

Voluntary exercise modulates the gut microbiota and improves skin inflammation in a mouse model

Wanchen Zhao¹, Ge Peng¹, Alafate Abudouwanli¹, Quan Sun¹, Mengyao Yang^{1,2}, Shan Wang^{1,3}, Yi Tan¹, Hideoki Ogawa¹, Ko Okumura¹, François Niyonsaba^{1,4}

¹Atopy (Allergy) Research Center, Juntendo University Graduate School of Medicine, Tokyo, Japan.

²Department of Dermatology, the First Affiliated Hospital of China Medical University, Liaoning, China

³Department of Dermatology, Beijing Children's Hospital, Capital Medical University, Beijing, China

⁴Faculty of International Liberal Arts, Juntendo University, Tokyo, Japan.

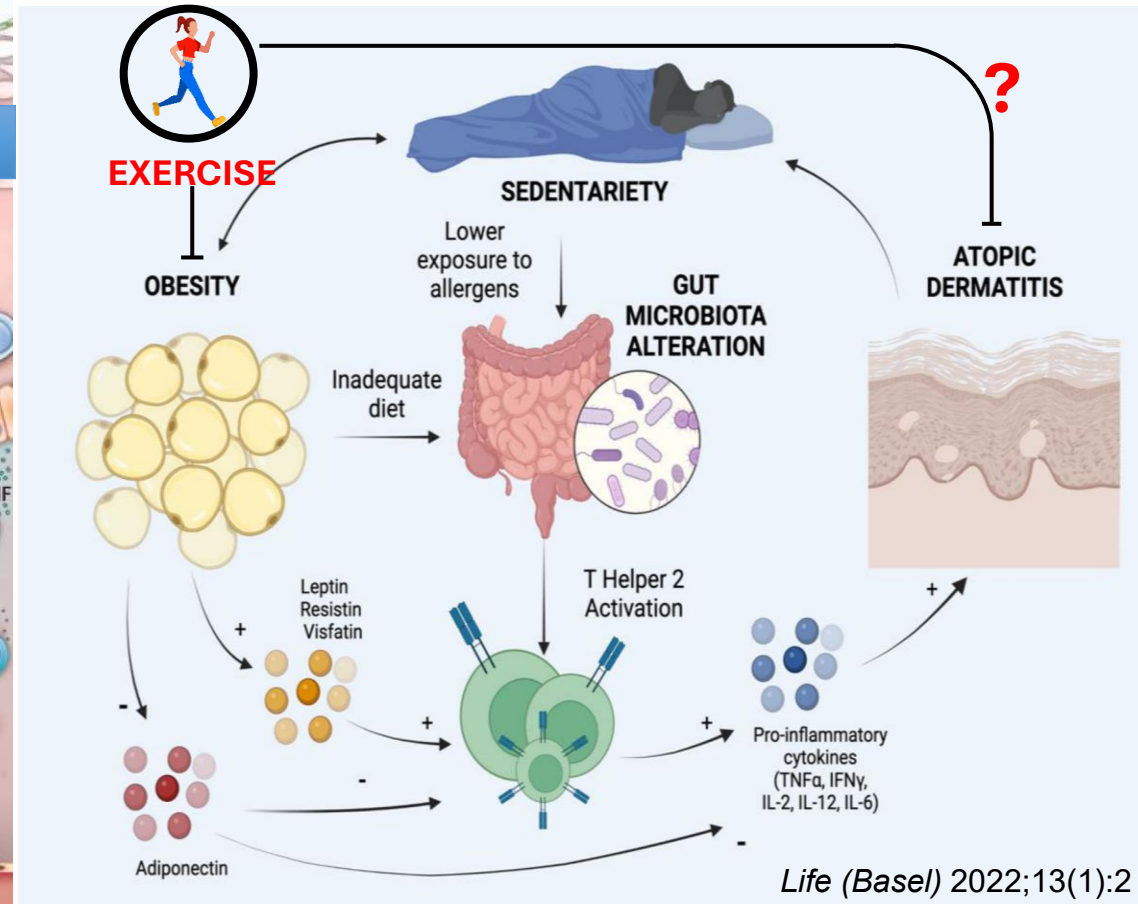
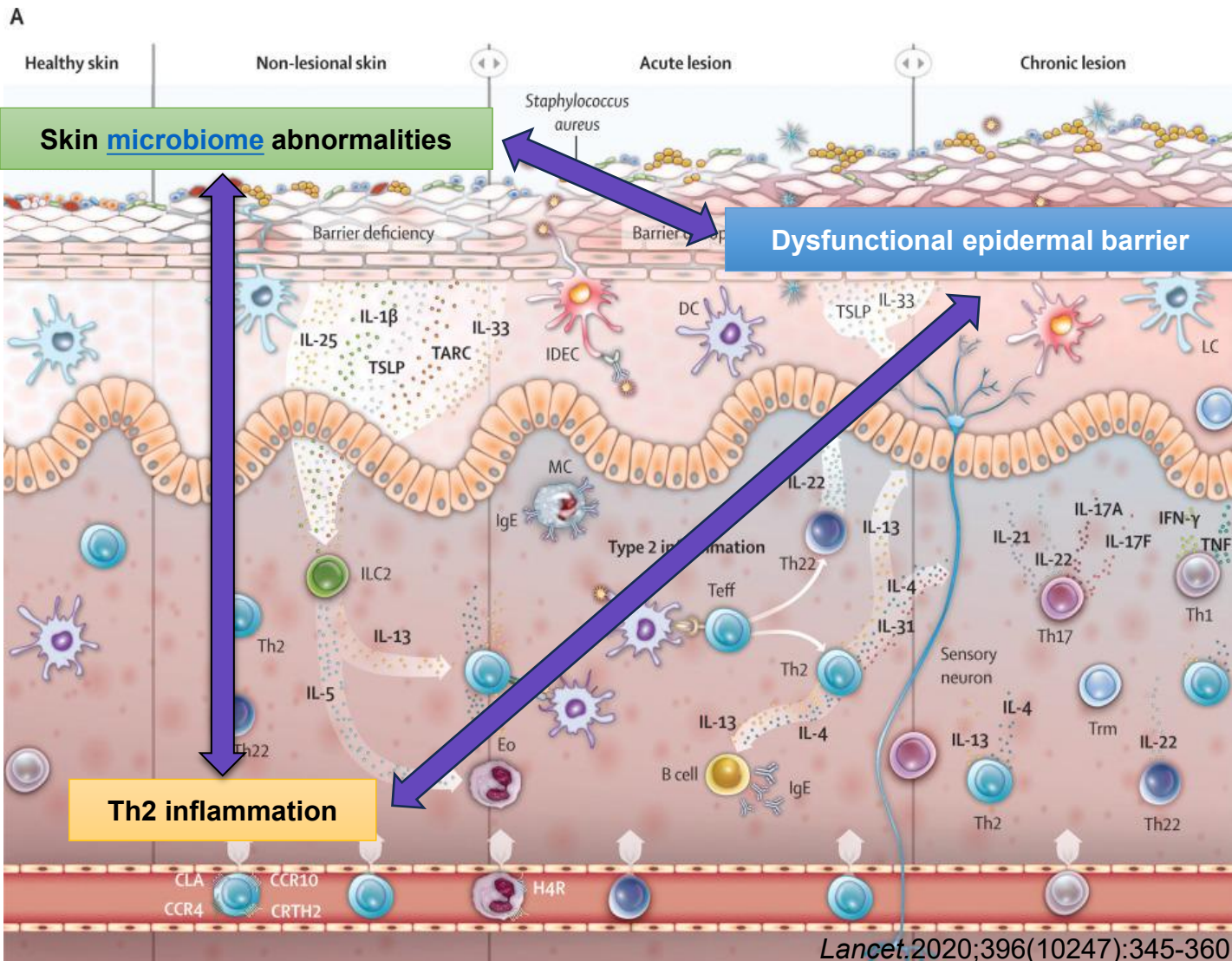
The 15th Georg RAJKA International Symposium on Atopic Dermatitis

COI Disclosure

Wanchen Zhao, et al.

The authors have no financial conflicts of interest to disclose concerning the presentation.

What is atopic dermatitis (AD)



Atopic Dermatitis Is Associated with Less Physical Activity in US Adults

Jonathan I. Silverberg^{1 2 3}  , Jing Song⁴, Daniel Pinto^{5 6}, Sherry H. Yu⁷, Abigail L. Gilbert⁸, Dorothy D. Dunlop^{2 4 6}, Rowland W. Chang^{4 5 6}

Table 1. Association of atopic dermatitis with physical activity as measured by daytime actigraphy in adults

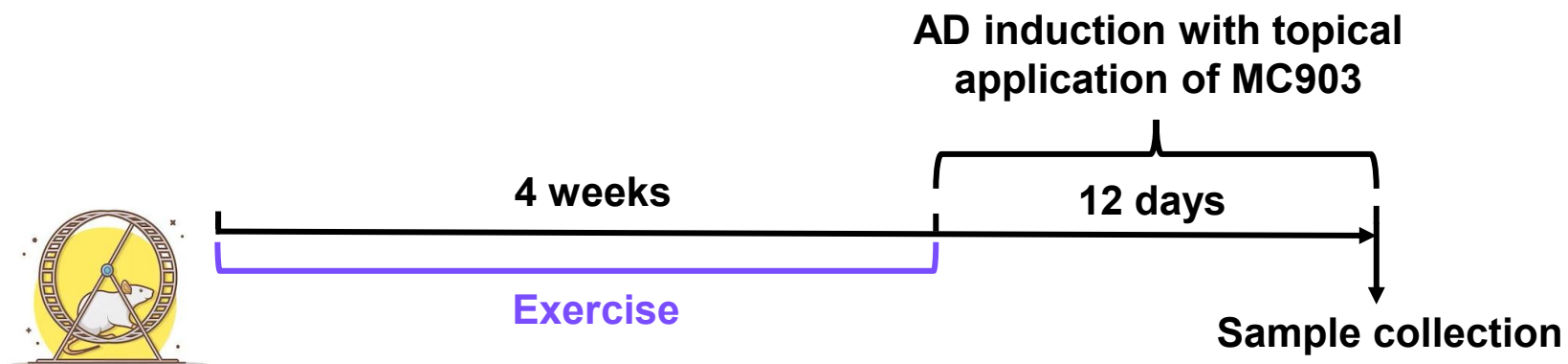
Variable	Atopic dermatitis					
	No (n = 3,061)	Yes (n = 189)				
	Mean (95% CI)	Mean (95% CI)	Crude beta (95% CI)	P	Adjusted beta (95% CI)	P
Average daily activity (count) ¹	261275 (254825.6–267725.3)	239245 (222411.3–256079.4)	–19562 (–35498 to –3627.32)	0.02	–15994 (–30536 to –1452.74)	0.03
Average sedentary time (min)	489.7 (485.0–494.4)	510.6 (494.8–526.4)	15.83 (–1.83 to 33.50)	0.08	12.74 (–4.30 to 29.79)	0.13
Average light activity (min)	344.4 (338.5–350.3)	329.6 (311.9–347.2)	–14.19 (–31.41 to 3.04)	0.10	–7.91 (–27.39 to 6.35)	0.20
Average moderate-vigorous activity (min)	21.2 (20.0–22.4)	17.9 (15.5–20.4)	–2.68 (–5.42 to –0.06)	0.04	–2.12 (–3.92 to –0.33)	0.02

Survey linear regression models were constructed with minutes of average daily activity, sedentary time, light activity, and moderate-vigorous activity as measured by actigraphy being the dependent (outcome) continuous variables and history of atopic dermatitis (binary) as the independent (explanatory) variable. Multivariate models included age (continuous), gender (binary), race/ethnicity (white vs. other), birthplace in the United States (binary), highest level of education in the household (less than high school vs. high school or greater), type of home (house vs. other), body mass index (<18, 18–24, 25–29, ≥30), and daily wear time of the actigraph (continuous) as covariates. Domain analysis was performed to yield appropriate estimates of variance. Crude and adjusted beta and 95% confidence intervals (95% CI) were determined.

