



Katherine L. Cook, Ph.D.

Disclosure of Commercial Interest

It is the policy of the Prevent Cancer Foundation and the Nurse Practitioners in Women's Health that the education presented at CE-certified activities will be unbiased and based on scientific evidence. To help participants make judgments about the presence of bias, the Prevent Cancer Foundation provides information that faculty have disclosed about financial relationships they have with commercial entities that produce or market products or services related to the content of this educational activity.

There will not be any off-label and/or investigational use of products discussed within the content at any of the presentations at this conference.

The Mediterranean Diet and the Breast Microbiome: Might the Right Diet Reduce the Risk of Breast Cancer?

Dr. Katherine Cook has indicated she has no relevant financial relationships within the past 12 months.



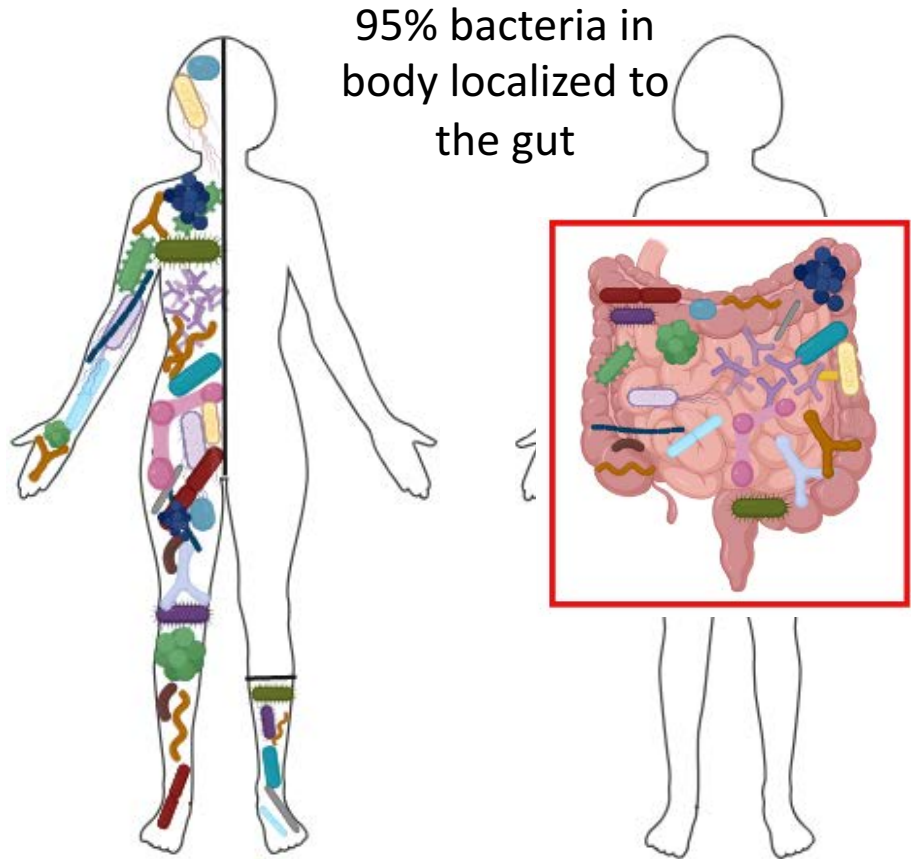
The Mediterranean Diet and the Breast Microbiome: Might the Right Diet Reduce the Risk of Breast Cancer?

Dr. Katherine L. Cook, Ph.D.

**Assistant Professor, Department of Surgery, Cancer Biology, &
Comprehensive Cancer Center**

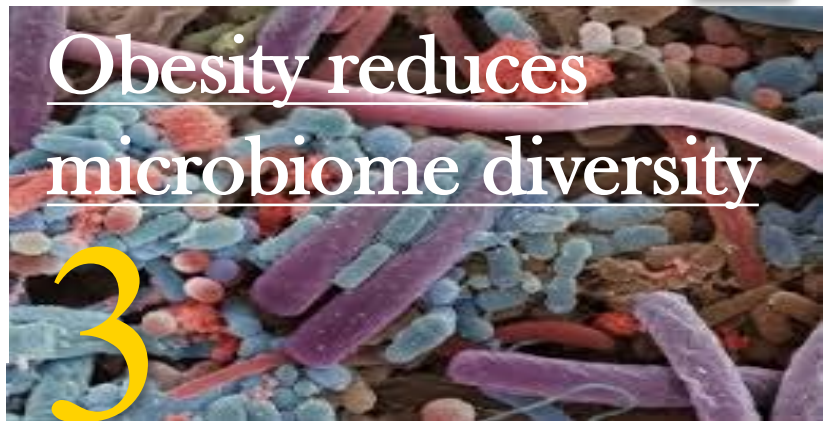
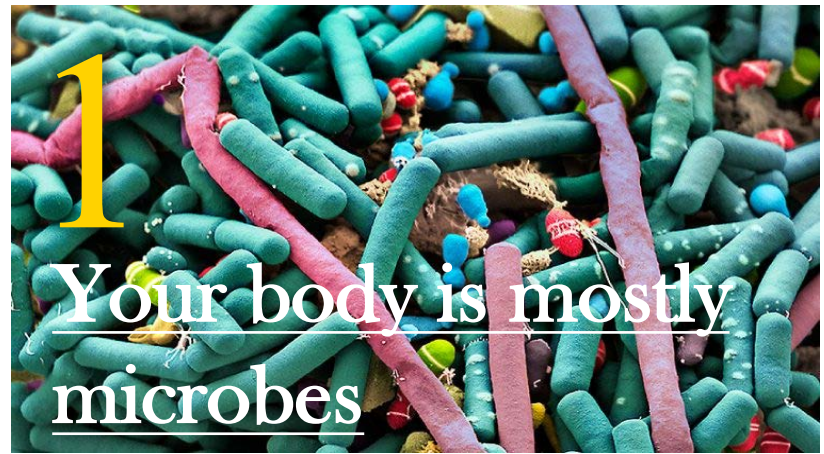


We are more microbial than human...

