



Dec 19, 2017

H29年度 アグリ技術シーズセミナー
@金沢商工会議所会館

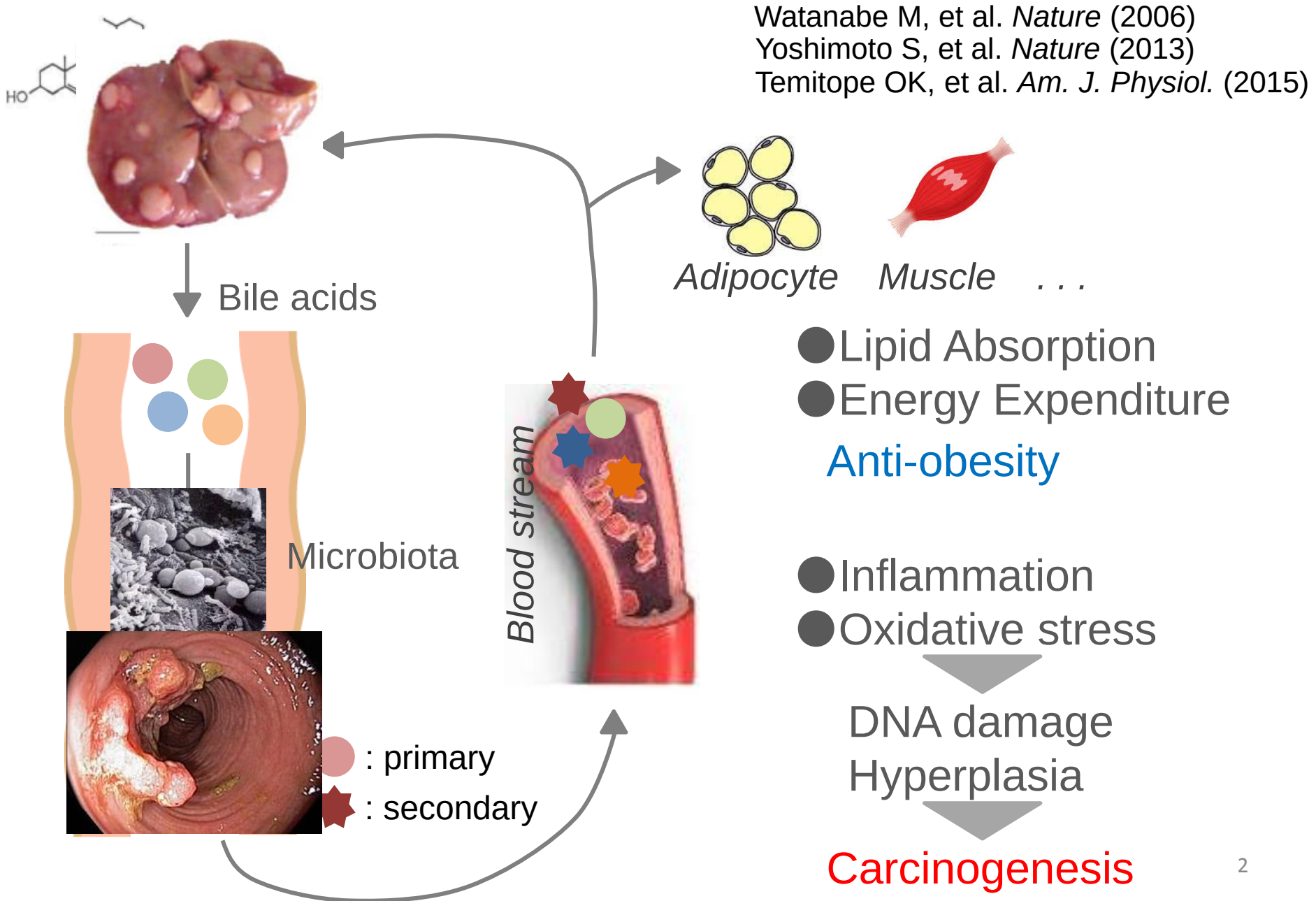


腸内環境を作用起点とした食品の 機能性について

石川県立大学 生物資源環境学部

東村 泰希

腸内細菌と胆汁酸代謝

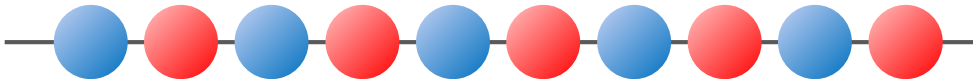


寒天由来のオリゴ糖(アガロオリゴ糖)

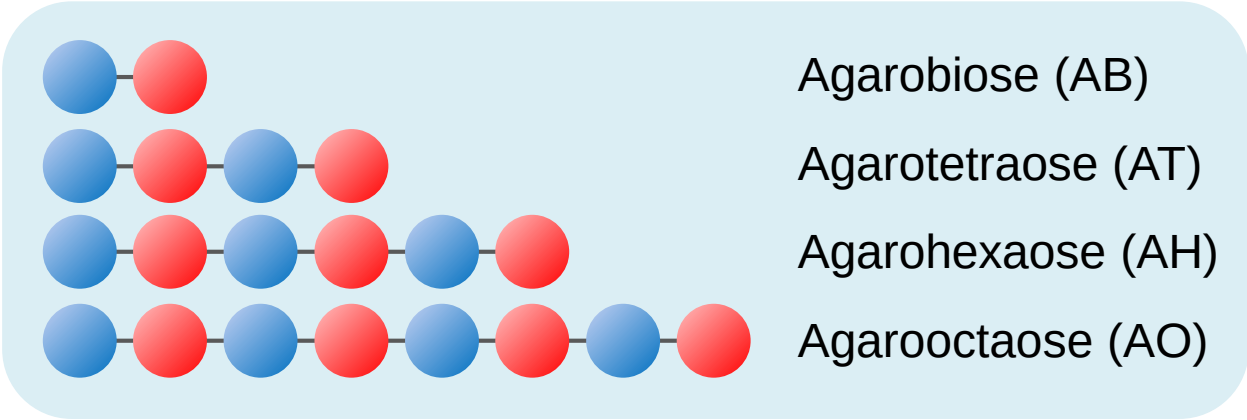


Agarose

- Galactose
- 3,6-Anhydro-galactose



↓ Hydrolysis of α -1,3 bond



Agaro-oligosaccharides
(AGO)

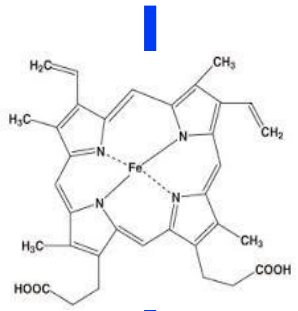


寒天由来のオリゴ糖(アガロオリゴ糖)

Enoki T, et al. *Biosci. Biotechnol. Biochem.* (2010)

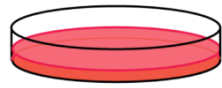
✓ *In vitro*において, HO-1の発現亢進を介して抗炎症作用を発揮する.