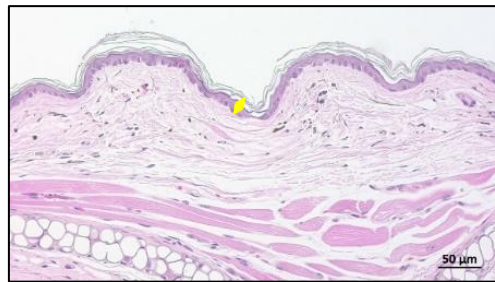
Boldface indicates significant value.

¹Average daily activity is the average total daily accelerometer count.

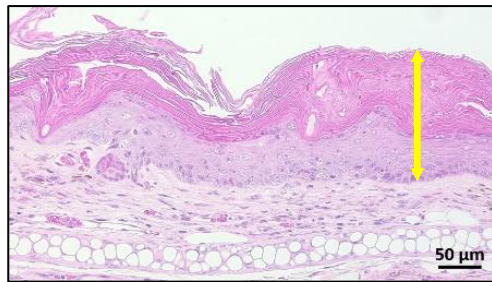
Induction of AD in exercised mice



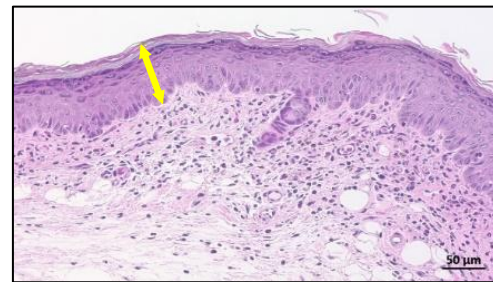
Voluntary running exercise may improve AD



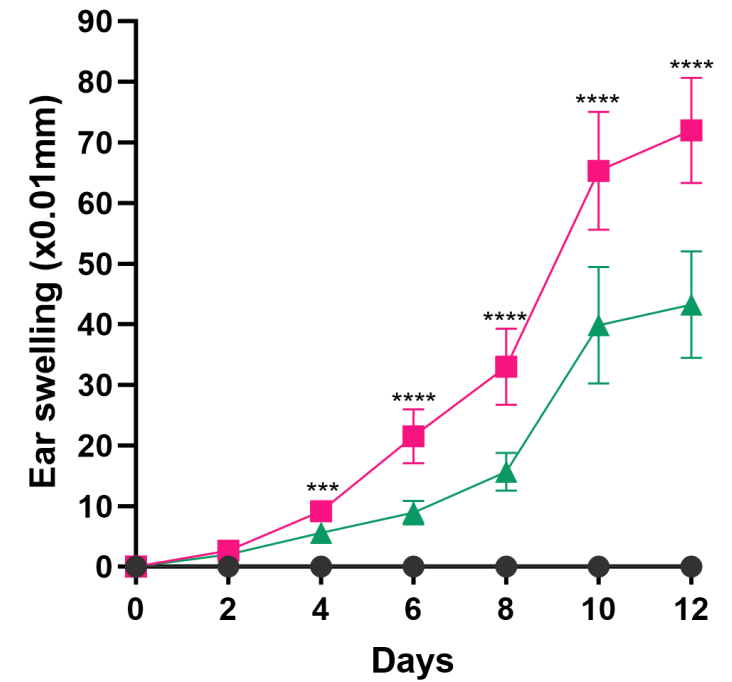
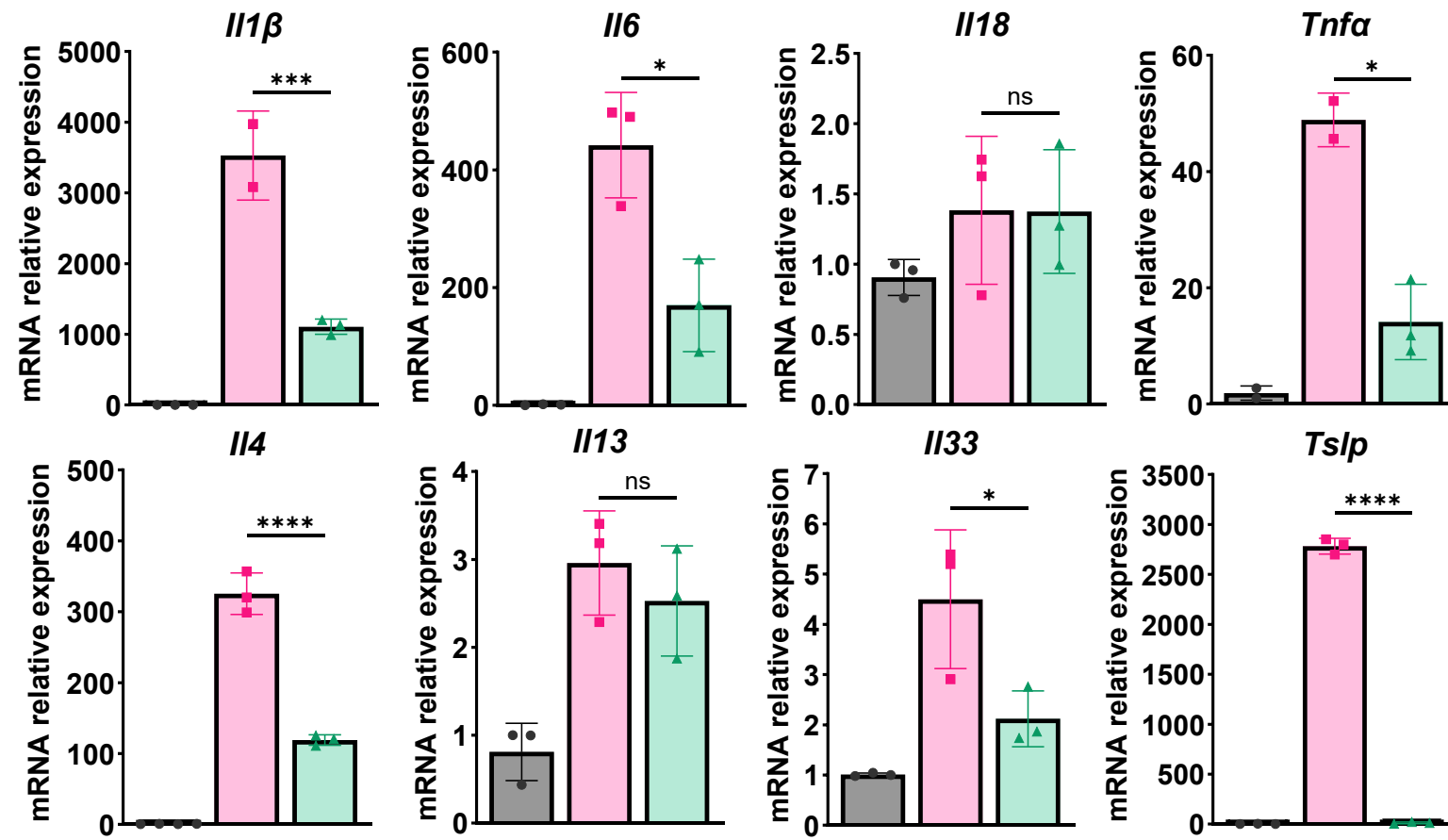
Sedentary + ethanol



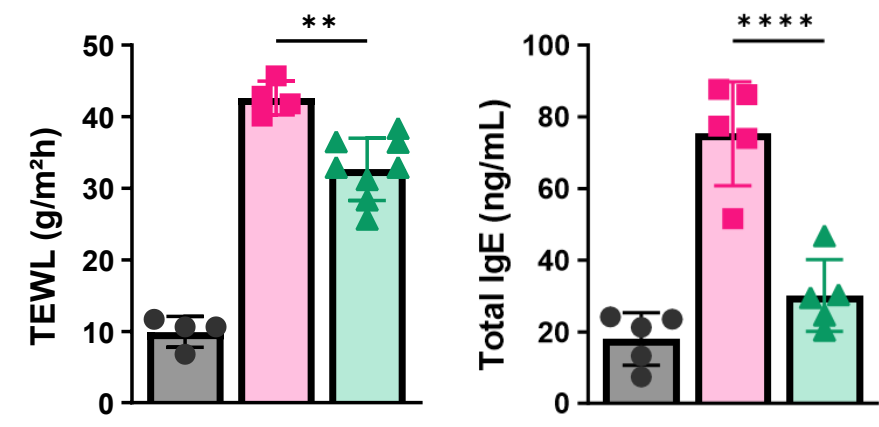
Sedentary + AD induction



Pre-exercise + AD induction



- Sedentary + ethanol
- Sedentary + AD induction
- ▲ Pre-exercise + AD induction



Co-housing with exercised mice alleviates AD symptoms

Co-housing $\longrightarrow$ **Gut microbiota modulation**

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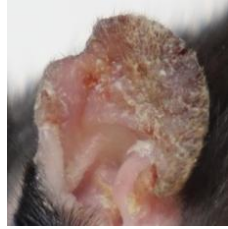
Sedentary + AD induction



Sedentary + AD induction



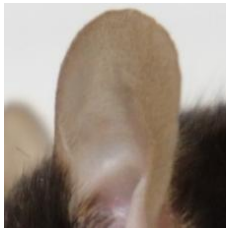
Sedentary + AD induction



Pre-exercised + AD induction



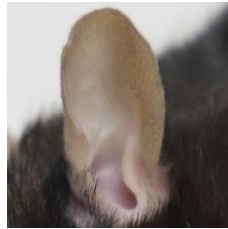
Pre-exercised + ethanol



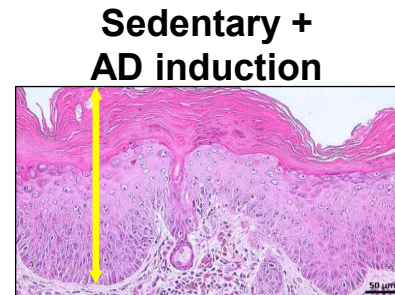
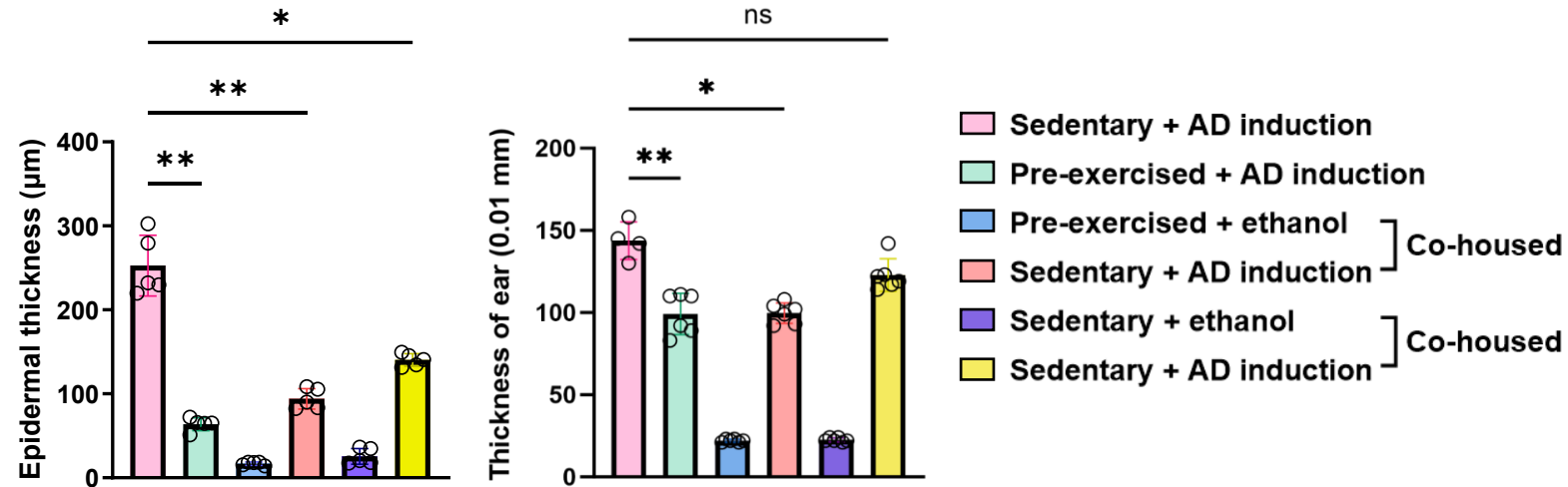
Co-housed



