

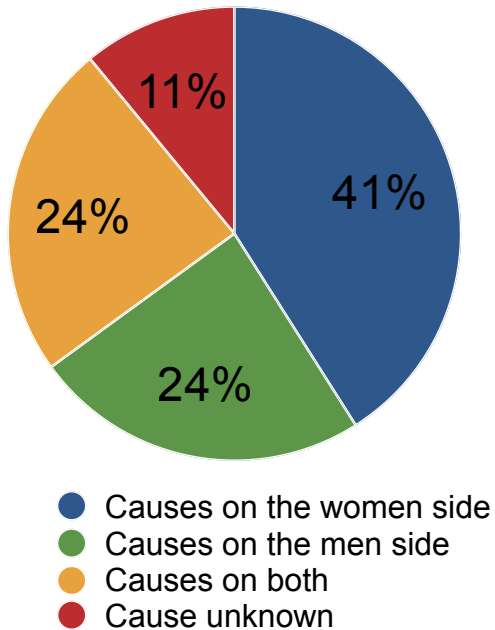
# Elucidation of the mechanisms of gut microbiota-sex hormone interaction

82024683, BI program, Haruno Takahashi

## Background / Aim of study

**【Problem】** About **186 million** people around the world are currently suffering from **infertility**.

Percentage of causes of infertility



(1998, WHO)

## Previous studies

*Lactobacillus reuteri* treatment raises testosterone levels. (2014, *PLoS one*)

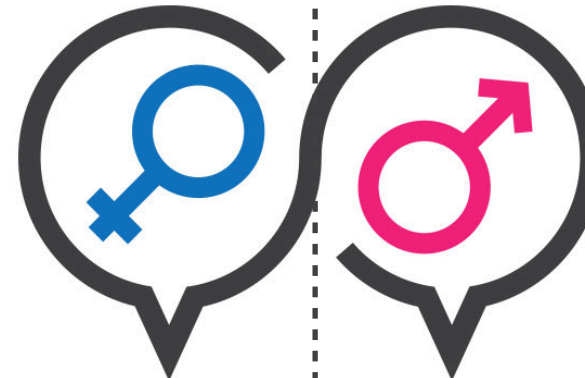
Ingestion of *Lactobacillus rhamnosus CECT8631* and *Bifidobacterium longum CECT7347* increases sperm motility. (2017, *Beneficial microbes*)

Prebiotics containing *Lactobacillus paracasei* cells are a safe treatment to improve ejaculatory volume and sperm quality and quantity in iOAT patients. (2017, *Andrology*)

Contamination to GF mice improved reproductive efficiency. (1998, *Exp Anim.*)

Administration of probiotics that settle in the vaginal canal is important for maintaining normal genitourinary health and preventing or treating infections. (2013, *Arch Gynecol Obstet*)

Intake of **Partially Hydrolyzed Guar Gum** increases the ratio of *Bifidobacterium* of infertility patients and may be involved in infertility treatment. (2020, *J Clin Biochem Nutr*)



Male

Female

Relationships between reproduction and gut microbiota is still unclear.