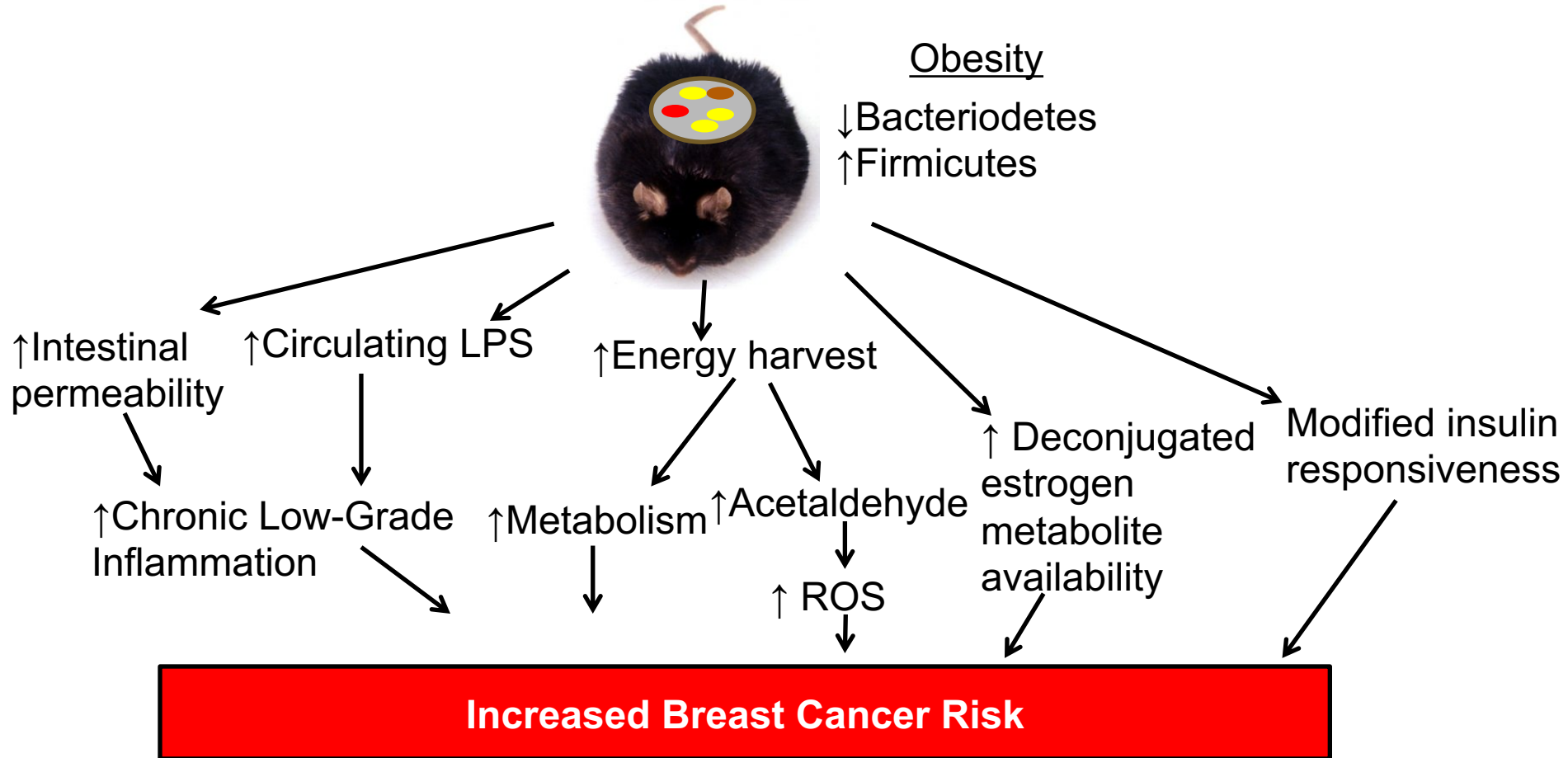


39 trillion bacteria cells: 30 trillion human cells
Our body is only 43% human!

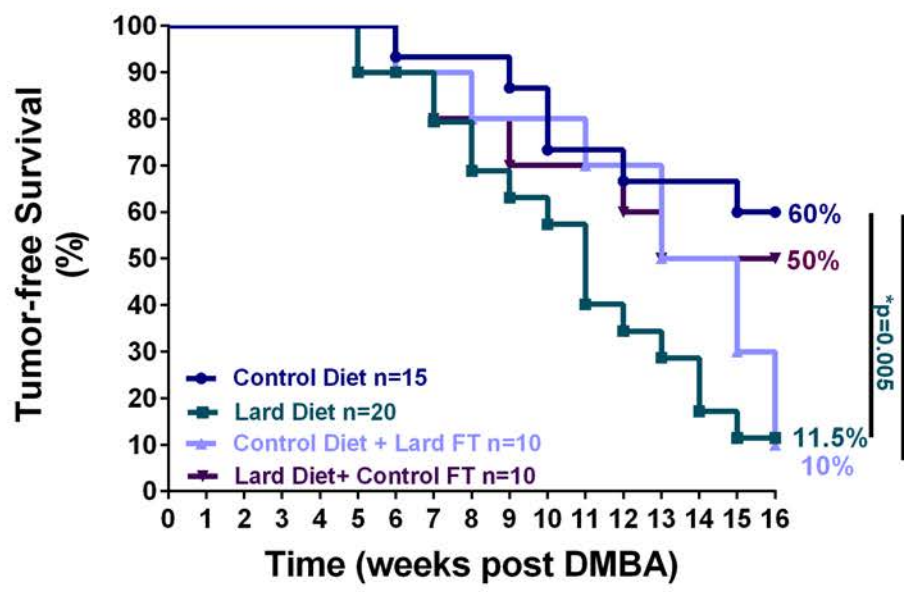
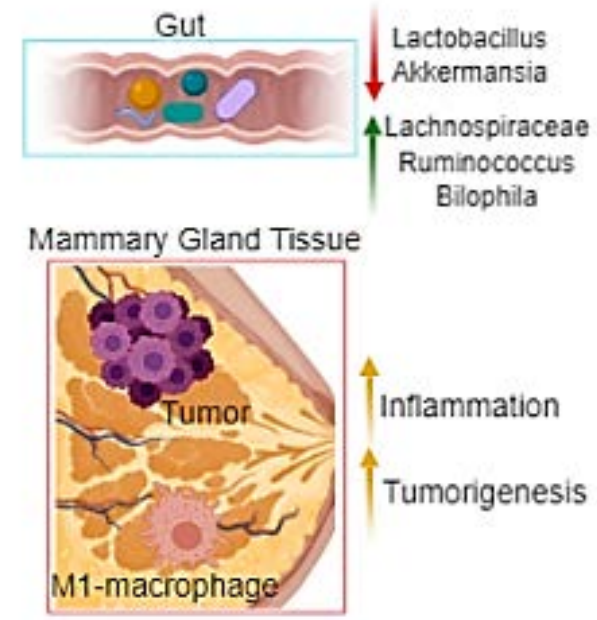
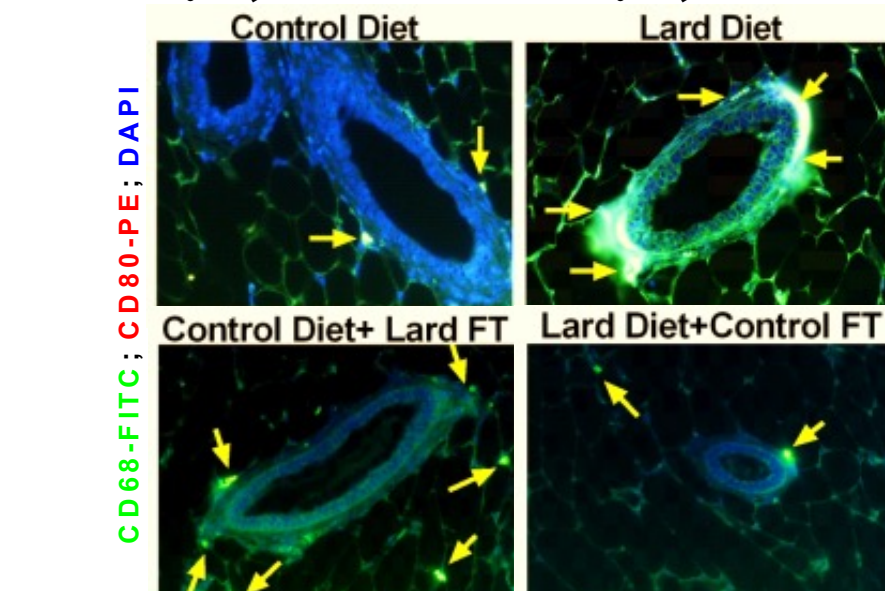
Wake Forest Baptist Medical Center