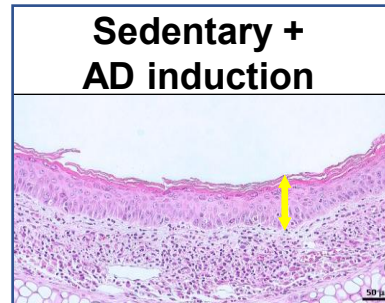
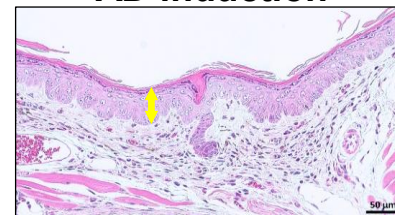
Sedentary + ethanol



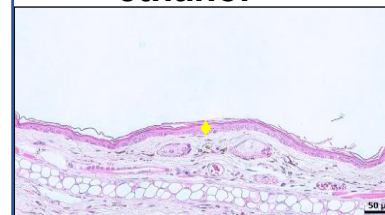
Co-housed



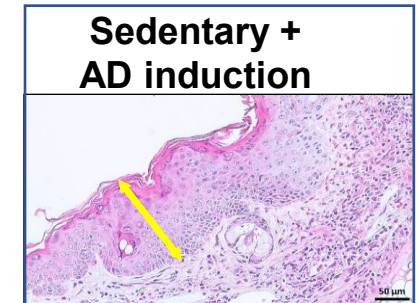
Pre-exercised + AD induction



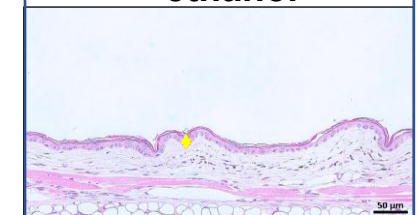
Pre-exercised + ethanol



Co-housed

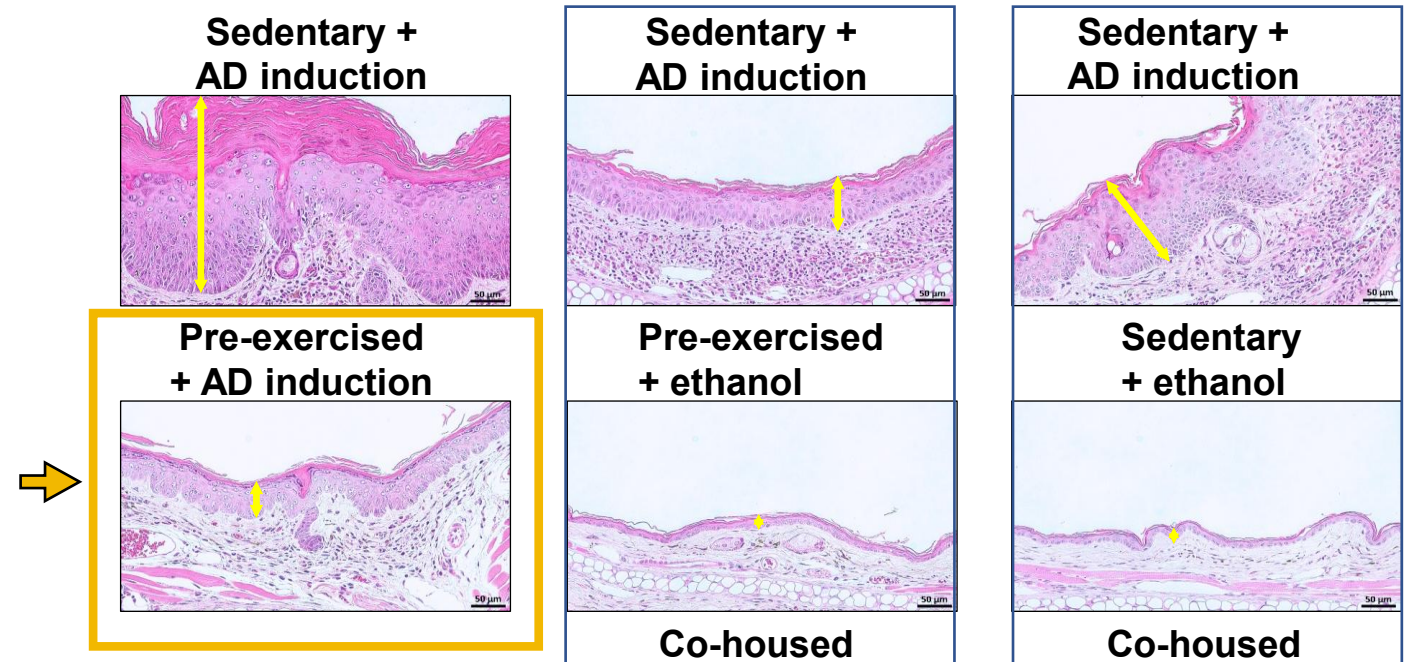
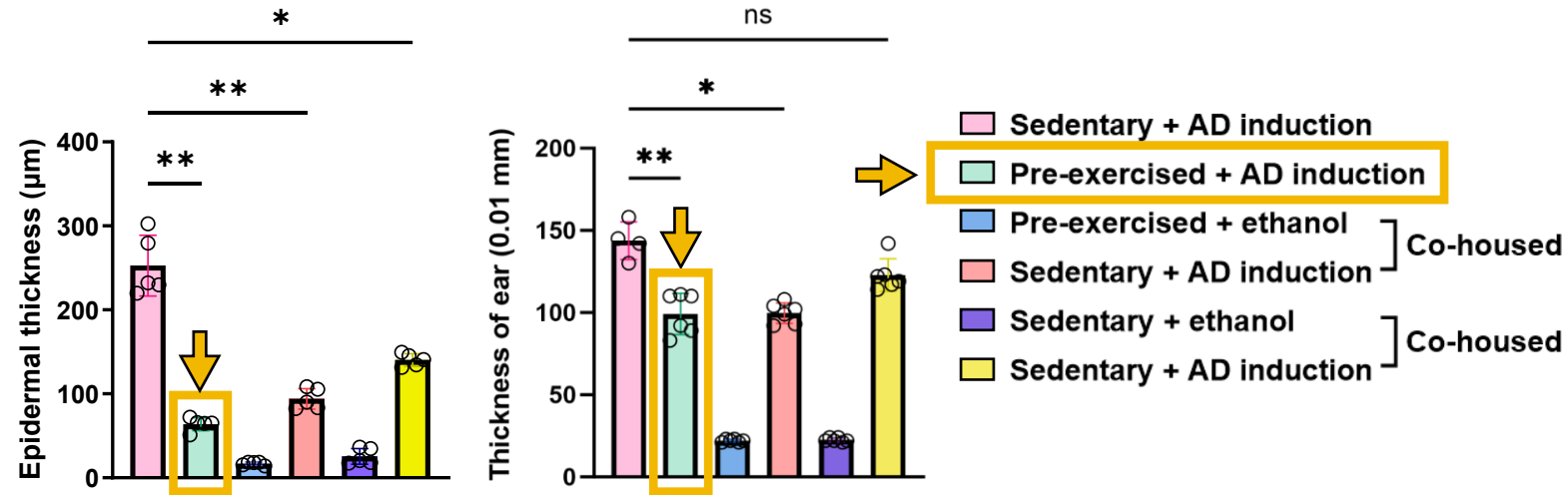
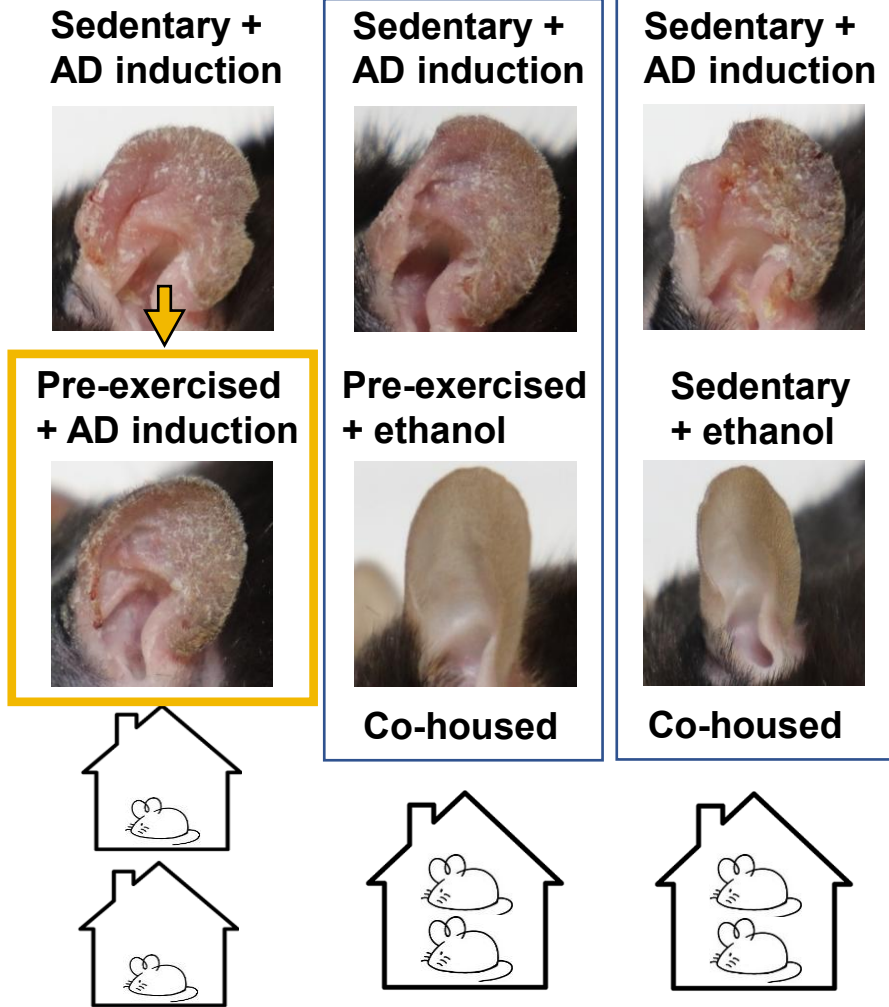


