



# Fecal Microbiota Transplantation affects post-antibiotics microbiome restoration and intestinal homeostasis in aging mice

Lei Dai

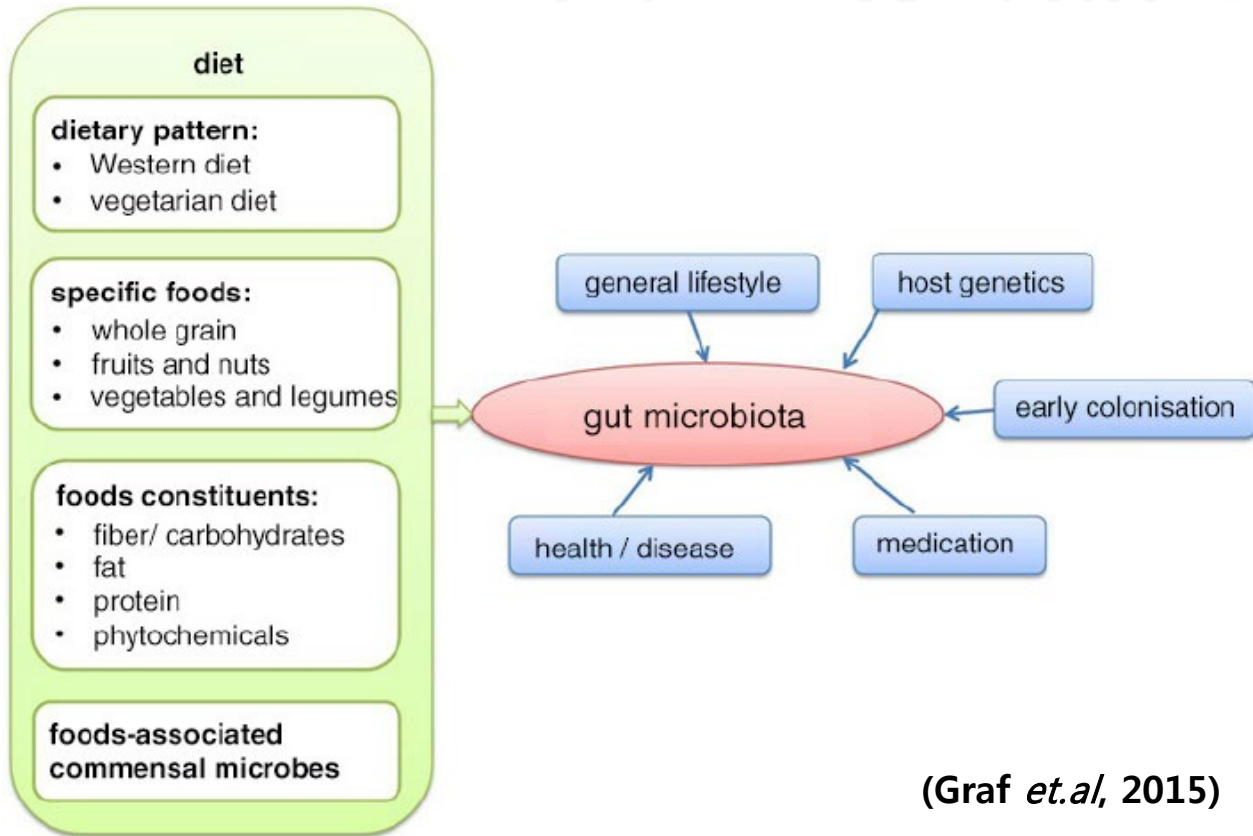
Shenzhen Institutes of Advanced Technology (SIAT)

Chinese Academy of Sciences

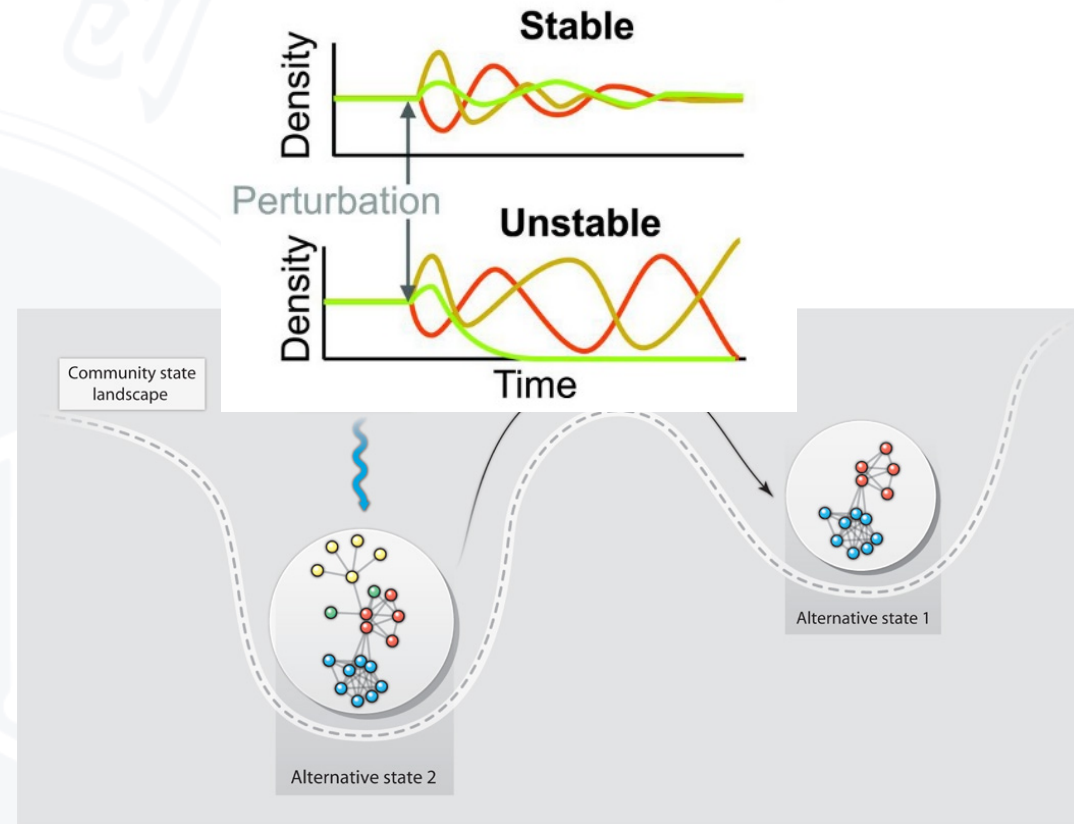
July 30, 2020



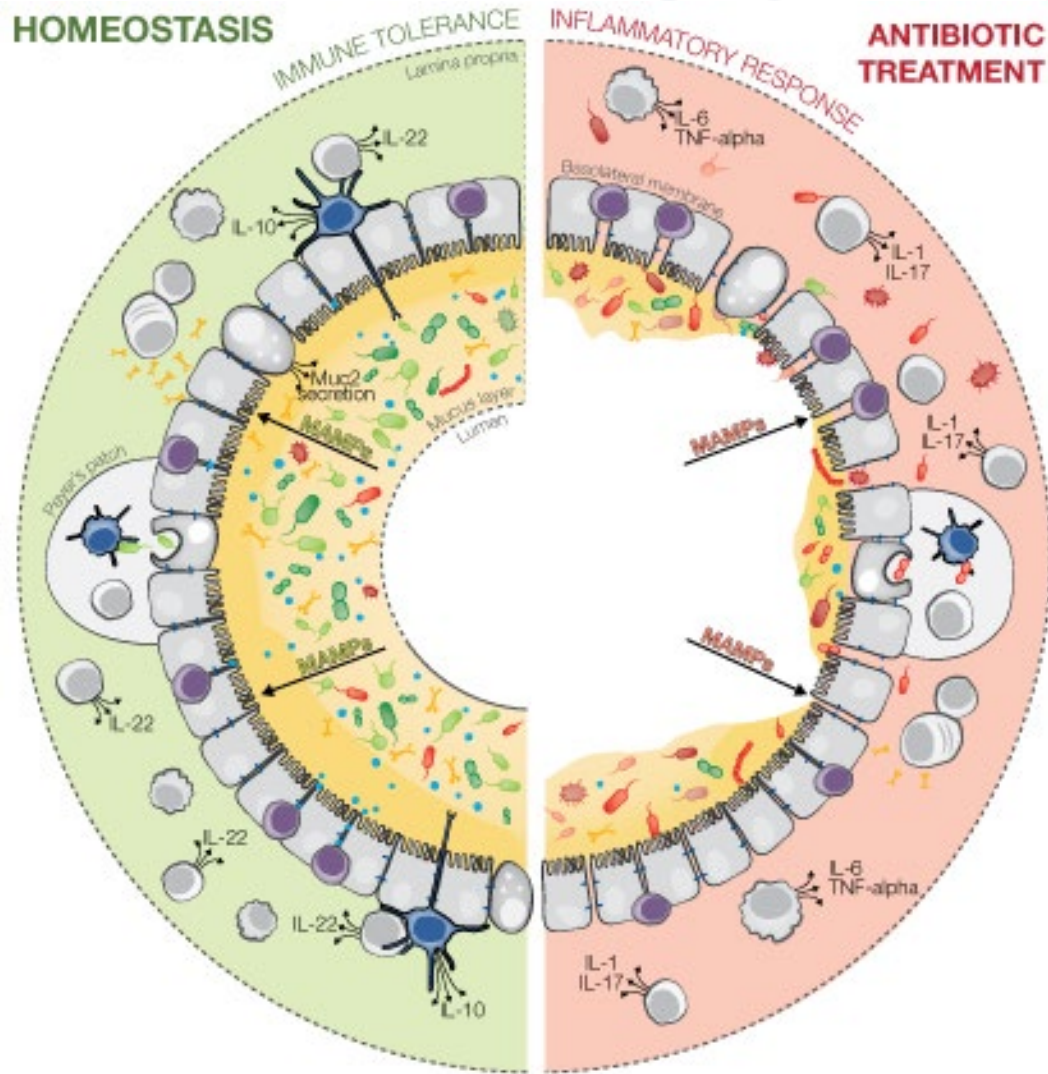
# Resilience of gut microbiota



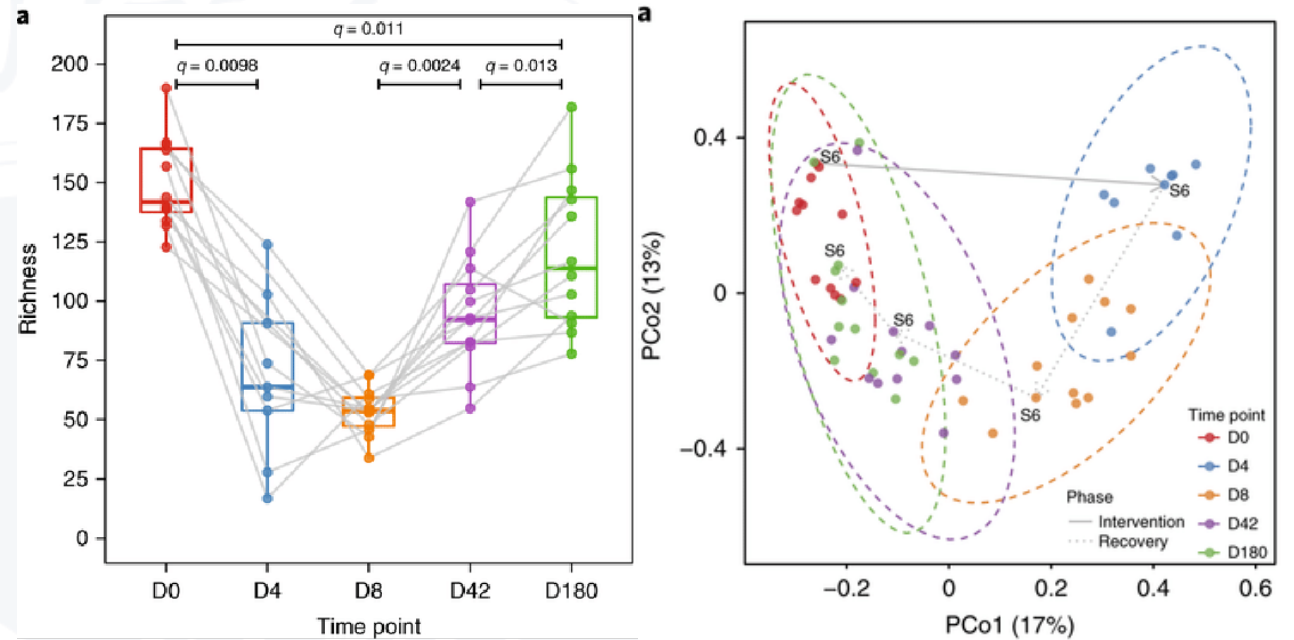
(Graf *et.al*, 2015)



