

## Intrinsically Connected: Prebiotics and Metabolic Function

Against the Grain: Innovative Foods/Ingredients with Prebiotic Activity for Supporting Cardiometabolic Health by Tiffany Weir



### Against the Grain: Innovative Foods/Ingredients with Prebiotic Activity for Supporting Cardiometabolic Health

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Dr. Valerie Stull



Dr. Chris Gentile



## Interception versus Therapeutic Models

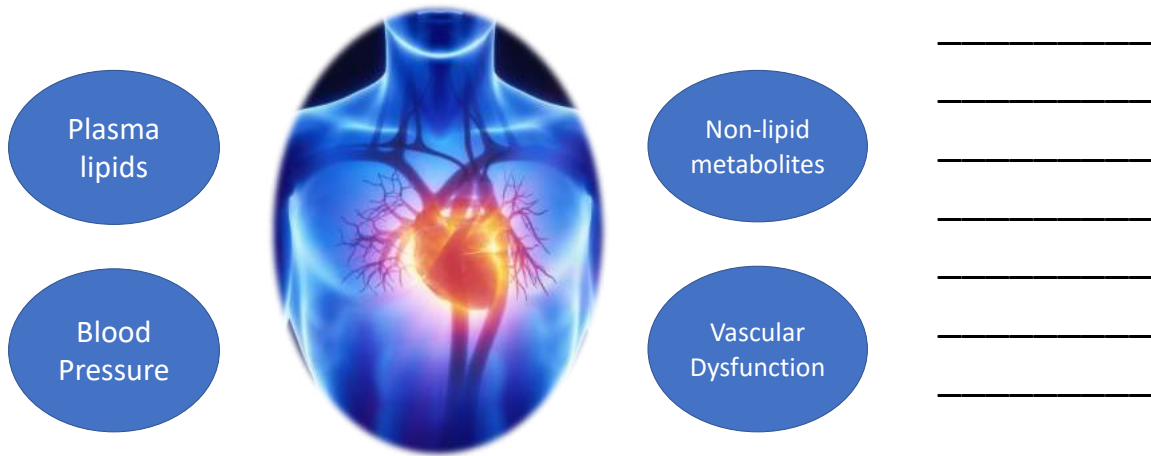
- No symptoms of disease.
- Detection of a **medical biomarker** that is a strong predictor of future disease
- Treatment is based on biomarker detection



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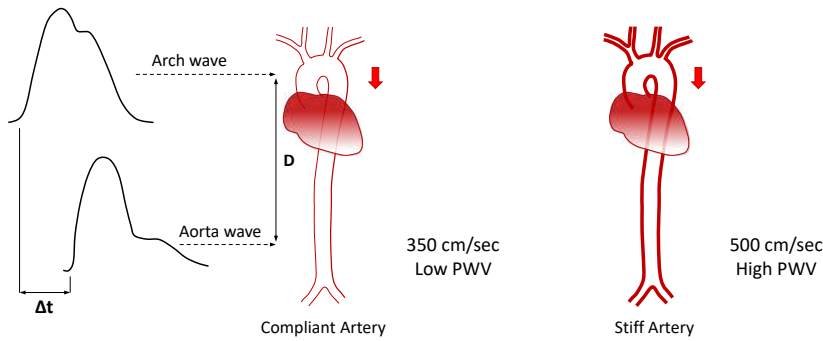
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## Case Study: Cardiovascular Disease

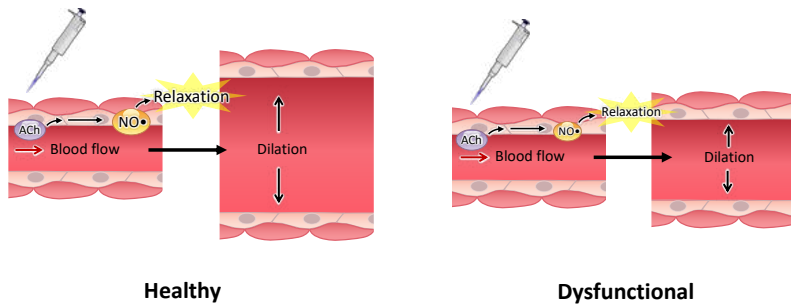


### Arterial Stiffness: Pulse Wave Velocity (PWV)

the speed at which the pulse wave travels through the blood vessels



## Endothelial Function



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## Prebiotics for Vascular Health: Case Studies



## Blueberry Polyphenols as Prebiotics



> J Nutr. 2018 Feb 1;148(2):209-219. doi: 10.1093/ntr/nwz027.