Sedentary + ethanol

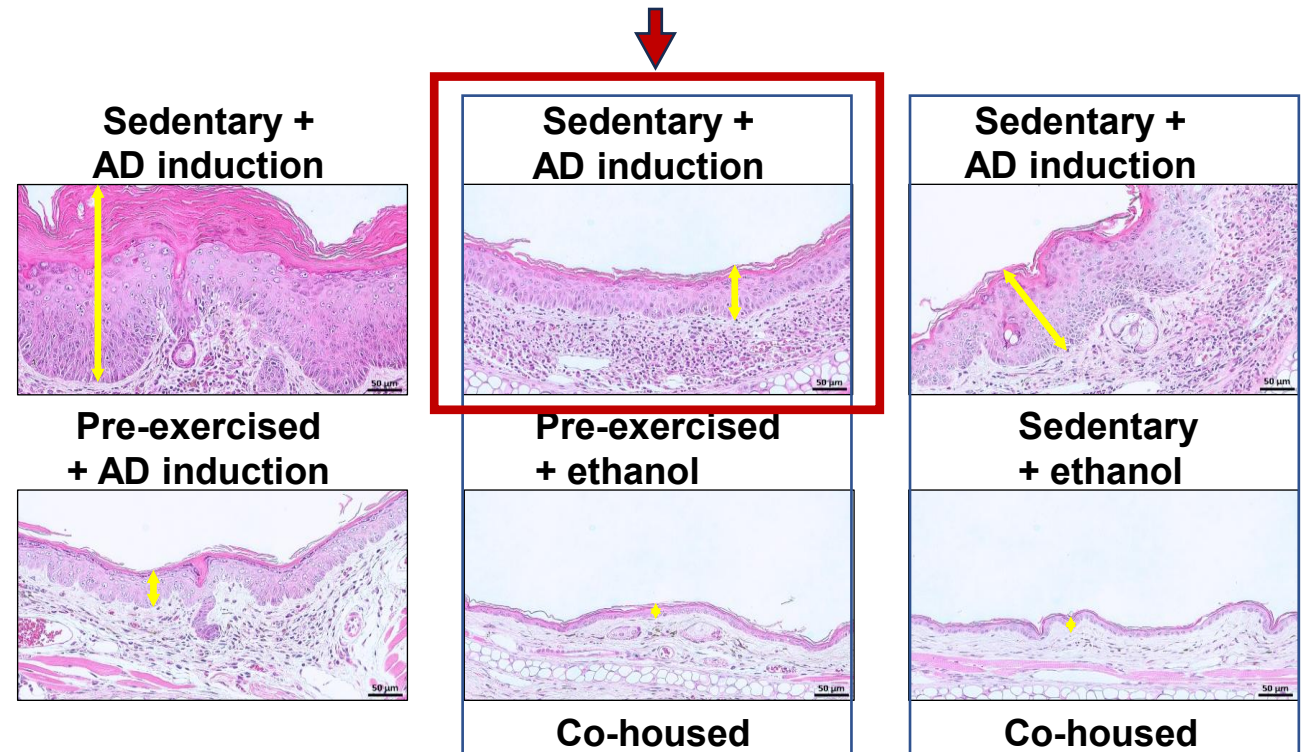
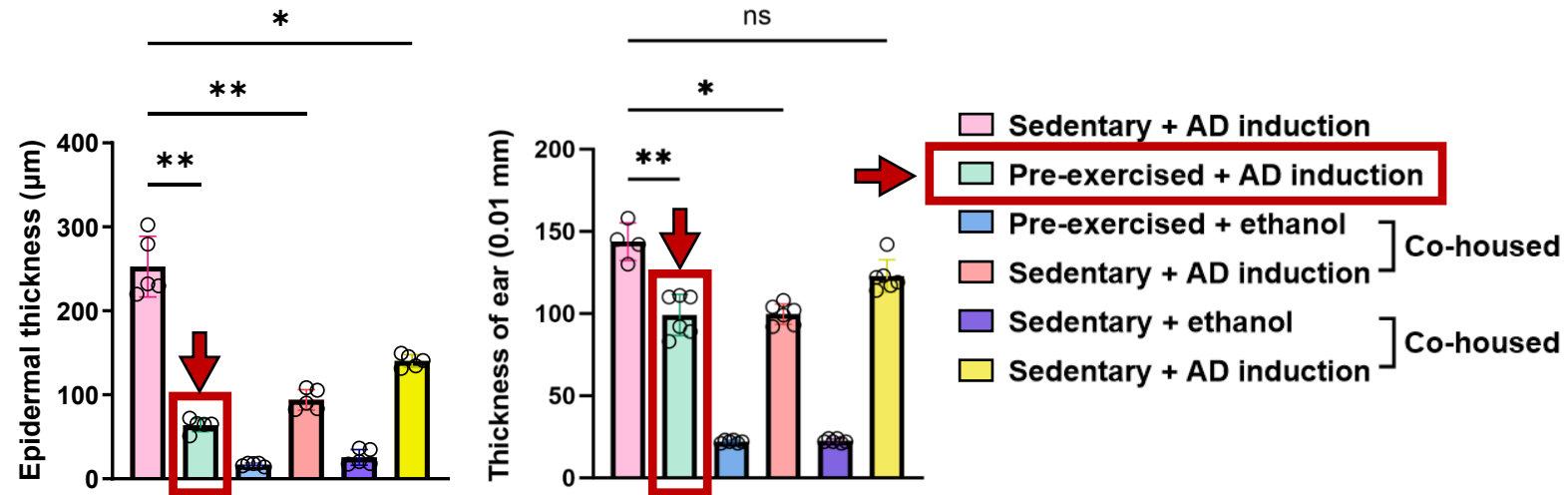
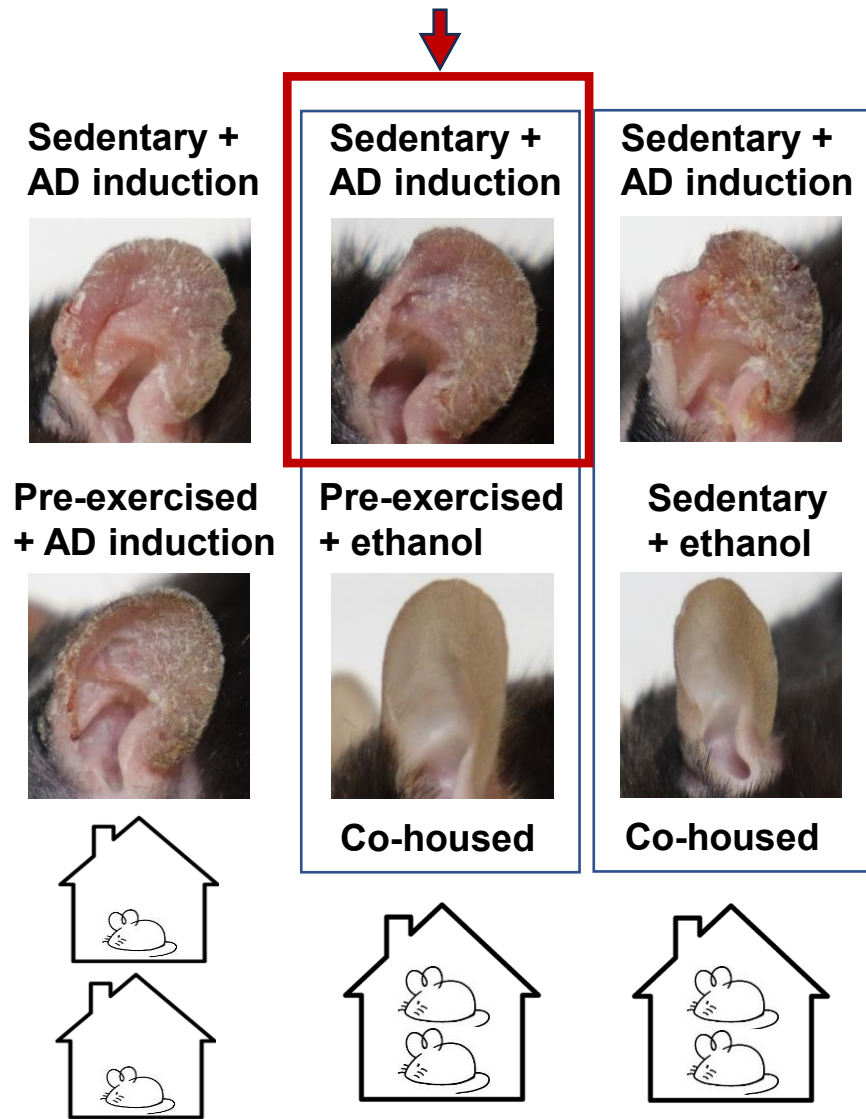


Co-housed

Co-housing with exercised mice alleviates AD symptoms



Co-housing with exercised mice alleviates AD symptoms



Co-housing with exercised mice alleviates AD symptoms

Sedentary +
AD induction



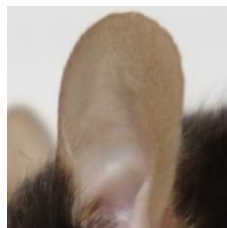
Pre-exercised
+ AD induction



Sedentary +
AD induction



Pre-exercised
+ ethanol



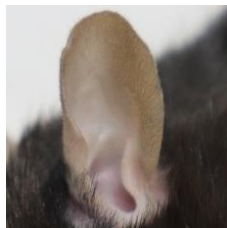
Co-housed



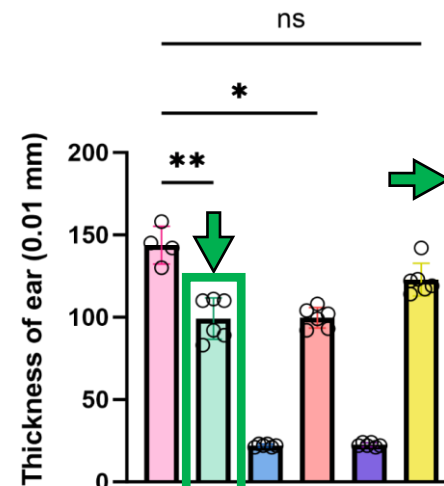
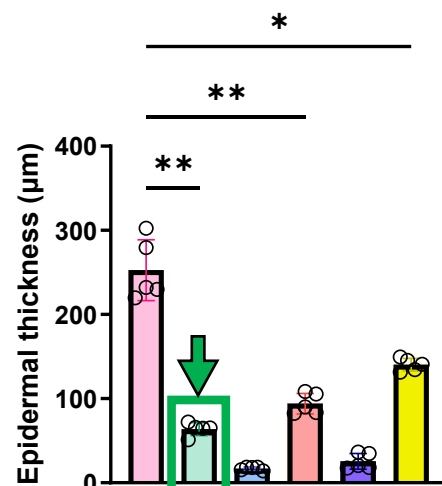
Sedentary +
AD induction



Sedentary
+ ethanol



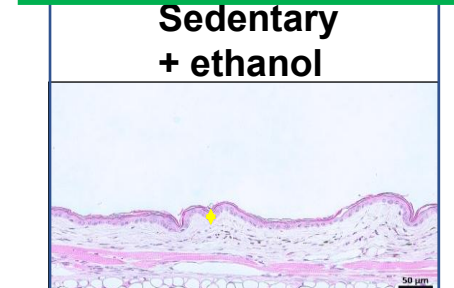
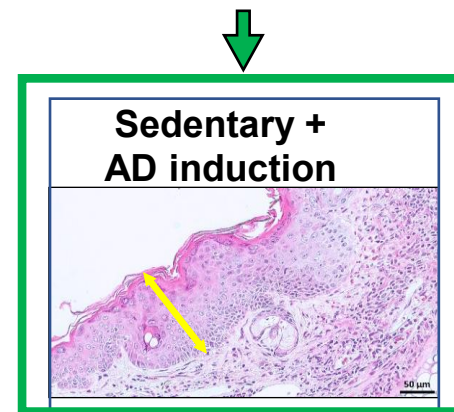
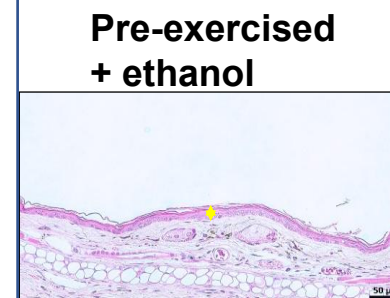
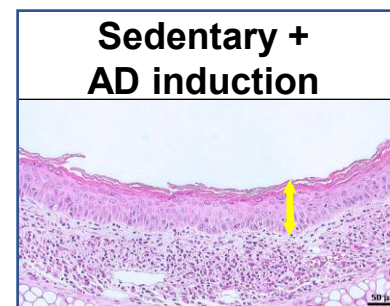
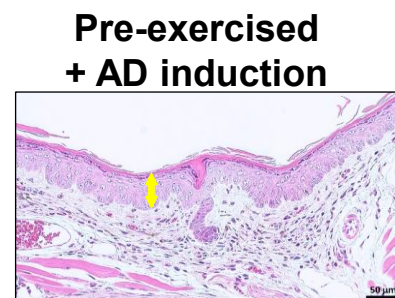
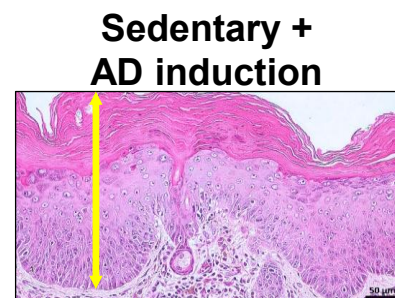
Co-housed



