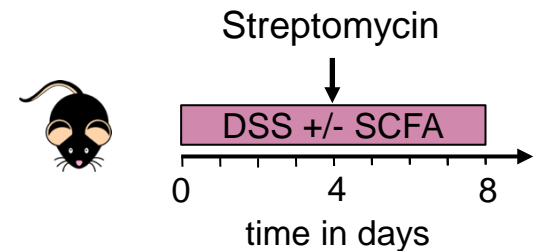
Hypothesis

Material & Methods

Results

Discussion

- DSS mouse model
  - 1% is sub-pathological
  - 20mg streptomycin worsens
- Short-chain fatty acid (SCFA) supplementation
  - 150mM in drinking water



# SCFA Supplementation

Introduction

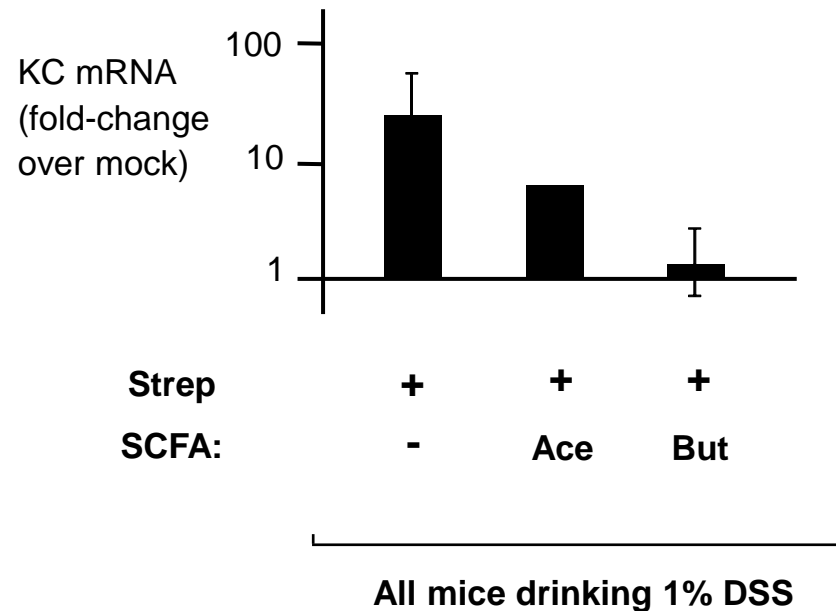
Hypothesis

Material & Methods

Results

Discussion

Microbial metabolites lower  
pro-inflammatory activity