Heme Oxygenase-1 (HO-1)



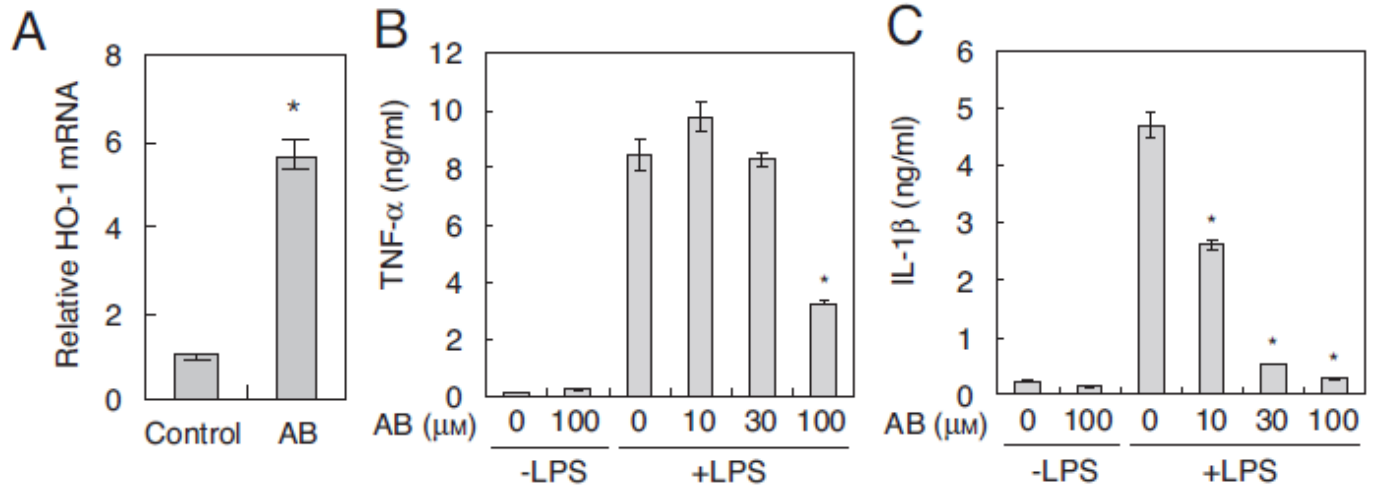
- Biliverdin
- Carbon monoxide
- Ferric ion

HO-1:抗酸化酵素
抗炎症作用



- Raw264.7
- Human monocyte

AGOs (AB)
LPS
→ anti-inflammatory effect

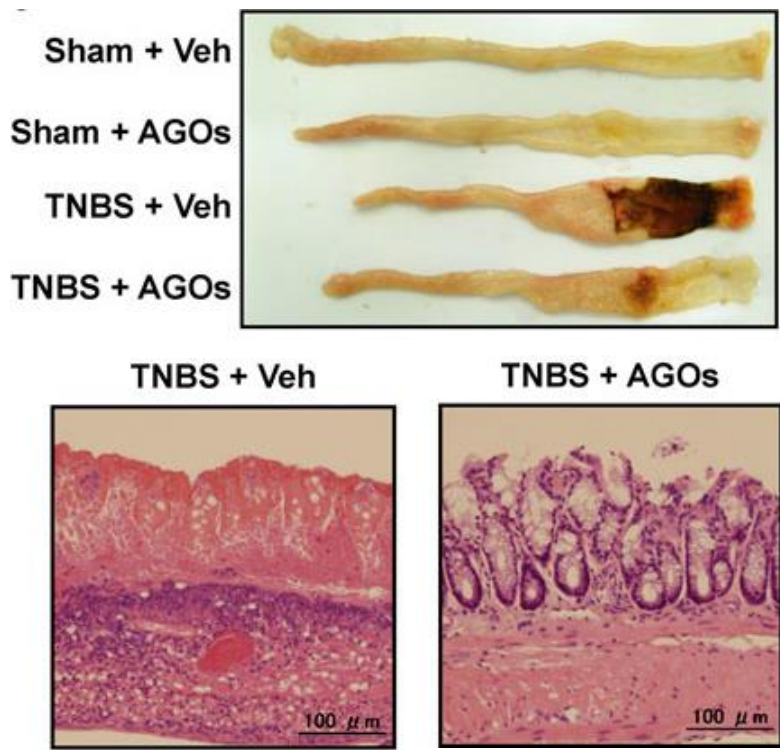
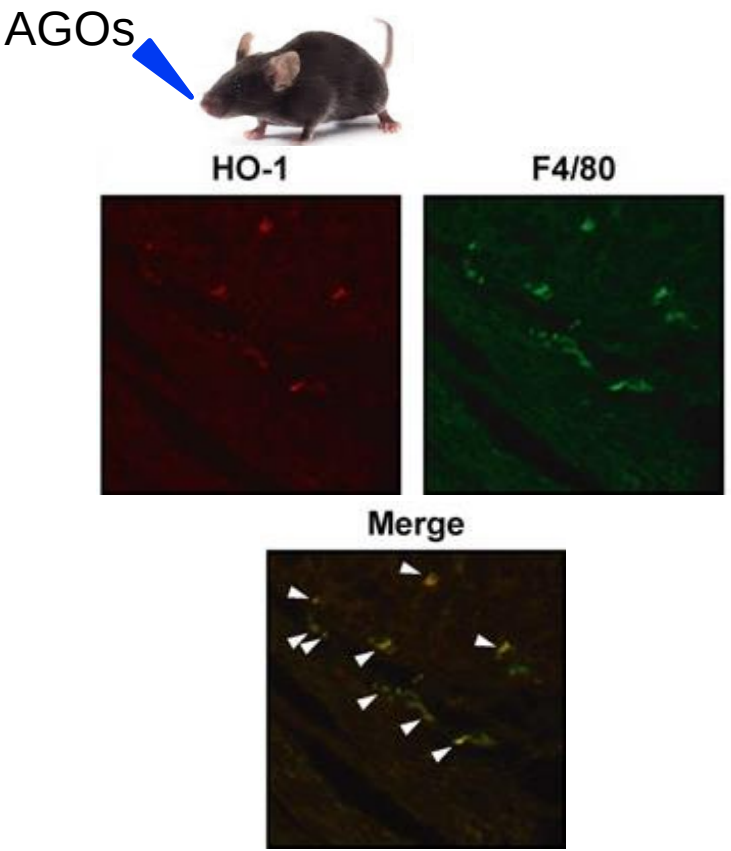


寒天由来のオリゴ糖(アガロオリゴ糖)

Higashimura Y, et al. *J. Gastroenterol.* (2013)

Naito Y, Higashimura Y, et al. *Arch. Biochem. Biophys.* (2014)

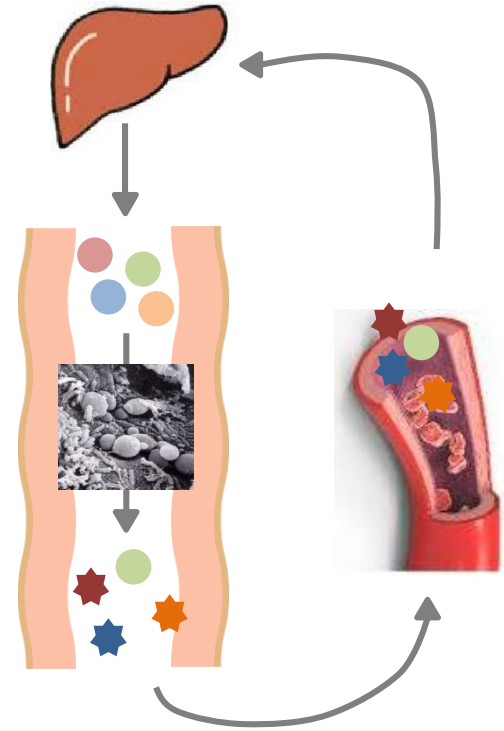
✓ AGOsの経口投与は、腸管粘膜内のマクロファージにおけるHO-1の発現亢進を介して、大腸炎の発症を抑制する。



