Association between OBESITY and *Firmicutes/Bacteroidetes* ratio in Breast cancer patients

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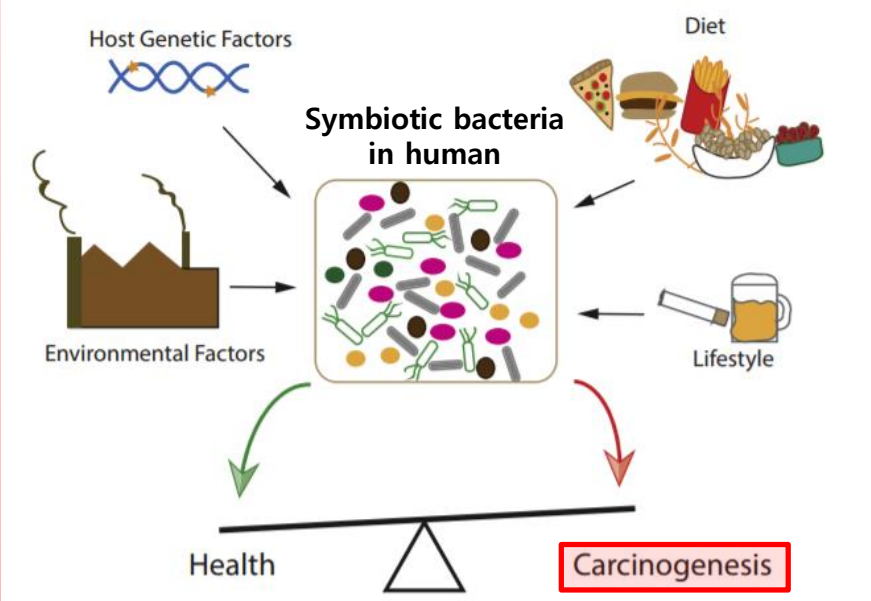
NIH HUMAN MICROBIOME PROJECT

Association between body mass index (BMI) and Firmicutes/Bacteroidetes (F/B) ratio

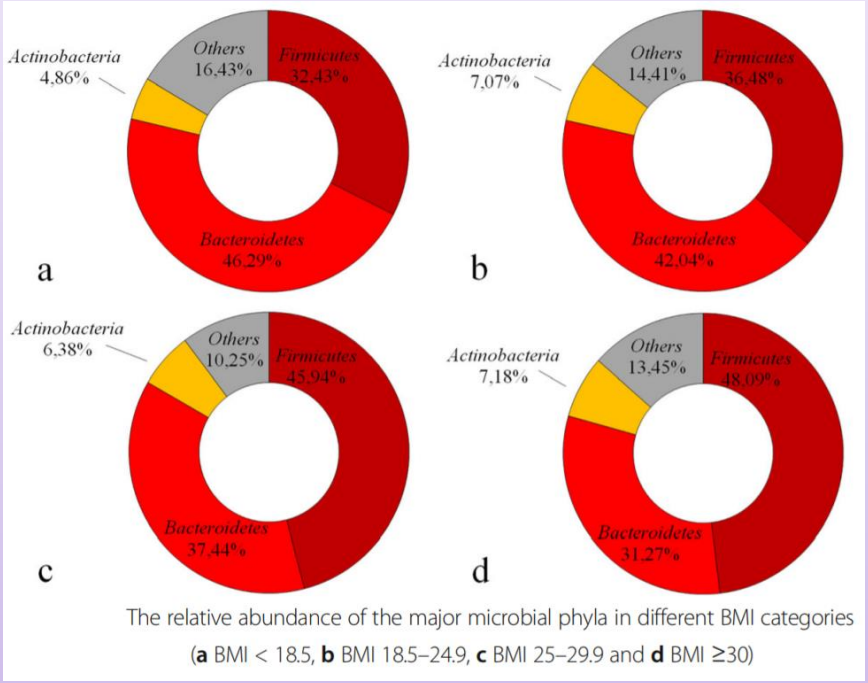
Symbiotic relationship with bacteria and human



The symbiotic relationship disturbed

Nature Reviews Cancer, 2013, 13.11: 800-812.

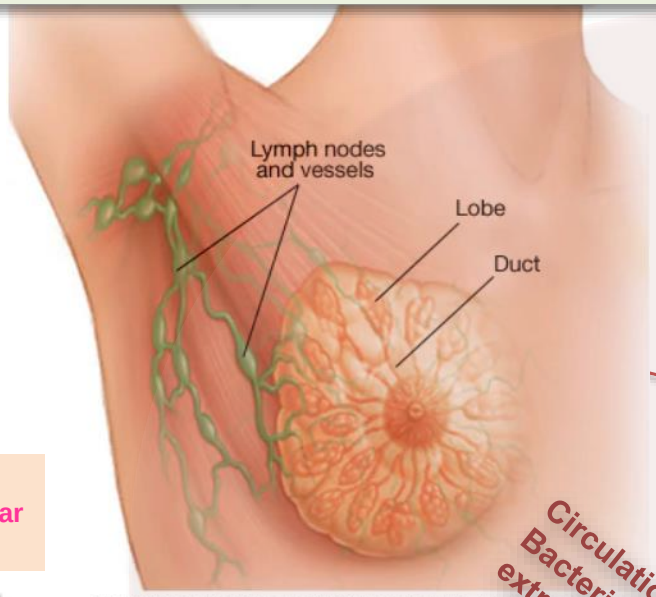
The relative abundance of the **major microbial phyla** in different **BMI** categories