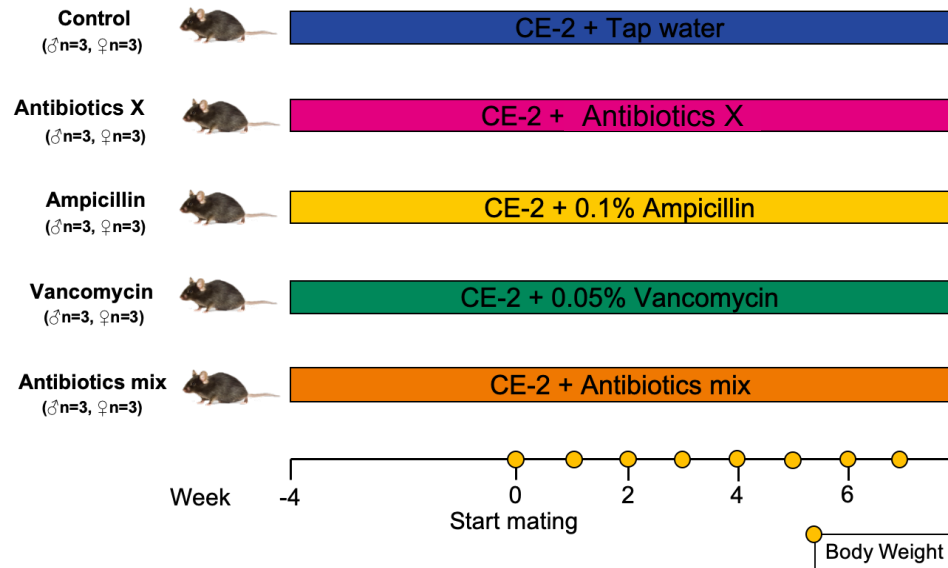


Clarify the effect of gut microbiota on reproductive function.

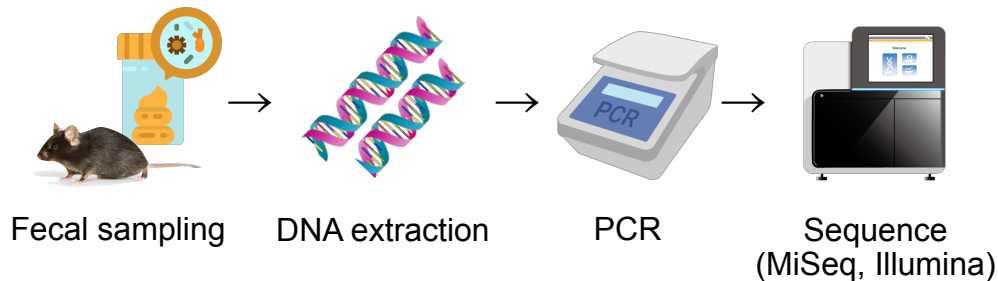
# Antibiotic treatment delayed the birth-delivery interval

## Reproductive efficiency evaluation test

@Tsuruoka CNV; free intake of CE-2 (n=3 pairs)