### Blueberry Supplementation Influences the Gut Microbiota, Inflammation, and Insulin Resistance in High-Fat-Diet-Fed Rats

Sunhye Lee<sup>1</sup>, Katherine I Kainer<sup>2</sup>, Rebecca Kridand<sup>3</sup>, Zachary J Grunwald<sup>4</sup>, Joan G Fischer<sup>5</sup>, Claire B de La Serre<sup>1</sup>

> PLoS One. 2013; 18(8):e67407. doi: 10.1371/journal.pone.0067407. Print 2013.

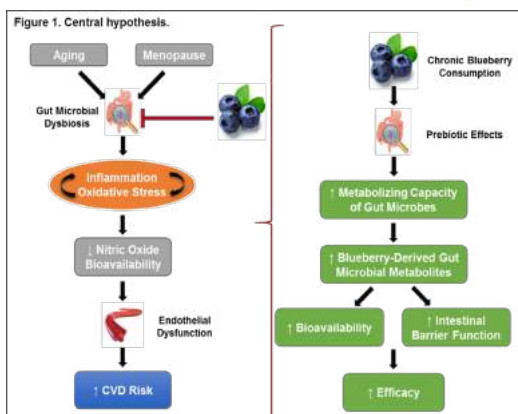
### Lowbush wild blueberries have the potential to modify gut microbiota and xenobiotic metabolism in the rat colon

Alison Lacombe<sup>1</sup>, Robert W Li, Dorothy Klima-Zacas, Aleksandra S Krista, Shweta Todopoli, Emily Kozak, Ryan Young, Vivian C H Wu

Randomized Controlled Trial > J Agric Food Chem. 2013 Aug 28;61(34):8134-40. doi: 10.1021/jf402495k. Epub 2013 Aug 19.

### Differential modulation of human intestinal bifidobacterium populations after consumption of a wild blueberry (*Vaccinium angustifolium*) drink

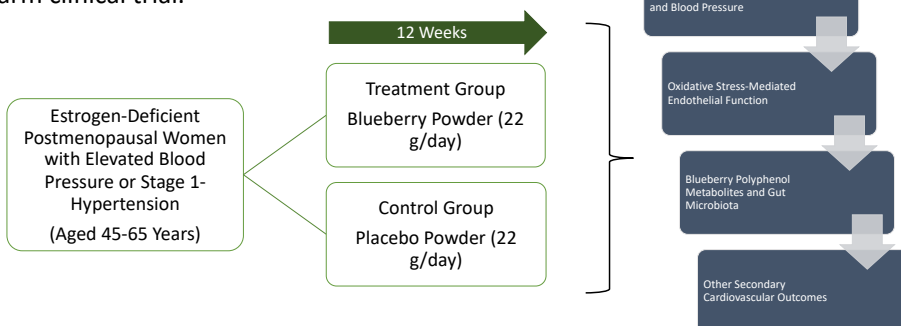
Simone Guglielmetti<sup>1</sup>, Daniela Fracassetti, Valentina Taverniti, Cristian Del Bo<sup>2</sup>, Stefano Vendrame, Dorothy Klima-Zacas, Stefania Arioli, Patrizia Rast, Maria Porri



## Blueberry Consumption for Improving Vascular Endothelial Dysfunction in Postmenopausal Women with Above-Normal Blood Pressure



- Randomized, double-blind, placebo-controlled, parallel-arm clinical trial.



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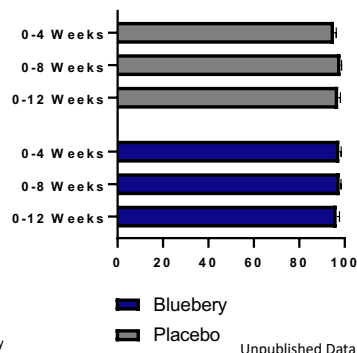
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## Participants & Compliance