Microbiome Composition Effects on Breast Cancer Risk



Modulating Gut Microbiome Shifts Mammary Gland Inflammation and Breast Cancer Risk



Soto-Pantoja et.al., under review at *Nature Communications*

DO NOT POST- unpublished data

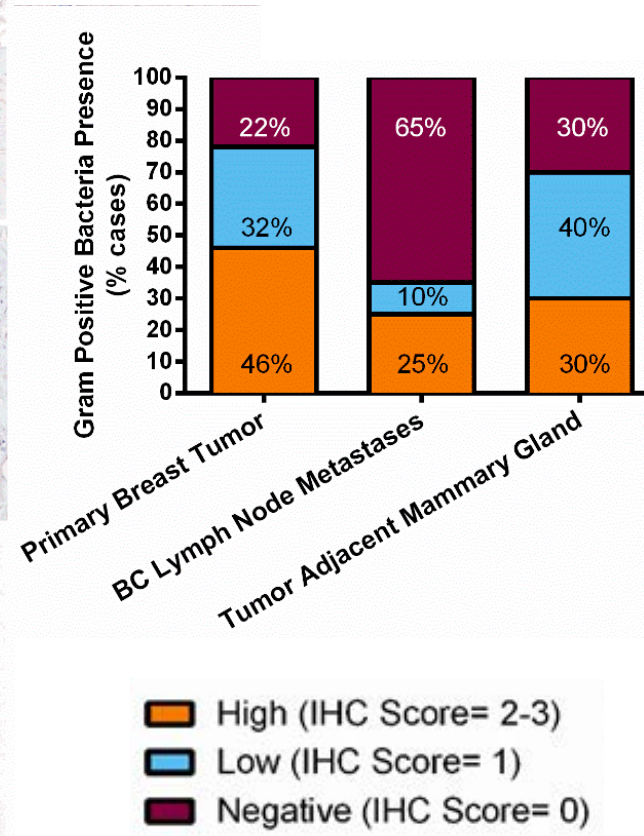
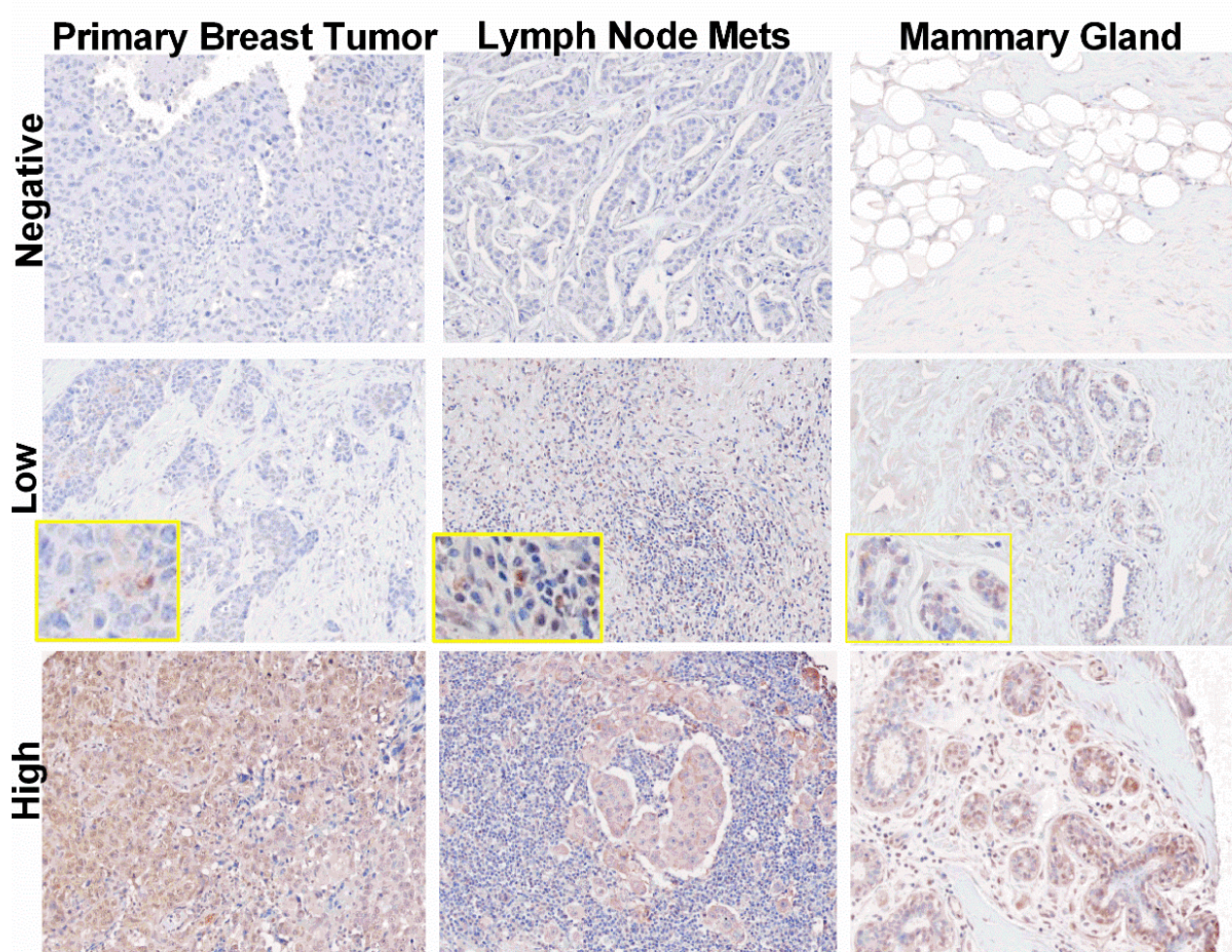
The Breast Microbiome and Cancer

- **Microbiota of human breast tissue.** Urbaniak et al, 2014

Microbiota Genus	Canadian breast tissue (% of microbiota population)	Irish breast tissue (% of microbiota population)
Bacillus	11.4%	<2%
Acinetobacter	10%	<2%
Enterobacteriaceae	8.3%	30.8%
Pseudomonas	6.5%	5.3%
Staphylococcus	6.5%	12.7%
Propionibacterium	5.8%	10.1%
Prevotella	5%	<2%
Listeria	<2%	12.1%