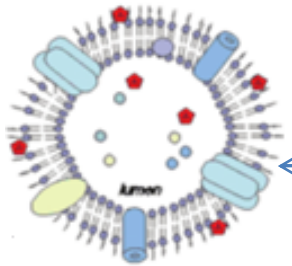
The relative abundance of the major microbial phyla in different BMI categories (**a** BMI < 18.5, **b** BMI 18.5–24.9, **c** BMI 25–29.9 and **d** BMI ≥30)

BMC Microbiology 2017 17:120

● This study has analyzed the microbiome of **blood** in breast cancer patients to investigate the F/B ratio.



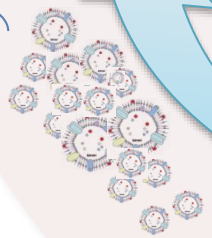
Bacterial extracellular vesicle

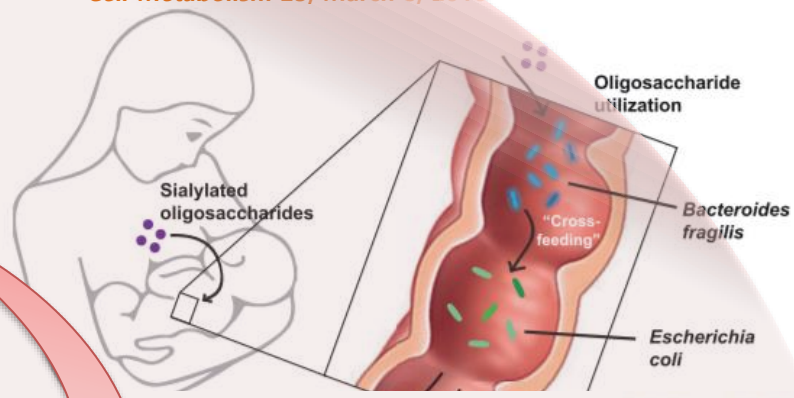


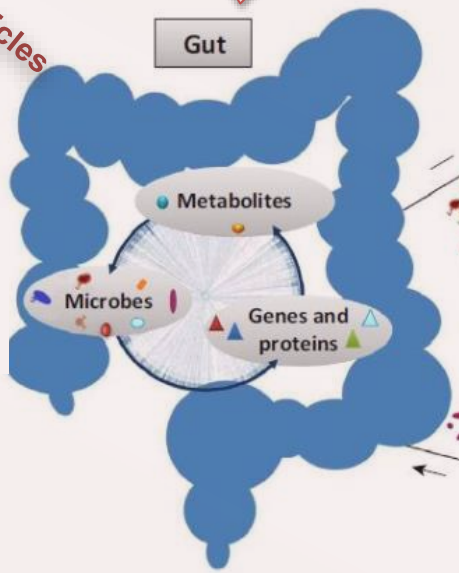
Genes & Dev. 2005. 19: 2645-2655

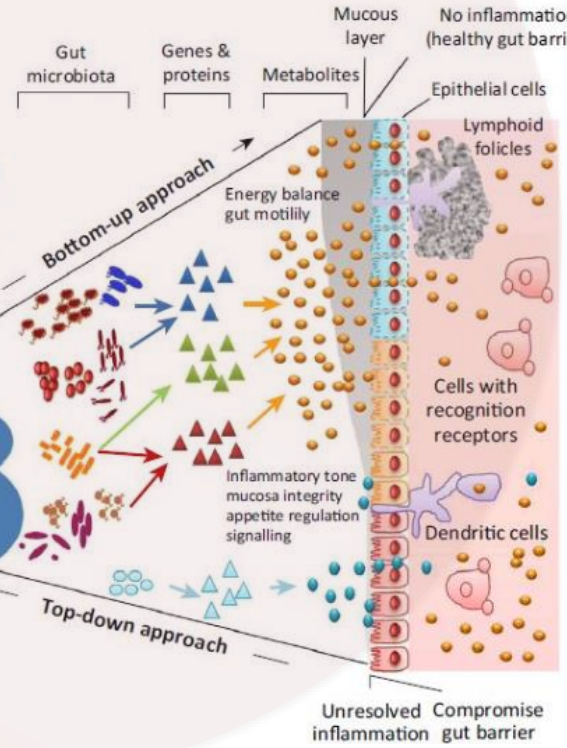
Circulation of Bacterial extracellular vesicles

blood, lymphatics









● **Bacterial extracellular vesicles (EVs) which include nucleic acids, and proteins such as enzyme and metabolites in the lipid bilayer.**

● **EVs circulate the whole body throughout the body fluids like blood and lymphatics.**

Method for metagenomic analysis

- **Patients characteristics**
  - Blood samples: **95** breast cancer patients & **187** healthy individuals

    females at Ewha Womans University Mokdong Hospital & Inje University Paik hospital, Haeundae
  - Duration of data collection: 4.2011 ~ 8. 2015
  - **Age adjustment** was performed in all analyses.
  - The **preoperative blood samples** were collected.
- **Extracellular vesicles(EV)**: EV isolation and EV DNA prep
- **Bacterial 16S rDNA sequencing(NGS)**