# Multiple Targets of SCFAs

Introduction

Hypothesis

Material & Methods

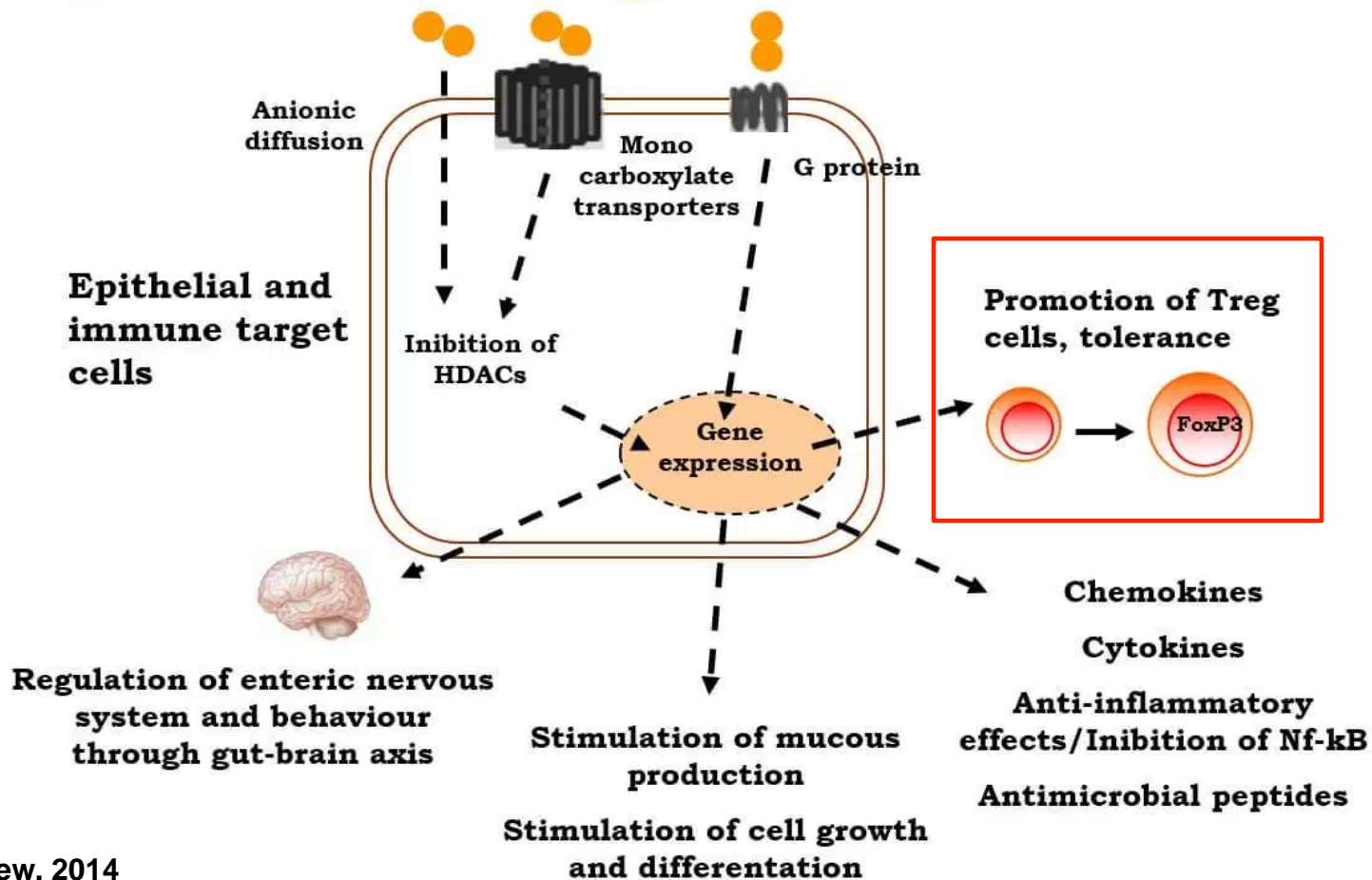
Results

Discussion

Dietary fibers

Microbiota

SCFAs



# Treg depletion

Introduction

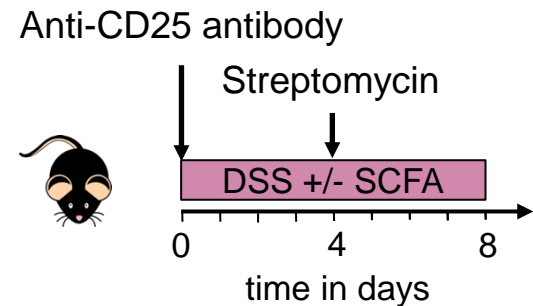
Hypothesis

Material & Methods

Results

Discussion

- DSS mouse model
  - 1% is sub-pathological
  - 20mg streptomycin worsens
- Short-chain fatty acid (SCFA) supplementation
- Regulatory T-cell depletion
  - Anti-CD25 antibody