# Restoration of gut microbiota following antibiotics treatment



(FX Medicine, 2019)

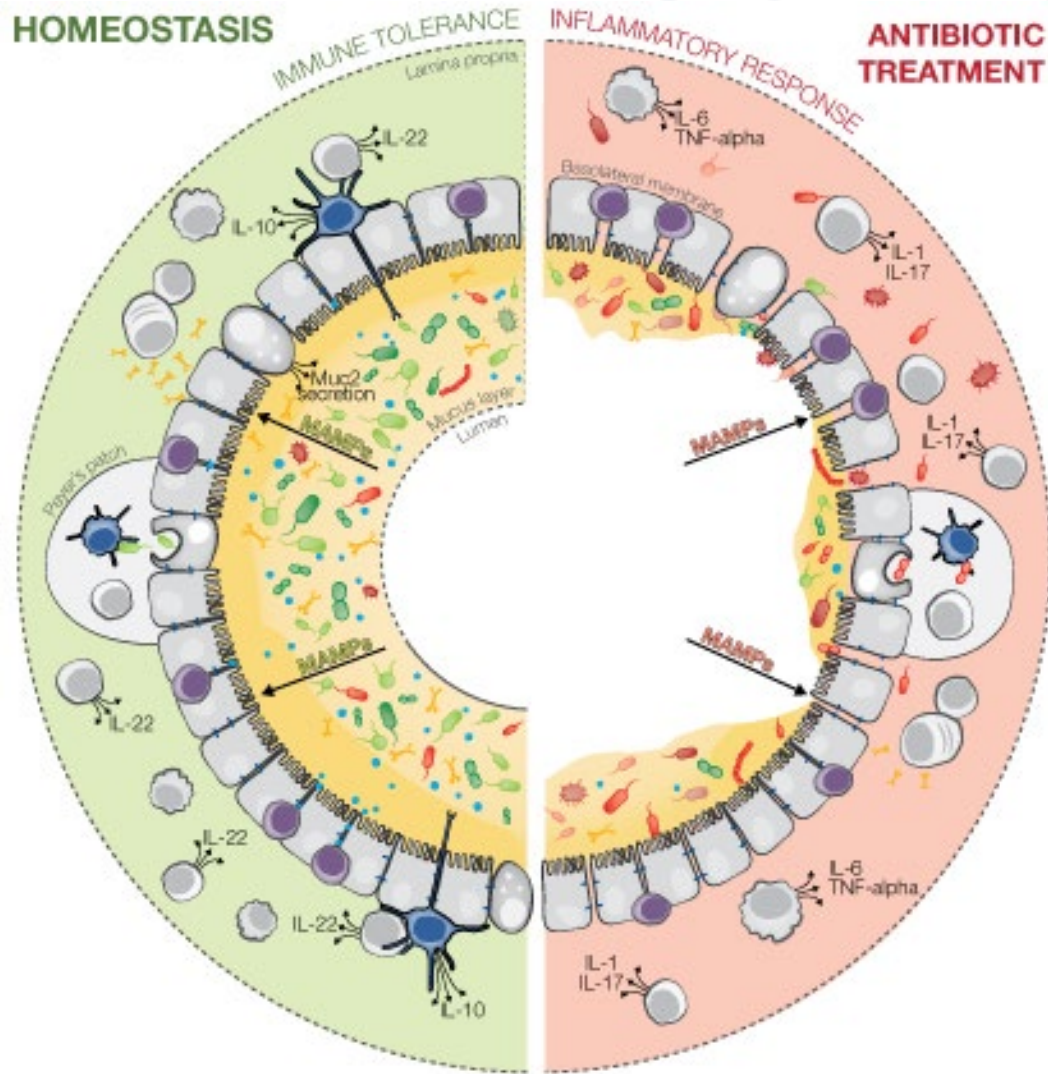


(Palleja *et al*, 2018)

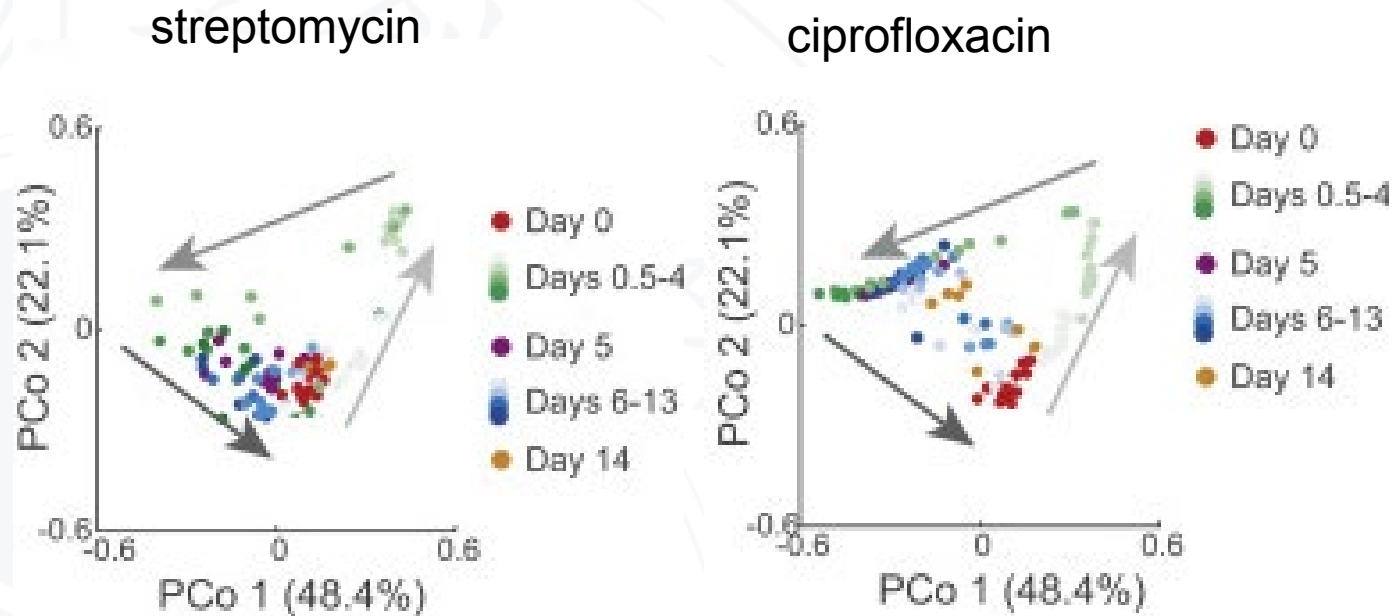


human  
volunteers

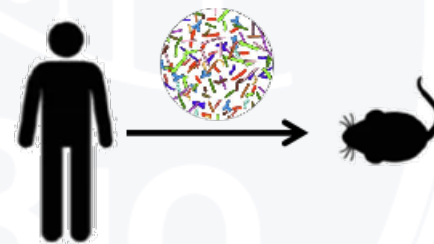
# Restoration of gut microbiota following antibiotics treatment



(FX Medicine, 2019)

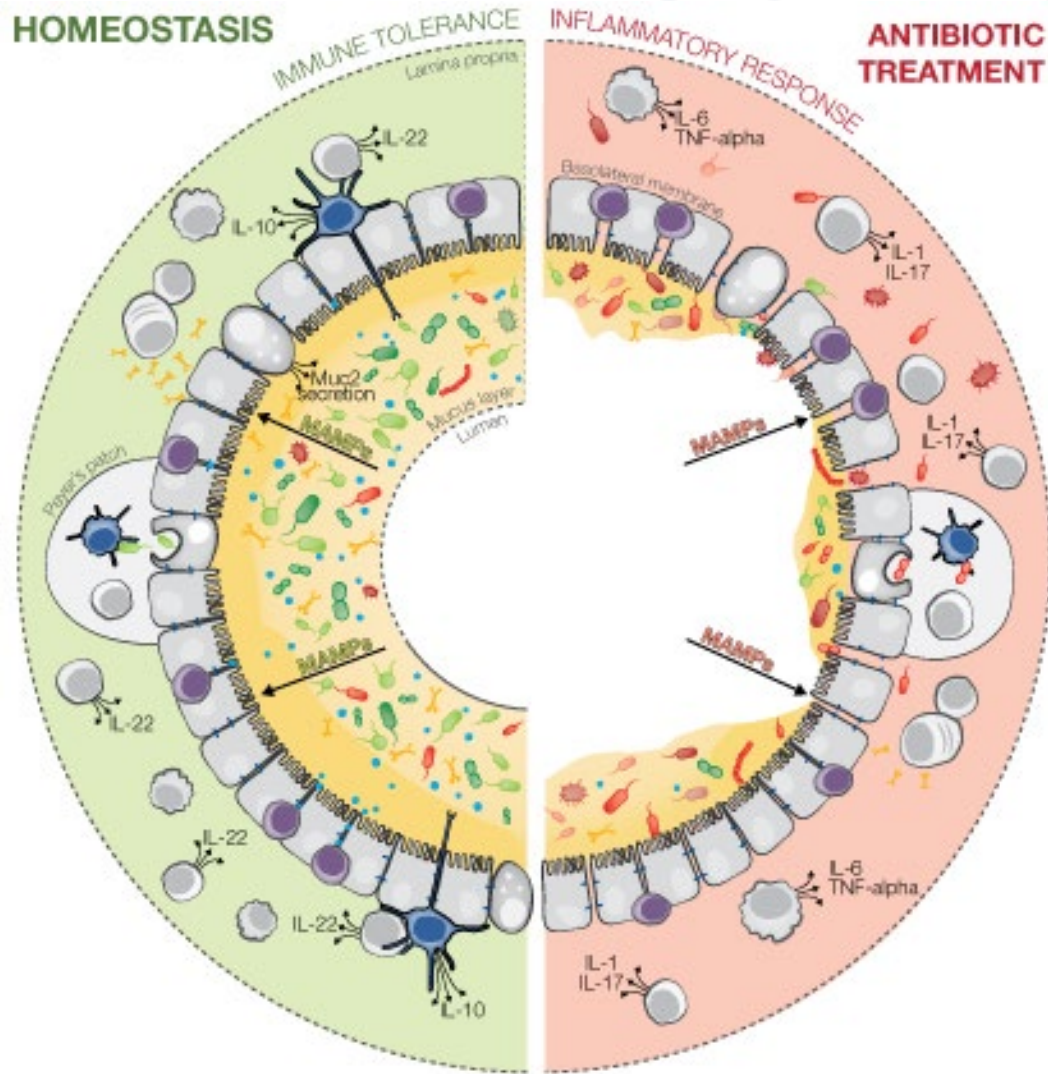


(Ng *et.al*, 2019)