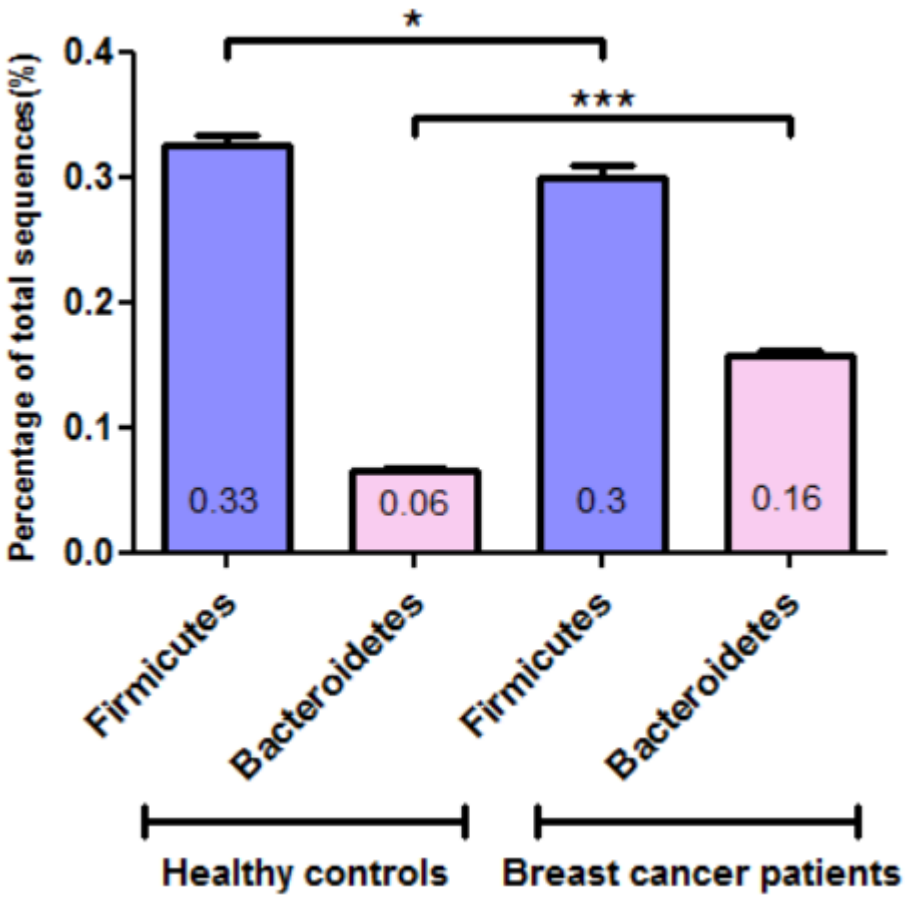
  using a **universal bacterial primer of 16S rDNA** (Miseq)

  taxonomic assignment: **profiling program** MDx-Pro ver.1
- **Statistic analysis**: **T-test, Kaplan-meier survival analysis**

Comparison of Fermicutes and Bacteriodetes

in healthy controls and breast cancer patients

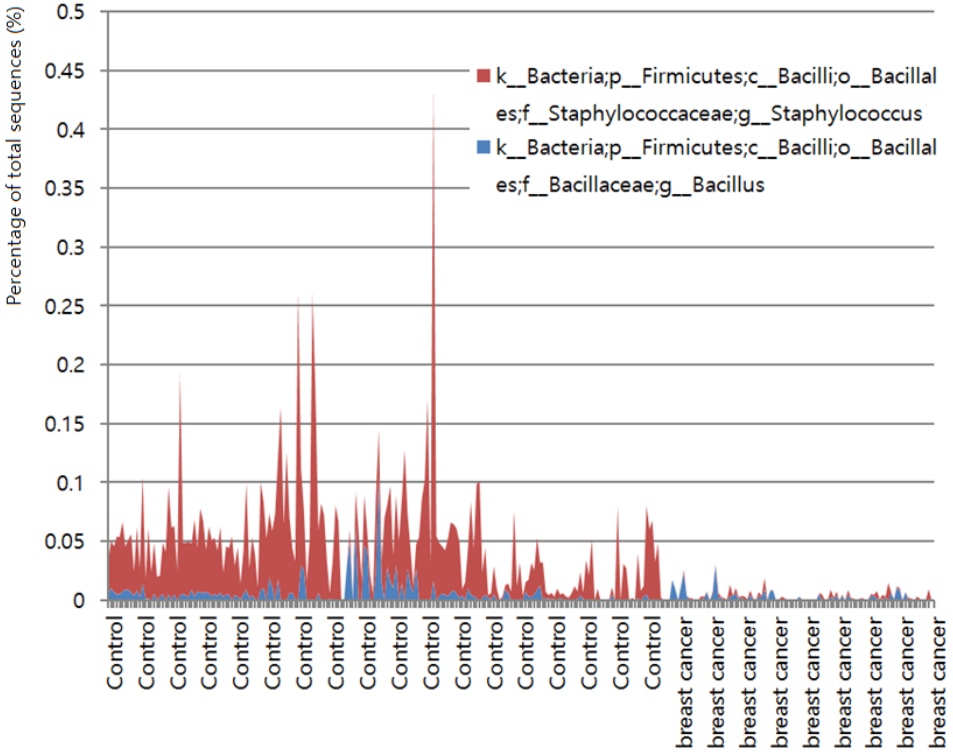
Firmicutes and *Bacteroidetes* ratios differ between breast cancer patients and healthy controls.