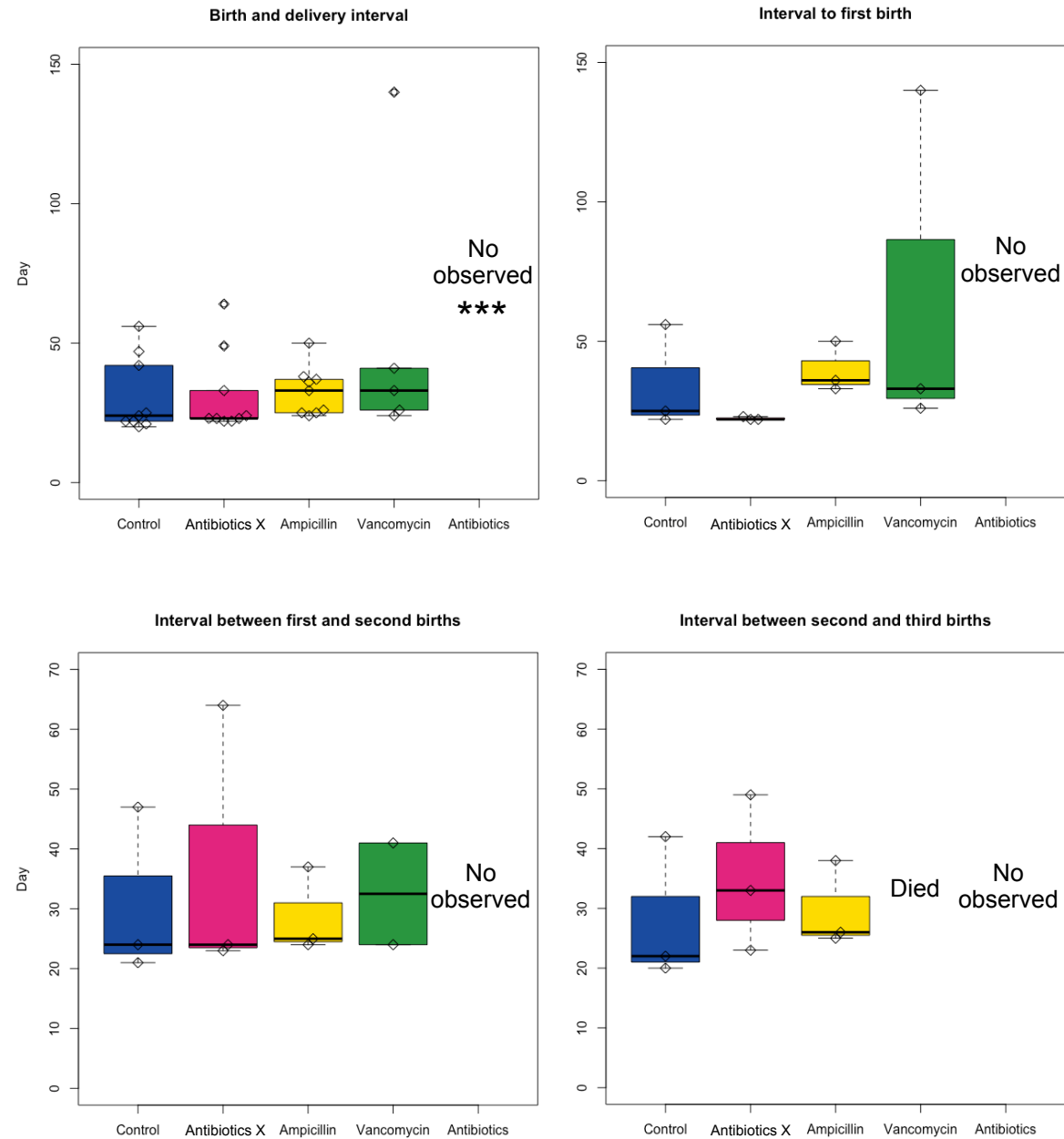


## 16S rRNA gene analysis



➔ Searched for gut bacterial candidates associated with reproductive efficiency.