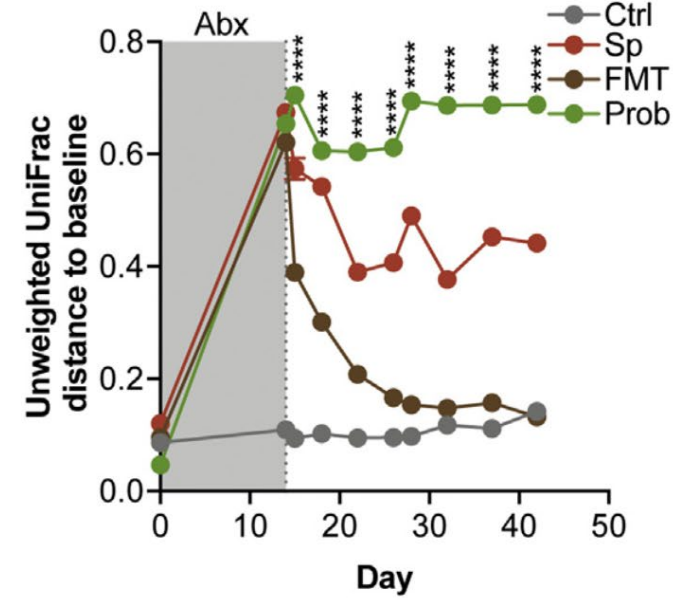
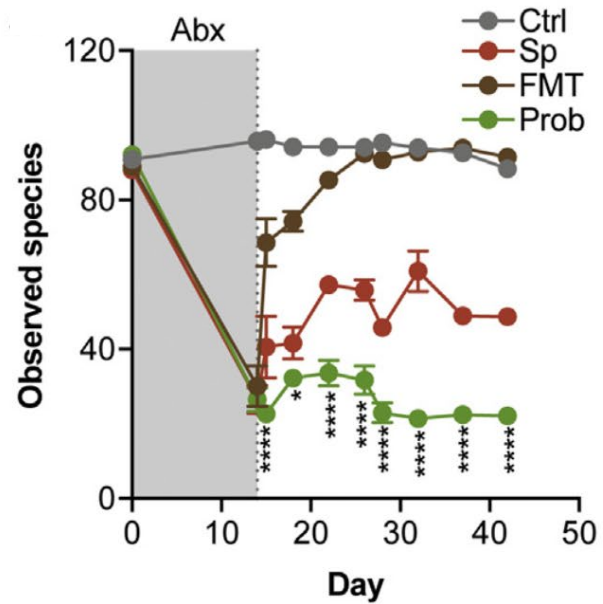


humanized mice

# Restoration of gut microbiota following antibiotics treatment



(FX Medicine, 2019)

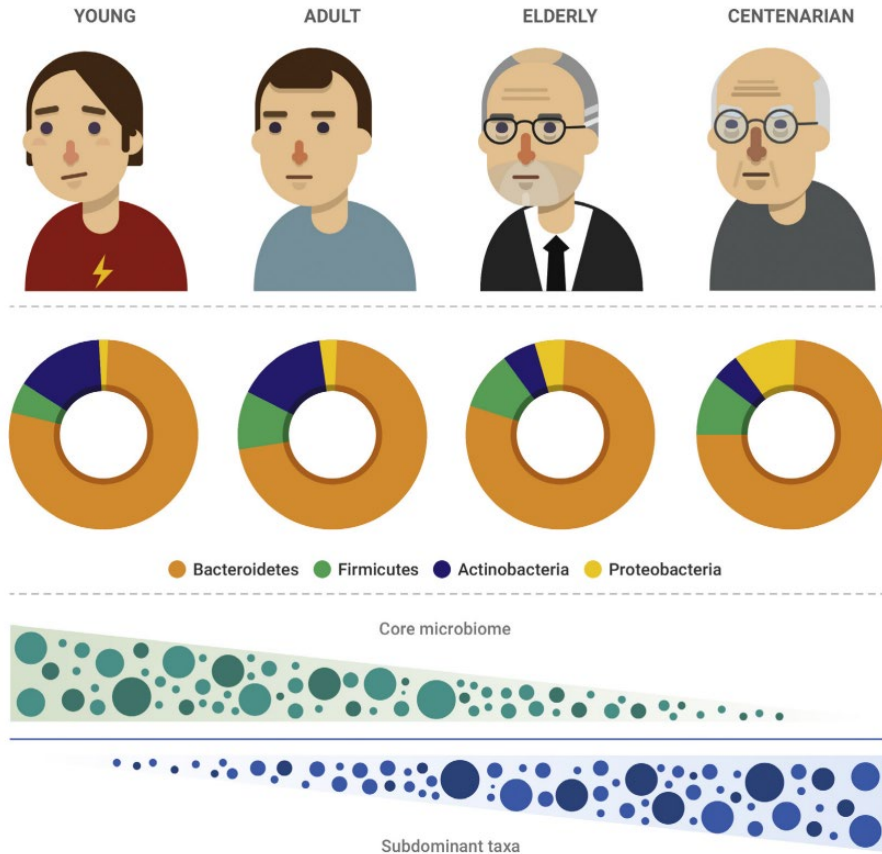


(Suez *et.al*, 2018)

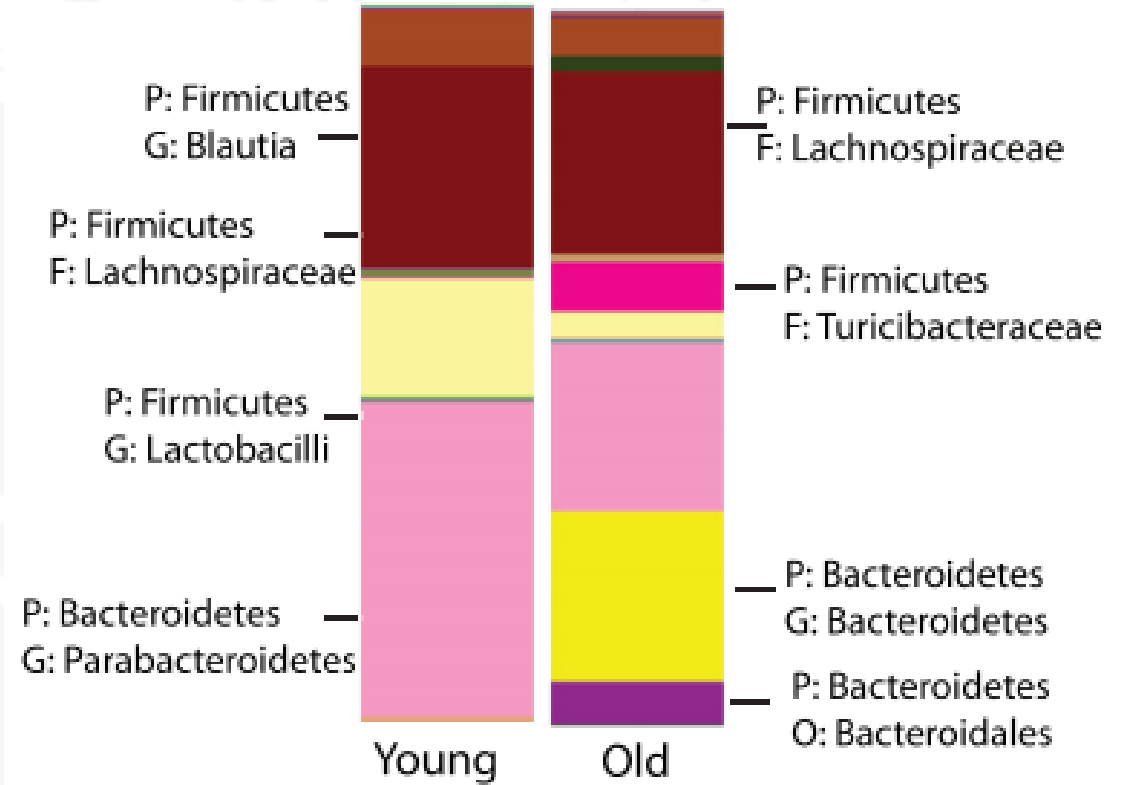


conventional mice

# Gut microbiota undergo substantial changes in composition and function during aging

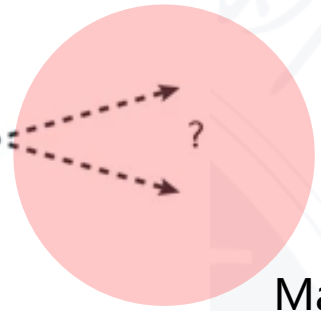
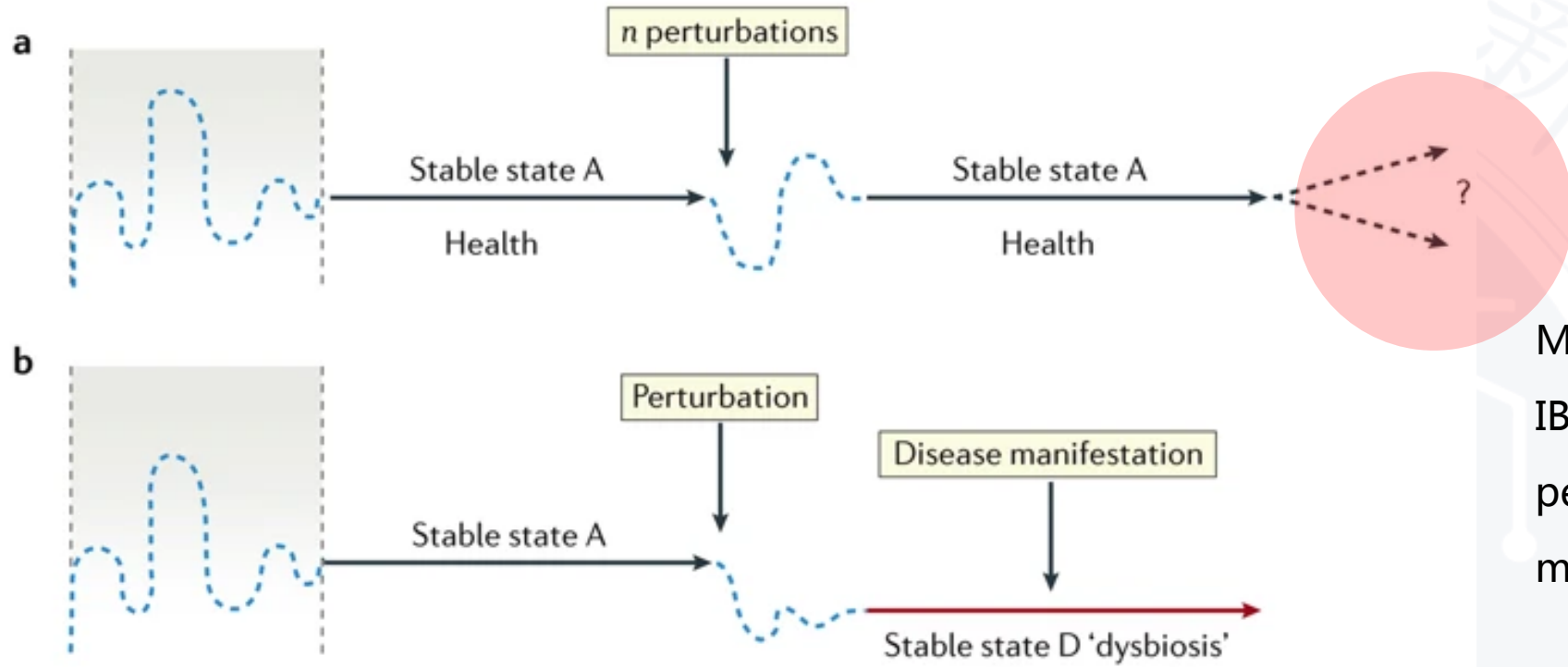
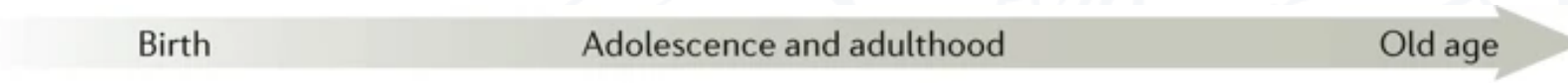


(Vaiserman *et.al*, 2017)



(Thevaranjan *et.al*, 2017)