Sedentary + AD induction
 Pre-exercised + AD induction
 Pre-exercised + ethanol
 Sedentary + AD induction
 Sedentary + ethanol
 Sedentary + AD induction

Co-housed

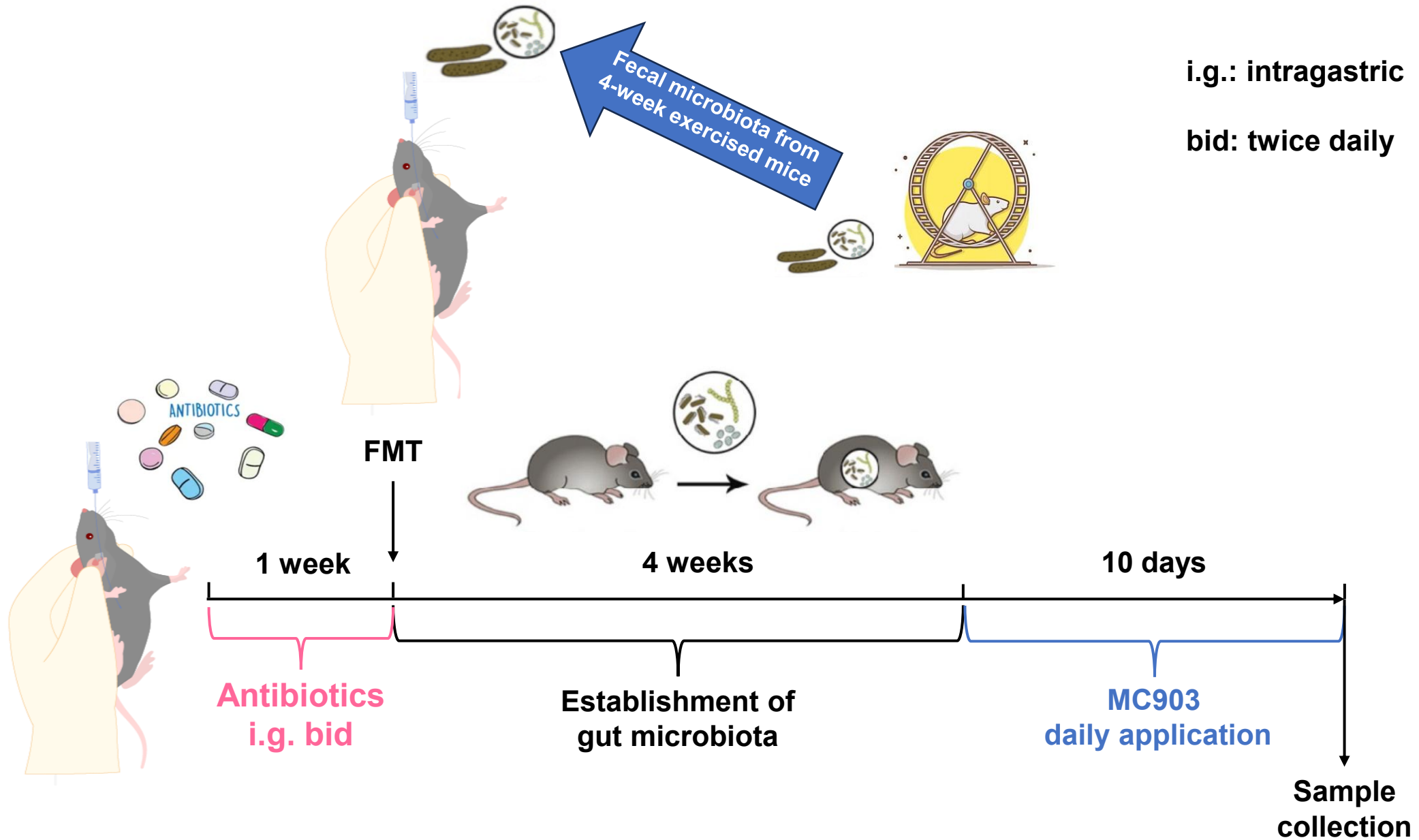
Co-housed



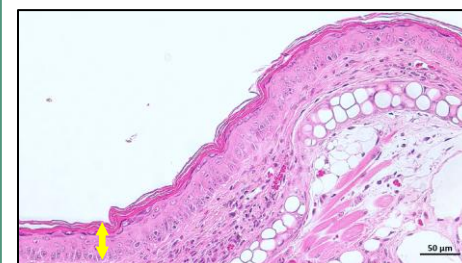
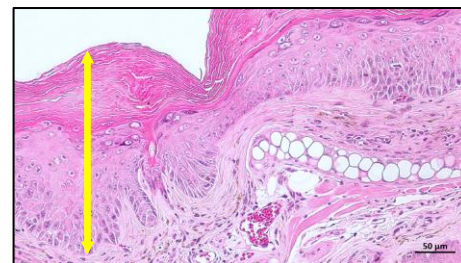
Co-housed

Co-housed

Fecal microbiota transplantation (FMT) from exercised mice



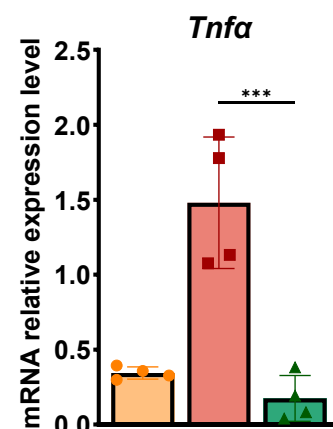
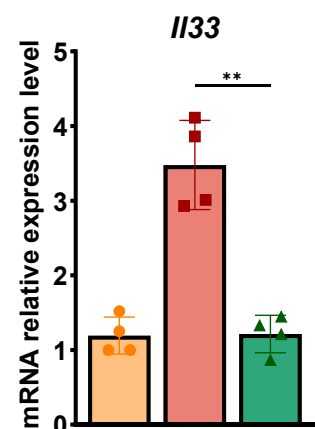
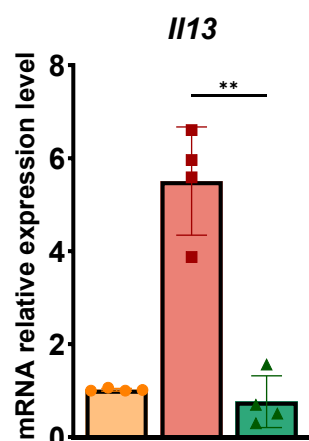
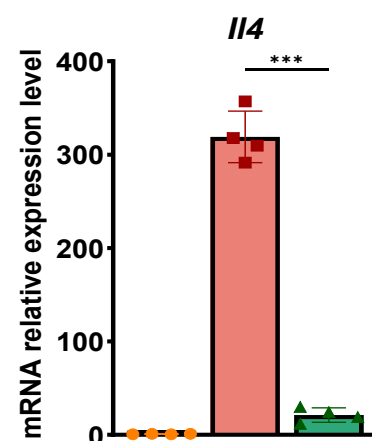
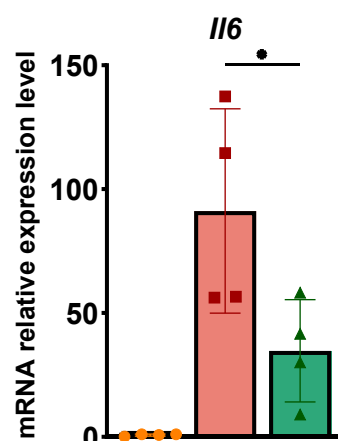
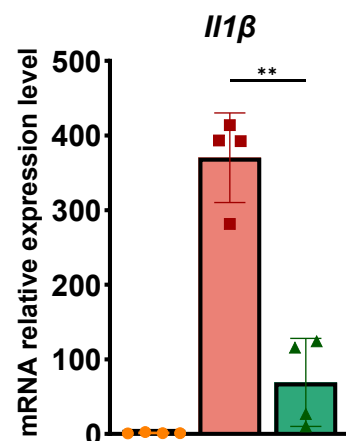
FMT from exercised mice improves AD



Sedentary fecal transplantation before ethanol application

Sedentary fecal transplantation before AD induction

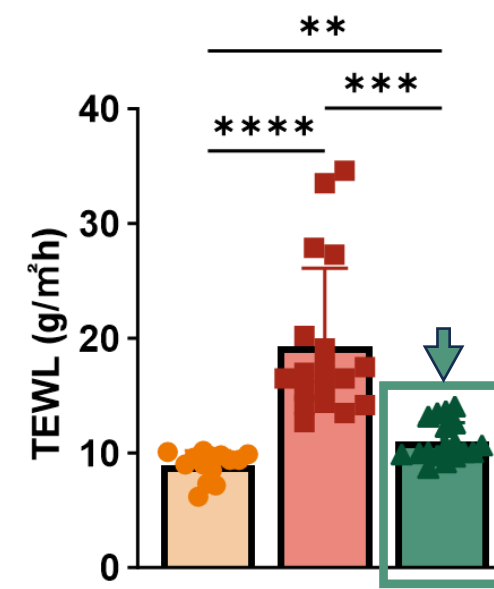
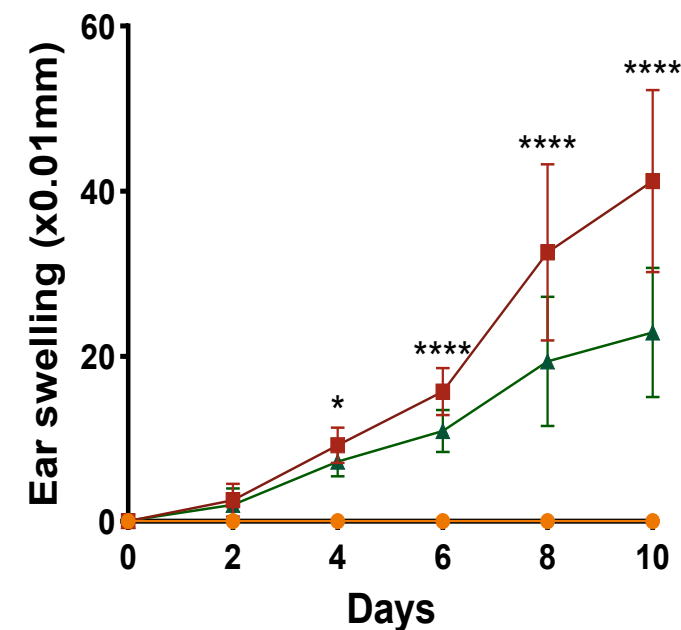
Pre-exercised fecal transplantation before AD induction



● Sedentary fecal transplantation before ethanol application

■ Sedentary fecal transplantation before AD induction

▲ Pre-exercised fecal transplantation before AD induction



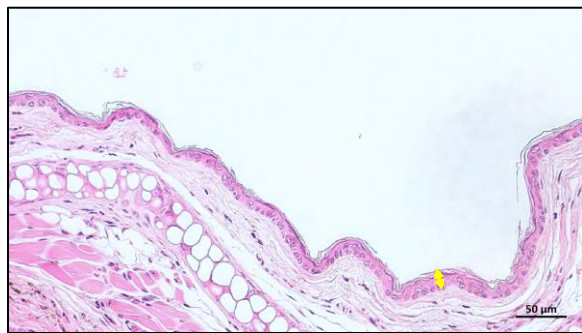
Depletion of gut microbiota in exercised mice

i.g.: intragastric

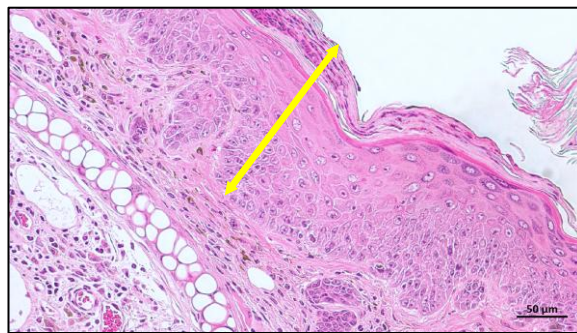
bid: twice daily



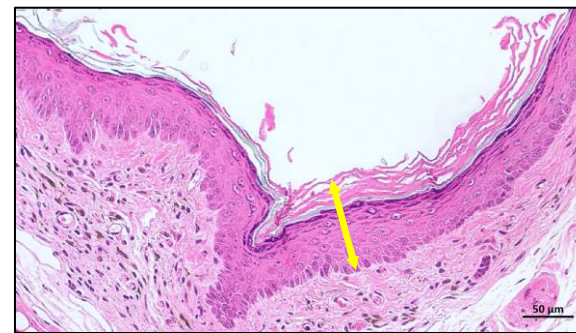
Gut microbiota is necessary for the protective effect of exercise in AD