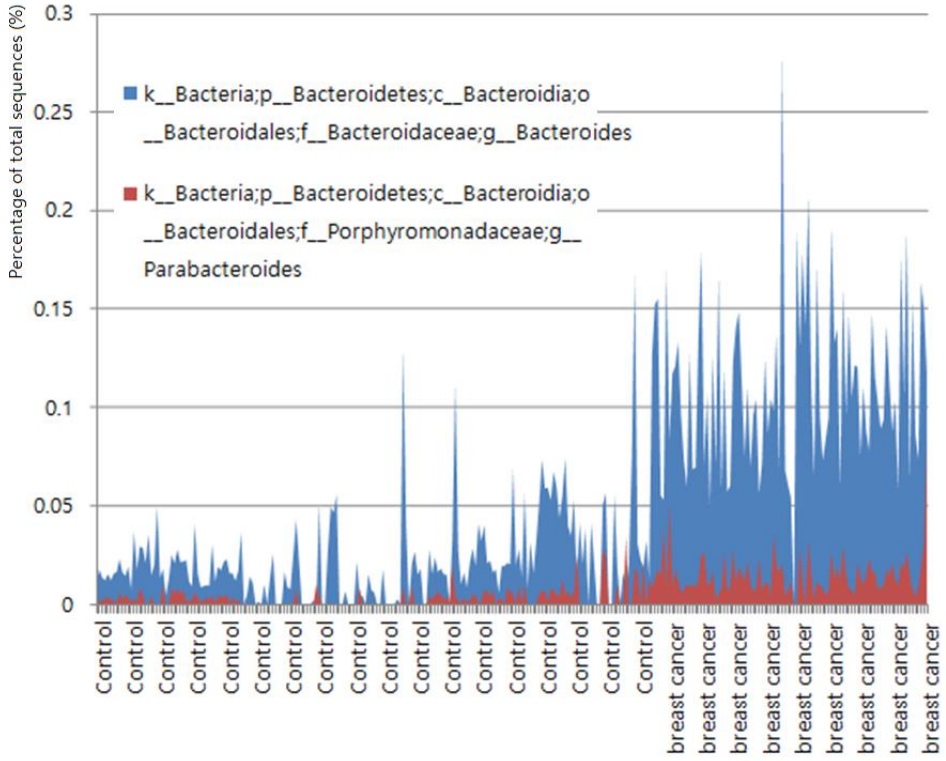


NS	P > 0.05
*	P ≤ 0.05
**	P ≤ 0.01
***	P ≤ 0.001

The different representative bacteria
between the control and breast cancer groups in *Firmicutes* and *Bacteroides*

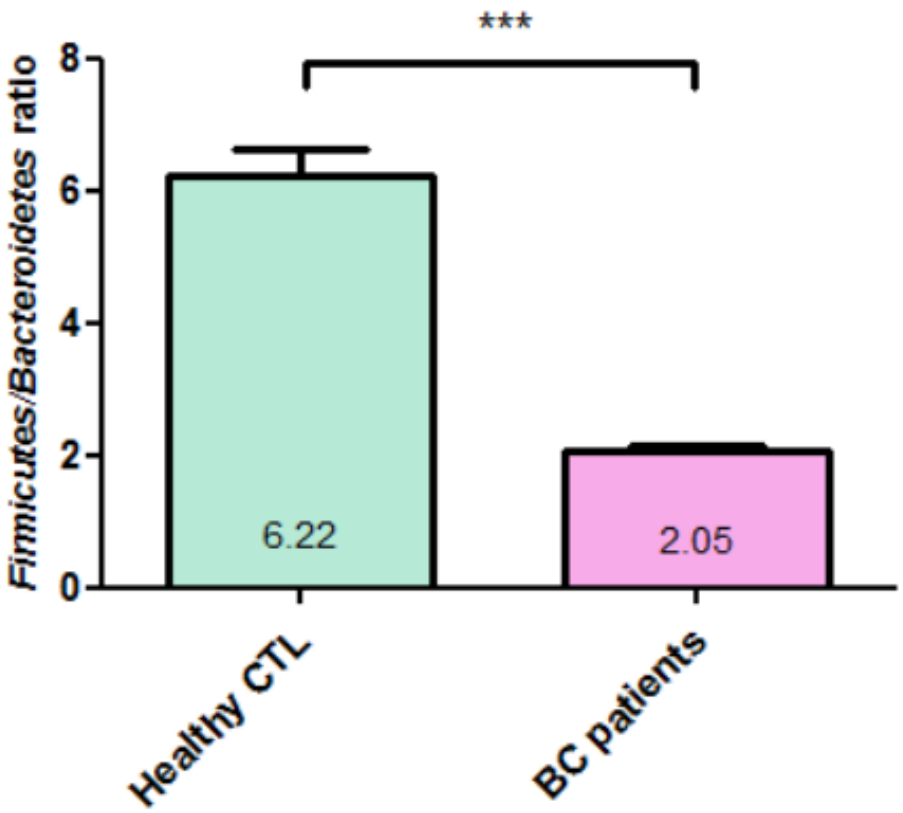
Firmicutes are abundant in healthy controls, and ***Bacteroidetes*** are abundant in breast cancer patients.