- **The microbiota of breast tissue and its association with breast cancer.** Urbaniak et al, 2016
 - Increased Staphylococcus in breast tissue from women with BC when compared with healthy controls
- **The microbiome of aseptically collected human breast tissue in benign and malignant disease.** Hieken et al, 2016
 - Decreased Lactobacillus in breast tissue from women with malignant BC

Breast Tumors Contain Bacteria

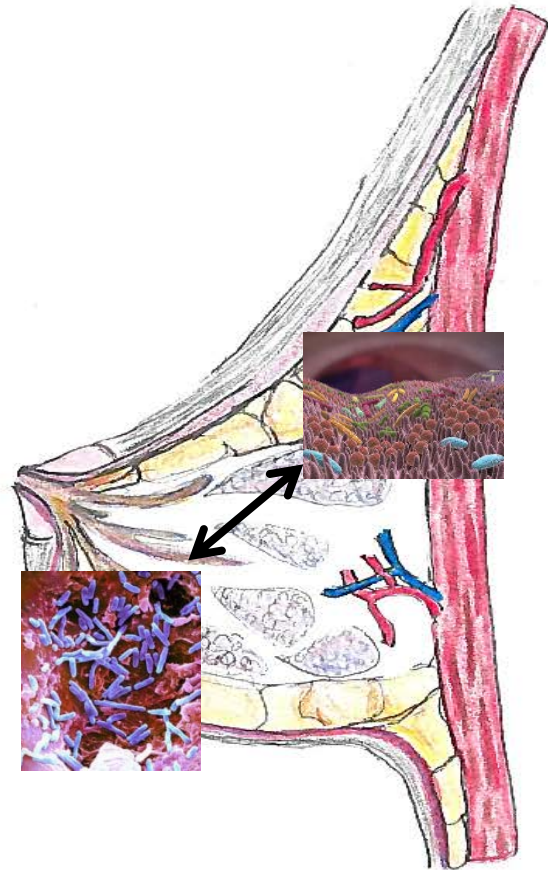


Primary breast tumors n=50;
 Breast cancer lymph node metastases n=40
 Tumor adjacent normal mammary gland tissue n=10

Soto-Pantoja et.al., under review at *Nature Communications*

DO NOT POST- unpublished data

Since diet is main determinant of the gut microbiome, can what you eat modify you breast microbiome?



Non-human Primate Diet Composition



Western Diet		Mediterranean Diet	
DIET #: 1523		DIET #: 1530 (1497 + Banana)	
INGREDIENT	g/ 100g	INGREDIENT	g/100 g
Casein, USP	8.50	Casein, USP	1.74
Whey Protein 895	8.50	Whey protein - 895	1.74
		Dried Egg white	2.61
		Fishmeal (Menhaden)	2.61
		Walnuts	0.87
		Black Bean flour	4.35
		Garbanzo Bean flour	1.74
		Wheat Flour (S.Biscuit all purpose)	24.35
Dextrin	26.00	Dextrin	9.66
Sucrose	18.00	Sucrose	3.48
High Fructose Corn Syrup -55	7.00	Banana	13.04
		Applesauce	3.82
		Tomato paste	1.74
Cellulose (Alphacel)	7.94	Cellulose (Alphacel)	9.48
Total Fiber (% of diet)	7.94	Total fiber (% of diet)	12.7
Lard	4.15	Olive Oil (Filippo Berio)*	6.17
Beef Tallow HHR*	4.00	Menhaden Oil (Omegapure)	0.87
Butter, lightly salted	1.25	Butter, lightly salted	0.87
Corn Oil	3.50	Corn Oil	1.04
Flaxseed oil	0.30	Flaxseed oil	0.17
Dried Egg Yolk	0.60	Dried Egg Yolk	1.48
Crystalline Cholesterol	0.04		
Complete Vitamin Mix (Teklad)	2.50	Complete Vitamin Mix (Teklad)	2.17
Mineral Mix w/o Ca, P, NaCl	5.00	Mineral Mix w/o Ca, P, NaCl	4.35
Calcium Carbonate	0.43	Calcium Carbonate	0.37
Calcium Phosphate, Monobasic	0.75	Calcium Phosphate, Monobasic	0.65
NaCl (Table Salt)	1.60	NaCl (Table Salt)	0.63
TOTAL	100	TOTAL	100

Non-human Primate Diet Represents Dietary Patterns of Women

Diet Composition	Human		Nonhuman Primate*	
	Western	Mediterranean	Western	Mediterranean
	% of Calories	% of Calories	% of Calories	% of Calories
Protein	15 ₁	17 ₂	16	16
Carbohydrate	51 ₁	51 ₂	54	54
Fat	33 ₁	32 ₂	31	31
	% of Total Fats	% of Total Fats	% of Total Fats	% of Total Fats
Saturated	33 ₁	21 ₂	37	21
Monounsaturated	36 ₁	56 ₂	36	57
Polyunsaturated	24 ₁	15 ₂	25	20
ω6:ω3 Fatty Acids	15:1 ₅	2.1-3:1 ₆	14.9:1	2.9:1
Cholesterol mg/Cal	0.13 ₁	0.16 ₂	0.16	0.15
Fiber g/Cal	0.01 ₁	0.03 ₃	0.02 ₁	0.04 ₃
Sodium mg/Cal	1.7 _{1,4}	1.3 _{2,3}	1.7 _{1,4}	1.1 _{2,3}

1 US Dept of Agriculture 2014, women 40-49 from NHANES *What We Eat* 2011-2012 2 Bedard,A., Riverin,M., Dodin,S., Corneau,L., and Lemieux,S. (2012). Sex differences in the impact of the Mediterranean diet on cardiovascular risk profile. *Br. J. Nutr.* 108, 1428-1434. (23)

3 Kafatos,A., et al. (2000). Mediterranean diet of Crete: foods and nutrient content. *J. Am. Diet. Assoc.* 100, 1487-1493. (24)