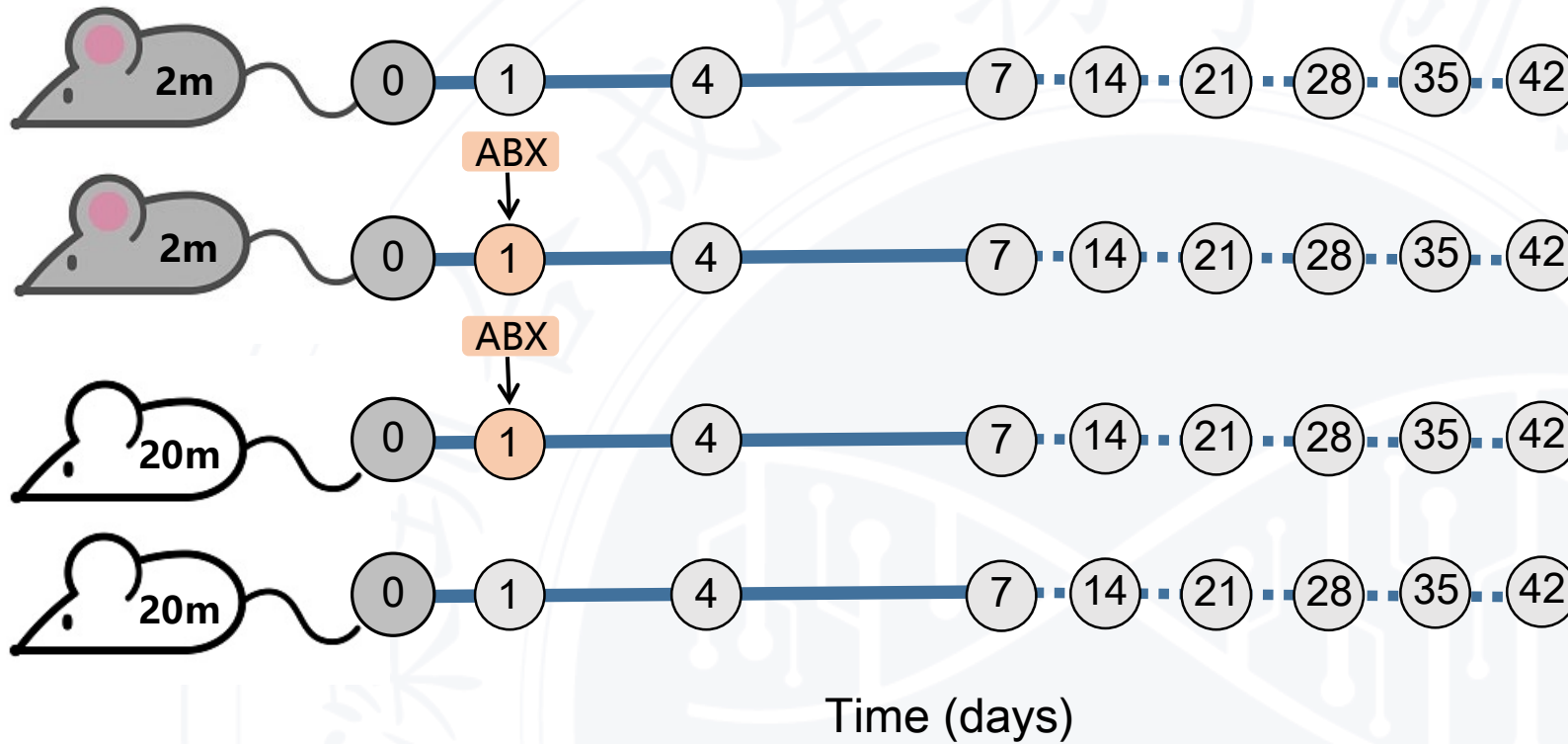
# Little is known about how gut microbiota in aging hosts respond to environmental perturbations



Many bowel diseases , like CDI , IBD , IBS , are more prevalent in elderly people , which may be affected by microbiota dysbiosis.

(Sommer *et.al*, 2017)

# Broad-spectrum antibiotic intervention in young and old mice

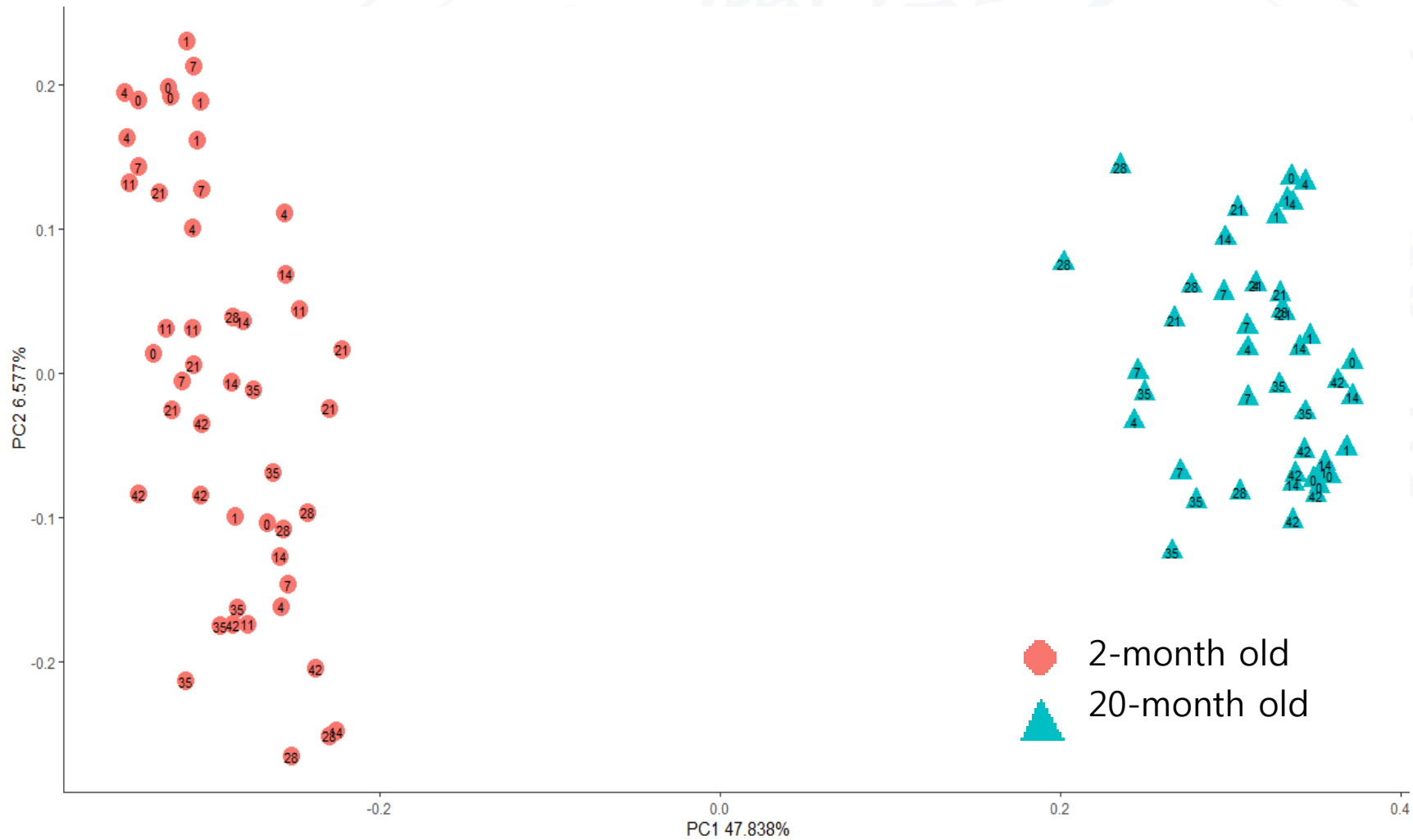


Ampicillin 1mg/mL  
Metronidazole 10mg/mL  
Neomycin 10mg/mL  
Vancomycin 5mg/mL

- Cocktail of four
- Last-resort antibiotic
- High concentration
- One time oral gavage

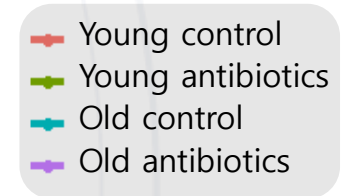
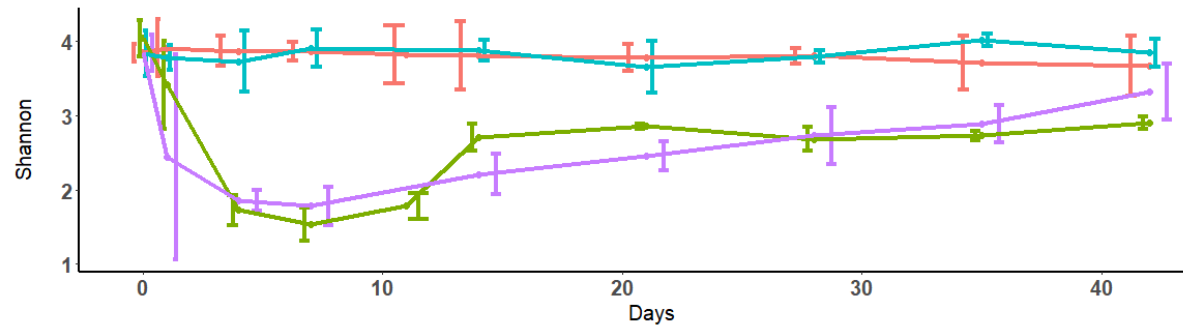
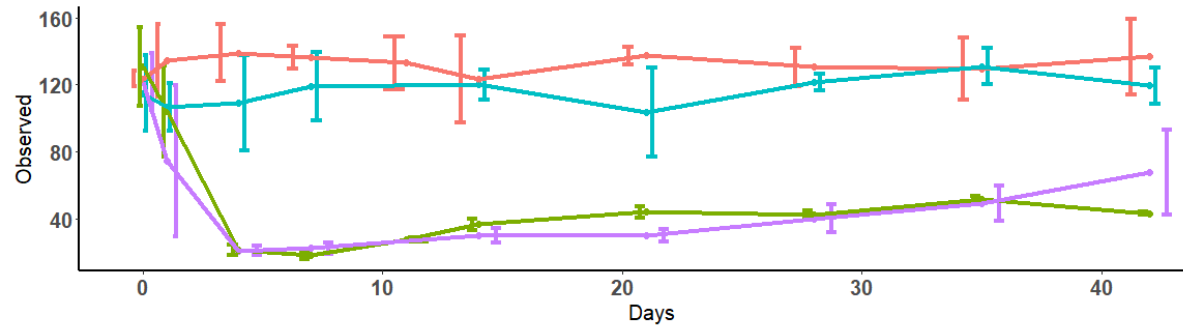
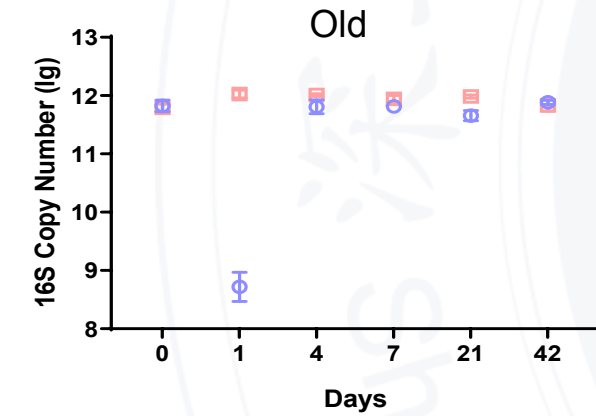
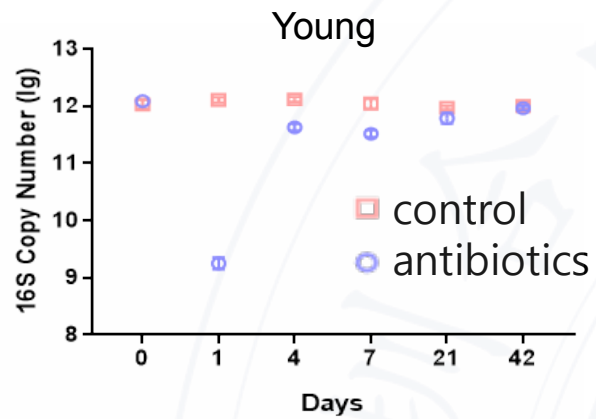


# Gut microbiome of young vs. old mice



(Wang *et al.*, unpublished data)

# Recovery of microbial load and diversity after antibiotics treatment



(Wang *et.al*, unpublished data)