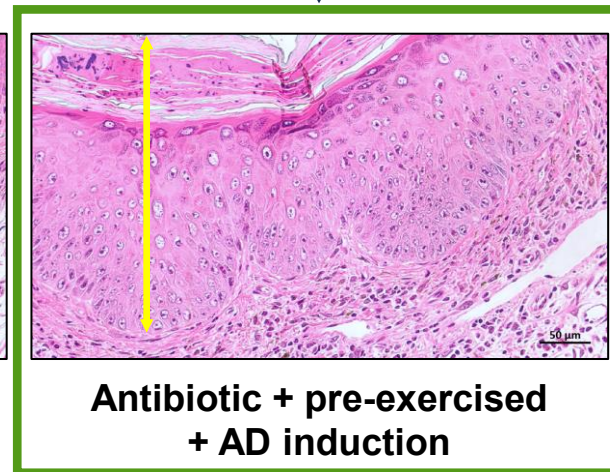
Sedentary + ethanol



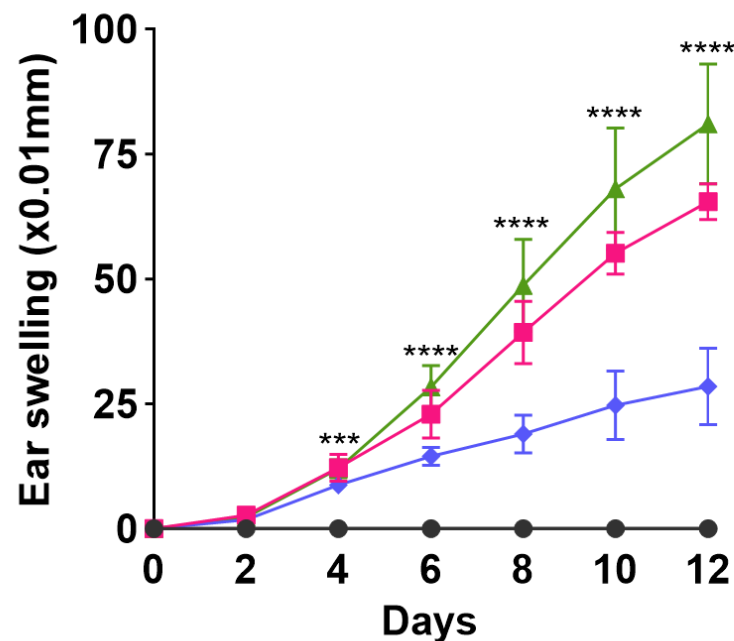
Sedentary + AD induction



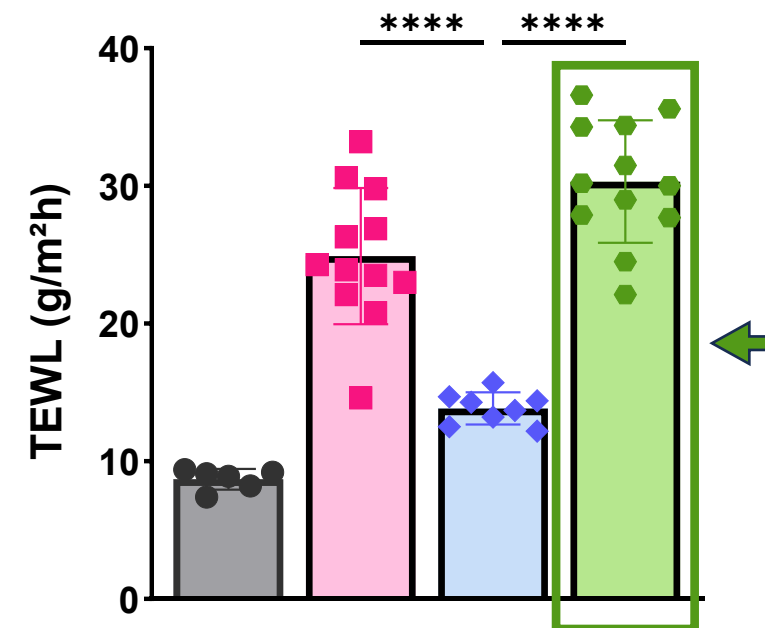
Pre-exercised + AD induction



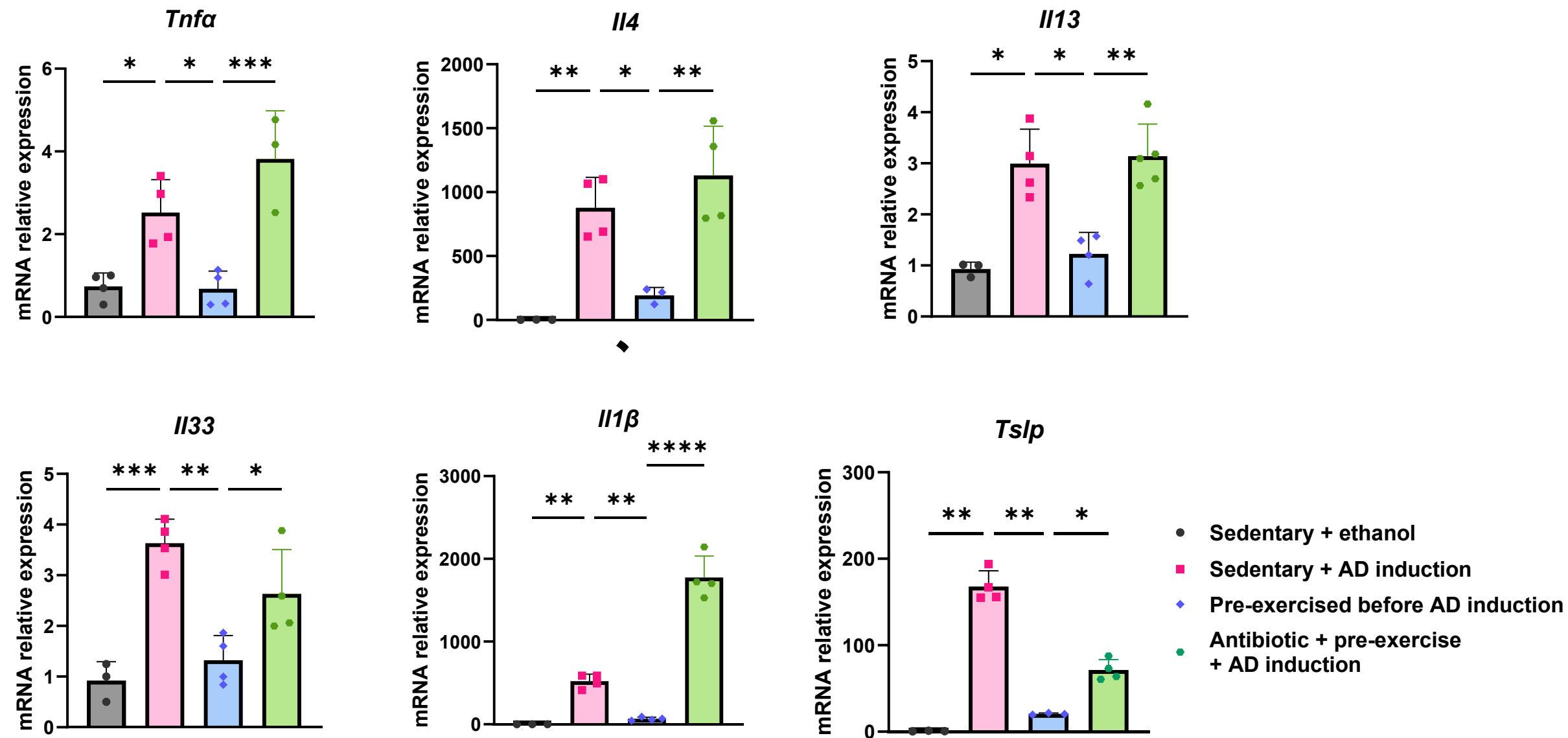
Antibiotic + pre-exercised
+ AD induction



- Sedentary + ethanol
- Sedentary + AD induction
- ◆ Pre-exercised + AD induction
- Antibiotic + pre-exercised + AD induction