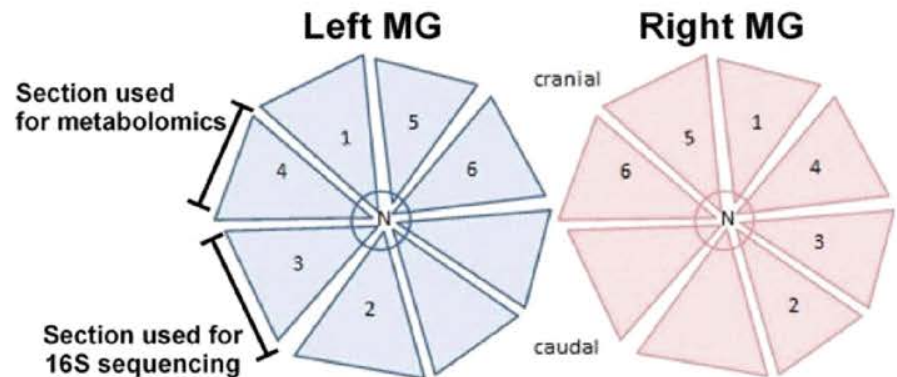
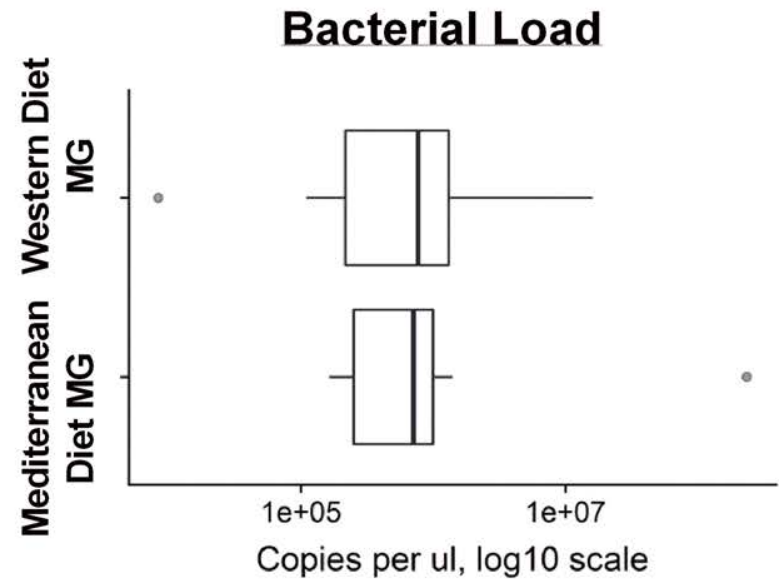
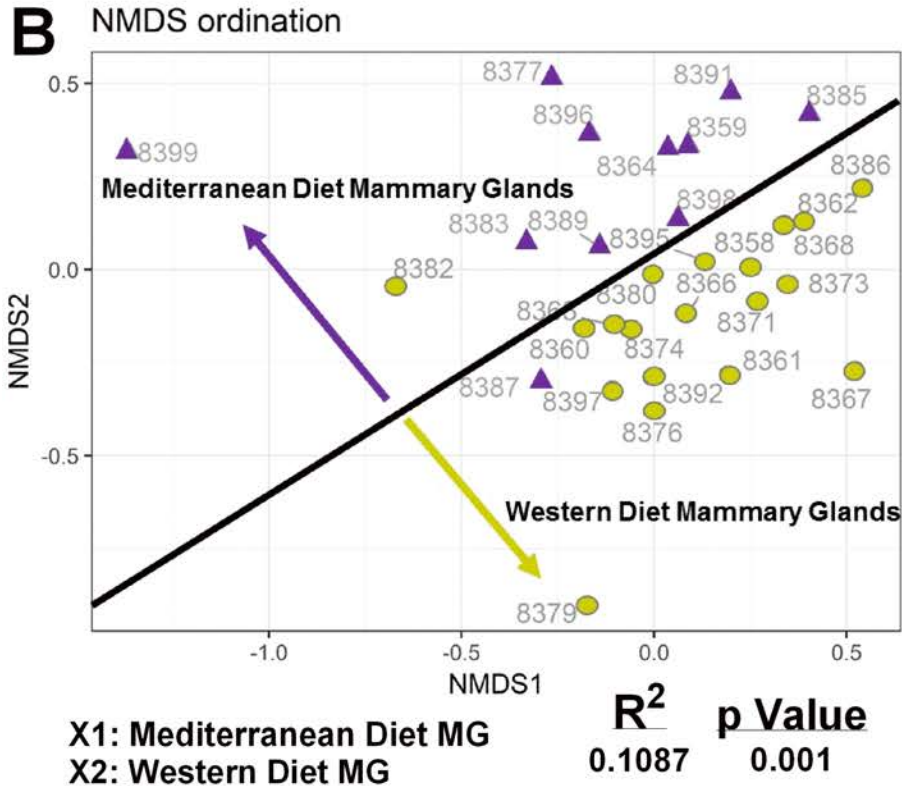
4 Powles,J., et al. (2013). Global, regional and national sodium intakes in 1990 and 2010: a systematic analysis of 24 h urinary sodium excretion and dietary surveys worldwide. *BMJ Open.* 3, e003733.(57)

5 Simopoulos,A.P. (2006). Evolutionary aspects of diet, the omega-6/omega-3 ratio and genetic variation: nutritional implications for chronic diseases. *Biomed. Pharmacother.* 60, 502-507. (58)

6 Cordain,L., et al. (2005). Origins and evolution of the Western diet: health implications for the 21st century. *Am. J. Clin. Nutr.* 81, 341-354.(25)

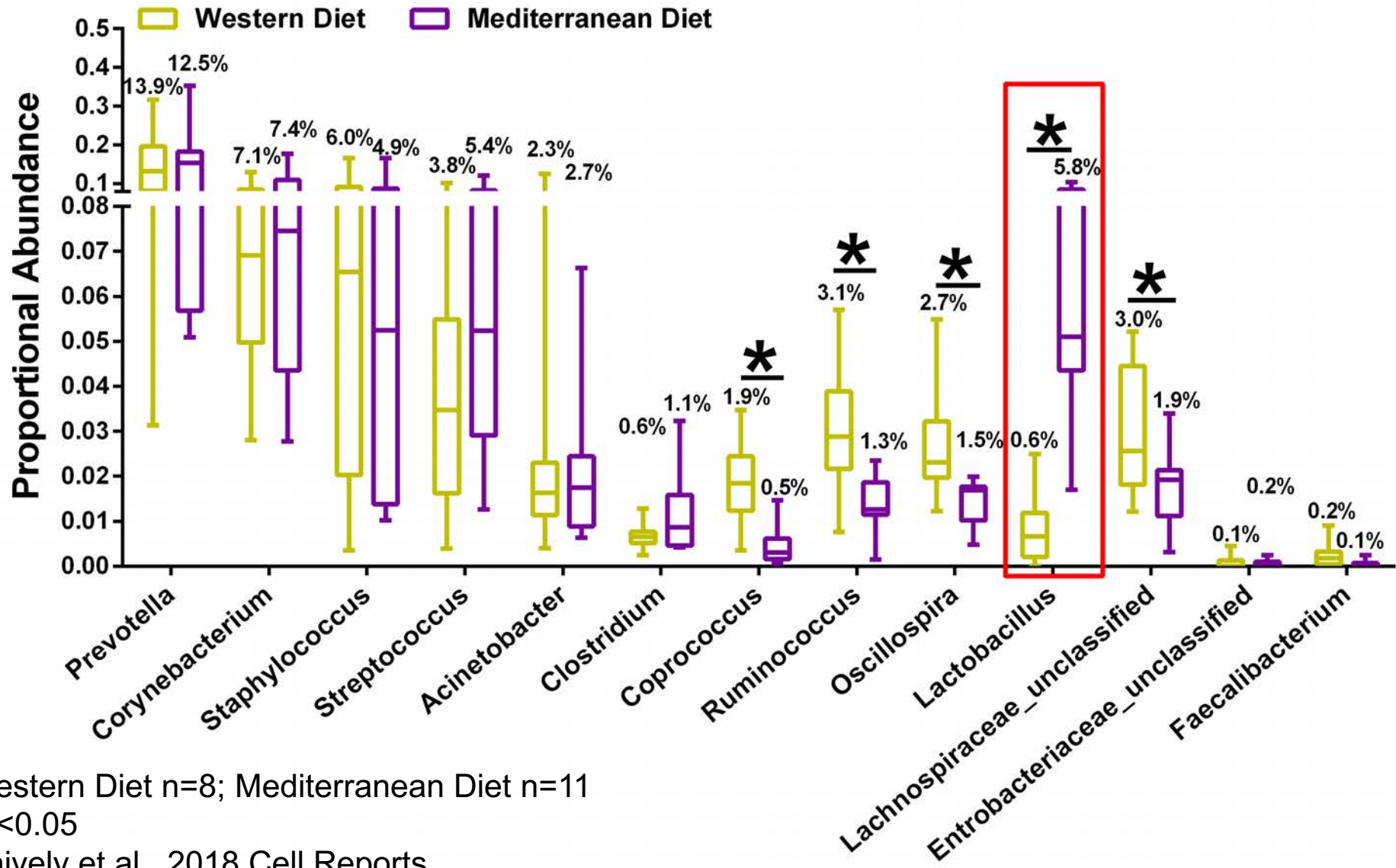
*These values were determined by diet composition analysis