# Drastic changes in gut microbiome composition after antibiotics treatment

Young

Old



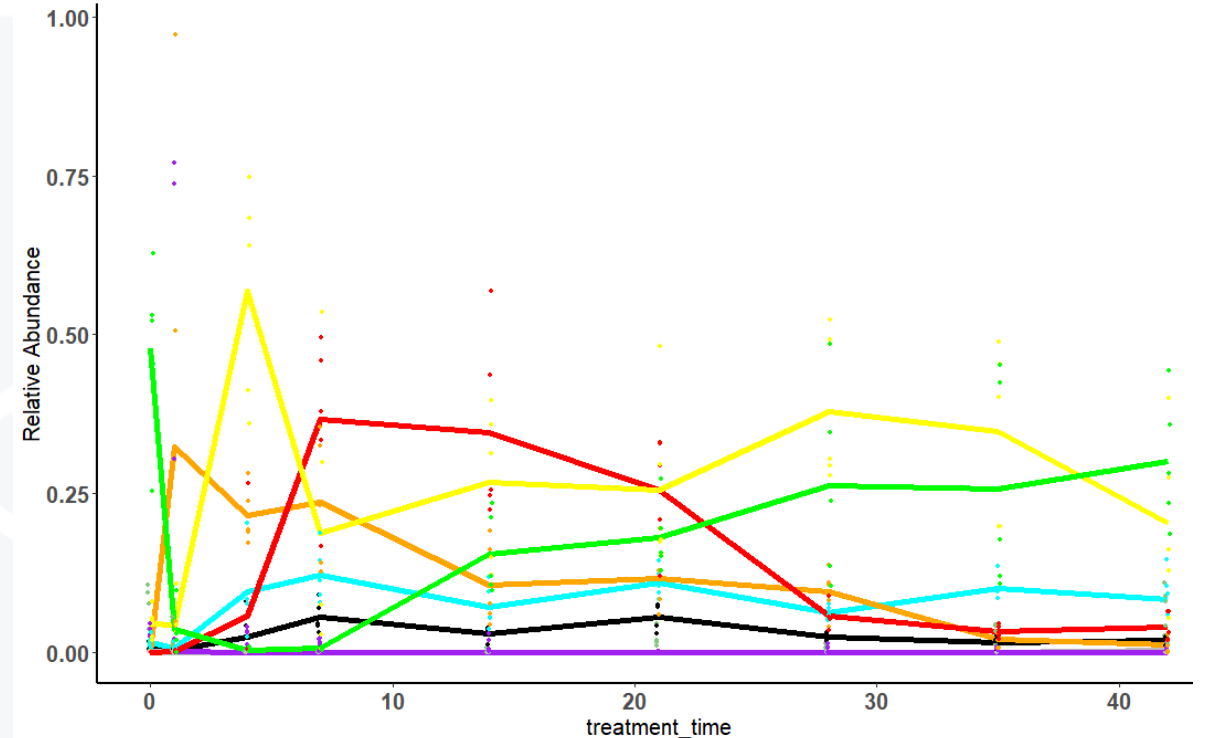
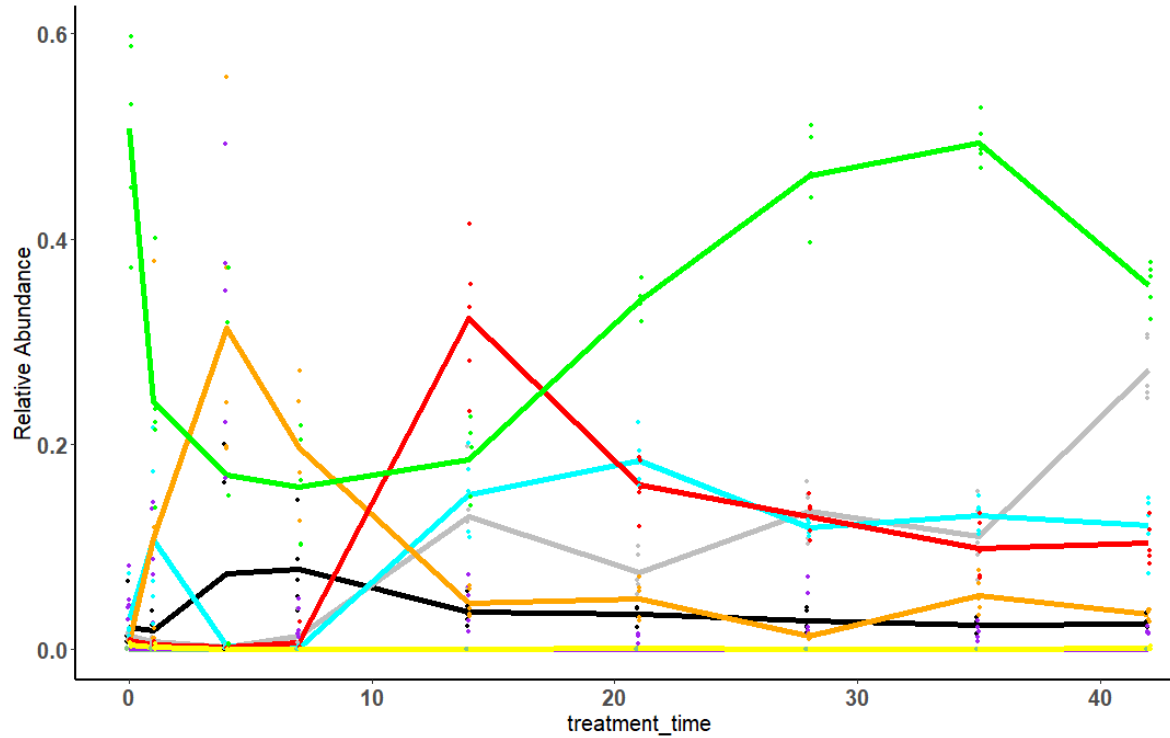
(Wang *et.al*, unpublished data)



# Succession of gut bacterial species during restoration

Young

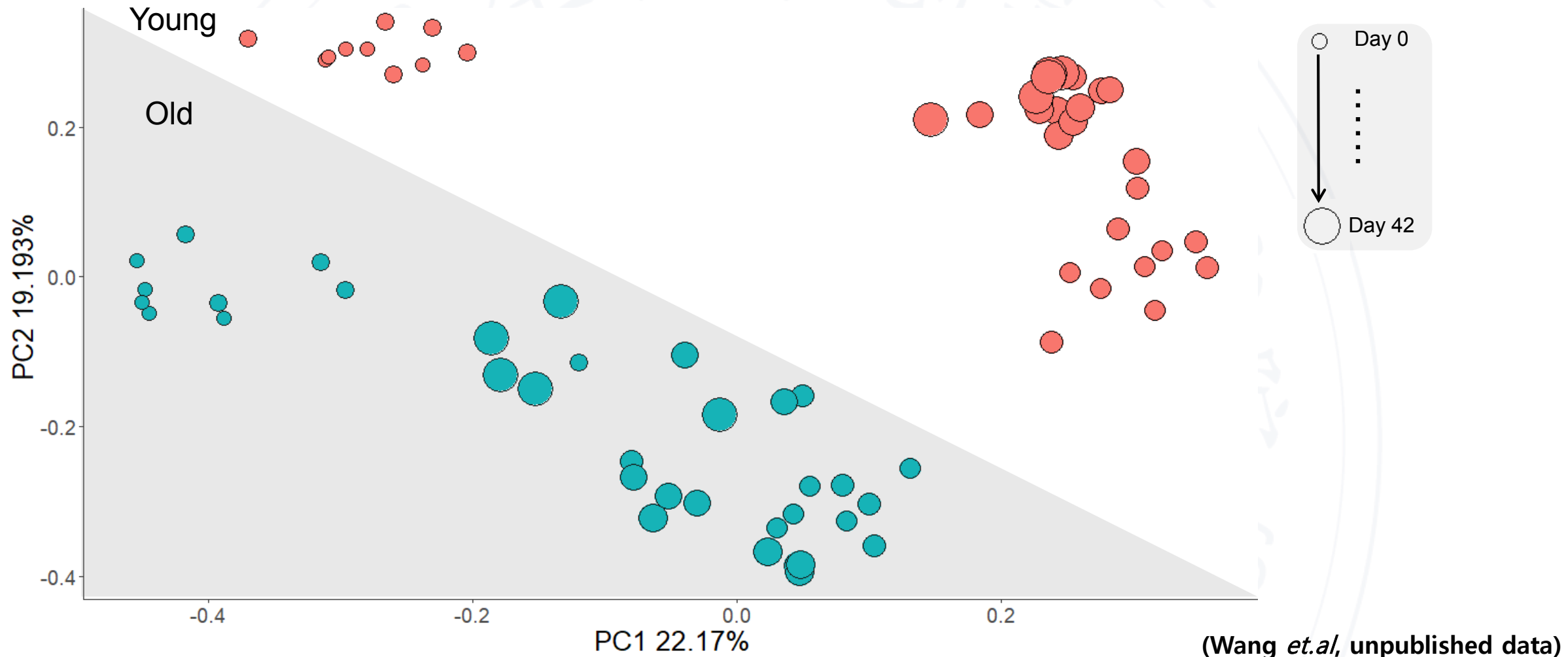
Old



- taxonomy
- F\_Desulfovibrionaceae
  - G\_Blautia
  - G\_Lachnoclostridium
  - G\_Lactobacillus
  - G\_Parasutterella
  - G\_Escherichia-Shigella
  - G\_Parabacteroides
  - G\_Bacteroides
  - F\_Muribaculaceae

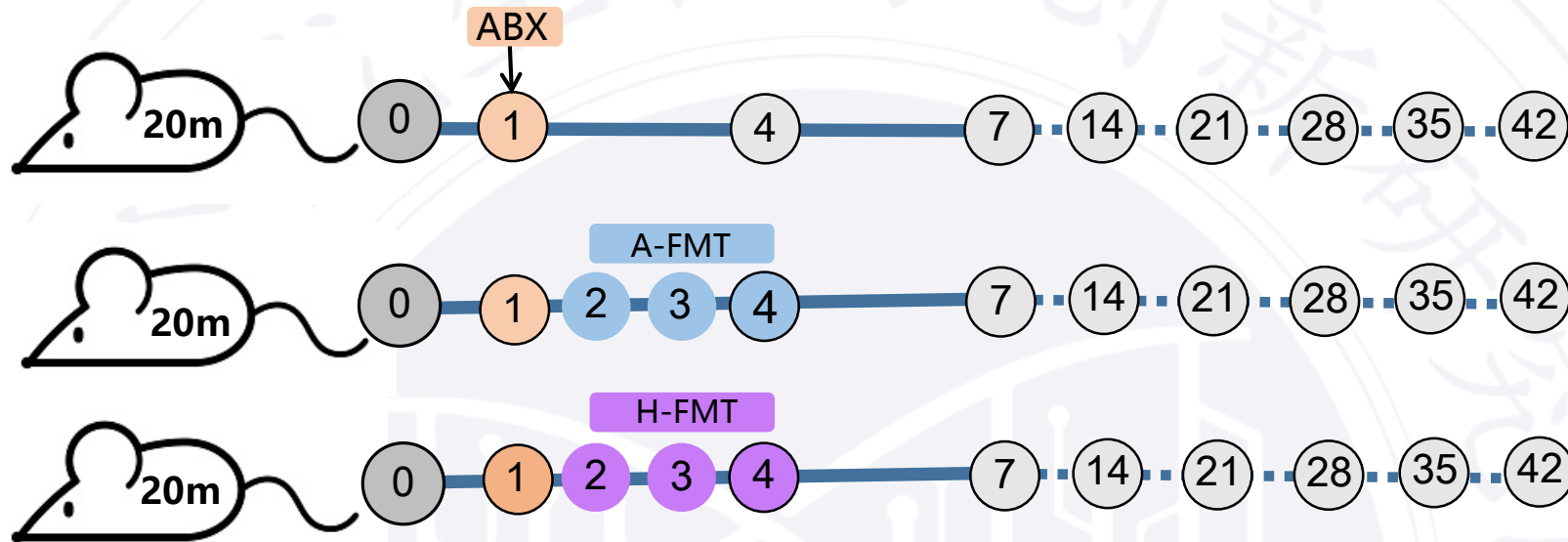
(Wang *et.al*, unpublished data)