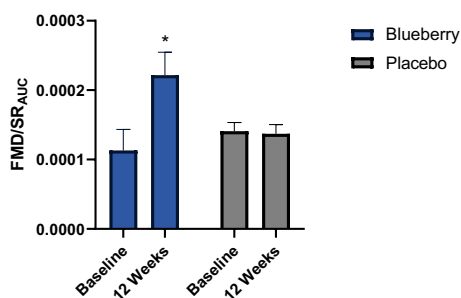
Variable	Blueberry (n=22)	Placebo (n=21)
Age (years)	60±1	61±1
Years After Menopause	10±1	10±2
Estradiol (pg/mL)	16.8±0.9	17.3±1.1
FSH (mIU/mL)	67.7±5.3	66.2±5.2
BMI (kg/m <sup>2</sup> )	27.6±1.0	27.7±1.1
WC:HC	0.84±0.02	0.82±0.01
SBP (mmHg)	134±3	131±2
DBP (mmHg)	80±2	78±1
TG (mg/dL)	118±11	114±14
HDL-C (mg/dL)	58±3	59±3
LDL-C (mg/dL)	132±5	139±5

Data are mean ± SEM. FSH, follicle-stimulating hormone; BMI, body mass index; WC:HC, waist circumference; hip circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol.

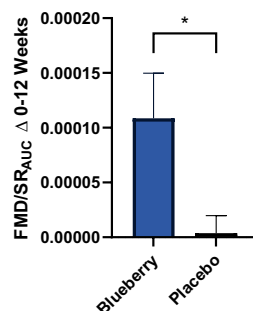
### % Compliance



## Blueberries Improve Endothelial Function

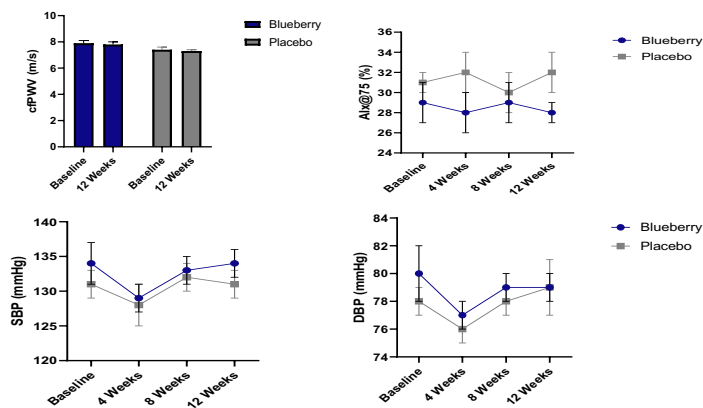


Values are mean ± SEM adjusted for age, BMI, years since menopause, hypertension stage, and hypertensive medication use. \*P<0.05 compared to baseline. FMD/SRAUC, flow-mediated dilation normalized to shear rate area under the curve.



Values are mean ± SEM adjusted for age, BMI, years since menopause, hypertension stage, and hypertensive medication use. \*P<0.05 between groups.

## No Effect on Central Arterial Stiffness, Blood Pressure



Values are mean ± SEM adjusted for age, BMI, years since menopause, hypertension stage, and hypertensive medication use. cPWV, carotid-femoral pulse wave velocity; AIx@75, augmentation index normalized to heart rate of 75 beats per minute.

Unpublished Data

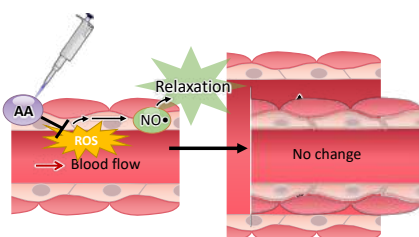
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## Assessing the Influence of Blueberries on Vascular Oxidative Stress



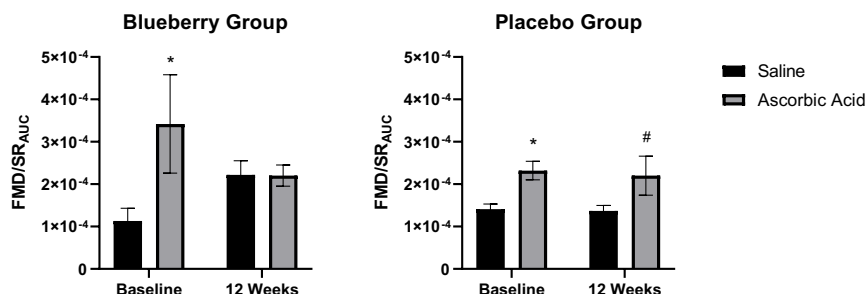
- Determined by measuring FMD post-intravenous infusion of supraphysiologic dose of ascorbic acid versus isovolemic saline control.



Treatment effects mediated through reductions in oxidative stress

Oxidative stress-mediated endothelial dysfunction

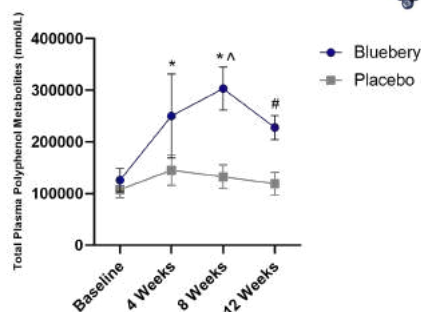
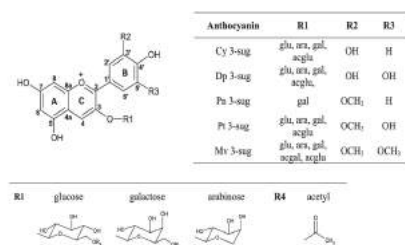
## Blueberries ↓ Oxidative Stress-Mediated Endothelial Dysfunction



Values are mean ± SEM adjusted for age, BMI, years since menopause, hypertension stage, and hypertensive medication use. \*P<0.05 vs. saline infusion; #P<0.1 vs. saline infusion. FMD/SR\_AUC, flow-mediated dilation normalized to, shear rate area under the curve.

Unpublished Data

## Polyphenol Metabolites Increase with Blueberry Consumption



Values are mean ± SEM adjusted for age, BMI, years since menopause, hypertension stage, and hypertensive medication use. \*P<0.05 compared to baseline. #P=0.06 compared to baseline. ^P<0.05 compared to placebo. Assessed using mass spectrometry. The sum of polyphenol metabolites assessed were summed for each individual.

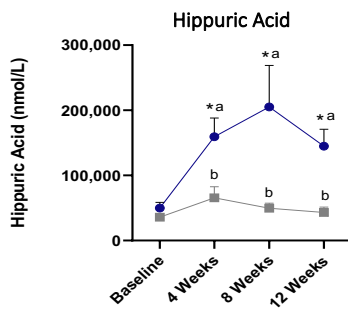
Unpublished Data



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## Increased Microbial Metabolites of Polyphenols Indicate Enriched Polyphenol-Associated Enzyme (PAZ-yme) Activity



Blueberry  
Placebo



Sci Rep. 2017; 7: 13670.

Published online 2017 Oct 20; doi:10.1038/s41598-017-13722-5

PMCID: PMC5651863

PMID: 29057086

Hippurate as a metabolomic marker of gut microbiome diversity: Modulation by diet and relationship to metabolic syndrome

Tessa Palmiter,<sup>1</sup> Matthew A. Jackson,<sup>1</sup> Tishana C. Martin,<sup>1</sup> Jonas Ziere,<sup>1,2</sup> Amy Jennings,<sup>3</sup> Robert P. Mohney,<sup>4</sup> Alexander MacGowan,<sup>5</sup> Claire J. Steves,<sup>1</sup> Aedin Cassidy,<sup>3</sup> Tim D. Spector,<sup>1</sup> and Cristina Meoni<sup>6</sup>

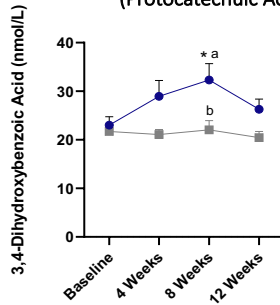
Values are mean  $\pm$  SEM adjusted for age, BMI, years since menopause, hypertension stage, and hypertensive medication use. \* $P < 0.05$  compared to baseline. Different letters indicate significant ( $P < 0.05$ ) differences between groups at that time point.

Unpublished Data

## Increased Microbial Metabolites of Polyphenols Indicate Enriched Polyphenol-Associated Enzyme (PAZ-yme) Activity

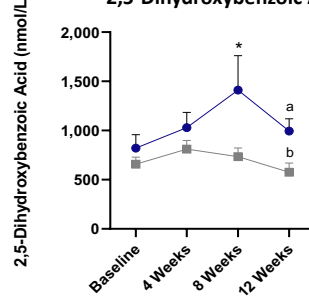


3,4-Dihydroxybenzoic Acid (Protocatechuic Acid)



Blueberry  
Placebo

2,5-Dihydroxybenzoic Acid



Blueberry  
Placebo

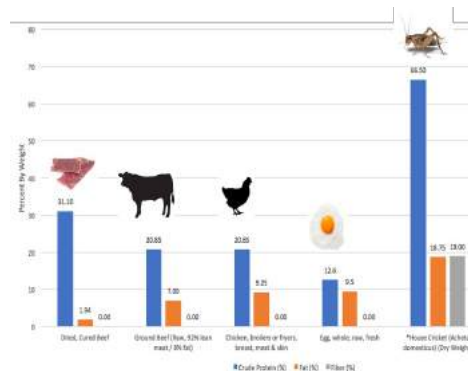
Values are mean  $\pm$  SEM adjusted for age, BMI, years since menopause, hypertension stage, and hypertensive medication use. \* $P < 0.05$  compared to baseline. Different letters indicate significant ( $P < 0.05$ ) differences between groups at that time point.

Unpublished Data

## Nutritional Benefits of Edible Insects



- More than 2 Billion people worldwide consume insects.
  - >1,000 species consumed
- Sustainability factors
  - Require less land, water, and food
  - 7-8 weeks to maturity
  - Produce fewer greenhouse gases



Rumpold & Schluter, 2013a; Ramos-Elorduy Blasquez et al., 2012a; Ramos-Elorduy et al., 2007a; Finke, 2002a; Entomo Farms; Finke 2005.; USDA, 2016 National Nutrient Database

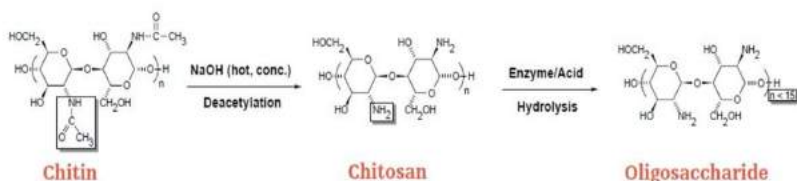
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## Can Insect Chitin Act as a Prebiotic?



English name	Latin name	Stage	Fiber content (% in dry matter)
African migratory locust*	<i>Locusta migratoria</i>	Nymph	27
Jamaican field cricket*	<i>Gryllus assimilis</i>	Nymph	8
Yellow mealworm*	<i>Tenebrio molitor</i>	Larva	18
House Cricket <sup>a</sup>	<i>Acheta domesticus</i>	Adult	16.35 – 22.08
Banded Cricket <sup>b</sup>	<i>Gryllobates sigillatus</i>	Adult	8.33

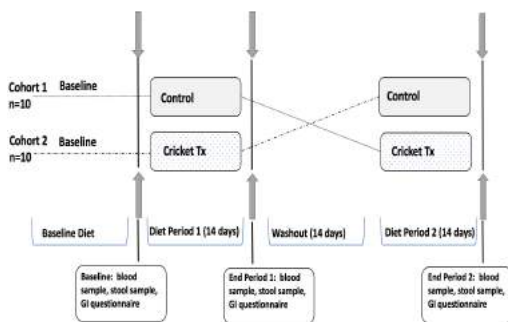


\*Slide by V. Stull- Univ. Wisc. Bednarova, 2013; <sup>a</sup>Ramos-Elorua et al, 2007; Finke, 2002; <sup>b</sup>Entomo Farms; Stull et al, 2018

## What's Hopping? Impact of Cricket Consumption on the Gut Microbiota in Healthy Adults.



Randomized, double-blind, placebo-controlled, crossover dietary intervention.



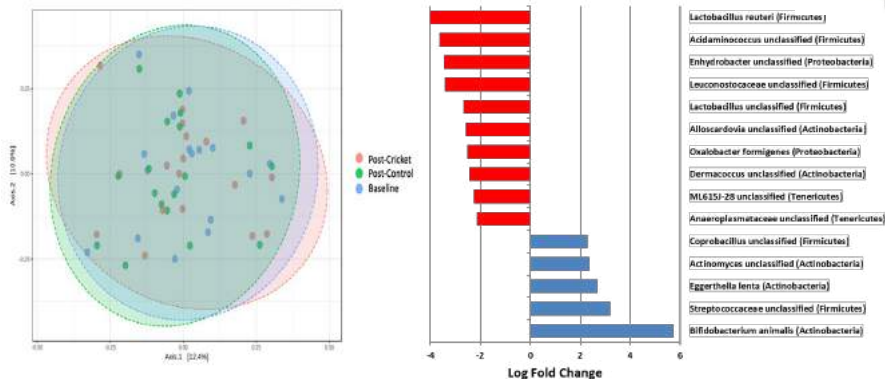
Characteristic	Value
Age (years)	26.45 ± 6.33
Sex	
Male (%)	9 (45%)
Female (%)	11 (55%)
BMI (kg/m <sup>2</sup> )	23.39 ± 2.46
Fasting blood glucose (U/L)	89.32 ± 6.94

Note: values presented as the mean ± the standard deviation

Nutrient Composition Prepared Breakfasts (values per serving: 1 shake, 2 muffins)		
Nutrient	CONTROL	CRICKET
Energy (kcal)	495.26	569.34
Total fat (g)	12.75	18.12
Total protein (g)	9.31	21.67
Total carbohydrate (g)	88.36	81.34
Sugars (g)	46.72	48.65
Total fiber (g)	5.35	5.57

Stull et al, 2018 *Scientific Reports*

## Cricket Powder Selectively Alters Gut Microbiota



\* We also observed cricket-associated decreases in TNF-α and increase in Alkaline Phosphatase

Stull et al, 2018 *Scientific Reports*

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## Chitin Derivatives Have Reported Cardioprotective Effects



[Oxid Med Cell Longev](#). 2019; 2019: 7658052.  
Published online 2019 Mar 10. doi: [10.1155/2019/7658052](#)

PMID: [30984339](#)

Chitosan Oligosaccharides Show Protective Effects in Coronary Heart Disease by Improving Antioxidant Capacity via the Increase in Intestinal Probiotics

Tiechao Jiang,<sup>1,2</sup> Xiaohong Xing,<sup>1</sup> Liang Zhang,<sup>3</sup> Zhen Liu,<sup>4</sup> Jixue Zhao,<sup>2,5</sup> and Xin Li<sup>2,6</sup>

## Chitin–glucan and pomegranate polyphenols improve endothelial dysfunction

Audrey M. Neyrinck, Emilie Catry, Bernard Taminiau, Patrice D. Cani, Laure B. Bindels, Georges Daube, Chantal Dessy & Nathalie M. Delzenne

[Scientific Reports](#) 9, Article number: 14150 (2019) | [Cite this article](#)

## Chitin–glucan supplementation improved postprandial metabolism and altered gut microbiota in subjects at cardiometabolic risk in a randomized trial

Harimalata Banerjee, Zhengqian Zhang, Maud Allinier, Laure Van Den Bergh, Monique Sothier, Stephanie Lambert-Derobert, Nathalie Faugier, Charlotte Guers, Christelle Macheson, Audrey M. Neyrinck, Benjamin Seathaler, Julie Rodriguez, Martin Beuermann, Giulio G. Mussioli, Veronique Maquet, Martine Lézelle, Stephen C. Bischoff, Jana Walter, Nathalie M. Delzenne & Julie-Anne Nazare

[Scientific Reports](#) 12, Article number: 8830 (2022) | [Cite this article](#)

## Additional Prebiotic Research Projects



Lutsiv T et al (2022) Relandscaping the gut microbiota with a whole food: dose response effects to common bean. *Foods* 11(8), 1153

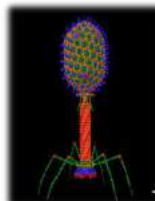
Lutsiv T et al (2021) Compositional Changes of the High-Fat Diet-Induced Gut Microbiota upon Consumption of Common Pulses. *Nutrients* 13 (11): 3992.



McGinley JN et al (2020) Pulse Crop Effects on the Gut Microbial Populations, Intestinal Function, and Adiposity in a Mouse Model of Dietary Induced Obesity. *Nutrients* 12:593

Neil E et al (2019) Common bean (*Phaseolus vulgaris* L.) consumption reduces fat accumulation in a polygenic mouse model of obesity. *Nutrients* doi: 10.3390/nu1112780

Sheflin AM et al (2016) Dietary Supplementation with Rice Bran or Navy Bean Alters Gut Bacterial Metabolism in Colorectal Cancer Survivors. *Mol Nutr Food Res*. 61(1).



Grubb DS et al. (2020) PHAGE-2 Study: Supplemental Bacteriophages Extend Bifidobacterium animalis subsp. lactis BL04 Benefits on Gut Health and Microbiota. *Nutrients* 12, 2474

Trotter RE et al (2020) Examining the Impact of Probiotic Supplement Intake on Endothelial Function and Lipid Metabolism in Healthy Adults. *Beneficial Microbes* 11 (7): 621-630.

Febvre HP et al (2019) PHAGE: Effects of bacteriophage consumption on gut microbiota, inflammation, and lipid metabolism. *Nutrients* 11 (3): 666.

Gindin M et al (2018) Bacteriophage for Gastrointestinal Health (PHAGE) Study: Evaluating the Safety and Tolerability of Supplemental Bacteriophage Consumption. *JACN* doi:10.1080/07315724.2018.1483783