Diet Impacts Mammary Gland Microbiota



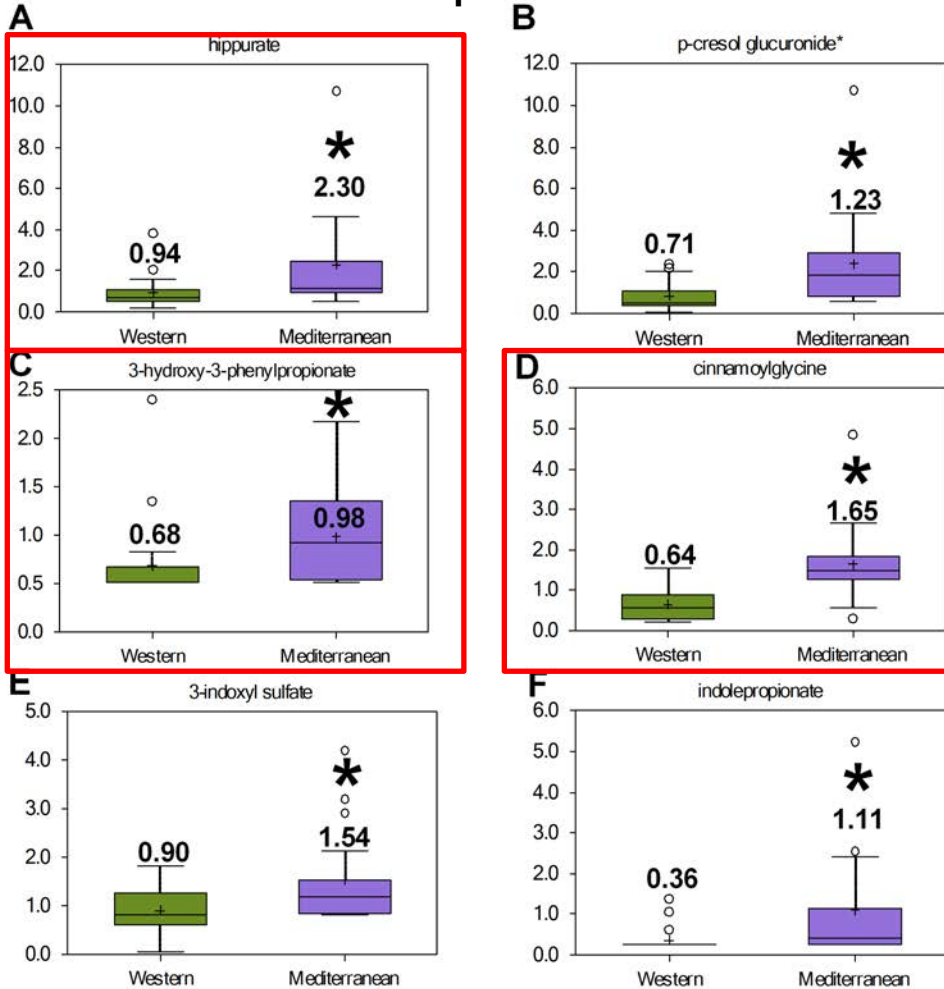
Western Diet n=18; Mediterranean Diet n=11
 Shively et al., 2018 Cell Reports