本日の内容

✓大腸がん抑制効果について

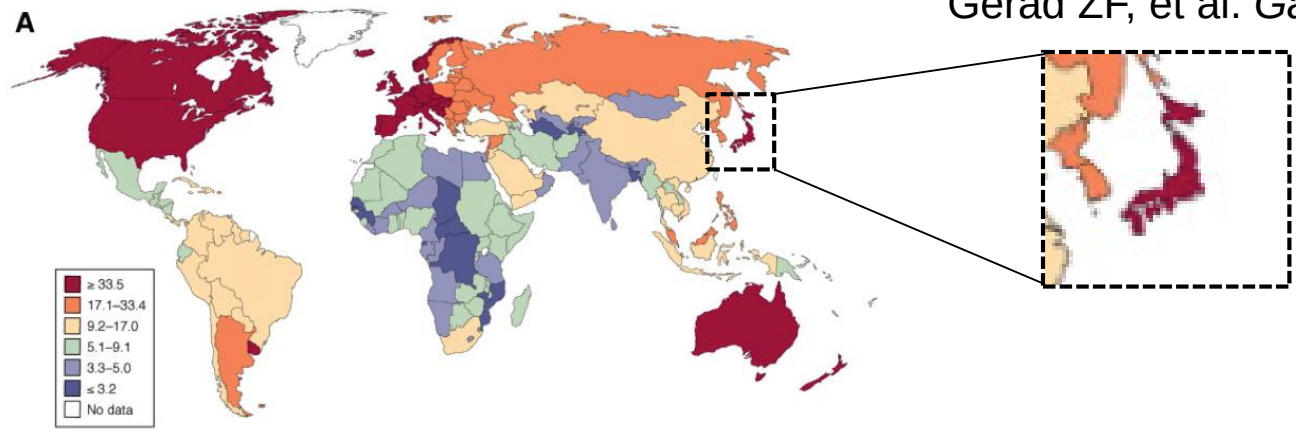
✓抗肥満作用について



大腸がんについて

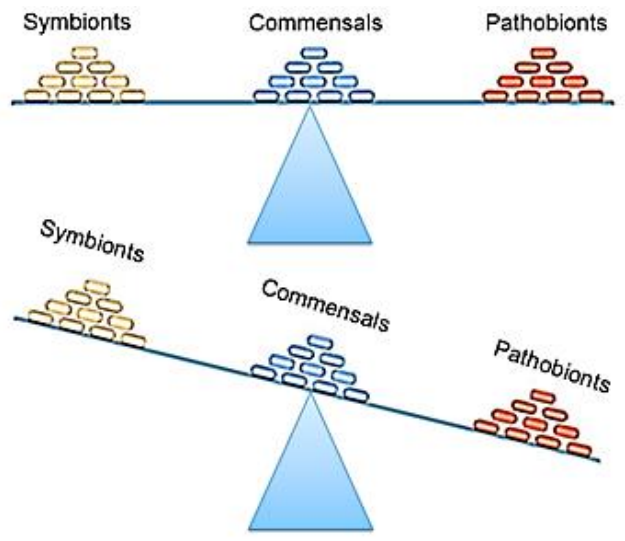
✓日本は世界で最も大腸がん死亡率の高い国である

Gerad ZF, et al. *Gastroenterology* (2010)



✓大腸がんリスクとしての“Gut dysbiosis”

Temitope OK, et al. *Am. J. Physiol.* (2015)

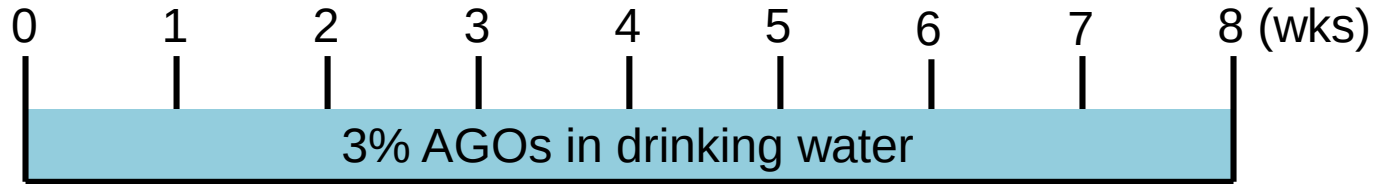


- Host genetics
- Antibiotics
- Hygiene
- Lifestyle (**High-fat diet**)
etc...



AGO

実験方法



Control diet: CE-2, Test diet: HFD32

< Microbiome: T-RFLP >



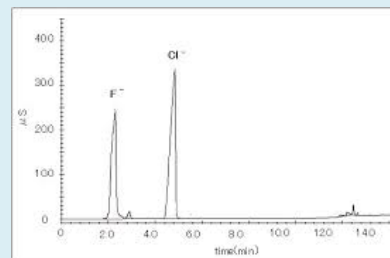
- *Bifidobacterium*
- *Lactobacillales* order
- *Bacteroides*
- *Prevotella*
- *Clostridium* cluster IV
- *Clostridium* subcluster XIVa
- *Clostridium* cluster XI
- *Clostridium* cluster XVIII