# Gut microbiome did not return to the original state after antibiotics treatment



# Could FMT help microbiome restoration in aging mice ?

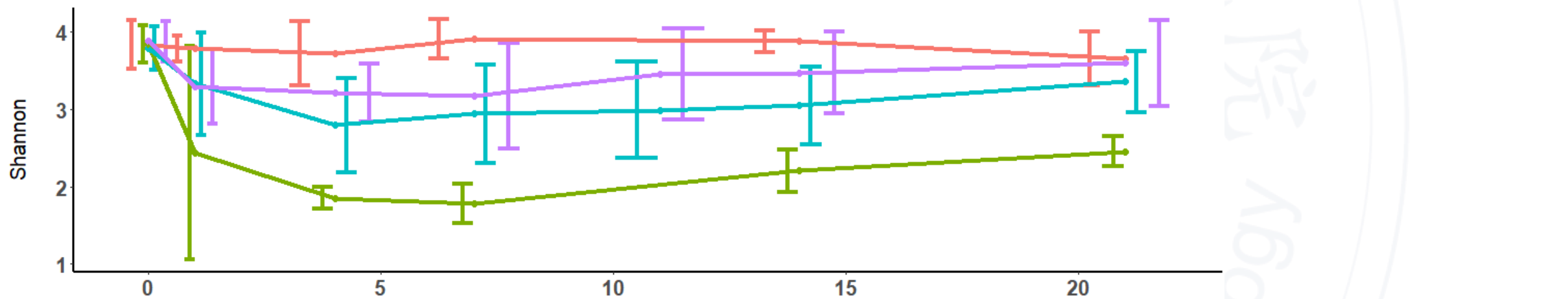
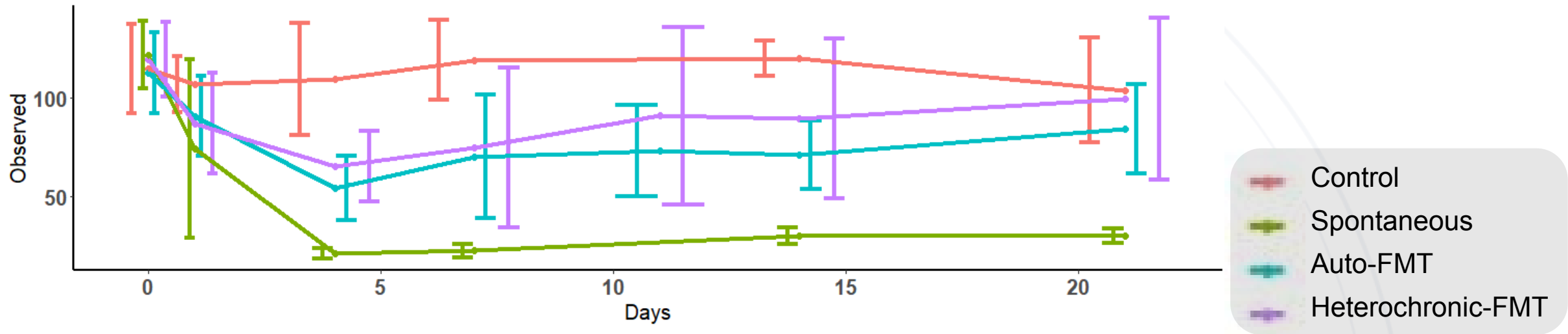
## FMT: Fecal Microbiota Transplantation



**Autologous Fecal Microbiota Transplantation (A-FMT):** Fecal samples collected from 20-month-old mice used as donor

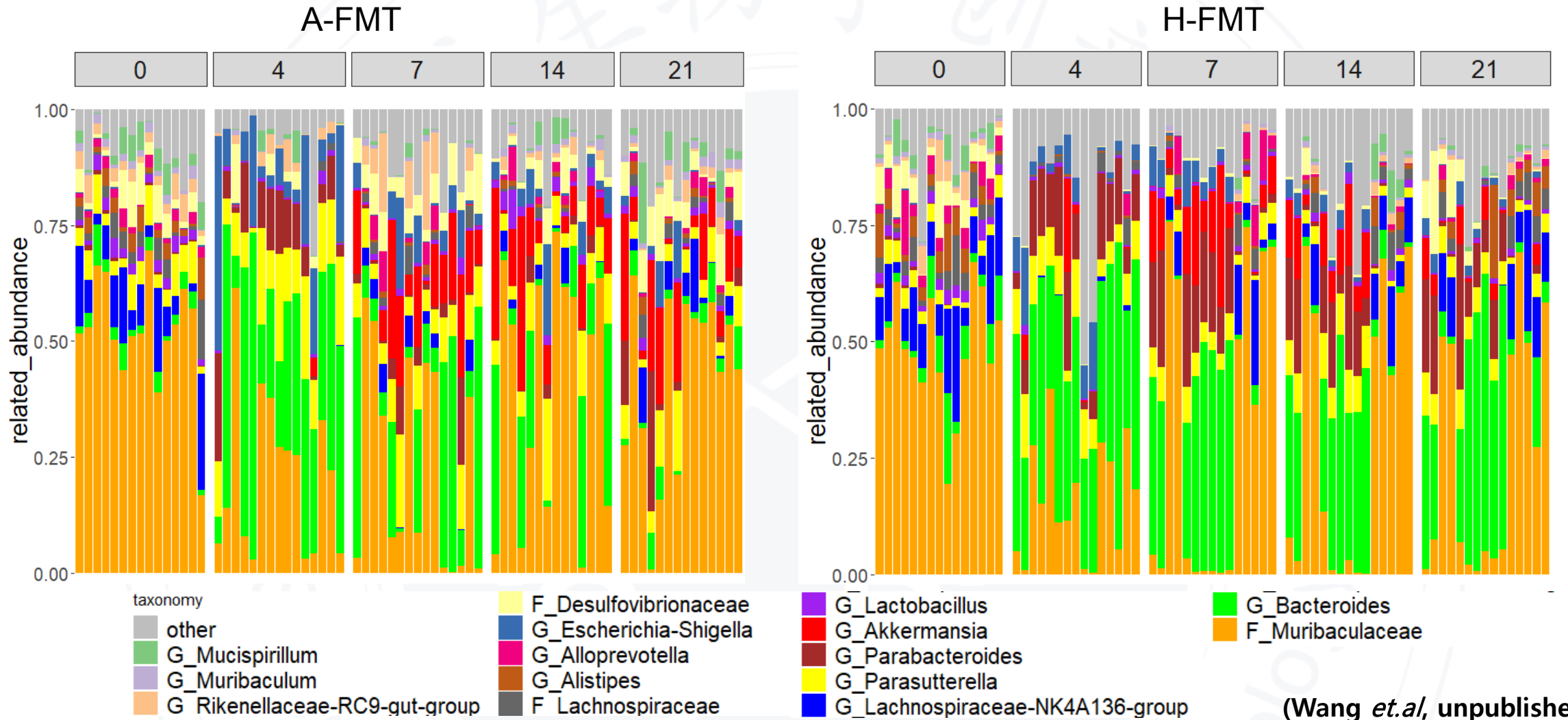
**Heterochronic Fecal Microbiota Transplantation (H-FMT):** Fecal samples collected from 2-month-old mice used as donor

# FMT after antibiotics treatment helps restoration of gut microbiome diversity in aging mice



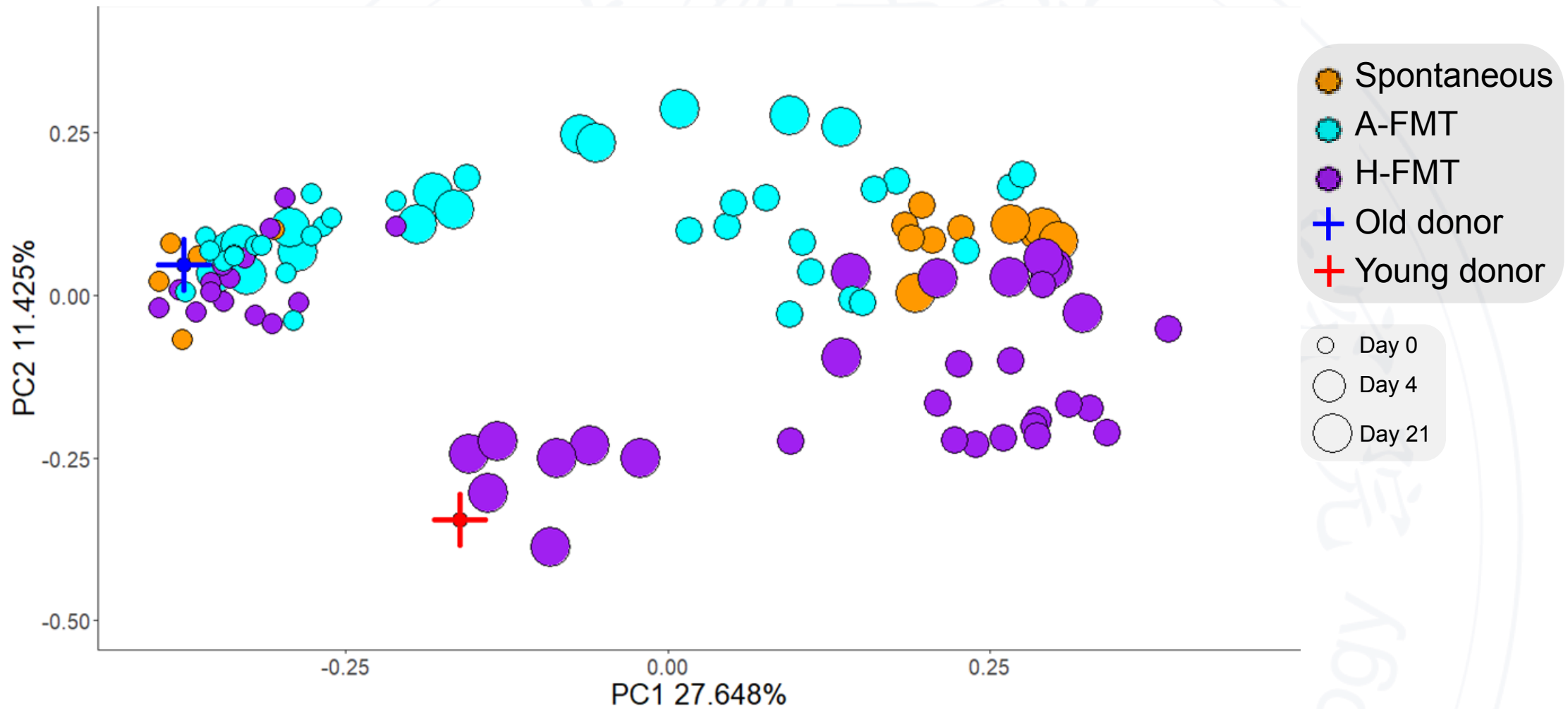
(Wang *et.al*, unpublished data)