Comparison of F/B ratio
in healthy controls and breast cancer patients

The F/B ratio is **three times higher** in **healthy controls** than in breast cancer patients.

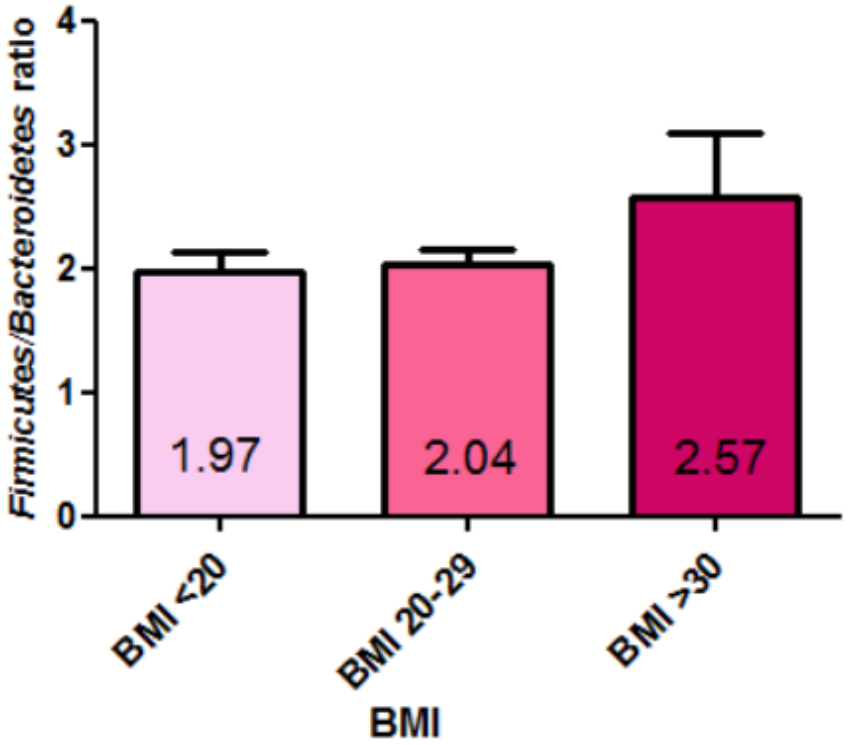


NS	P > 0.05
*	P ≤ 0.05
**	P ≤ 0.01
***	P ≤ 0.001

CTL: control
BC: Breast cancer

F/B ratio according to BMI
in breast cancer patients

The **higher** the **BMI** in breast cancer patients, the **higher** the **F/B ratio** is.



NS	P > 0.05
*	P ≤ 0.05
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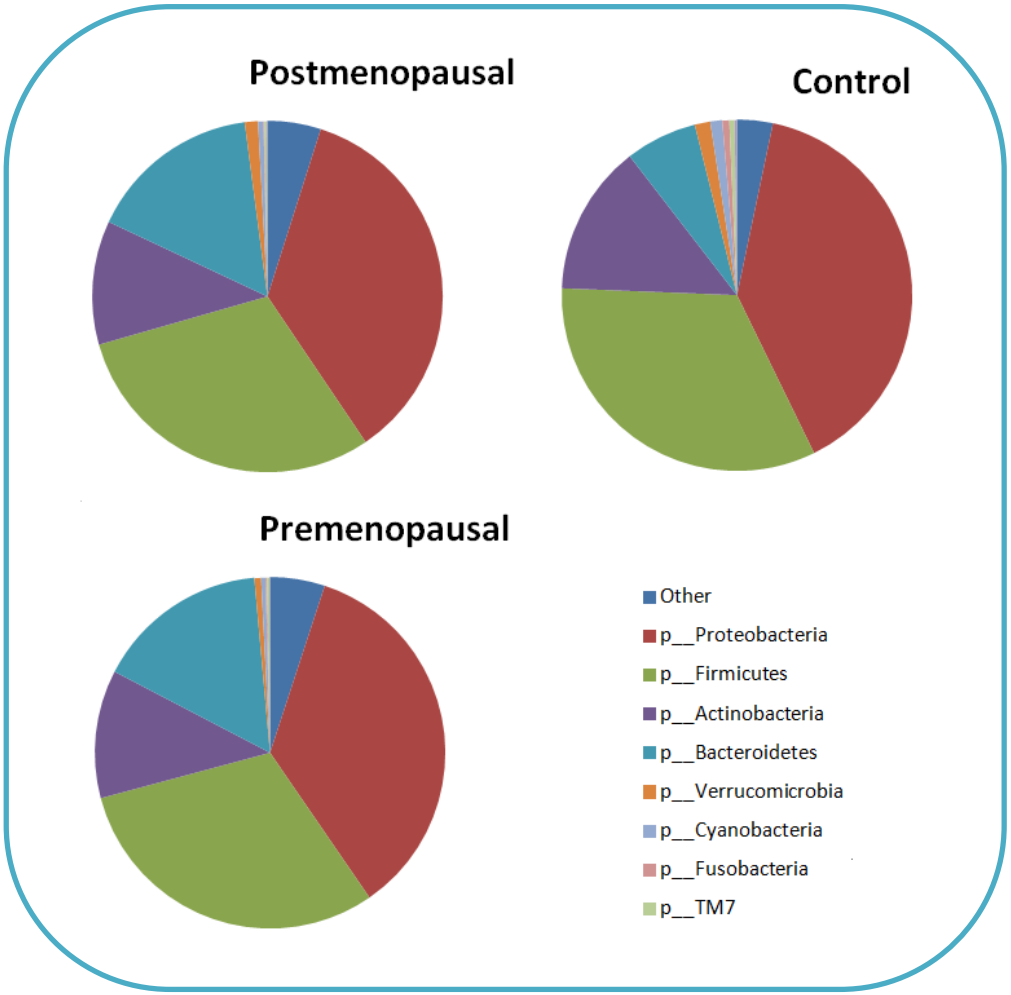
***	P ≤ 0.001

Comparison of F/B ratio

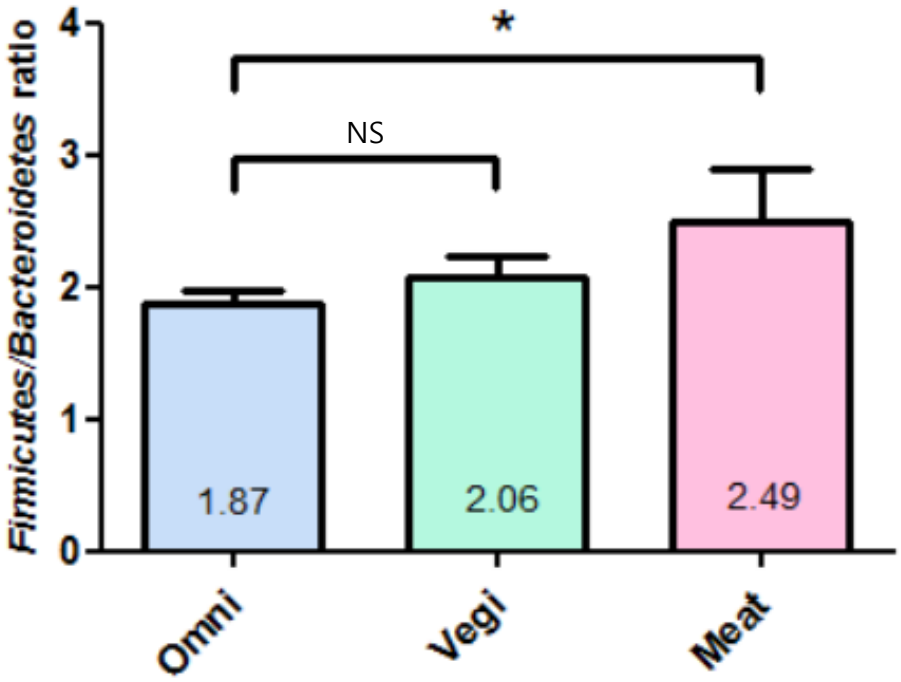
according to mensturation in breast cancer patients

There was no relationship between F/B ratio and menstruation in breast cancer patients.



Comparison of F/B ratio
according to diet in breast cancer patients

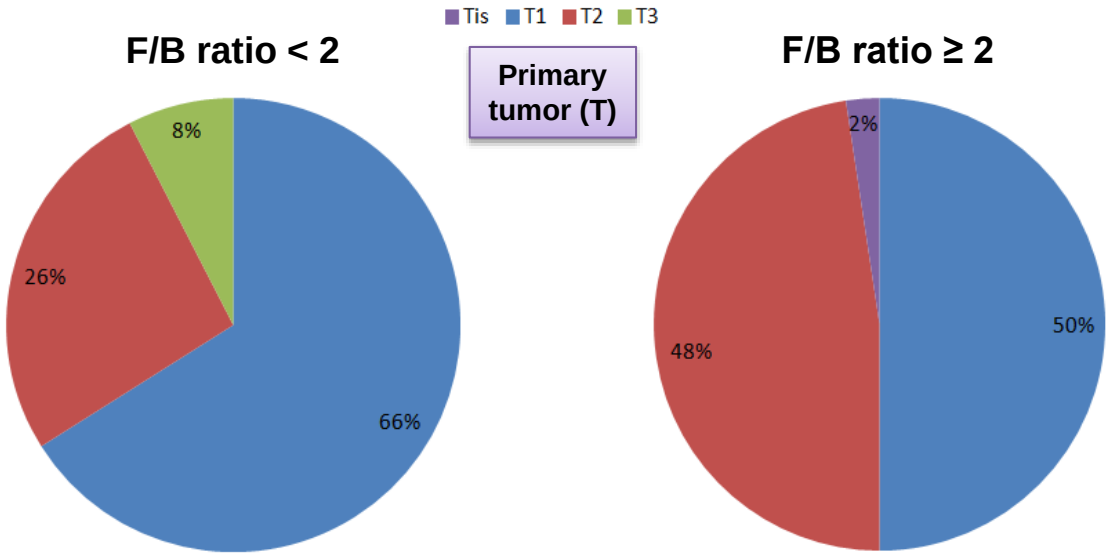
The F / B ratio was **higher** in the group that enjoyed **eating meat.**