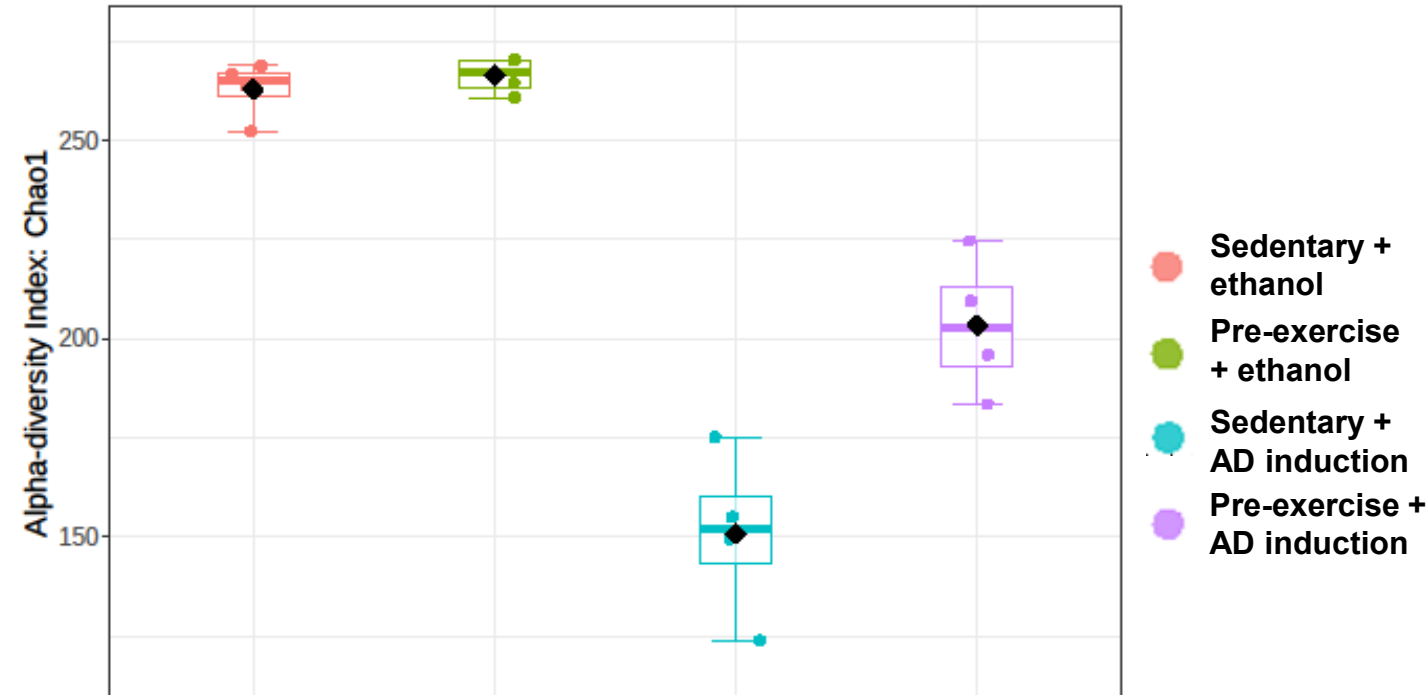


Gut microbiota is necessary for the protective effect of exercise in AD



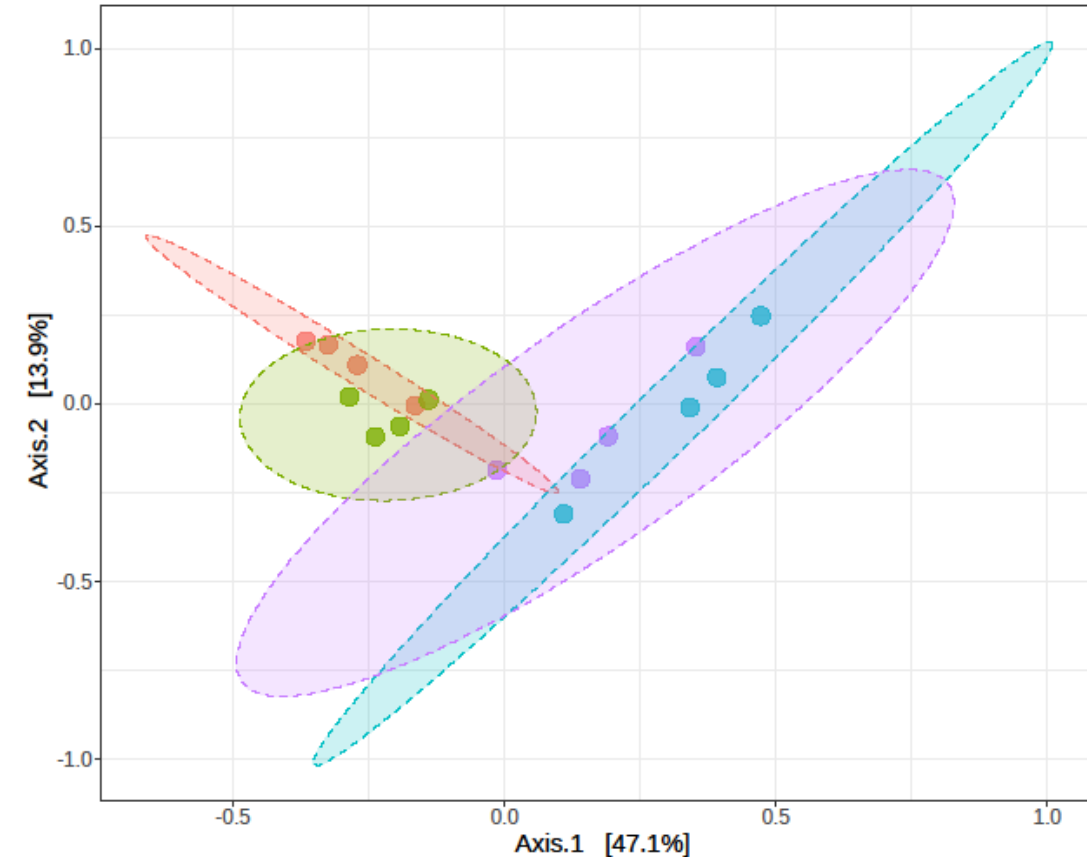
Exercise modulates the gut microbiota

p-value: 2.0694e-07; [ANOVA] F-value: 57.93



α -diversity analysis: reflects the richness and evenness of microbial species present in a given community

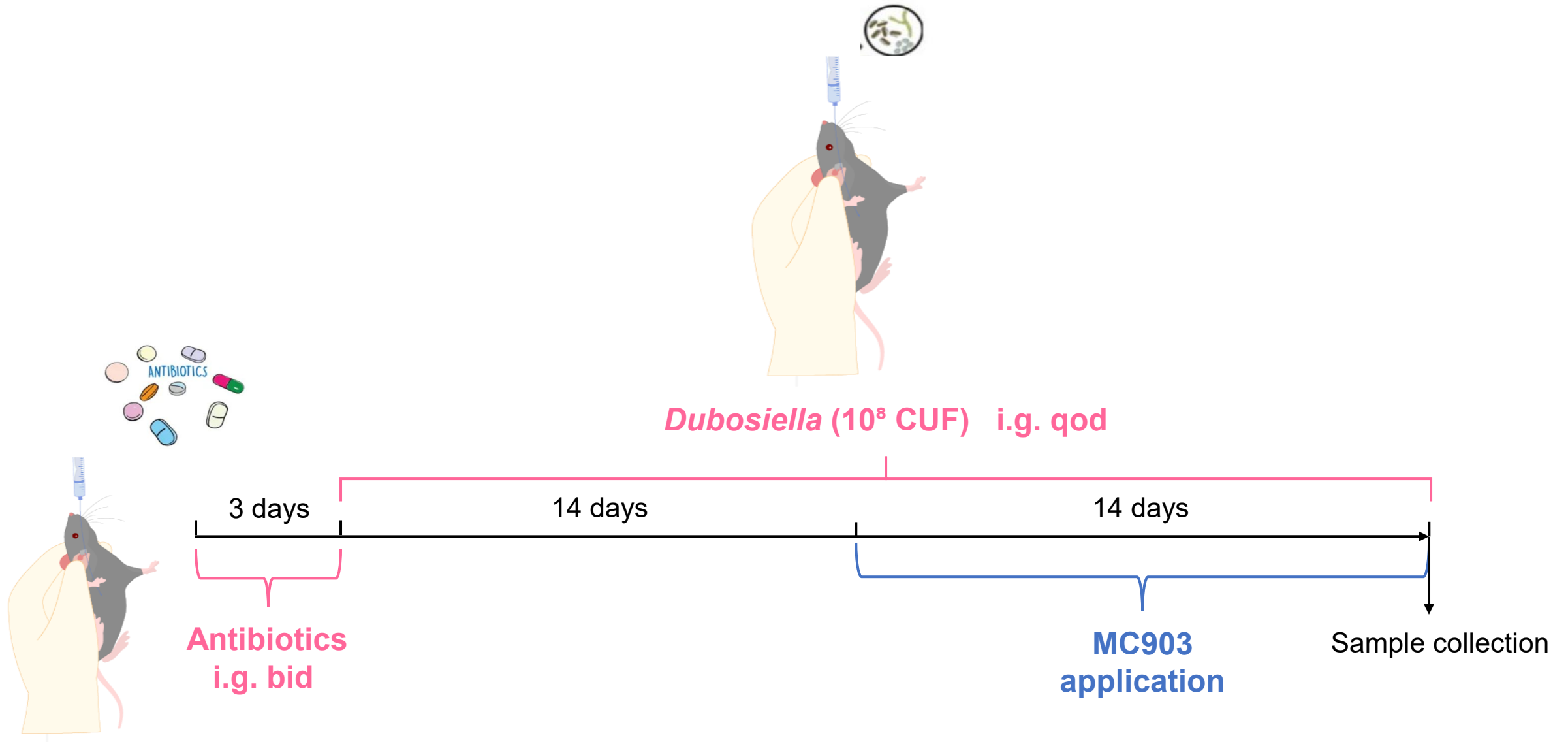
[PERMANOVA] F-value: 4.0674; R-squared: 0.50418; p-value: 0.001



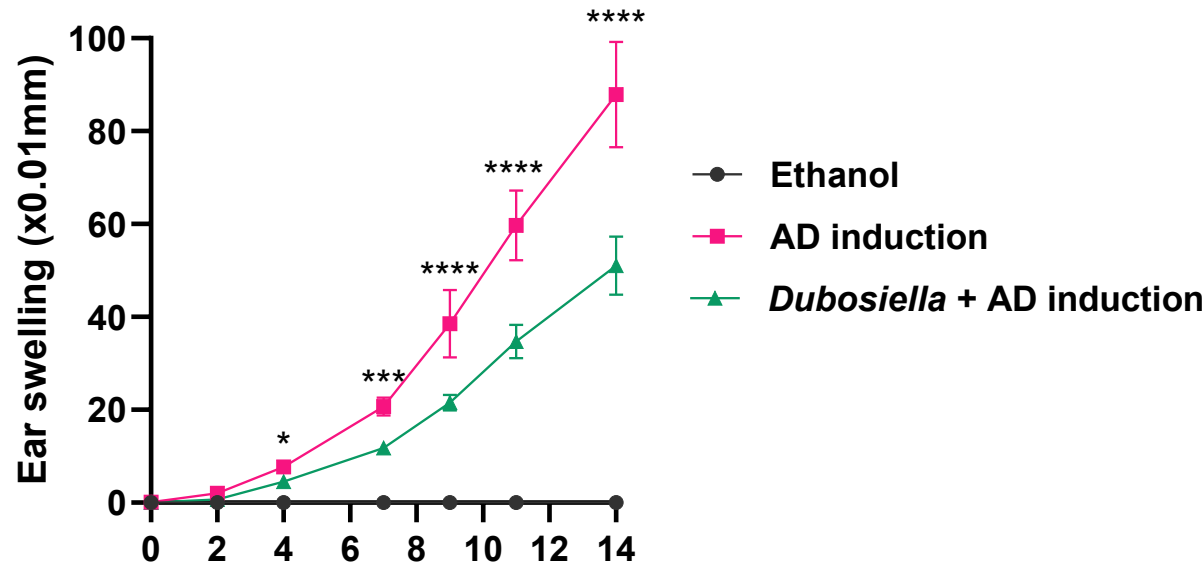
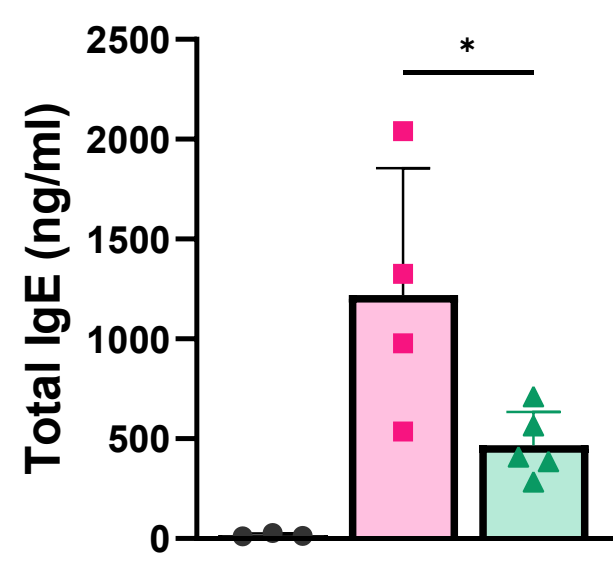
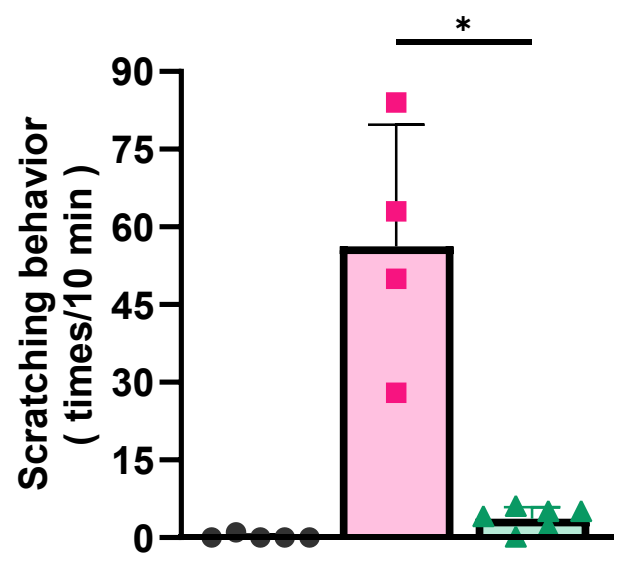
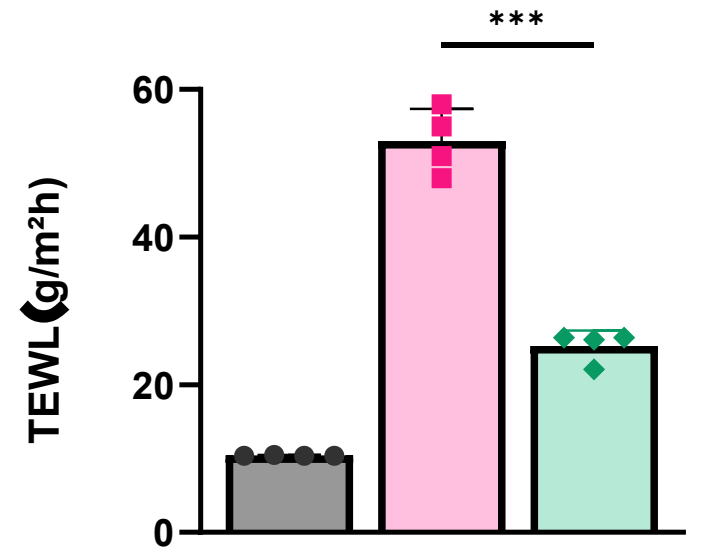
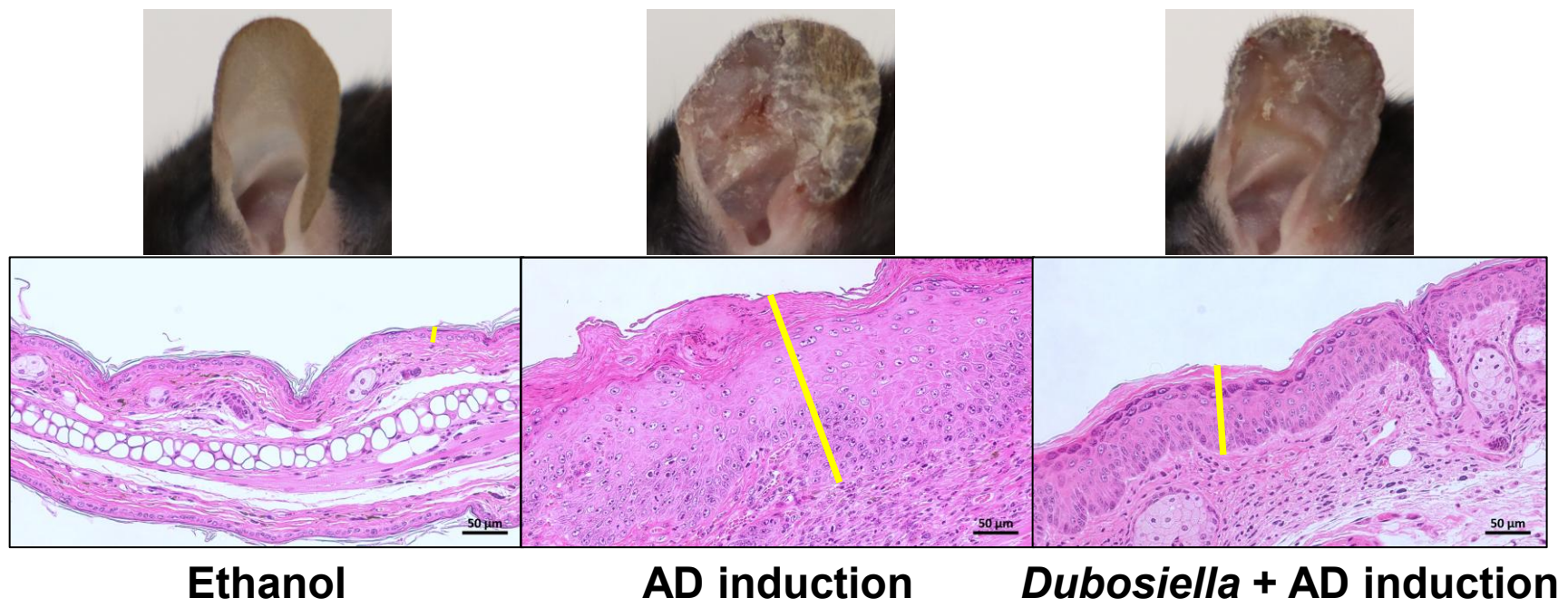
β -diversity analysis: helps to understand how microbial communities differ from one another in terms of species composition, structure, and abundance

Dubosiella transplantation in AD mice

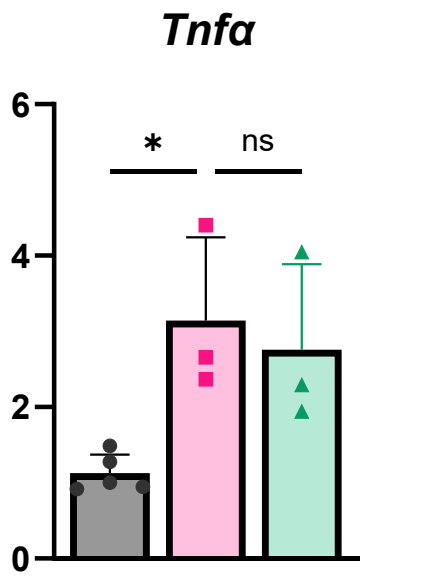
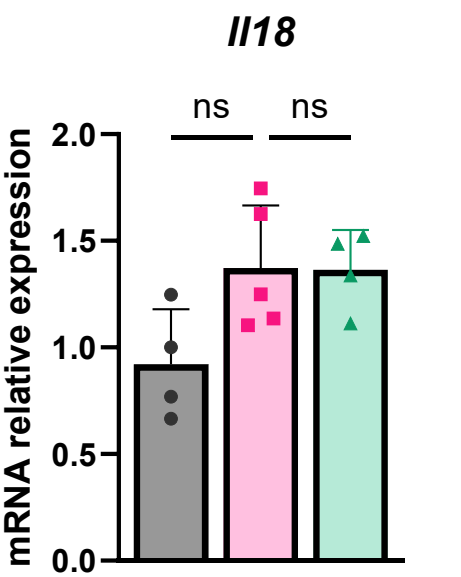
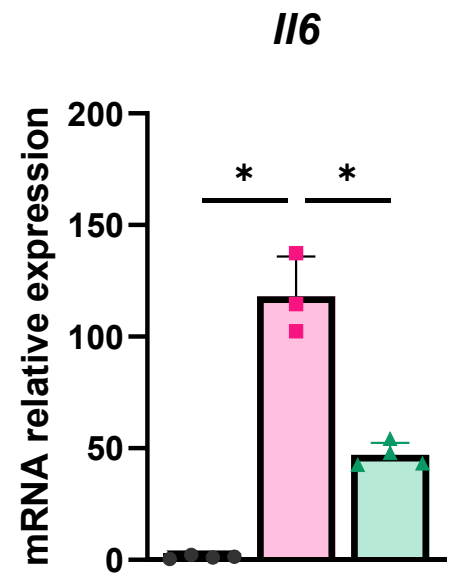
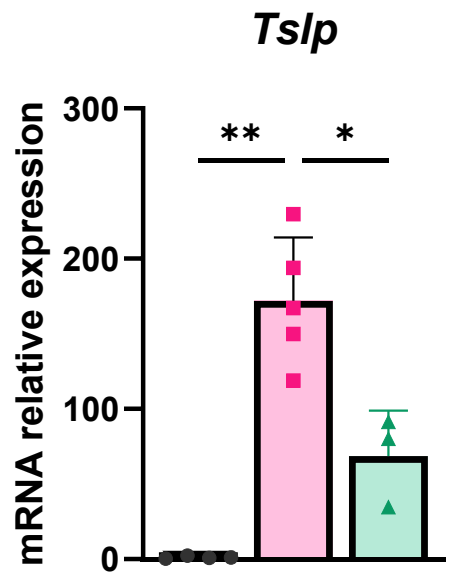
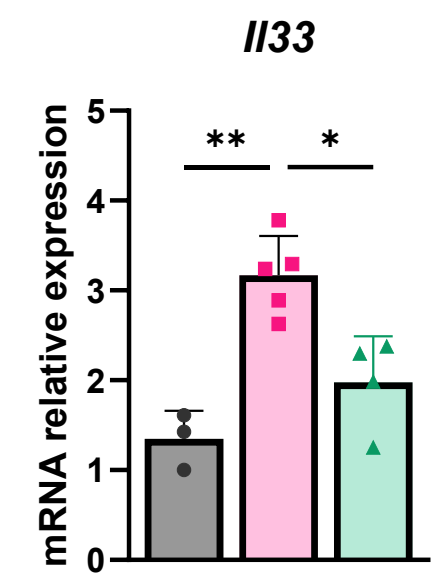
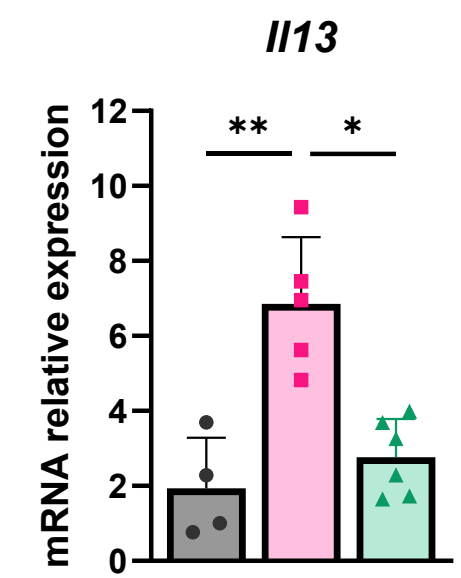
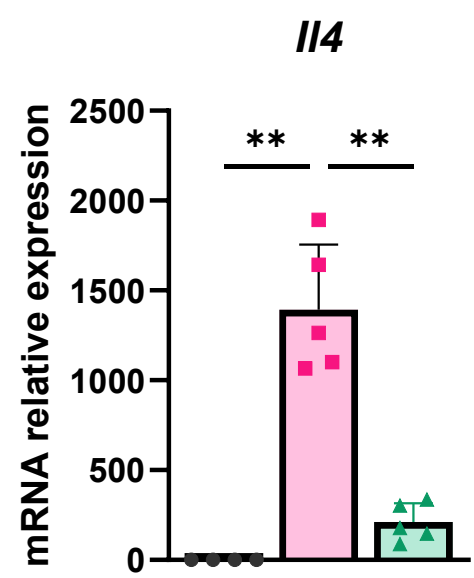
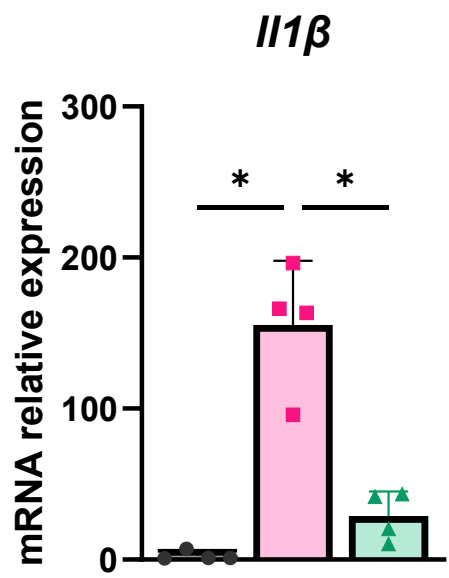
i.g.: intragastric administration



Dubosiella transplantation alleviated inflammation symptoms



Dubosiella transplantation alleviated inflammation symptoms



- Ethanol
- AD induction
- ▲ *Dubosiella* + AD induction

Conclusion

- Exercise may prevent AD by regulating the gut microbiota.
- *Dubosiella* transplantation alleviated inflammation in AD mouse model.

Exercise may serve as a preventive approach for AD.

Acknowledgement

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Quan Sun,
Mengyao Yang,
Shan Wang,
Yi Tan,
Yoshie Umehara,
Prof. Ko Okumura,
Prof. Hideoki Ogawa,
Prof. François Niyonsaba



JSPS

科研費
KAKENHI



アトピー疾患研究センター
Atopy Research Center

Thank you for your attention