# Gut microbiome after autologous and heterochronical FMT follows different paths



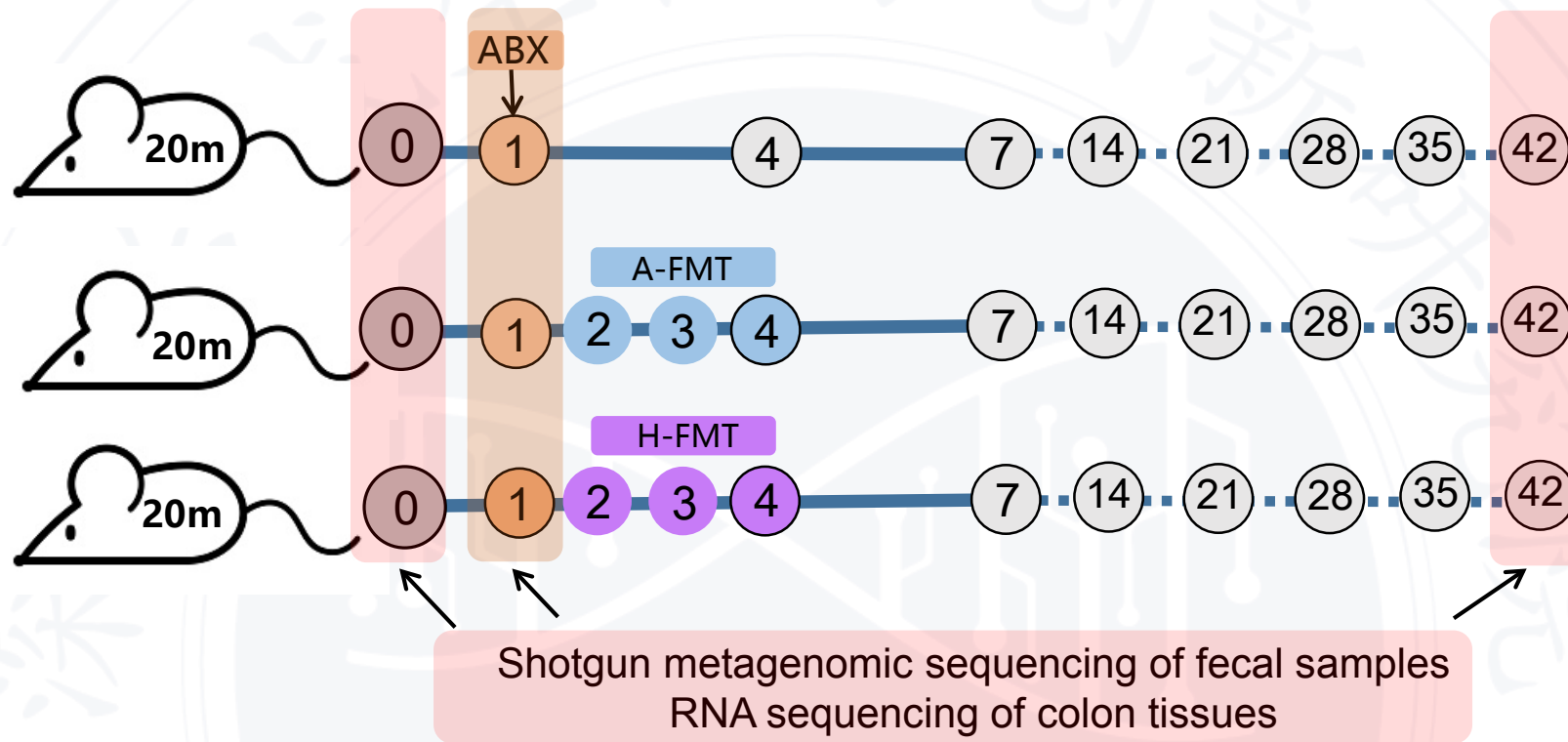


# The restored state of gut microbiome depends on FMT donor

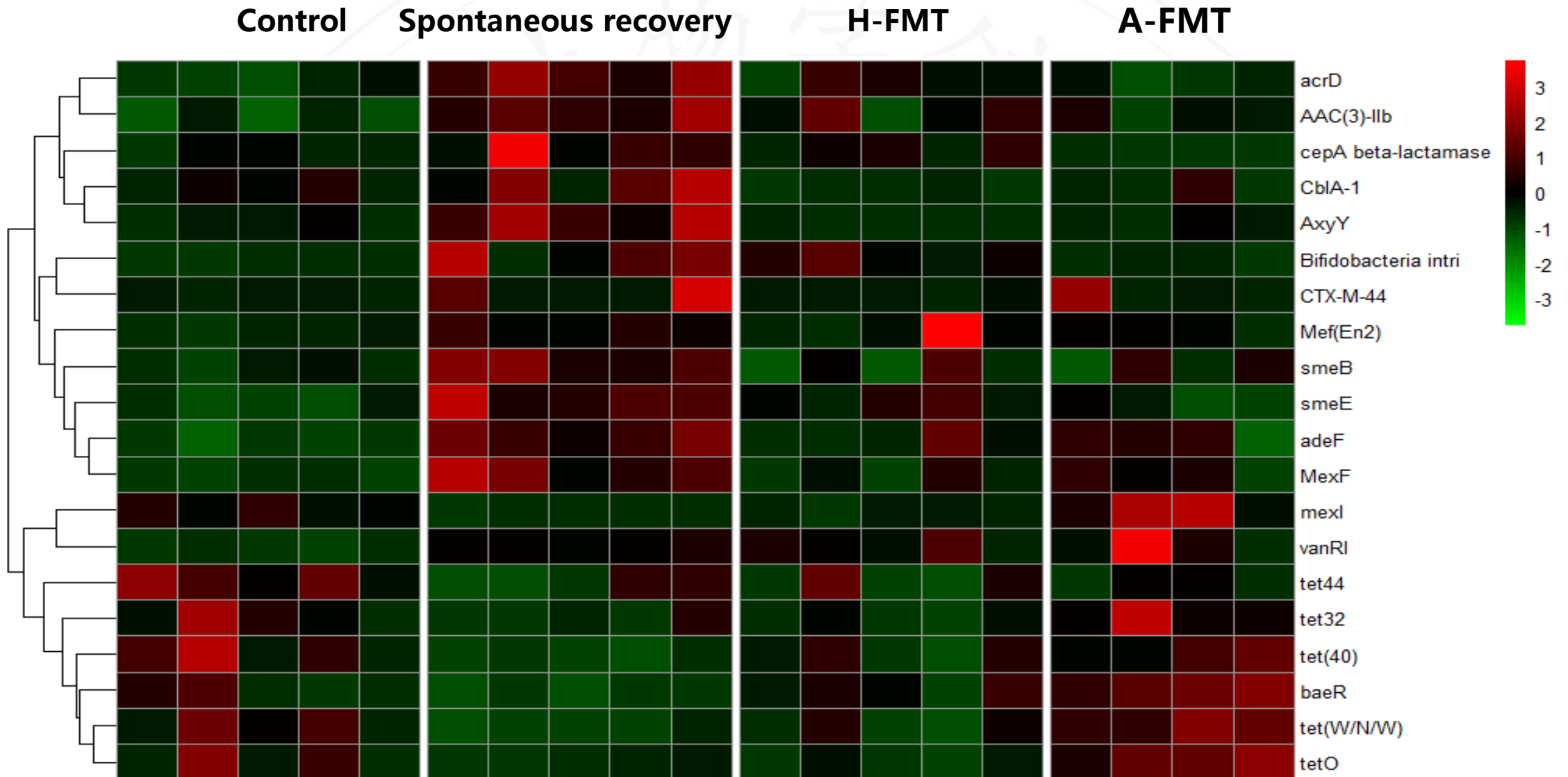


(Wang *et.al*, unpublished data)

# How does FMT affect the abundance of ARGs and the transcriptome of colon tissues?

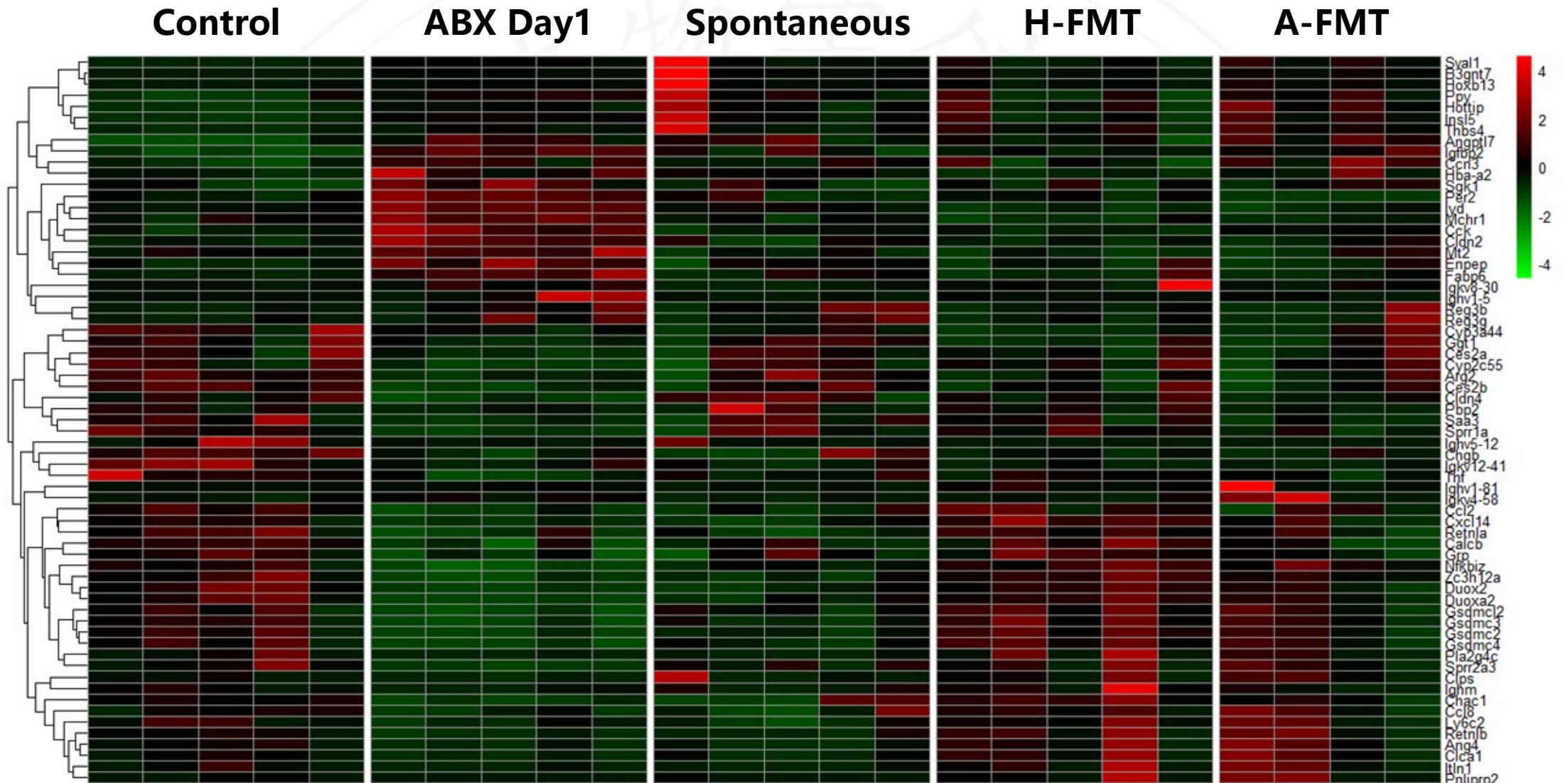


# The profile of Antibiotics Resistant Genes in gut microbiome



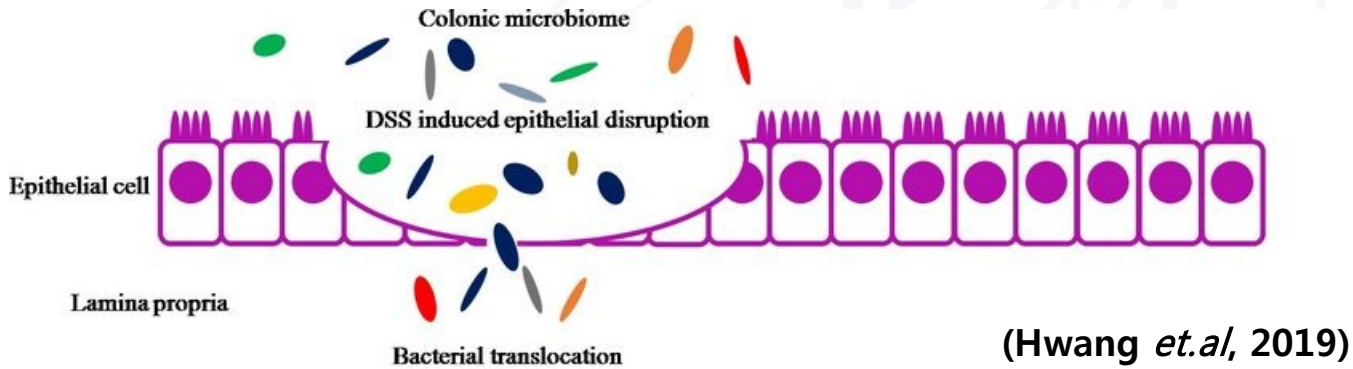
(Wang *et.al*, unpublished data)

# Host colon transcriptome is partially restored after FMT

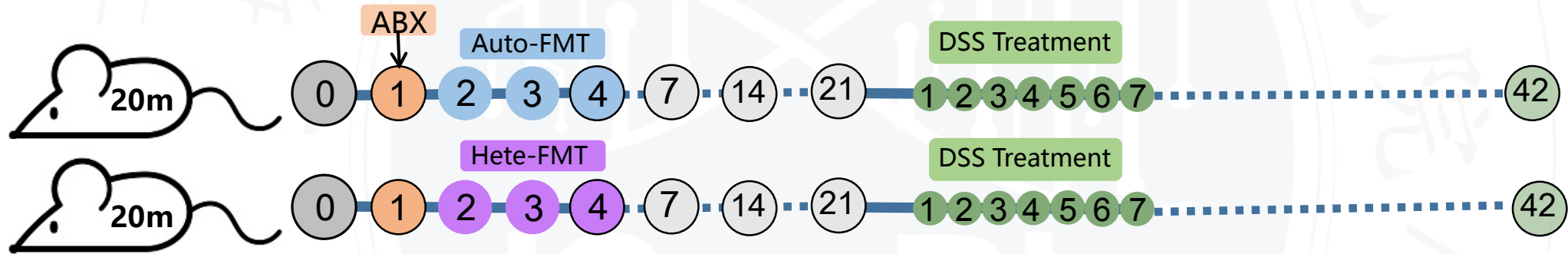


(Wang *et.al*, unpublished data)