Elevated Lactobacillus Populations in MG of Mediterranean Diet Fed Monkeys

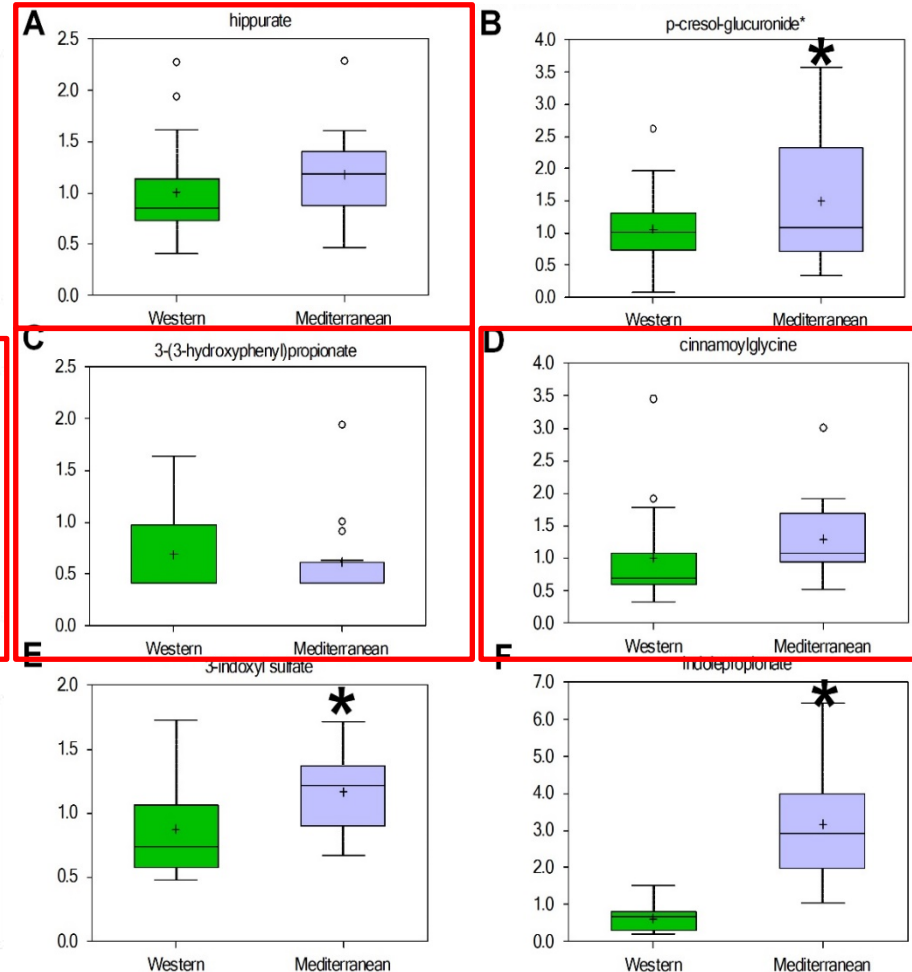


Regulation of Bacterial Modified Metabolites by Diet

Mammary Gland Bacterial Modified Bioactive Compounds



Plasma Bacterial Modified Bioactive Compounds

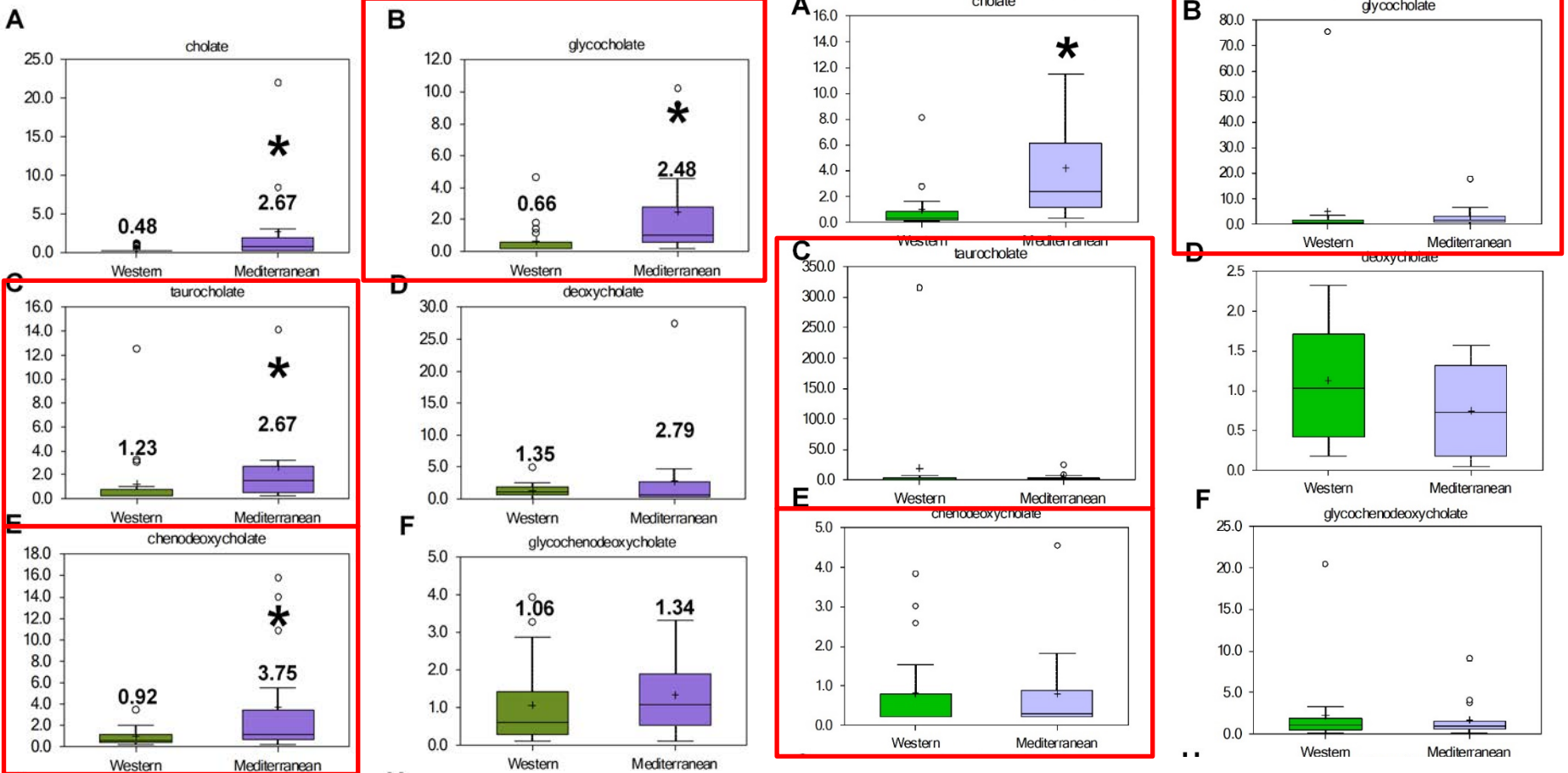


Upregulation of phenylalanine derived bacterial modified bioactive compounds in MG suggests regulation of these compounds may be site specific