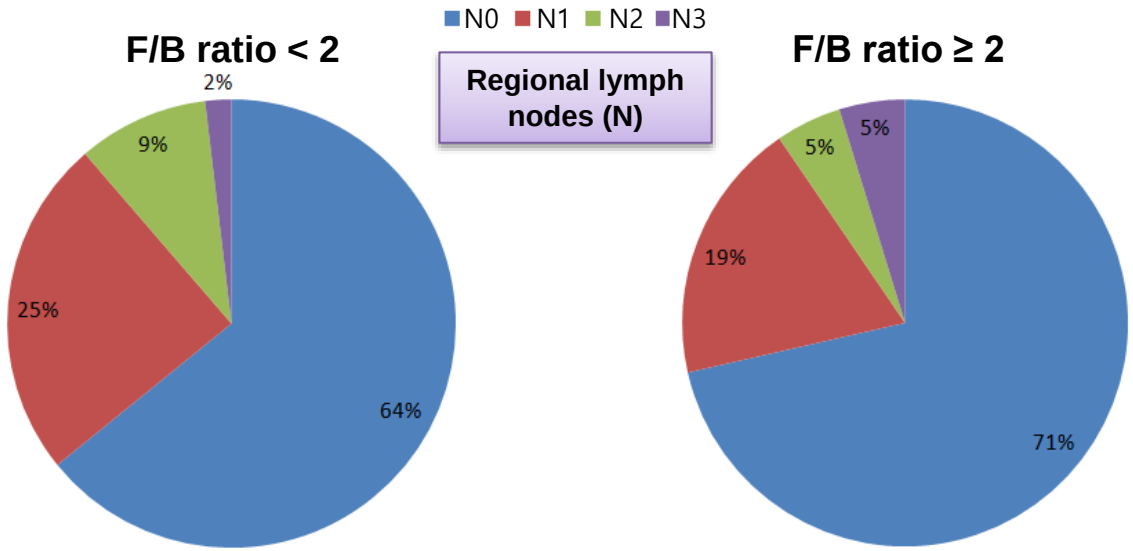
NS	P > 0.05
*	P ≤ 0.05
**	P ≤ 0.01
***	P ≤ 0.001

Omni : Omnivorous meal
Vegi : Vegetable-based meal
Meat : Meat-based meal

Comparison of Primary tumor and Regional lymph nodes according to F/B ratio in breast cancer patients



As the F/B ratio increases, the ratio of Tis is increased.

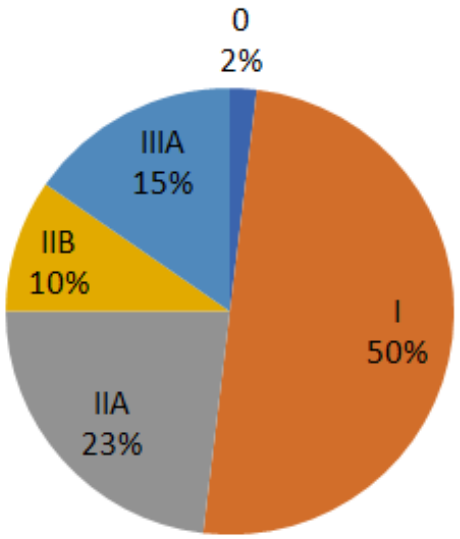


As the F/B ratio increases, The ratio of N0 is increased.

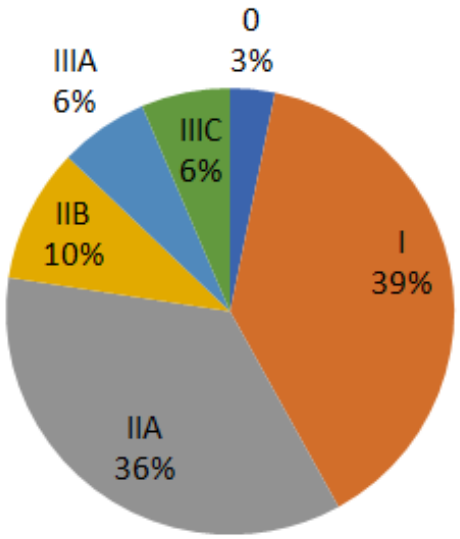
Comparison of Pathologic stage
according to F/B ratio in breast cancer patients

As the F/B ratio increases, the TNM stage is down-graded.