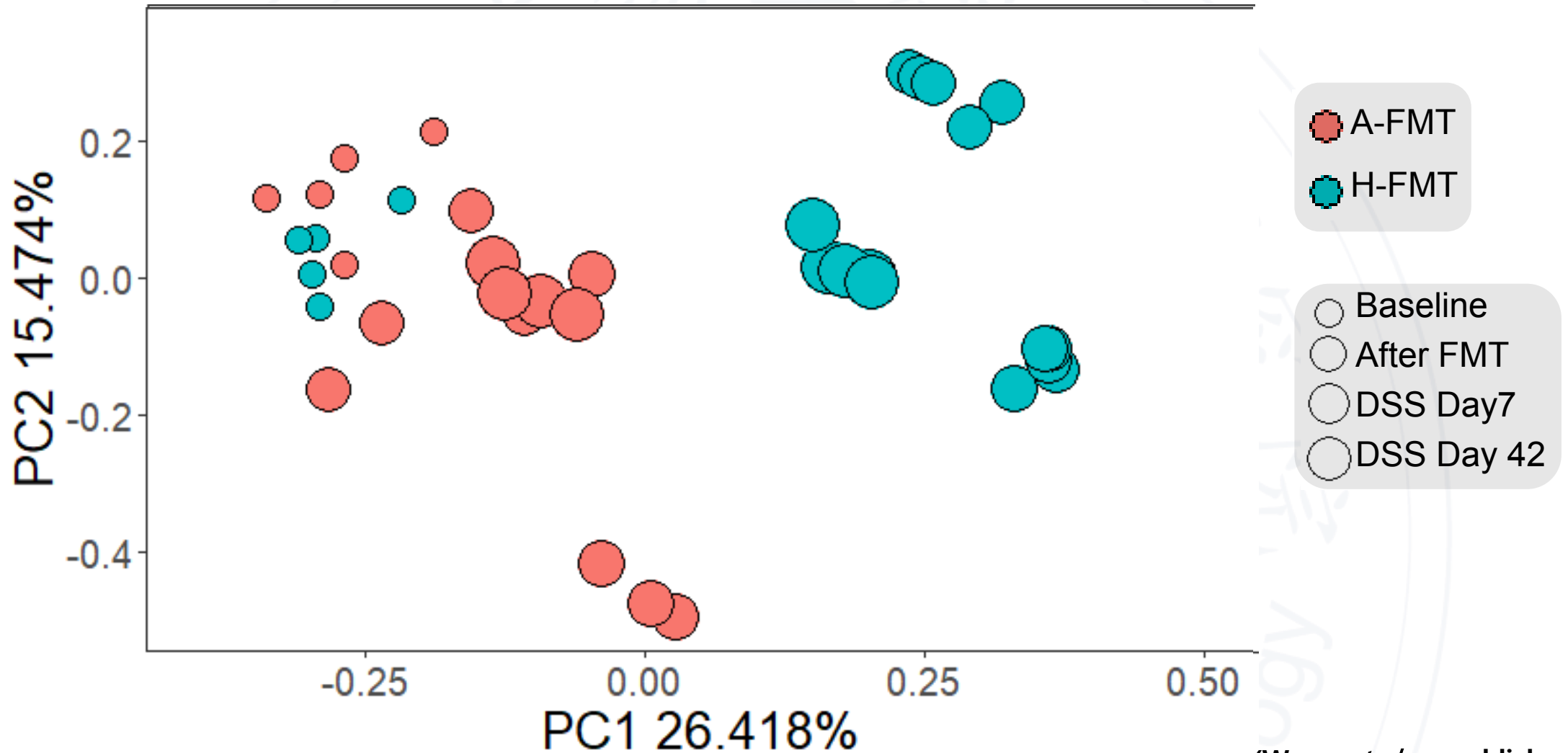
# Perturbation of microbiome: induced inflammation in aging mice after FMT



Dextran Sulfate Sodium (MW 36,000-50,000)  
 3% (w/v) in drinking water for 7 days  
 Induce colonical inflammation (colitis) and microbiome perturbation

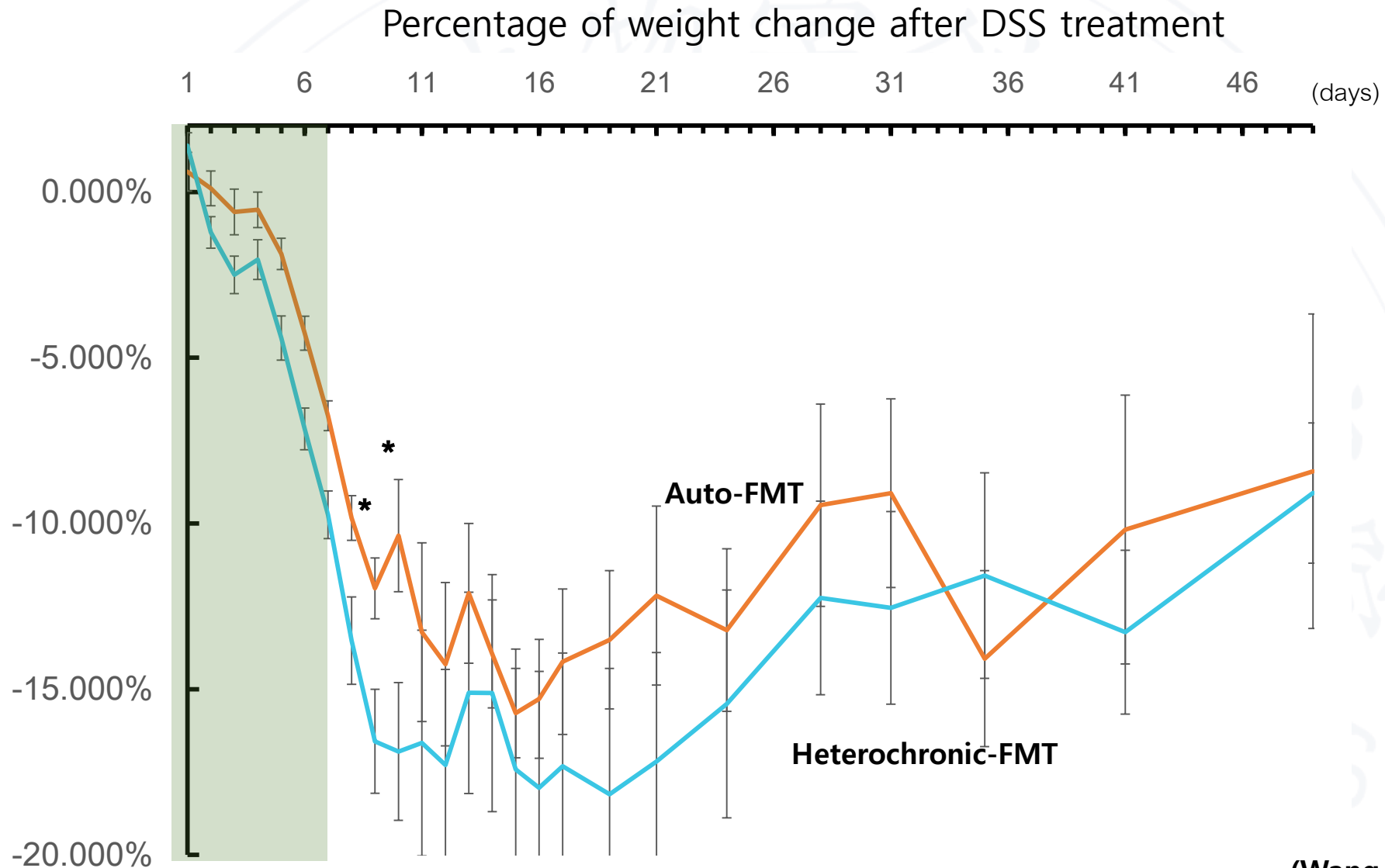


# Gut microbiome after A-FMT is more resilient to perturbation induced by inflammation



(Wang *et.al*, unpublished data)

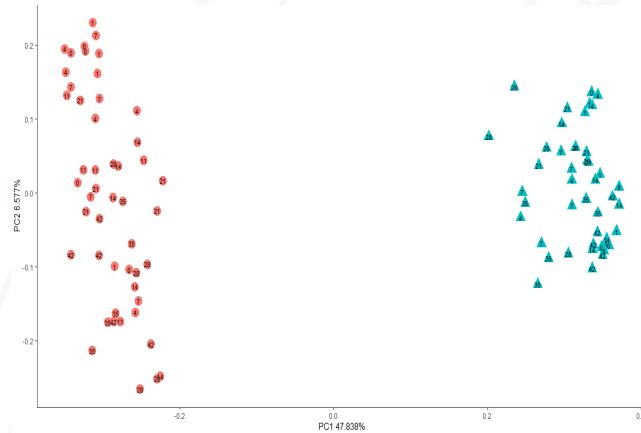
# Susceptibility to induced colitis in aging mice after FMT



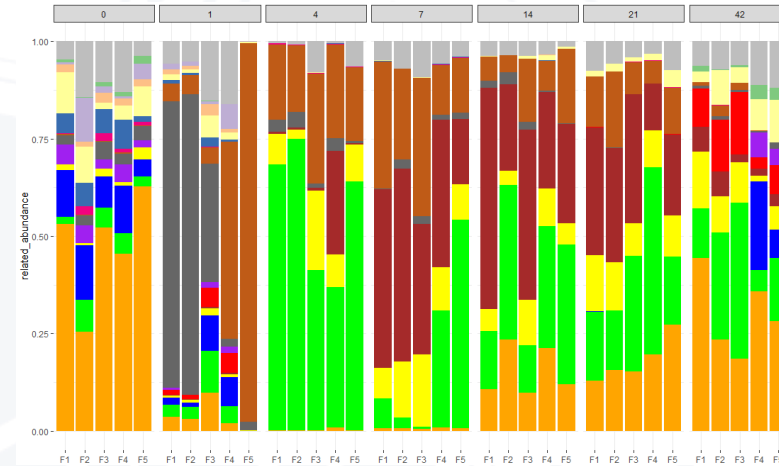
(Wang *et.al*, unpublished data)

# Summary

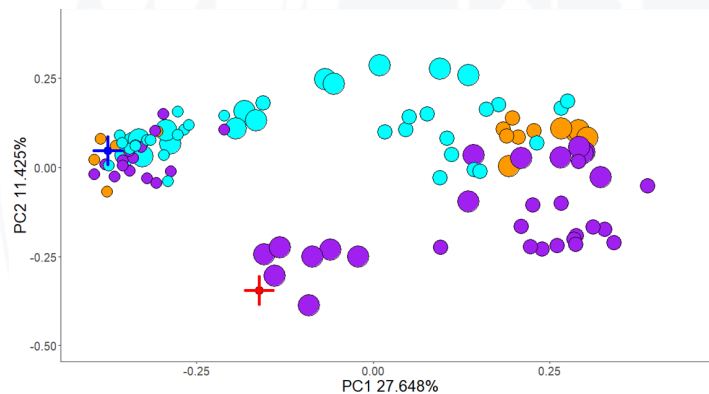
Young and aging hosts have different gut microbiome



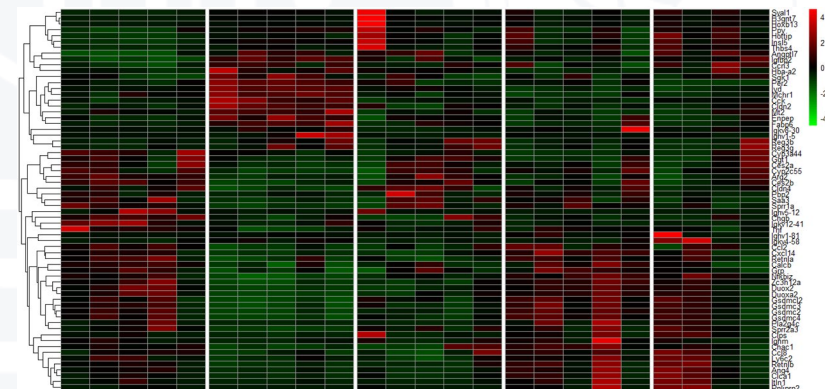
Gut microbiome does not return to the original state after antibiotics treatment



FMT following antibiotics treatment helps restore the gut microbiome diversity



Autologous FMT may be the best strategy for restoring intestinal homeostasis in aging hosts





# Acknowledgments

Lei Dai lab members



Experiments: Dr. Ying Wang, Qingqing Lv  
Data analysis: Jinhui Tang

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