# SCFA Supplementation

Introduction

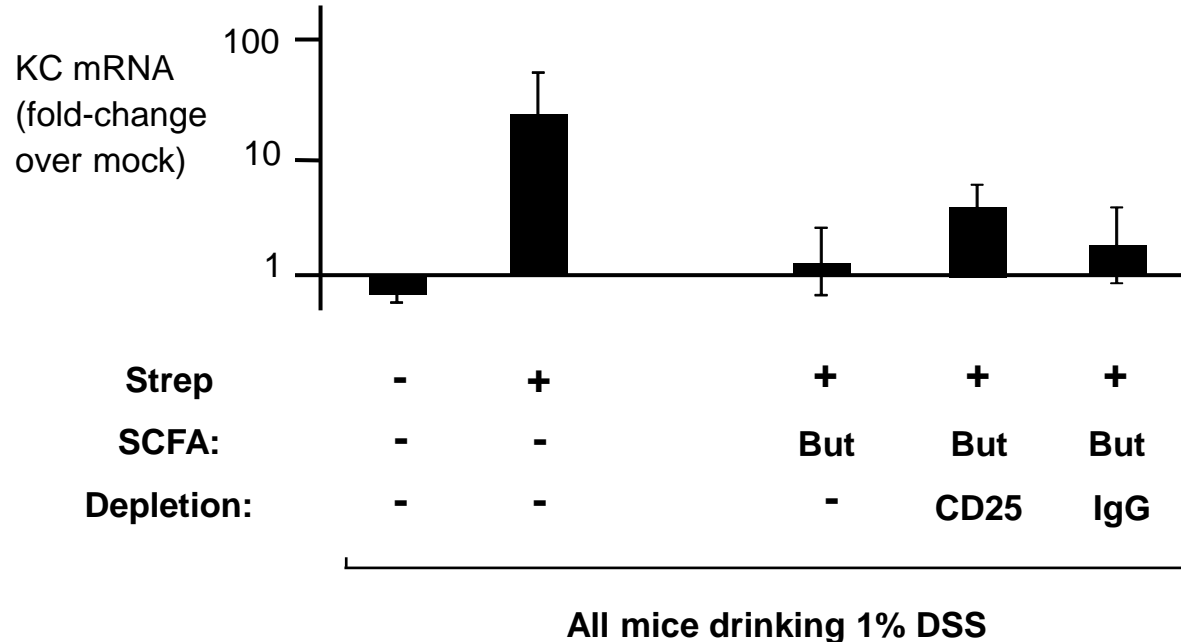
Hypothesis

Material & Methods

Results

Discussion

Butyrate may exert some protective effect via T-regs



# Multiple-Hits Model

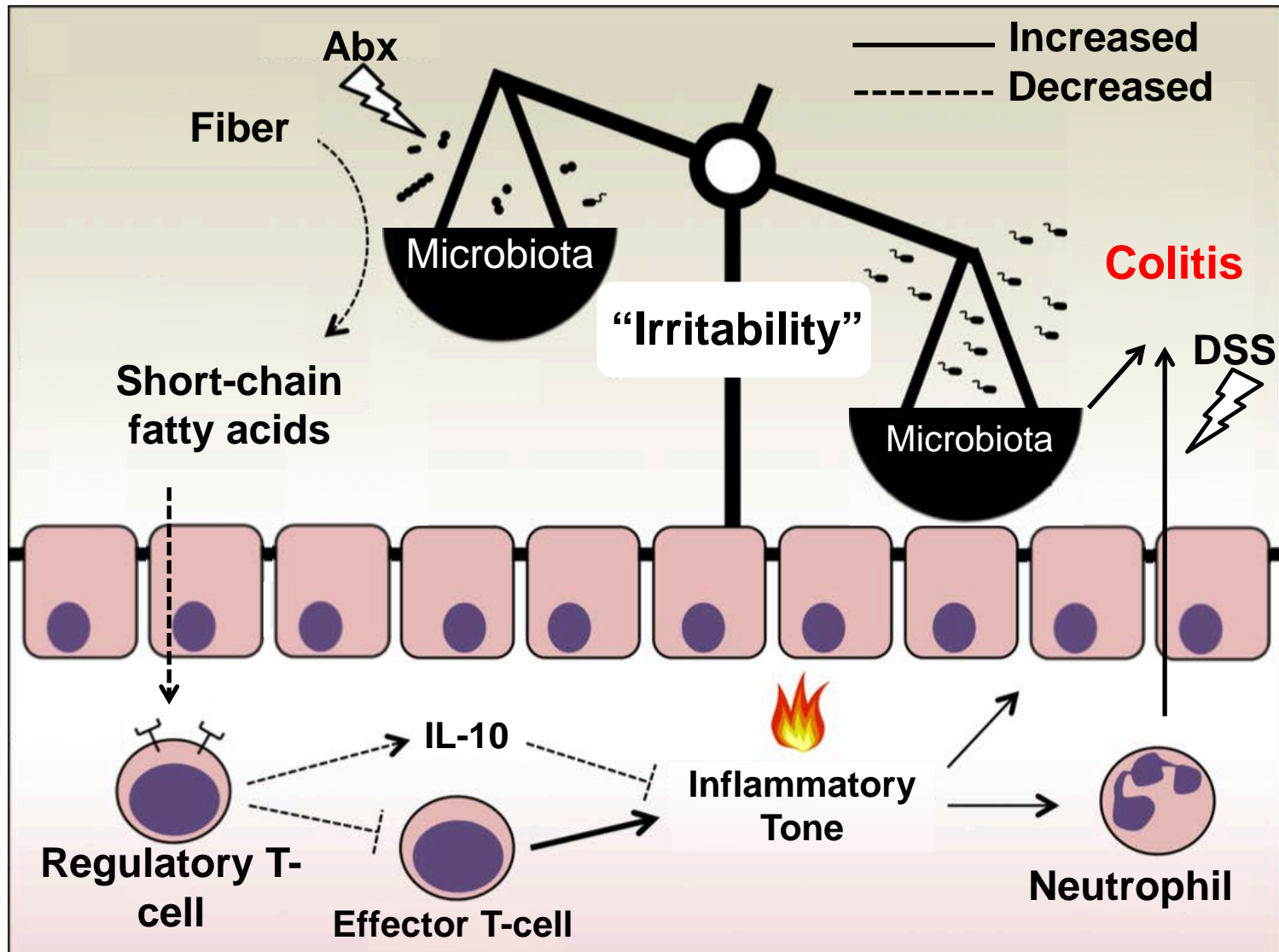
Introduction

Hypothesis

Material & Methods

Results

Discussion



# Acknowledgements

Introduction

Hypothesis

Material & Methods

Results

Discussion



- STAR 2016 Funding
- Baumler & Tsois Labs
- Everyone in this room!