

Polish Academy of Science-Academia Sinica research
forum in ecology and evolution 2022

**Biodiversity and molecular mechanisms
involved in sex steroid-mediated microbe-
host interactions**



(江殷儒副研究員/代理副主任)

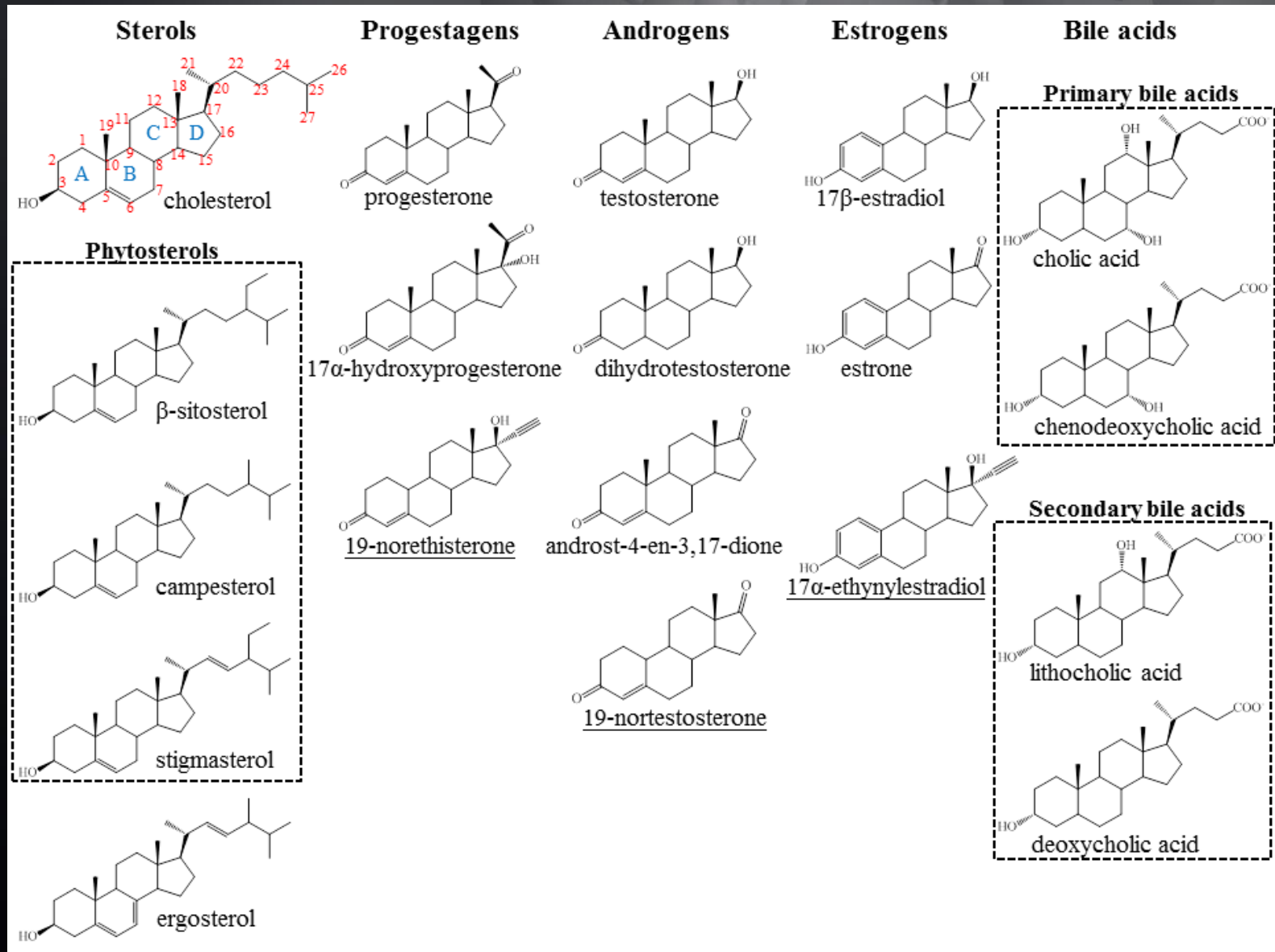
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March 16, 2022

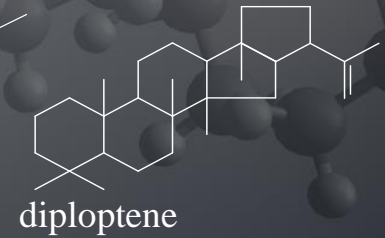
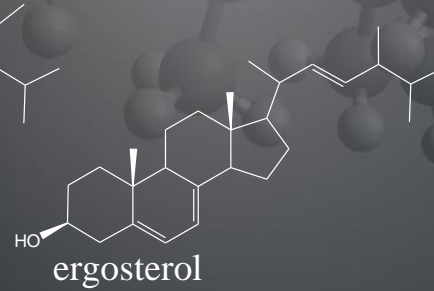
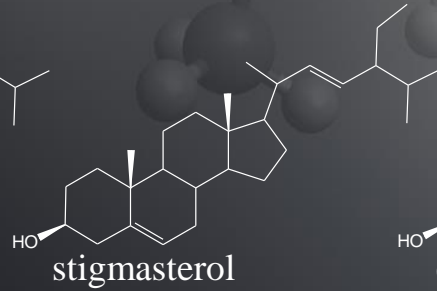
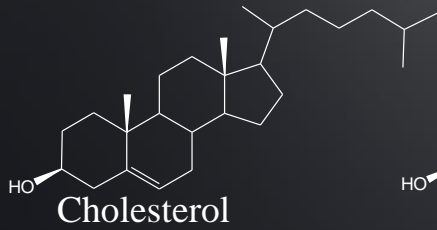
More than 1000 steroid structures have been found in nature



Steroids are exclusively produced by eukaryotes

O₂-dependent oxidosqualene cyclase (OSC)

O₂-independent
squalene cyclase (SC)



Cholesterol

Phytosterols

Ergosterol

Hopanoids



Adverse effects of steroid hormones on aquatic ecosystems

The development and reproduction of individuals

The sex ratio of populations

The animal community structure

Journal of Applied Ecology 2014, **51**, 582–591

doi: 10.1111/1365-2664.12237

An environmental oestrogen disrupts fish population dynamics through direct and transgenerational effects on survival and fecundity

Adam R. Schwindt^{1*}, Dana L. Winkelman², Kristen Keteles³, Mark Murphy³ and Alan M. Vajda⁴

Suburbanization, estrogen contamination, and sex ratio in wild amphibian populations

Max R. Lambert^{a,1}, Geoffrey S. J. Giller^a, Larry B. Barber^b, Kevin C. Fitzgerald^{b,2}, and David K. Skelly^a

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Edited by James H. Brown, University of New Mexico, Albuquerque, NM, and approved July 28, 2015 (received for review January 22, 2015)

Research on endocrine disruption in frog populations, such as shifts in sex ratios and feminization of males, has predominantly focused on agricultural pesticides. Recent evidence suggests that We compare ponds in landscapes ranging from highly suburban backyards to undeveloped forests (Fig. S1), and on sex ratios of green frogs (*R. clamitans*), which inhabit

PHILOSOPHICAL
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Direct and indirect responses of a freshwater food web to a potent synthetic oestrogen

Karen A. Kidd¹, Michael J. Paterson^{2,3}, Michael D. Rennie^{2,3}, Cheryl L. Podemski², Dave L. Findlay², Paul J. Blanchfield² and Karsten Liber⁴

Birth and death of steroids:

eukaryotic steroidogenesis and microbial degradation



Vertebrate gut

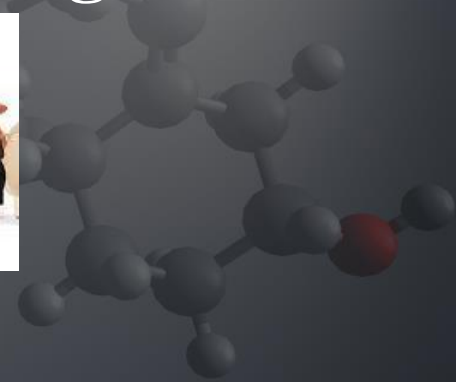
Bacteroidetes
Firmicutes
Actinobacteria
Proteobacteria



Estuarine sediments



WWTP



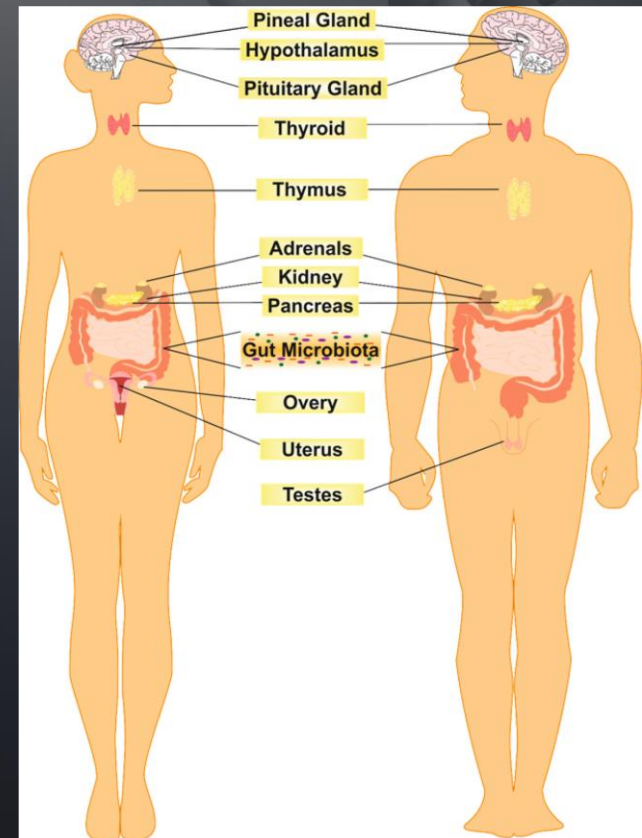
Steroid-mediated gut microbe-host interactions

MINIREVIEW

Minireview: Gut Microbiota: The Neglected Endocrine Organ

Gerard Clarke, Roman M. Stilling, Paul J. Kennedy, Catherine Stanton, John F. Cryan, and Timothy G. Dinan

Alimentary Pharmabiotic Centre (G.C., R.M.S., P.J.K., C.S., J.F.C., T.G.D.) and Departments of Psychiatry (G.C., C.S., T.G.D.) and Anatomy and Neuroscience (J.F.C.), University College Cork, Cork, Ireland; and Teagasc (C.S.), Moorepark, Fermoy, Cork, Ireland



We aim to answer the following questions:

- ♣ How many steroid catabolic pathways are still undiscovered?
- ♣ How do bacteria metabolize steroids in oxygen-limited or oxygen-fluctuating environments?
- ♣ What kinds of microorganisms are responsible for steroid metabolism in anaerobic ecosystems?
- ♣ Do sex steroids play a role in microbe-host interactions?

A pioneering and leading group in anaerobic steroid metabolism



microbial biotechnology

Open Access

Minireview

Microbial degradation of steroid sex hormones: implications for environmental and ecological studies

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Po-Hsiang Wang,^{1,†} Pei-Hsun Wu² and
Chang-Ping Yu²

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Introduction

Thus far, more than 1000 different steroids are found to naturally occur (Haubrick and Assmann, 2006; Hannich *et al.*, 2011; Valliova *et al.*, 2016; Zubair *et al.*, 2016; Staley *et al.*, 2017; Stonik and Stonik, 2018), including commonly distributed sterols (e.g. cholesterol, phytosterols and ergosterol), steroid hormones (e.g. 17 β -oestradiol, progesterone and testosterone) and bile acids (e.g. cholic acid) (see Fig. 1 for the common steroid structures). A remarkable characteristic of steroids is their extremely low aqueous solubility; that is, cholesterol has a maximum solubility of 4.7 μ M (= 1.8 mg l⁻¹) in aqueous solutions (Haberland and Reynolds, 1973). The aqueous solubility of steroid hormones is also extremely low; for example, in neutral aqueous solutions, the solubility of natural oestrogens [e.g. oestrone (E1) and 17 β -oestradiol (E2)] is approximately 1.5 mg l⁻¹ at room temperature (Shareef *et al.*, 2006), whereas the experimental aqueous solubility of testosterone can reach 23 mg l⁻¹ at 25°C (Barry and El Eini, 1976). Similarly, the synthetic 17 α -ethynyoestradiol (EE2) also has a low solubility in water (4.8 mg l⁻¹ at 20°C) (Aris *et al.*, 2014).

In animals, cholesterol is the precursor of all classes of steroid hormones, namely glucocorticoids, mineralocorticoids and sex hormones (androgens, oestrogens and progestogens). The biosynthesis of steroid hormones involves the elimination of the cholesterol side chain and hydroxylation of the steroid nucleus (Ghayee and Auchus, 2007). All these hydroxylation reactions require NADPH and molecular oxygen; thus, steroid biosynthesis only occurs in the aerobic biosphere. Among sex steroids, progestogens (such as progesterone) function in preparing the lining of the uterus for implantation of an ovum and are also essential for maintaining pregnancy. The biotransformation of progesterone into androgens includes a hydroxylation at C-17 and the subsequent cleavage of the side chain. Androgens regulate the development and maintenance of male characteristics in vertebrates, and the major androgens naturally produced in males are testosterone, dihydrotestosterone and androstenedione (also named androst-4-en-3,17-dione, AD) (see Fig. 1 for structures) (O'Connor *et al.*, 2011). Oestrogens are responsible for

Summary

Steroid hormones modulate development, reproduction and communication in eukaryotes. The widespread occurrence and persistence of steroid hormones have attracted public attention due to their endocrine-disrupting effects on both wildlife and human beings. Bacteria are responsible for mineralizing steroids from the biosphere. Aerobic degradation of steroid hormones relies on O₂ as a co-substrate of oxygenases to activate and to cleave the recalcitrant steroidal core ring. To date, two oxygen-dependent degradation pathways – the 9,10-*seco* pathway for androgens and the 4,5-*seco* pathways for oestrogens – have been characterized. Under anaerobic conditions, denitrifying bacteria adopt the 2,3-*seco* pathway to degrade different steroid structures. Recent meta-omics revealed that microorganisms able to degrade steroids are highly diverse and ubiquitous in different ecosystems. This review also summarizes culture-independent approaches using the characteristic metabolites and catabolic genes to monitor steroid biodegradation in various ecosystems.

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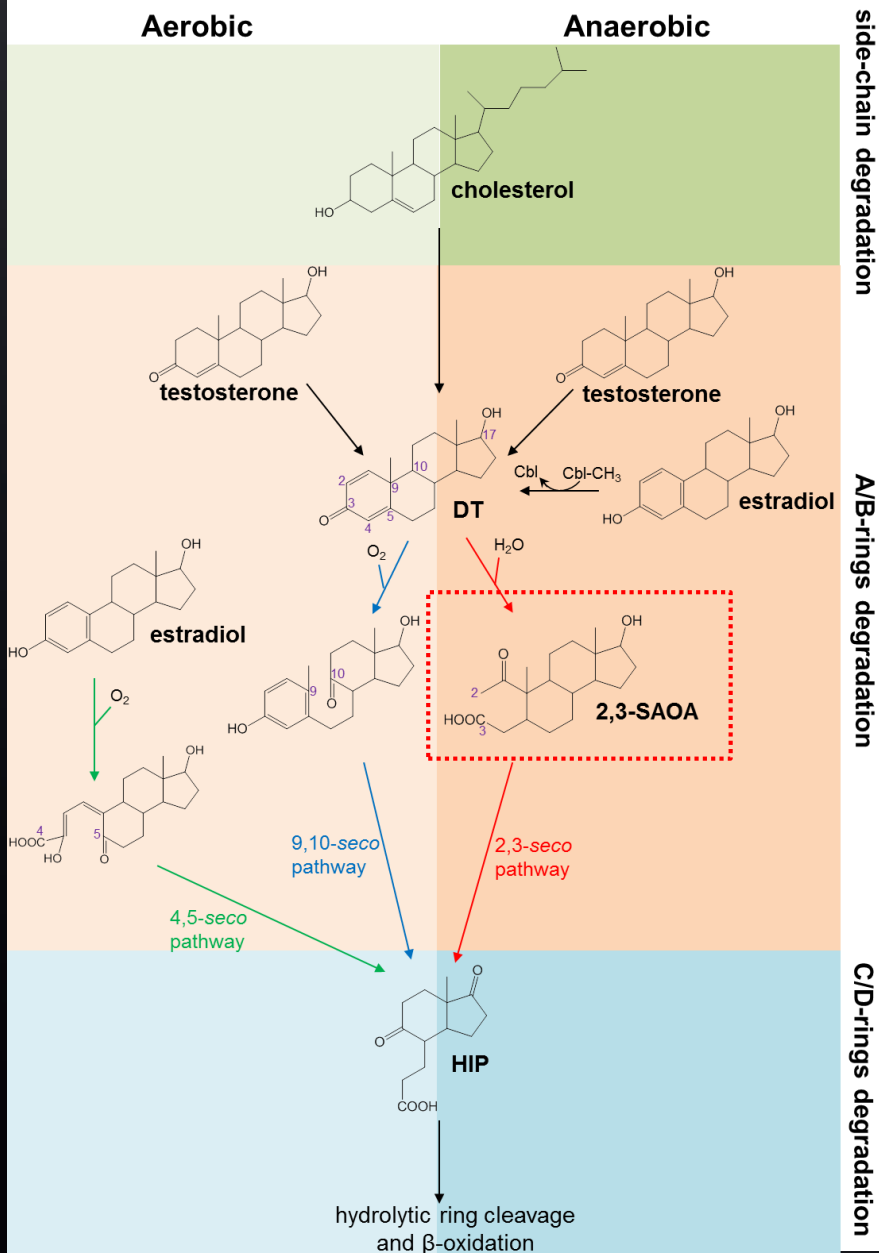
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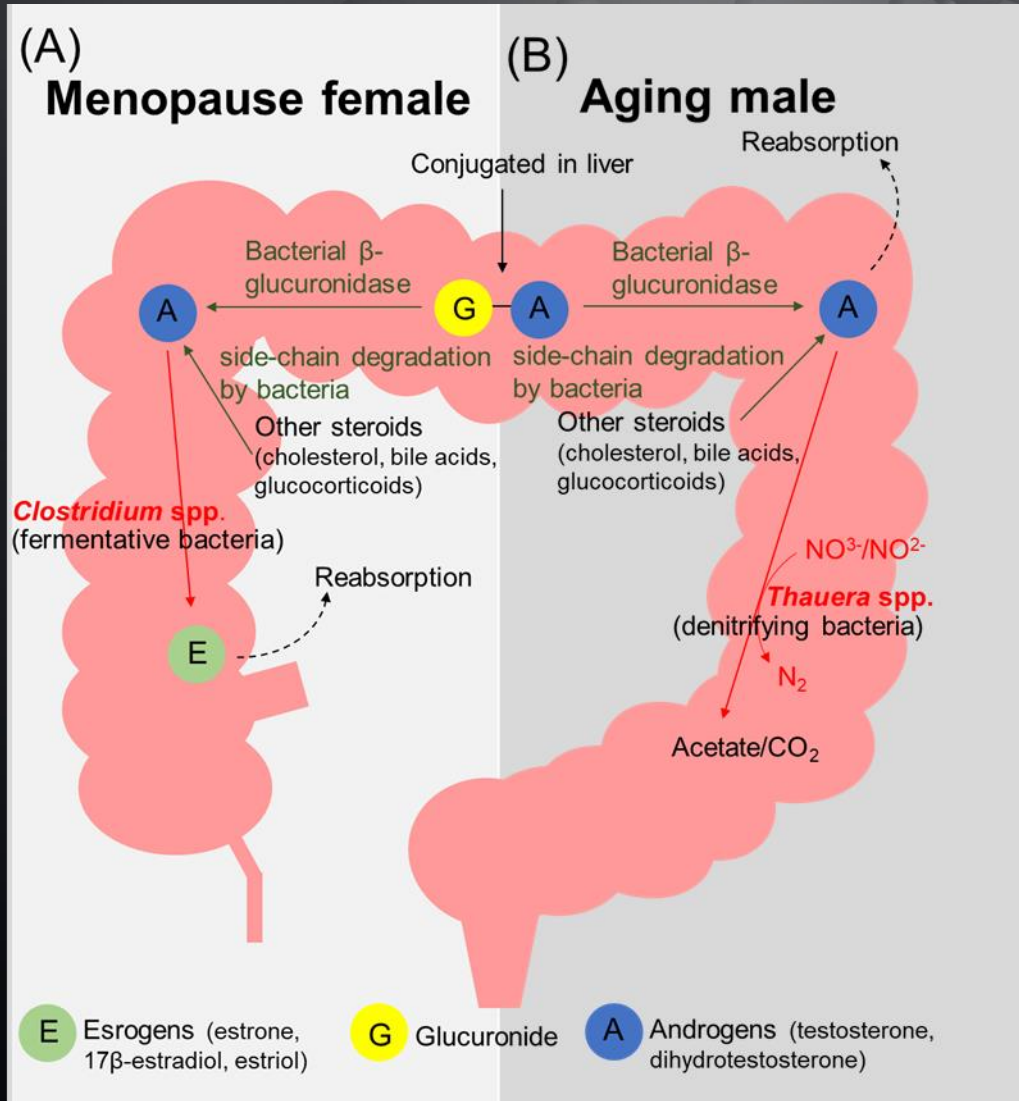


side-chain degradation

A/B-rings degradation

C/D-rings degradation

Potential applications of the steroid-metabolizing anaerobes in prostatic cancer and polycystic ovary syndrome (PCOS; 卵巢多囊症)



Gene clusters of strain GDN1 for androgen catabolism

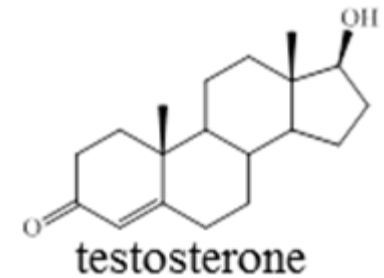
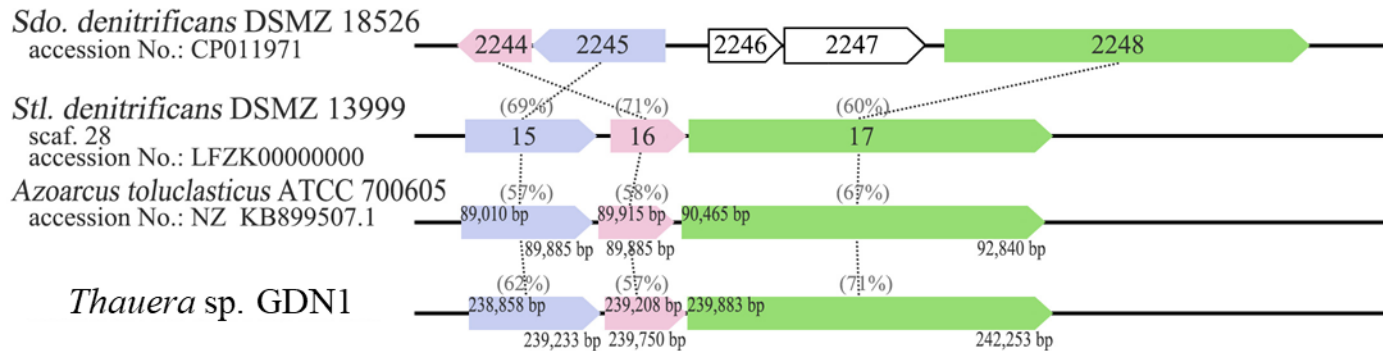
(A)

● β -oxidation-related genes ● meta-cleavage genes ● others

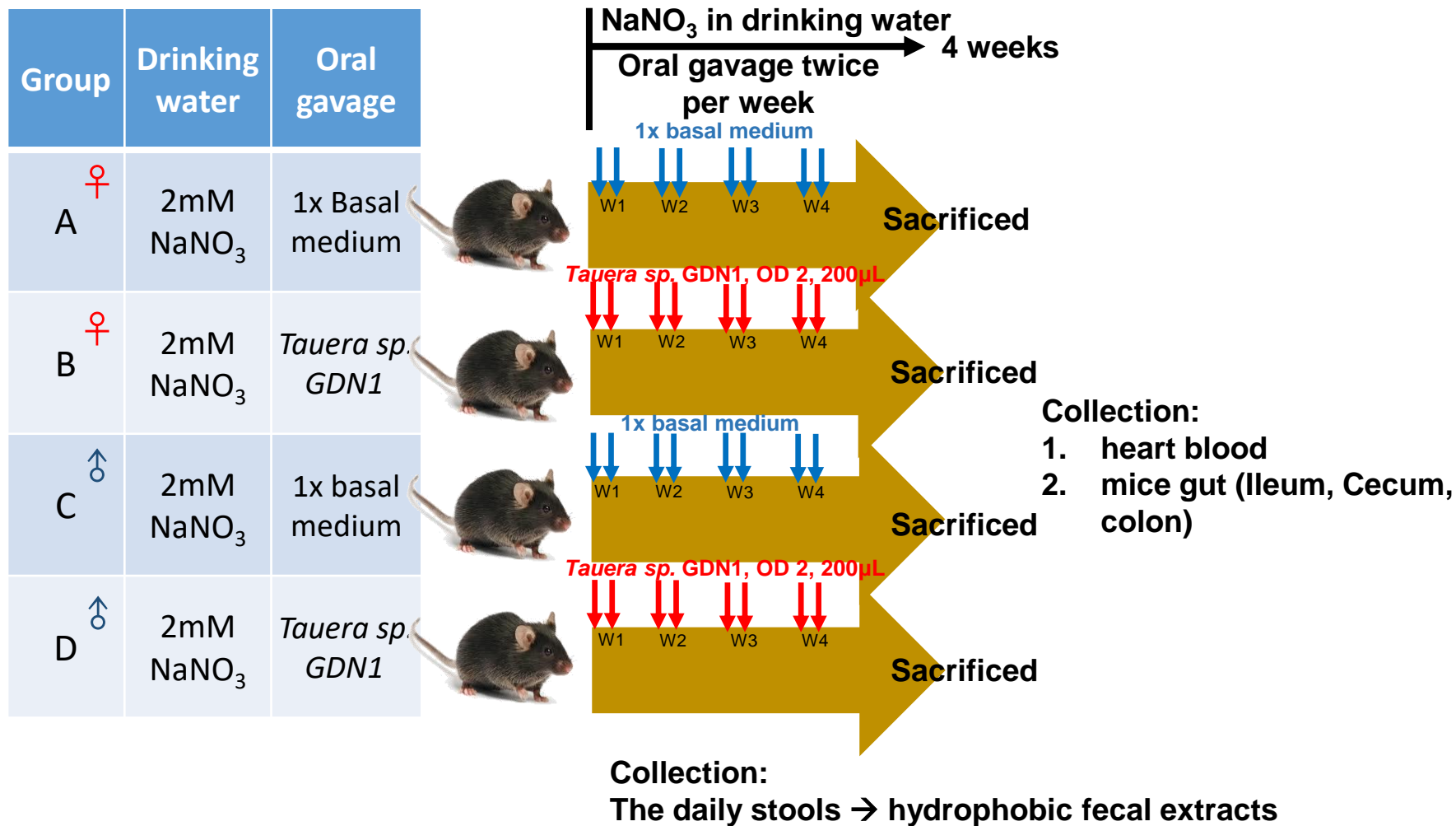


(B)

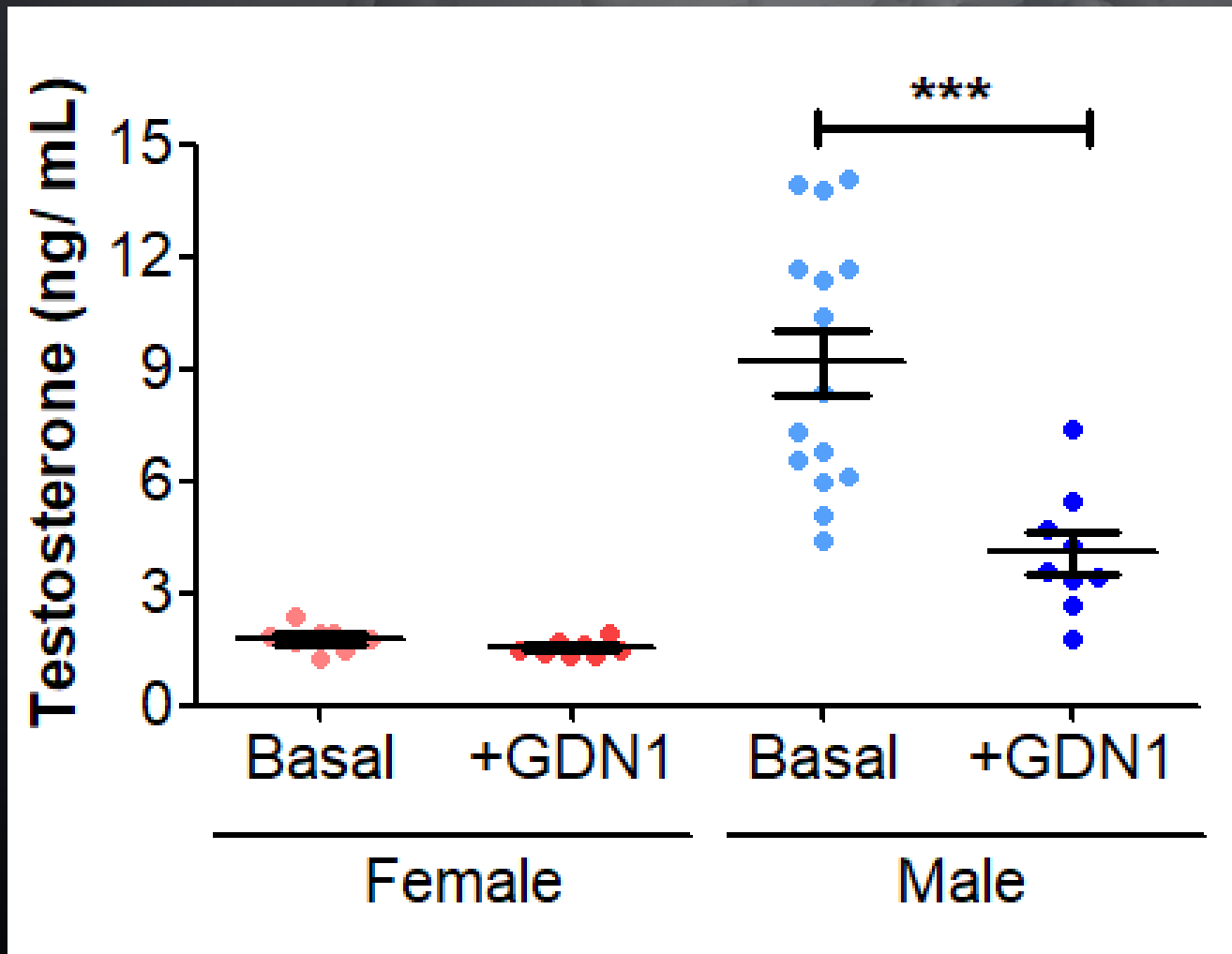
● [2Fe-2S]-binding subunit ● FAD-binding subunit ● Mo-binding subunit



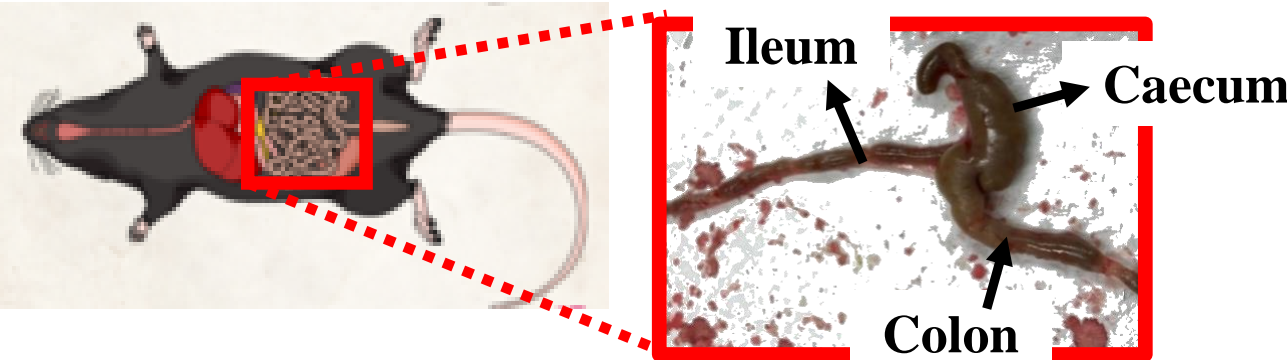
Administration of *Thauera* sp. strain GDN1 into mice gut through oral gavage



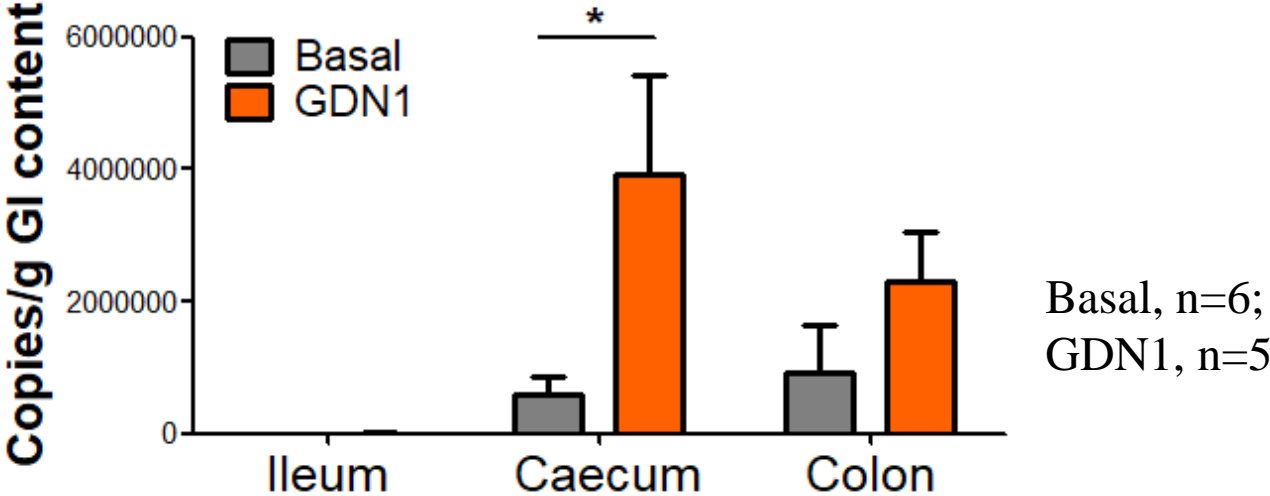
***Thauera* sp. strain GDN1 administration reduced the serum testosterone level in male mice**



Strain GDN1 mainly colonized in mice caecum, in which enterohepatic circulation occurs

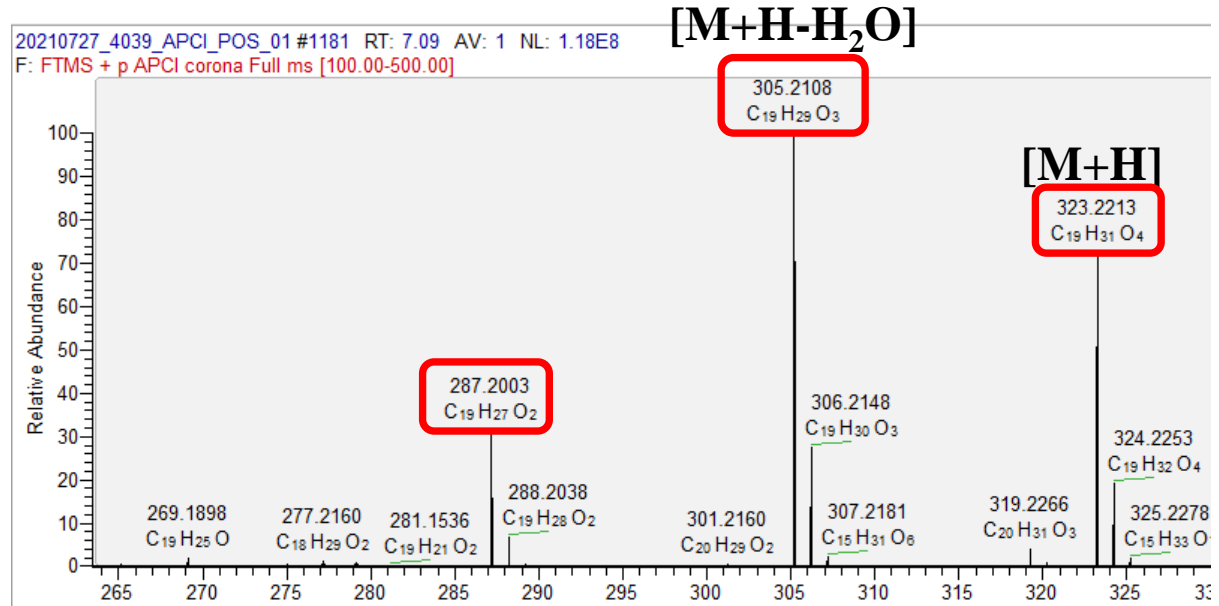


qPCR with GDN1-16S primer

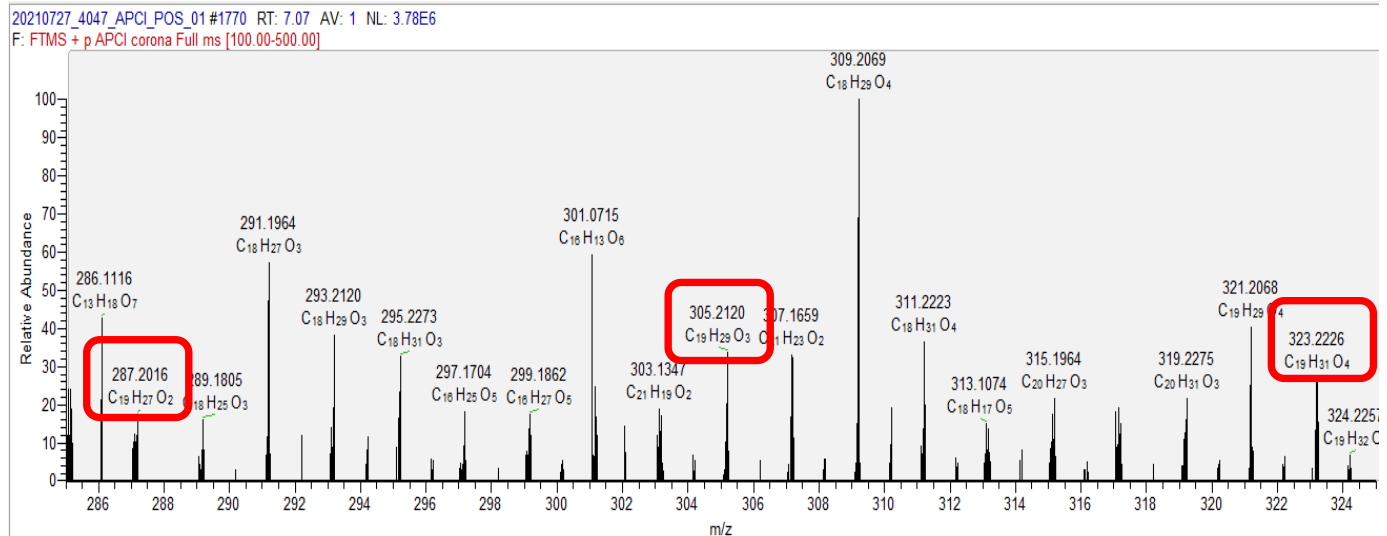


Characteristic androgen metabolites were identified in mouse fecal extracts

**Authentic
standard
(2,3-SAOA)**



**Fecal
extract of
GDN1-fed
mice**



**Thank you for your
attention & questions**