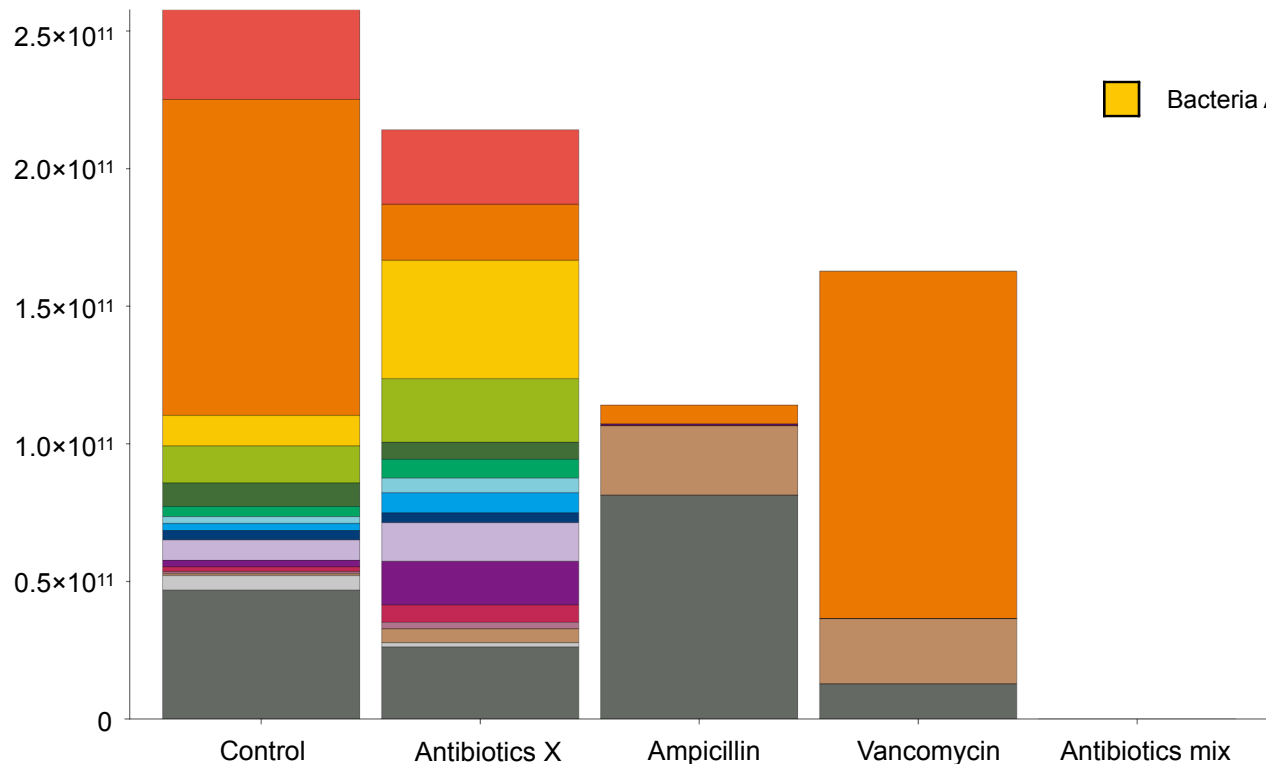
## Birth and delivery intervals



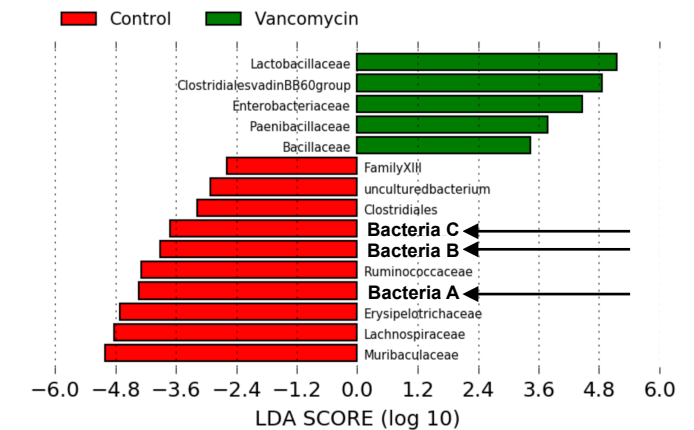
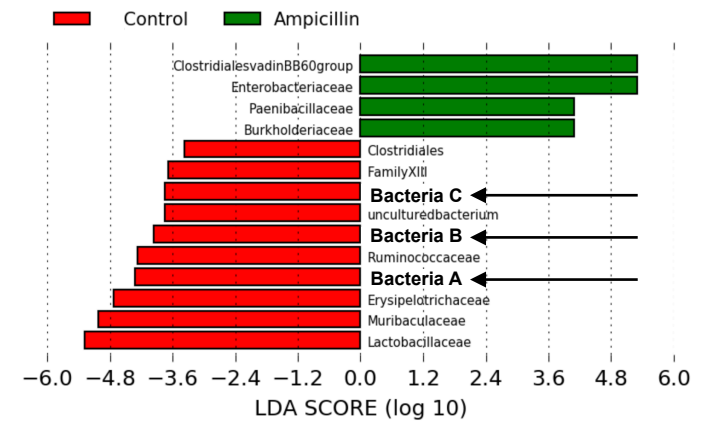
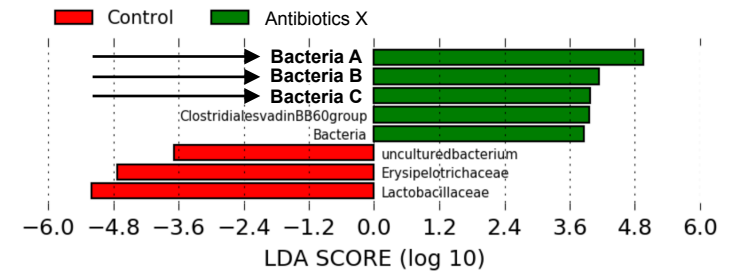
Dunnett's test (\*\*\*)  $P < 0.001$