×

< SCFA content >

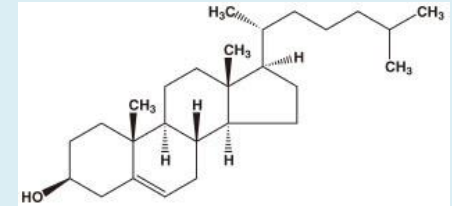


- Succinic acid
- Lactic acid
- Acetic acid
- Propionic acid
- *n*-Butyric acid



×

< Bile acid profile >



Primary

- Cholic acid
- Chenodeoxycholic acid
- Muricholic acid

Secondary

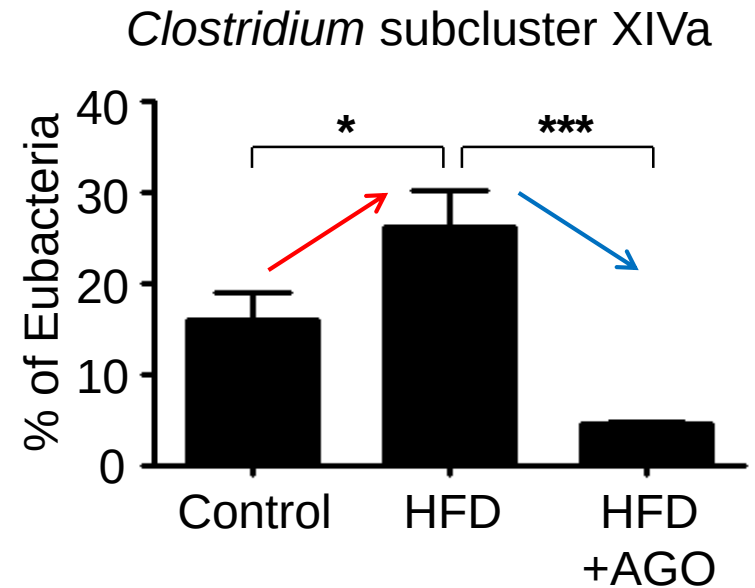
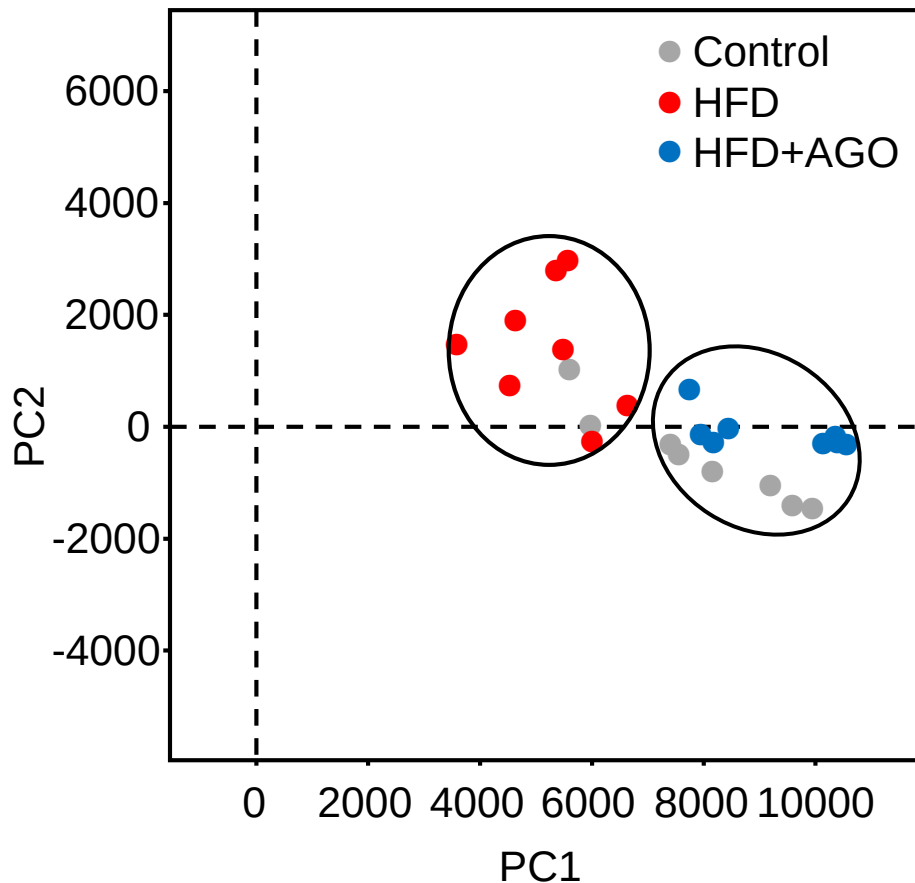
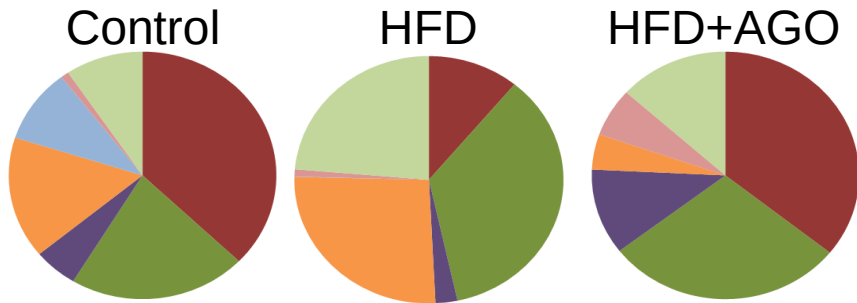
- Deoxycholic acid
- Ursodeoxycholic acid
- Lithocholic acid
- Hyodeoxycholic acid

Free-xxx

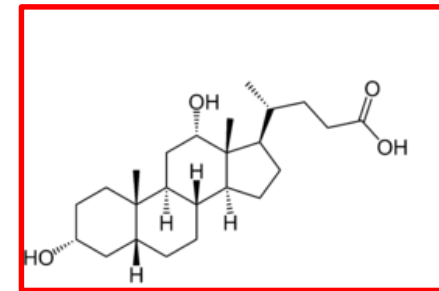
Tauro-xxx

Glyco-xxx

腸内細菌叢に及ぼすAGOの効果



Carcinogenic

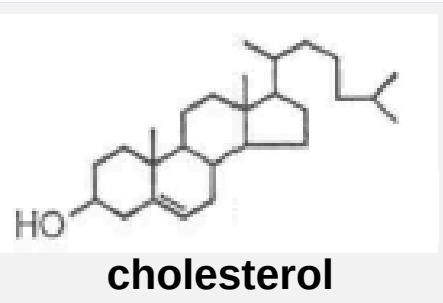


DCA
(deoxycholic acid)

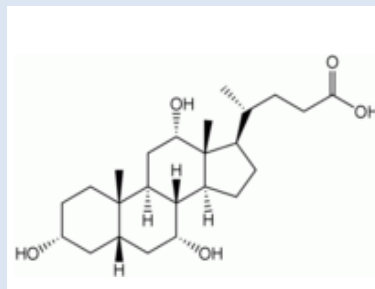
* $p < 0.05$
** $p < 0.01$
*** $p < 0.001$

胆汁酸の代謝について

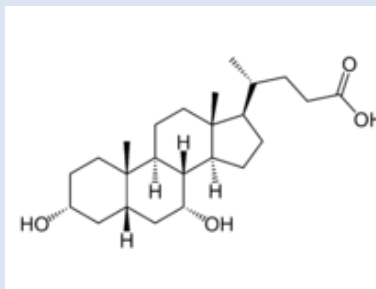
Primary
Secondary



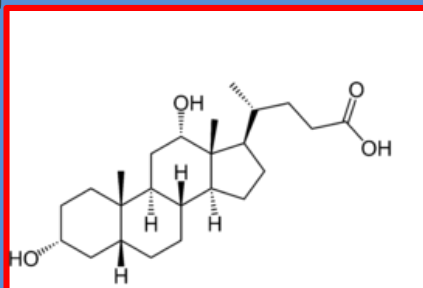
- ✓ Free-
- ✓ Glyco-
- ✓ Tauro-



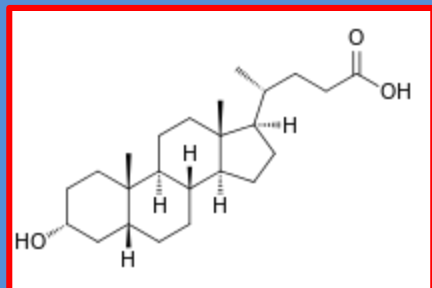
CA
(cholic acid)



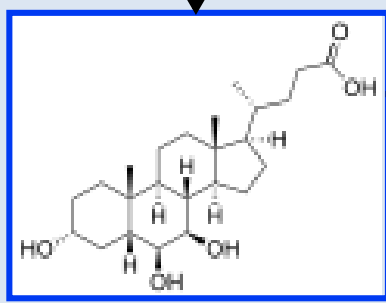
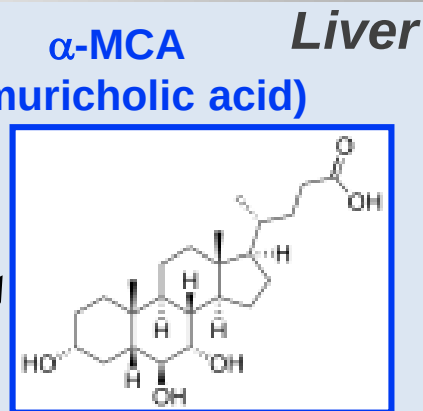
CDCA
(chenodeoxycholic acid)



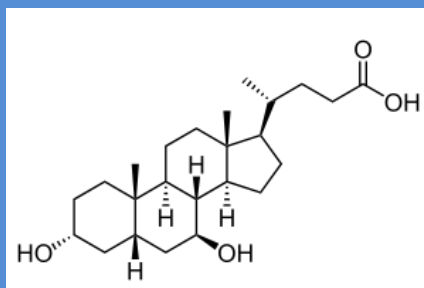
DCA
(deoxycholic acid)



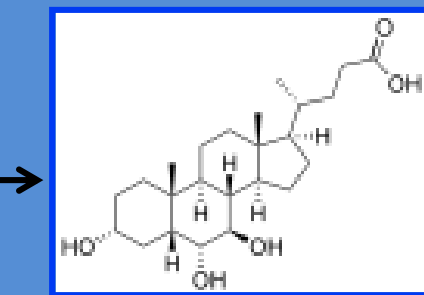
LCA
(lithocholic acid)



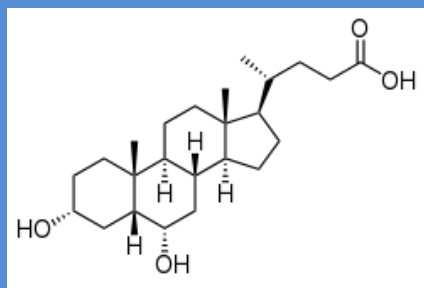
β -MCA



UDCA
(ursodeoxycholic)



ω -MCA

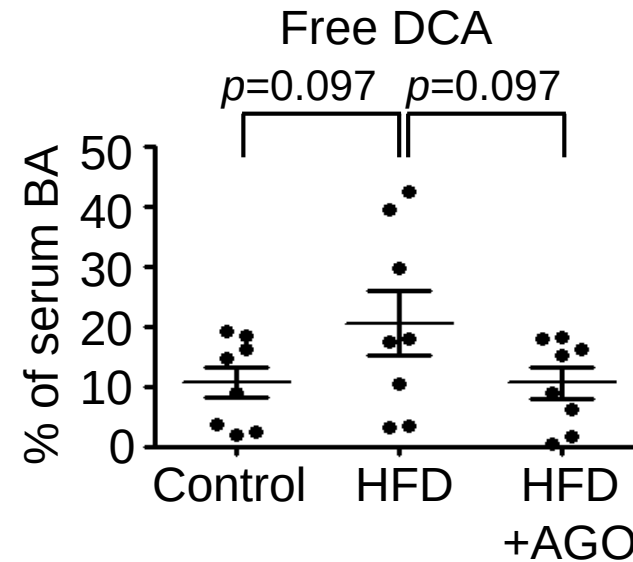
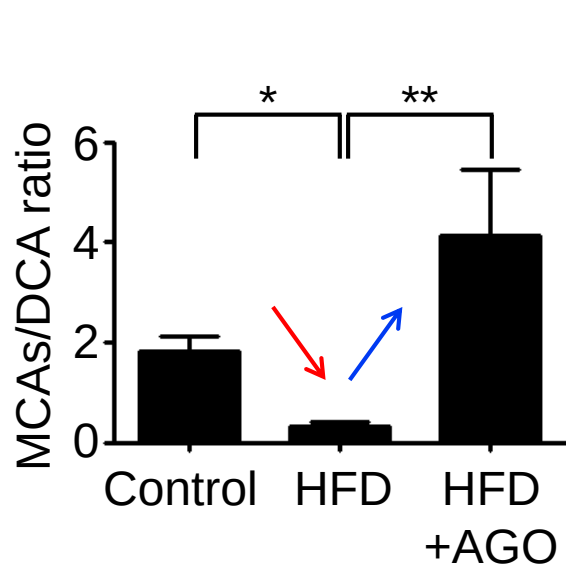


HDCA
(hyodeoxycholic)

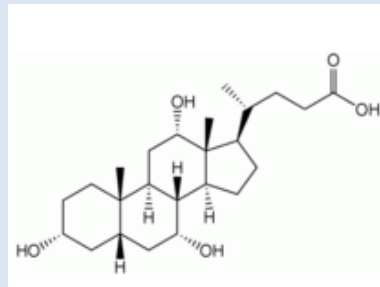
Liver

Intestine

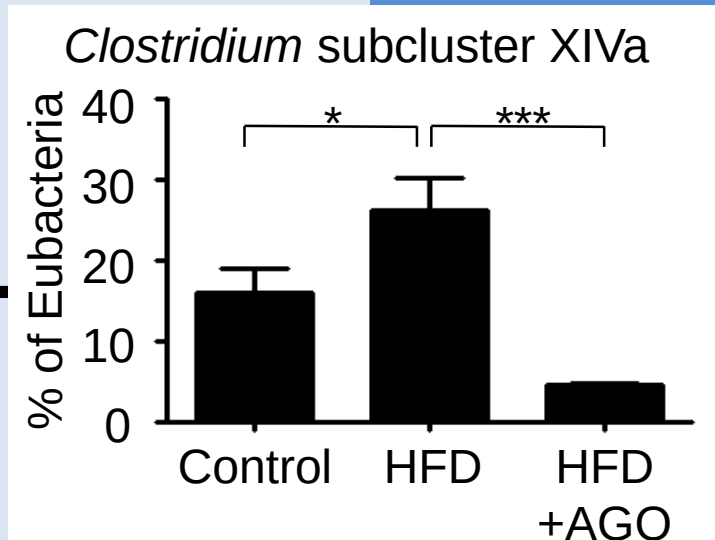
胆汁酸代謝に及ぼすAGOの効果



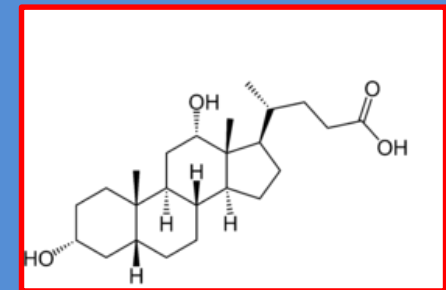
*p<0.05
**p<0.01
***p<0.001



CA
(cholic acid)



Carcinogenic

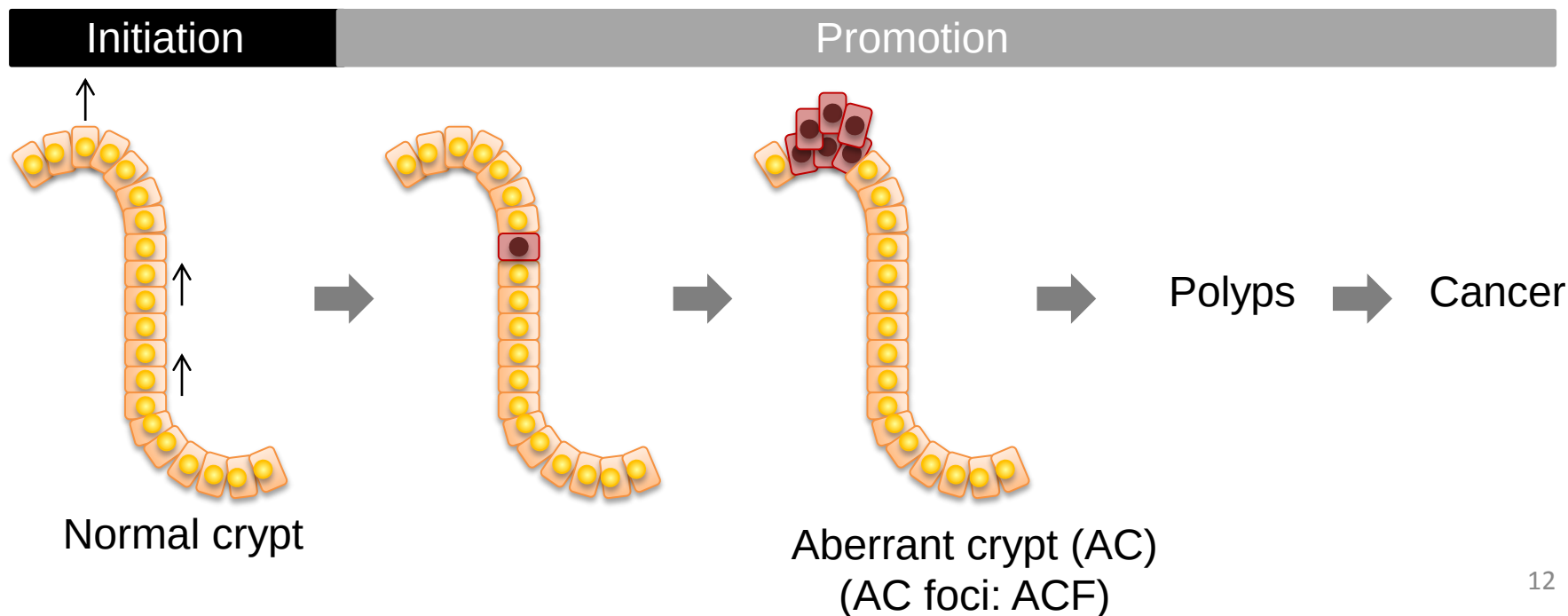
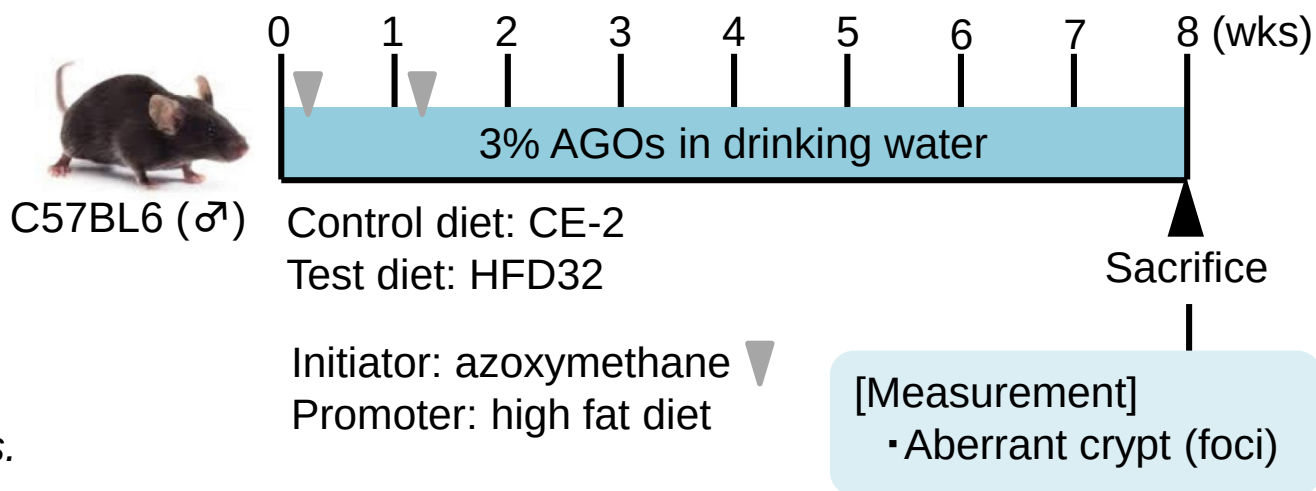


DCA
(deoxycholic acid)

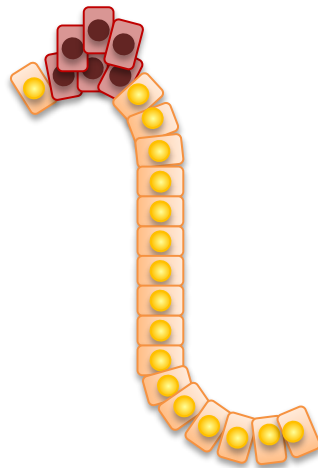
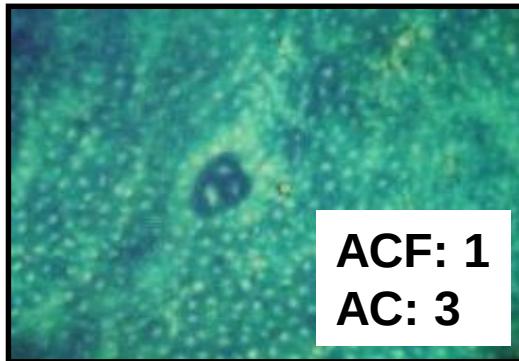
実験方法



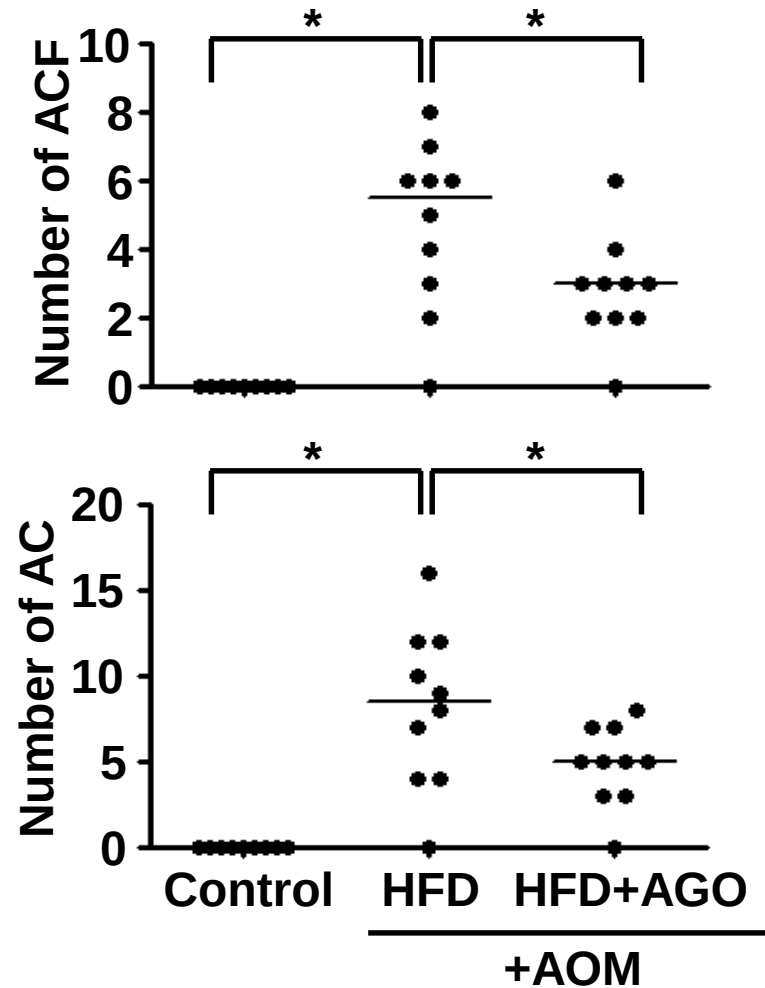
The Company of Biologists.



大腸前がん病変の発生に及ぼすAGOの効果



Aberrant crypt (AC)
(AC foci: ACF)



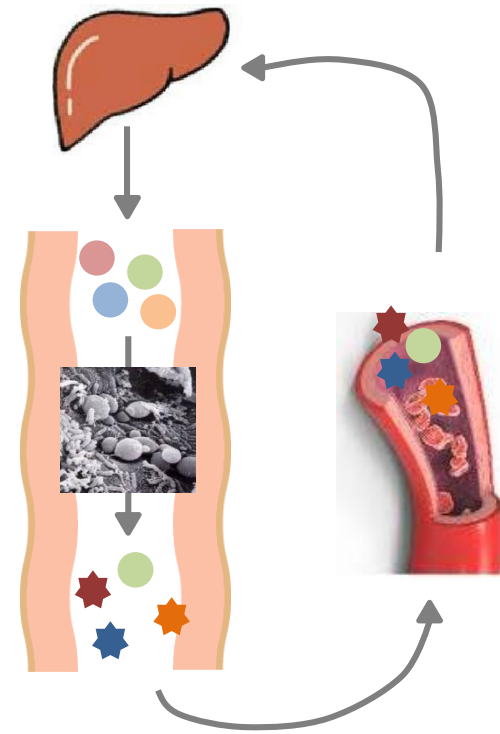
***p<0.05**

本日の内容

✓大腸がん抑制効果について

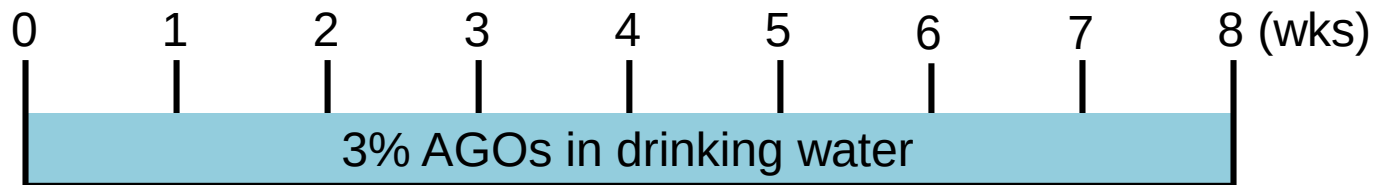
AGOの摂取は、高脂肪食により惹起されるdysbiosisを改善し、大腸前がん病変である異常腺管構造の形成を抑制した。

✓抗肥満作用について

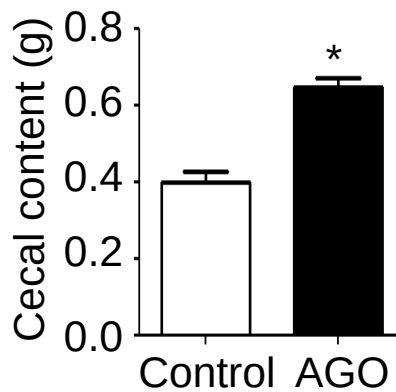
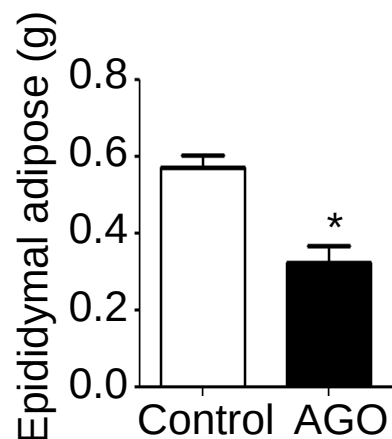


実験方法

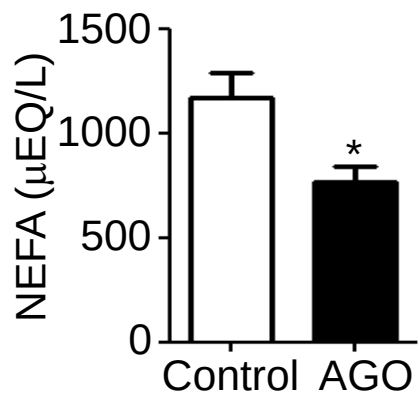
C57BL6 (♂)



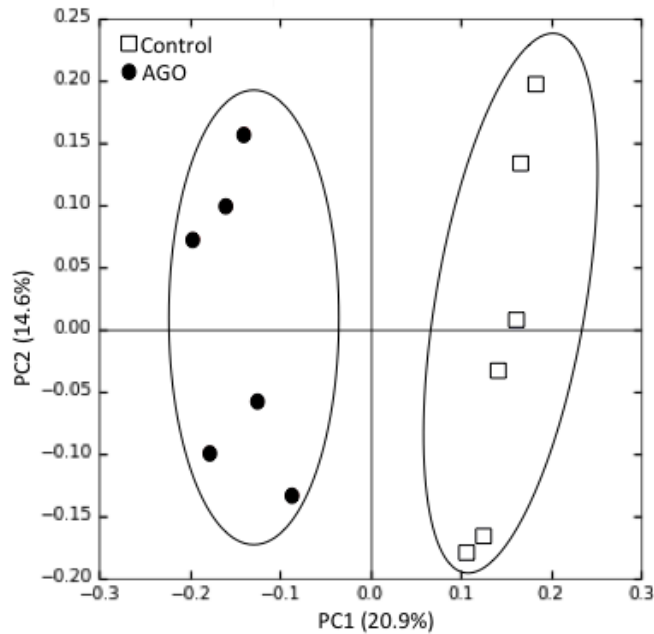
Control diet: CE-2



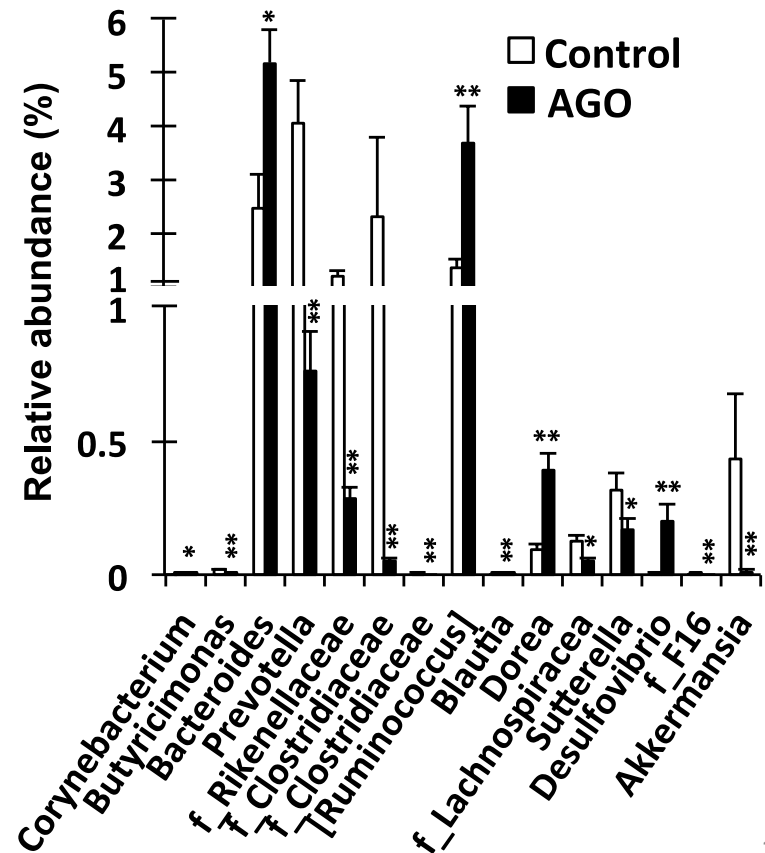
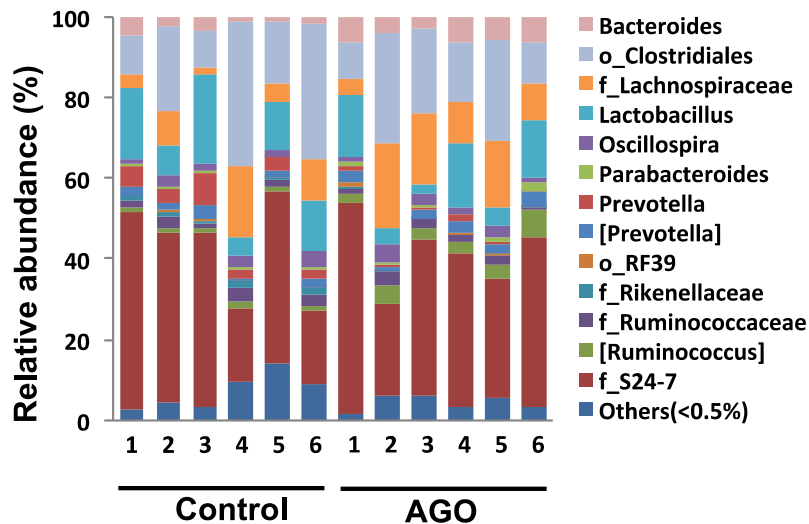
次世代シーケンサーを用いて
腸内細菌叢を解析



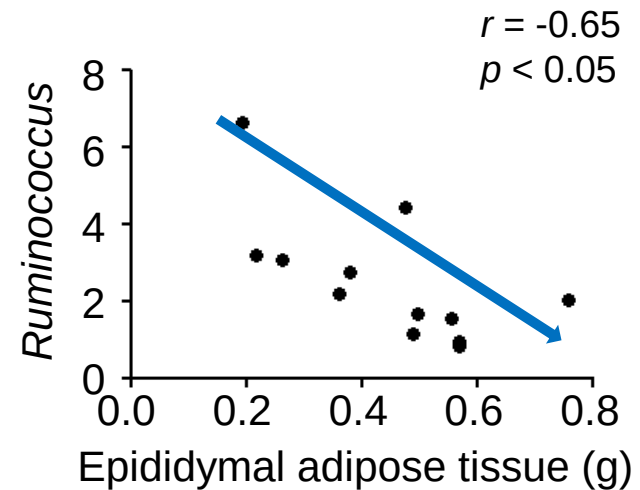
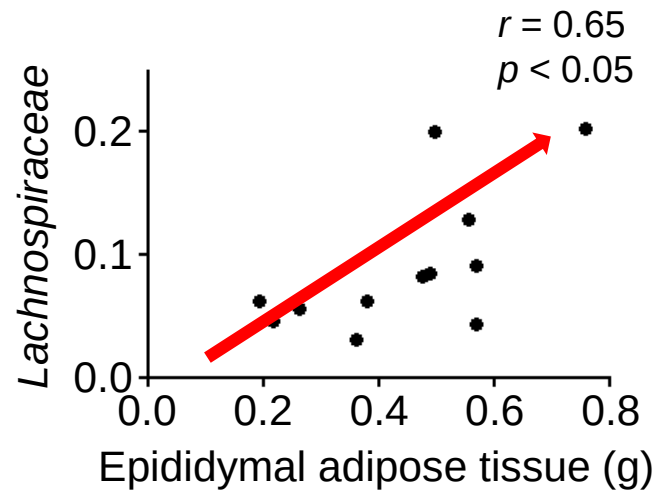
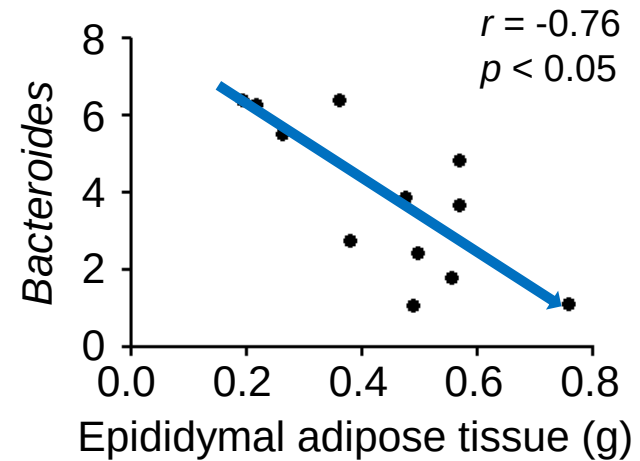
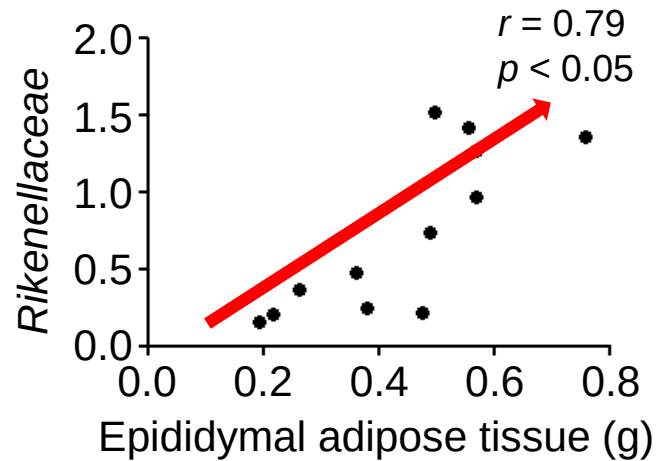
腸内細菌叢に及ぼすAGOの効果



AGO摂取により, 15 taxaの存在比が有意に変動した.



腸内細菌叢と精巣周囲脂肪重量との相関解析



まとめ

Higashimura Y, et al. *Am. J. Physiol.* (2016)

Higashimura Y, et al. *J Nutr Sci Vitaminol.* (2017)



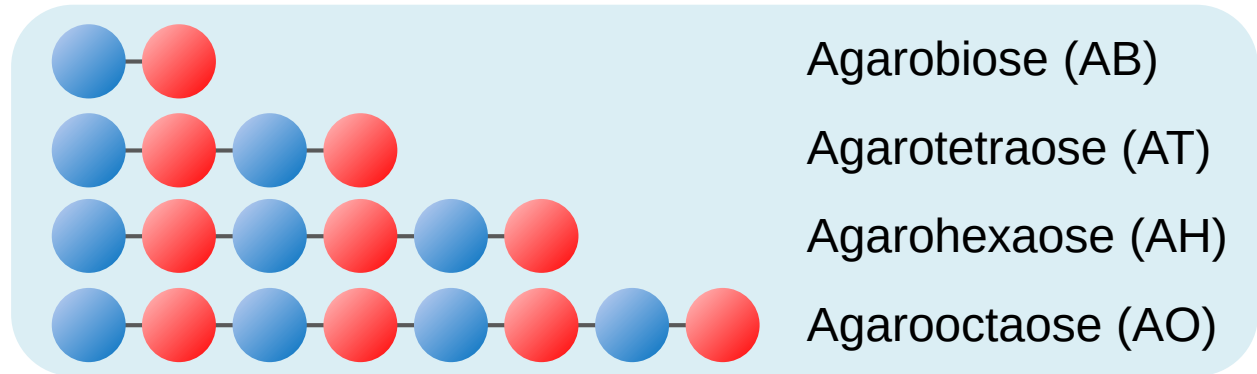
AGO



Dysbiosis



Carcinogenesis
Anti-obesity



- ✓ Microbiome
- ✓ SCFA content
- ✓ Bile acid metabolism