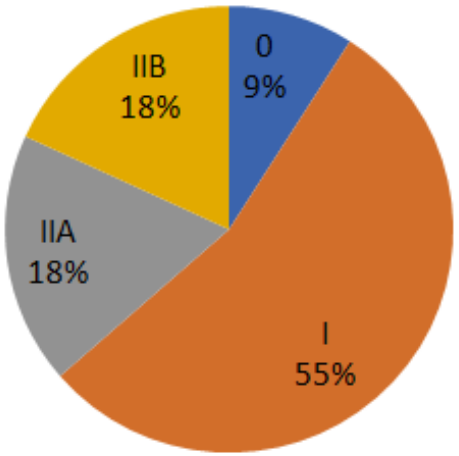
F/B ratio<2



2≤ F/B ratio<3



F/B ratio≥3



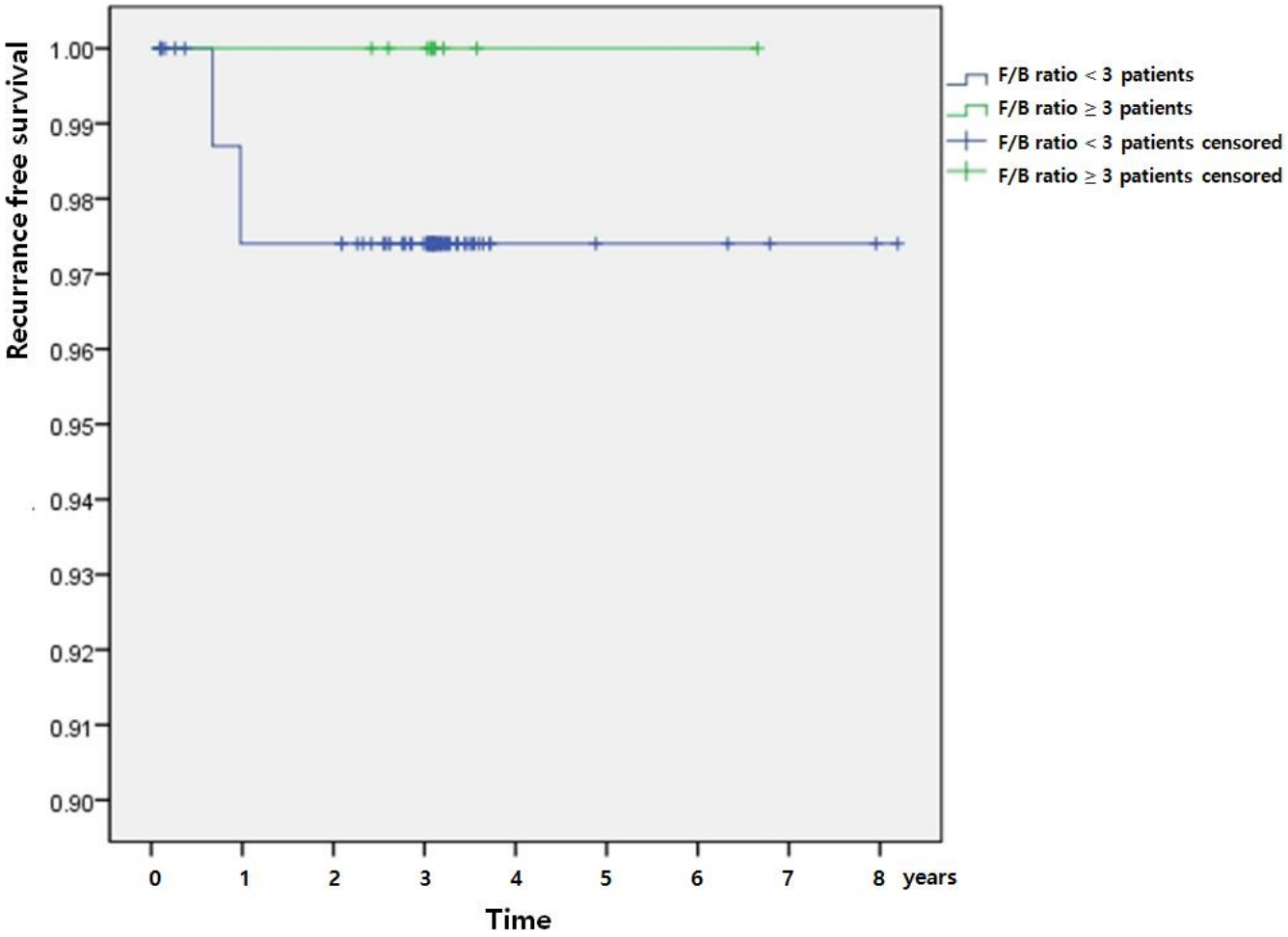
stage \ F/B ratio	F/B ratio<2	2≤ F/B ratio<3	F/B ratio≥3
0	2 %	3 %	9 %
I	50 %	39 %	55 %
II	33 %	46 %	36 %
III	15 %	12 %	0 %

Recurrance related to FB ratio

Patients with high FB ratio have a better prognosis

As the F/B ratio is low, the recurrence is increased.

- **Kaplan-meier survival analysis**



Conclusion

- The F / B ratio is higher in healthy control group.
- In breast cancer patients, **high-level of BMI** group and **meat-lover group** show the **F / B ratio high**, and the higher the F / B ratio, the lower TNM stage.
- Obesity was associated with the onset or bad prognosis of breast cancer. However, this study has been shown high BMI is one of a good prognostic factor concerning the microbiome F / B ratio.
- ***In conclusion, if the F / B ratio is high in the group of breast cancer patients as healthy control group, it may have a good prognosis.***
- This study keeps going on through clinical trials in the near future with MD healthcare company.