# Administration of antibiotics X significantly increased bacteria A

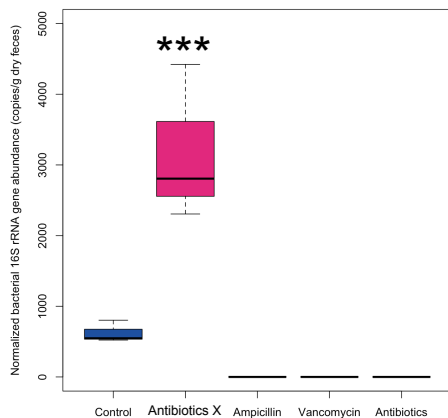
Bacterial abundance of gut microbiota of females (4 weeks after mating)



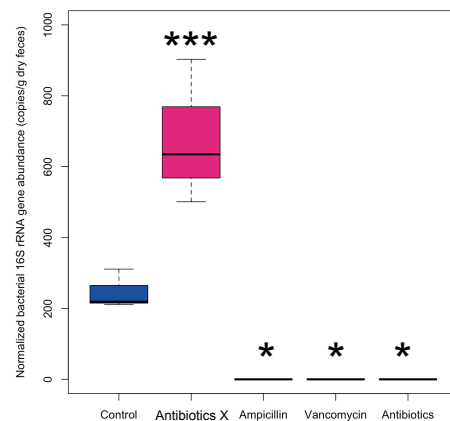
Comprehensive analysis by LEfSe



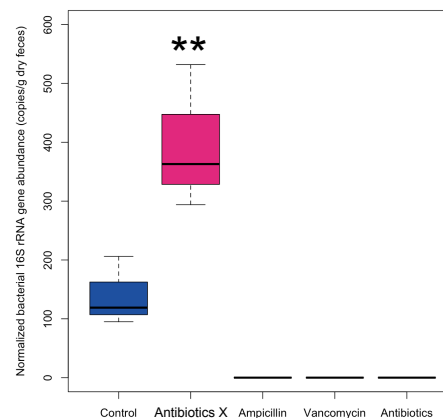
Bacteria A



Bacteria B



Bacteria C

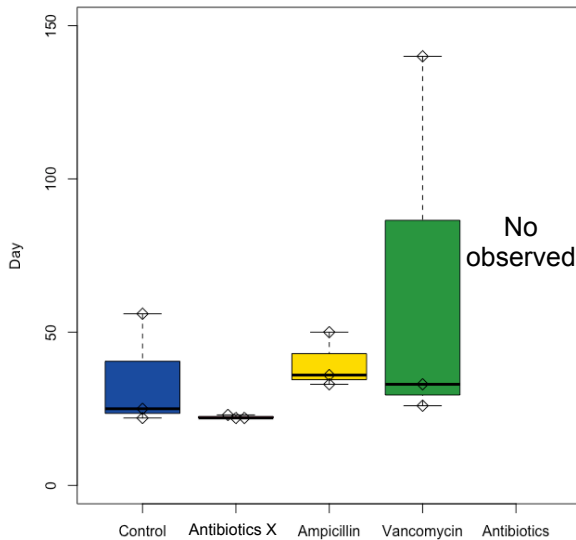


Dunnett's test (\*\* $P < 0.01$ , \*\*\* $P < 0.005$ )

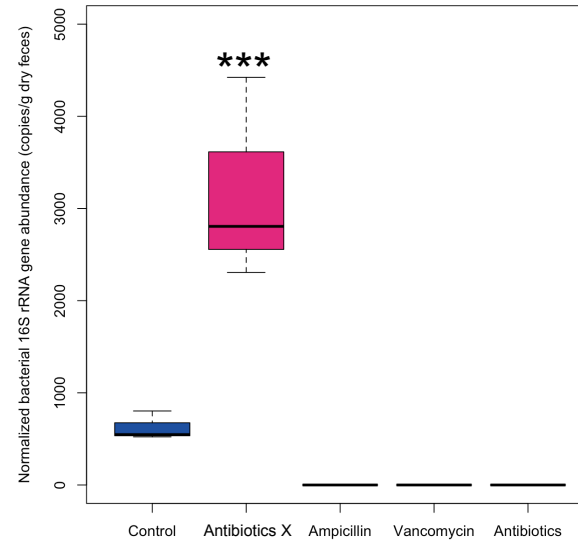
# Bacteria A may promote pregnancy in mice

Dunnett's test ( $***P < 0.001$ )

Interval to first birth



Bacteria A



## Suggestion baed on the results

- ✓ Antibiotics treatment delayed the birth-delivery interval.
  - Dysbiosis of gut microbiota leads infertility in mice.
  - Pregnancy may be accelerated by administration of antibiotics X.
- ✓ Administration of antibiotics X significantly increased bacteria A, B and C.
  - The amount of these bacteria may be related to the reproductive function.



**Track more detailed effects of gut microbiota on reproductive function.**

## Future plans

### Biomarker analysis



- ✓ Gut microbiota analysis
- ✓ Metabolome analysis



- ✓ Measurement of sex hormone



- ✓ Gene expression analysis

### Aged mice antibiotics X treatment experiment

**Control**  
(♂n=5, ♀n=5)



CE-2 + Tap water

**Antibiotics X**  
(♂n=5, ♀n=5)



CE-2 + Antibiotics X

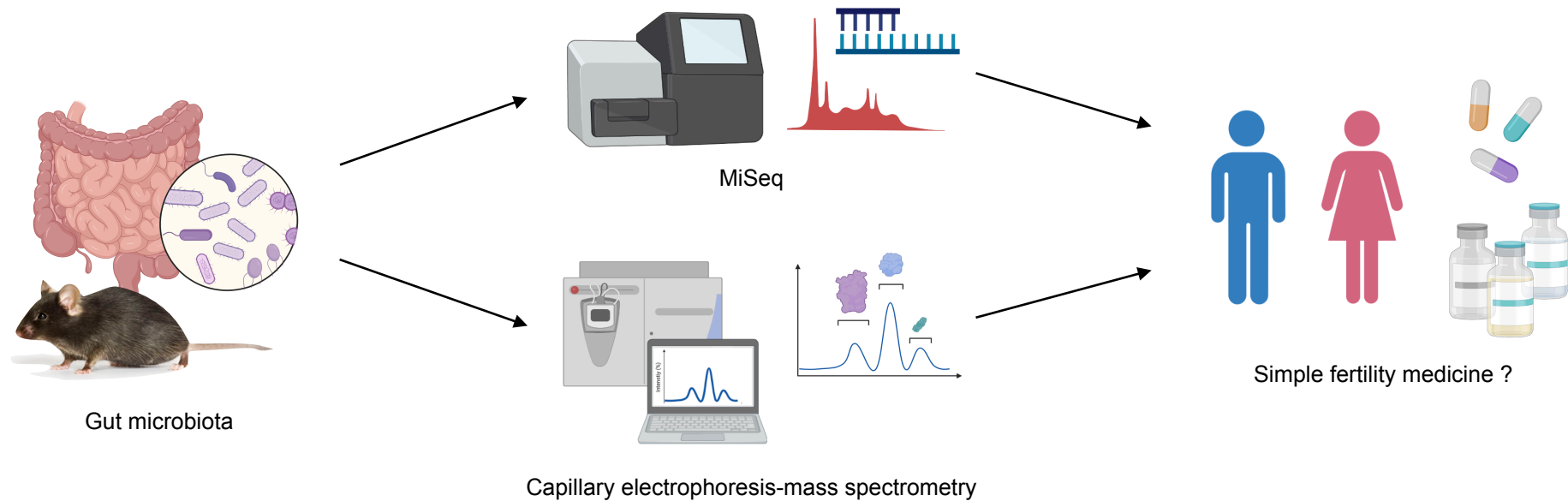
Antibiotics treatment

Week

-3 -2 -1 0 1 2

Start mating

# Expected outcome



# Acknowledgement

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