Regulation of Bile Acid Metabolites by Diet

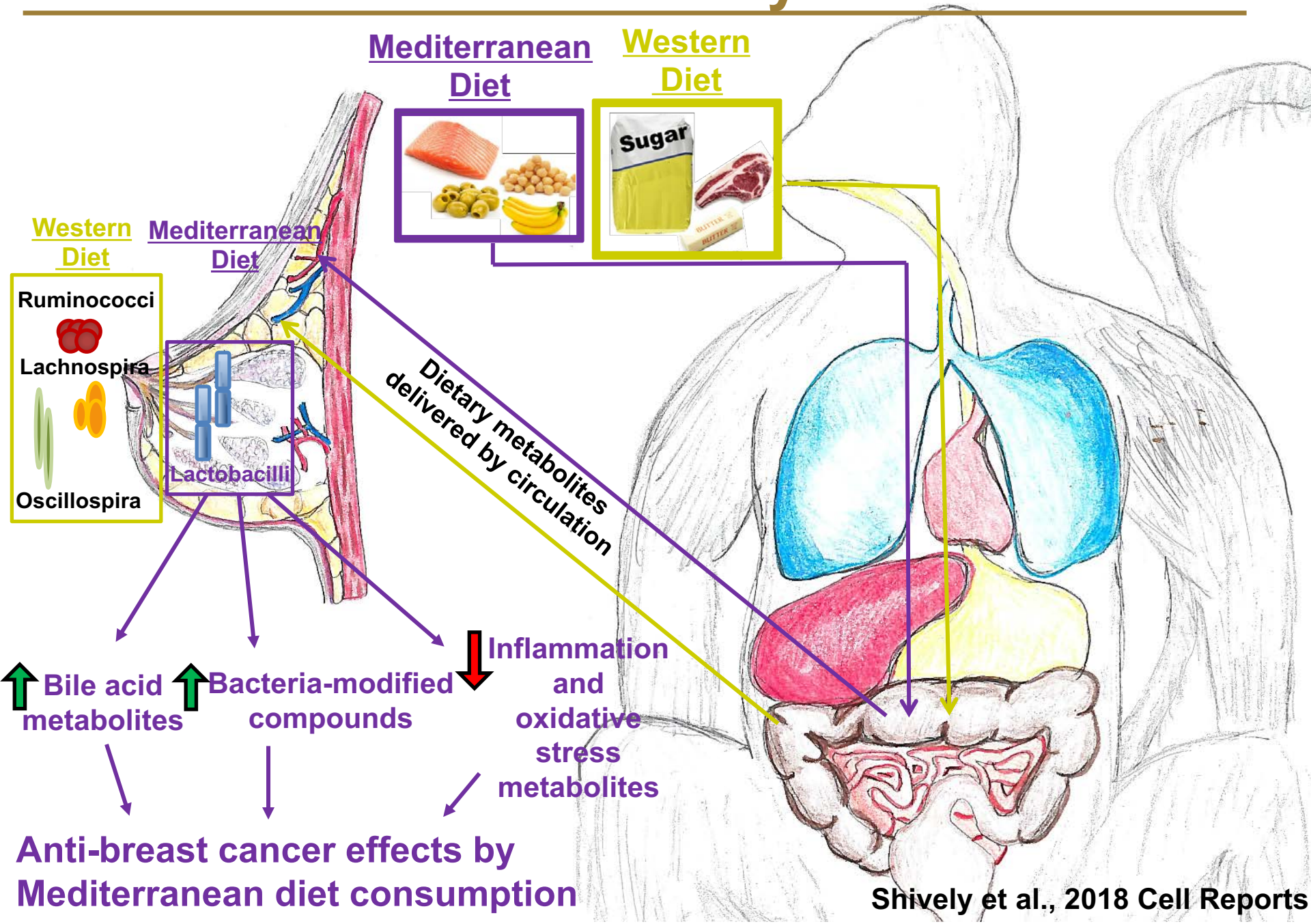
Mammary Gland Bile Acid Metabolites

Plasma Bile Acid Metabolites



Concentration of specific conjugated bile acid metabolites in MG but not in the plasma suggests regulation of these compounds may be site specific and due to localized microbiota

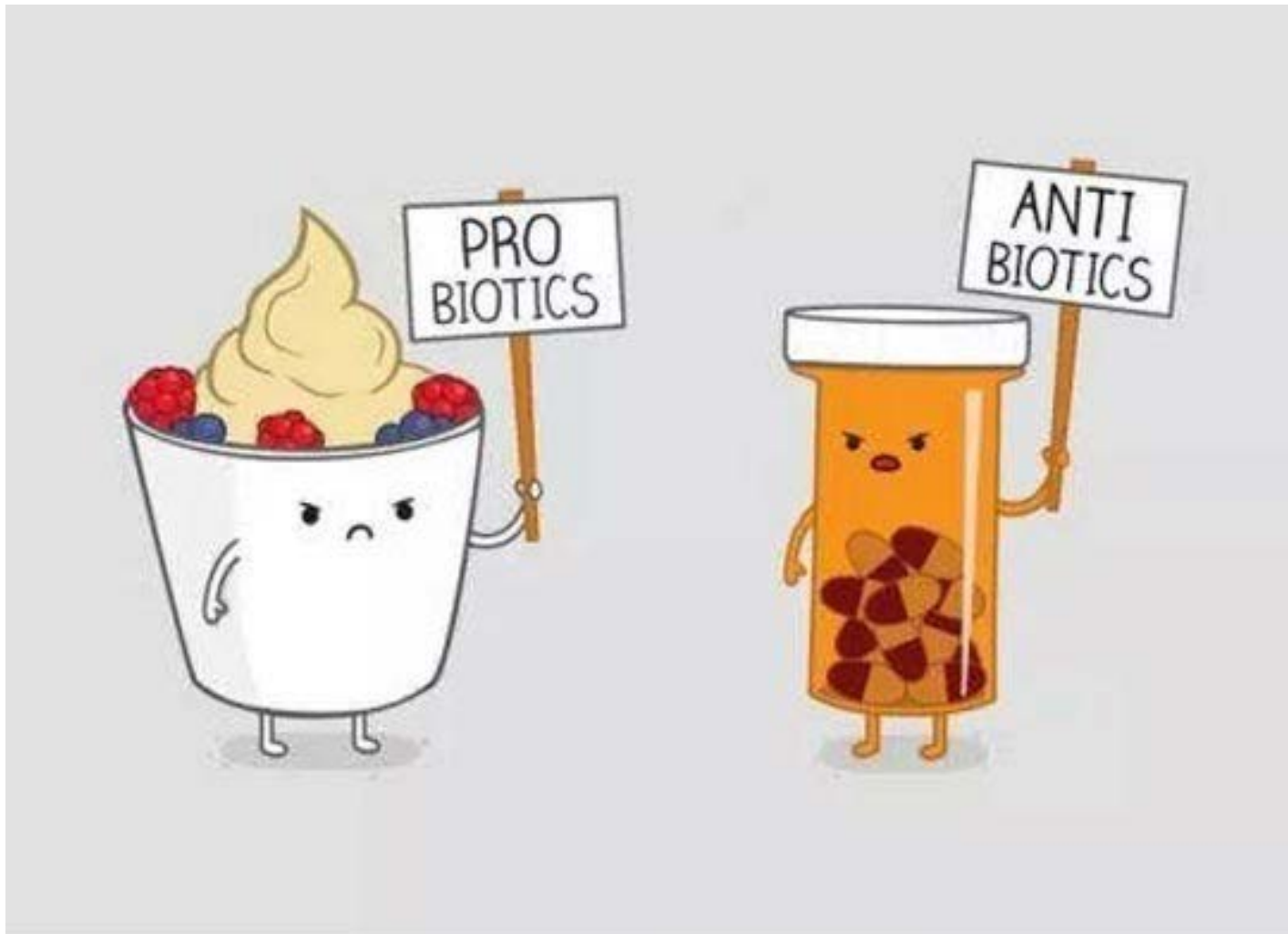
Summary



Future Studies

- Determine interventions to modulate breast tumor microbiota
 - Dietary intervention: Piggybacking off of Dr. Kucera and Dr. Levine's Breast Cancer Fish Oil Study funded by AICR
 - Determine timeline for oral consumption modifying breast microbiome
 - 2.5 years versus 2 weeks
 - Determine whether single component can shift breast microbiome
 - Dietary pattern vs supplements
- Mammary gland microbiota shifts in response to therapy
 - Menopause, antiestrogen therapies, hormone replacement therapy
 - Can we use mammary gland microbiota as biomarkers of tamoxifen response in postmenopausal women on antiestrogen therapies for breast cancer prevention?

Questions?



Acknowledgements:

Cook Group:

Technicians:

Adam Wilson

Kenysha Clear

Graduate Students:

Alaa Bawaneh (IPP)

Tiffany Newman (MCB)

Yismeilin Feliz-Mosquea (IPP)

Wake Forest Collaborators:

Dr. Akiko Chiba

Dr. Carol Shively

Dr. Janet Tooze

Dr. David Soto-Pantoja

Dr. Ann Tallant

Dr. Peg Gallagher

PRIME Postdoctoral fellows:

Dr. Manuel Ramirez

Funding:

