Sustainable foods for gastrointestinal health across the lifespan

Elizabeth P. Ryan
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College of Veterinary Medicine and Biomedical Sciences
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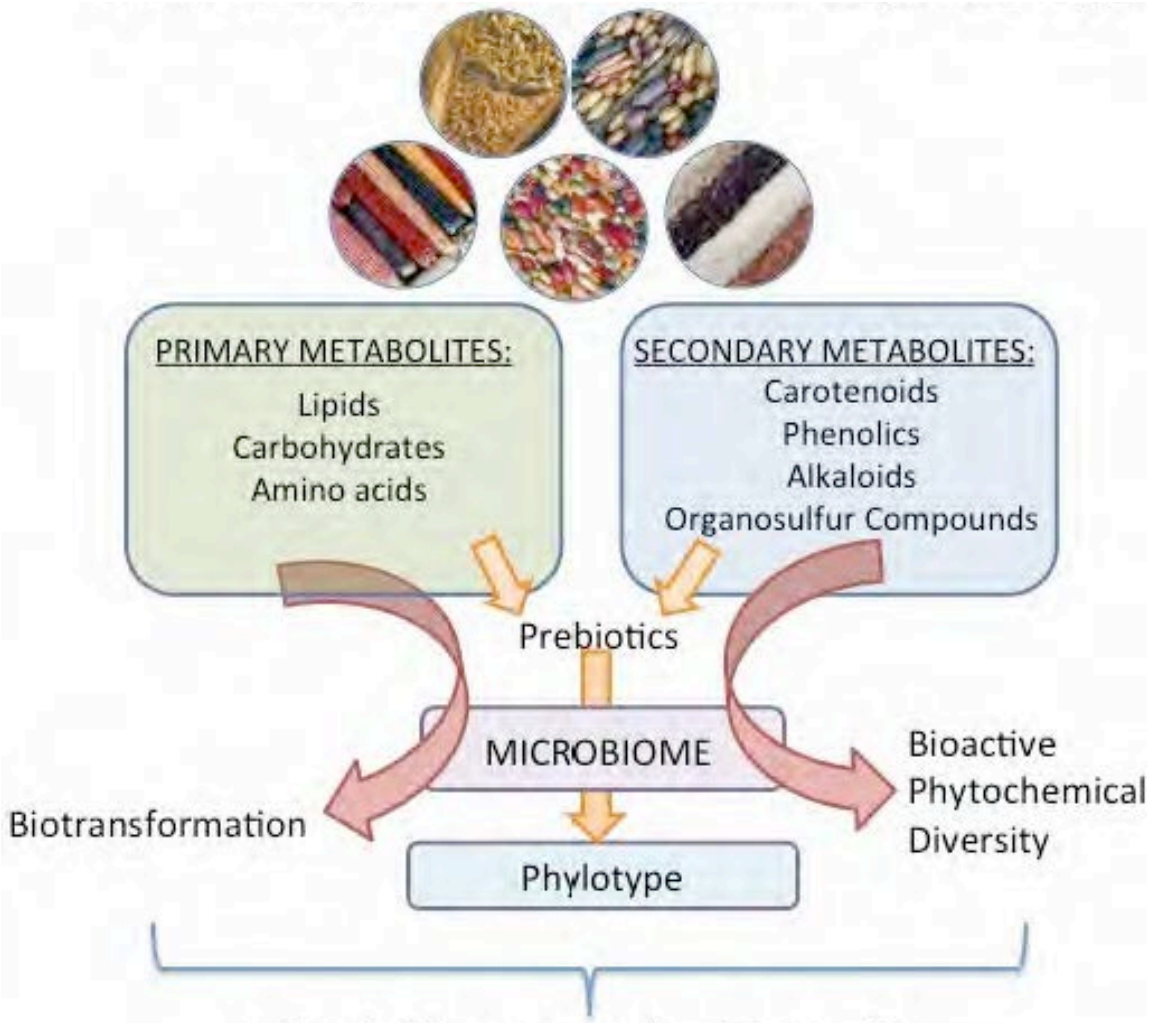
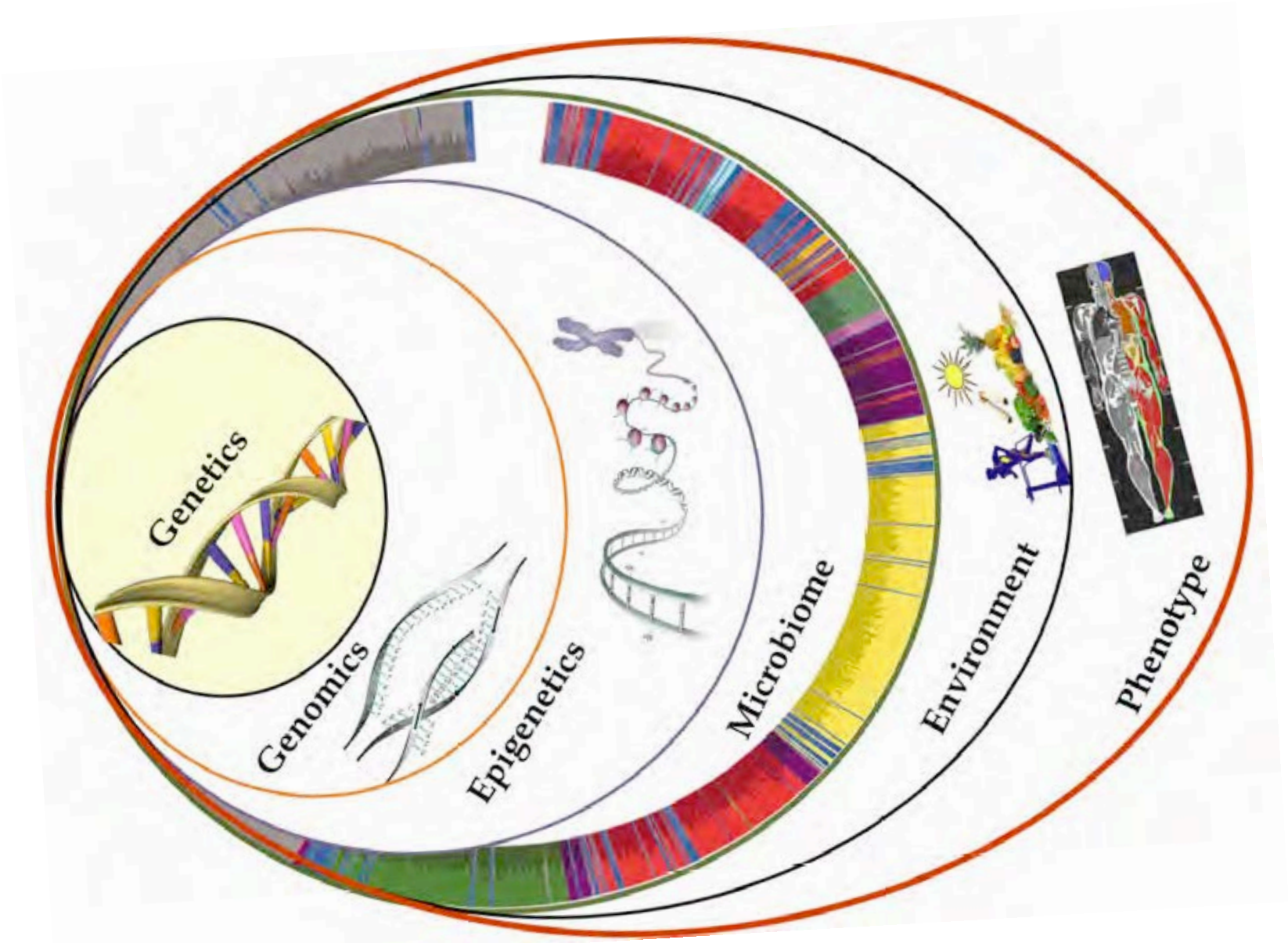
Microbiome mediated metabolism of whole foods and the components



Gastrointestinal Disease Control and Prevention

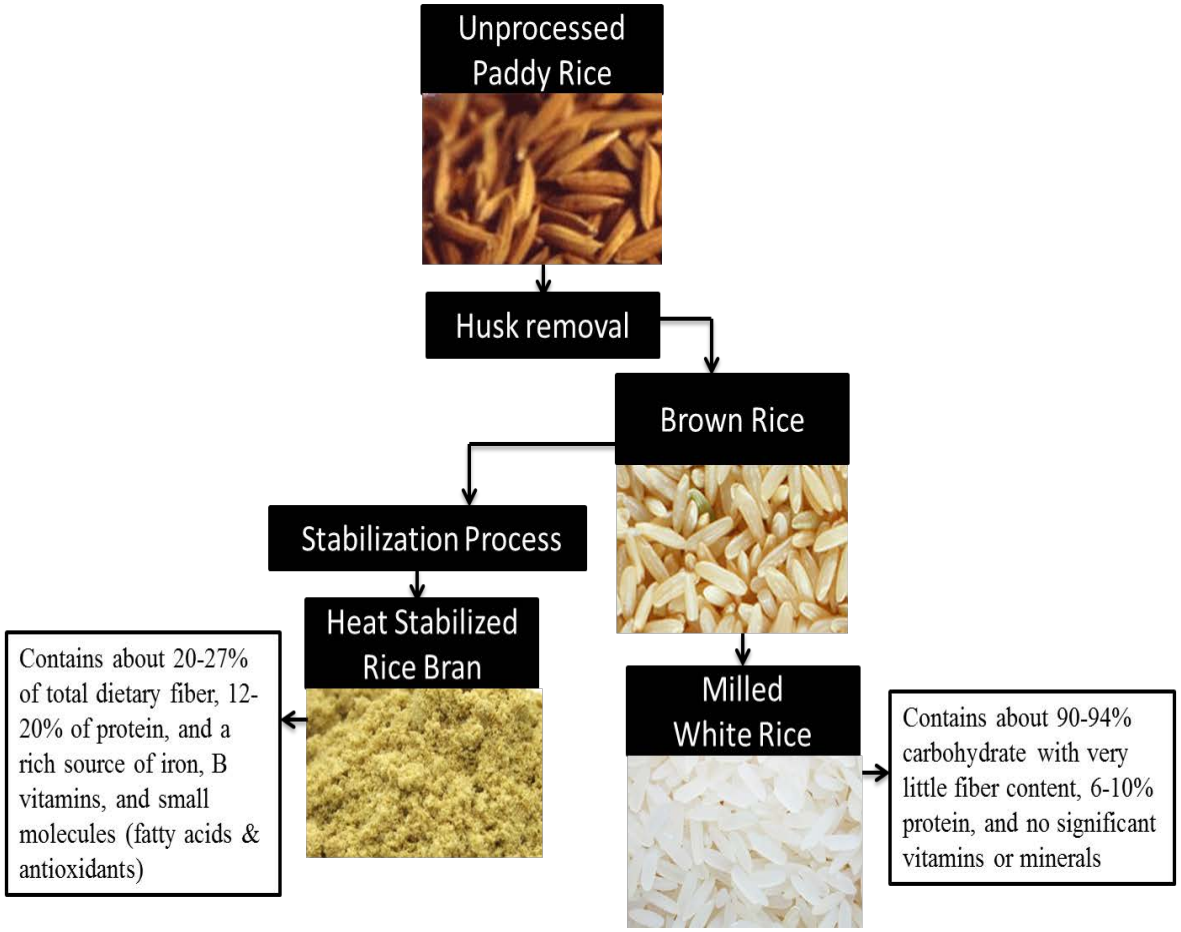
Daniell and Ryan (2012). The Nutrigenome and Gut Microbiome: Chronic Disease Prevention with Crop Phytochemical Diversity

Gut Health across the lifespan



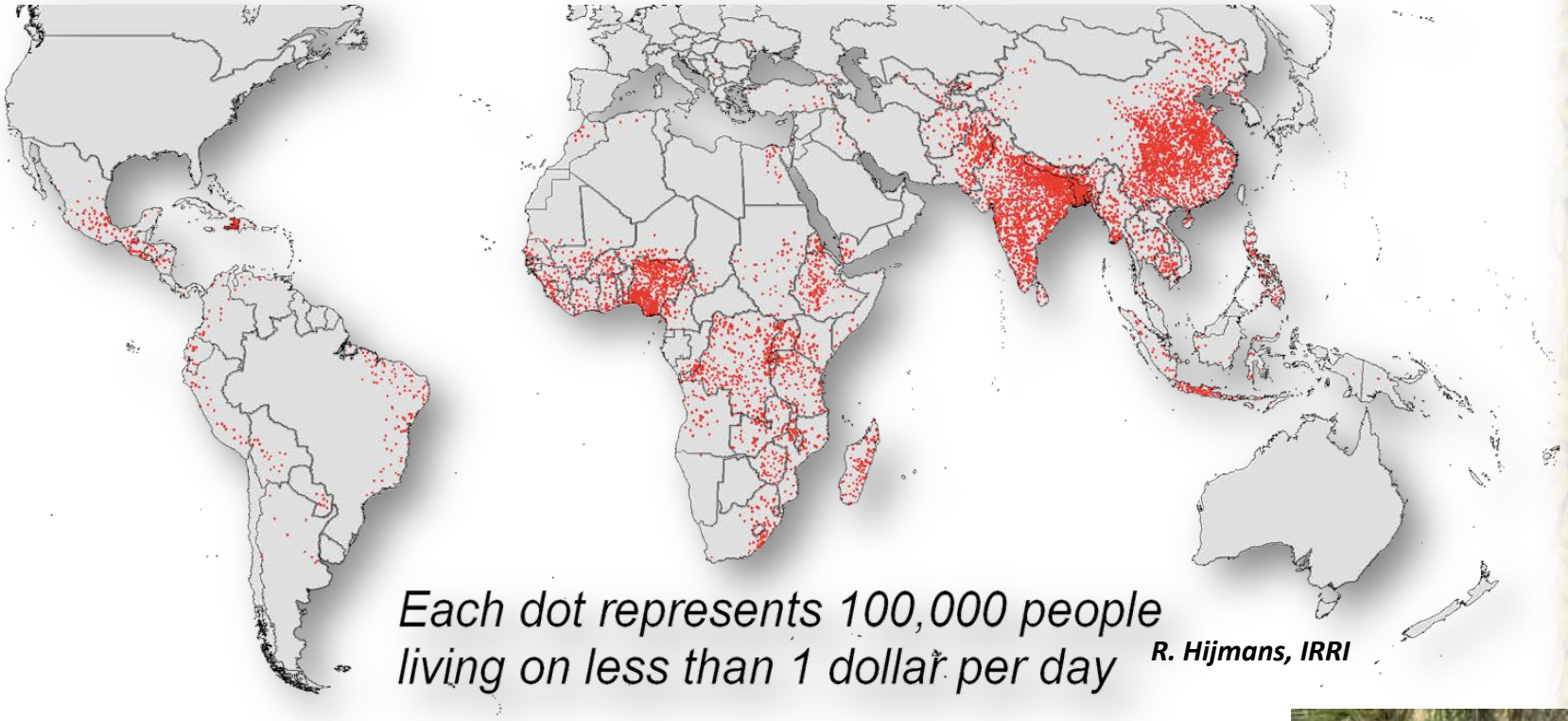
Daniell and Ryan (2012). The Nutrigenome and Gut Microbiome: Chronic Disease Prevention with Crop Phytochemical Diversity

Rice bran: an agricultural by-product of whole grain rice



Borresen, E.C. and Ryan, E.P. Rice Bran: A food ingredient with global public health opportunity (2014)

Nearly half of the people in the world eat rice



- many live in rice-producing areas where malnutrition and diarrheal diseases are prevalent and chronic diseases are on the rise.

Rice Bran (1g)

Fat (0.21g)

Saturated (g)	0.04
Monounsaturated (g)	0.08
Polyunsaturated (g)	0.07
MFA 18:1, Oleic (g)	0.07
PFA 18:2, Linoleic (g)	0.07

Protein (0.13g)

Essential Amino Acids (mg)

Histidine	3.55
Isoleucine	5.68
Leucine	10.2
Lysine	6.5
Methionine	3.06
Cystine	3.17
Phenylalanine	6.35
Tyrosine	4.11
Threonine	5.55
Tryptophan	1.08
Valine	8.81

Non-Essential Amino Acids (mg)

Alanine	9.7
Aspartic Acid	13.08
Glutamic Acid	18.54
Glycine	8.75
Proline	6.68
Serine	6.62
Arginine	10.58

CHO (0.50g)

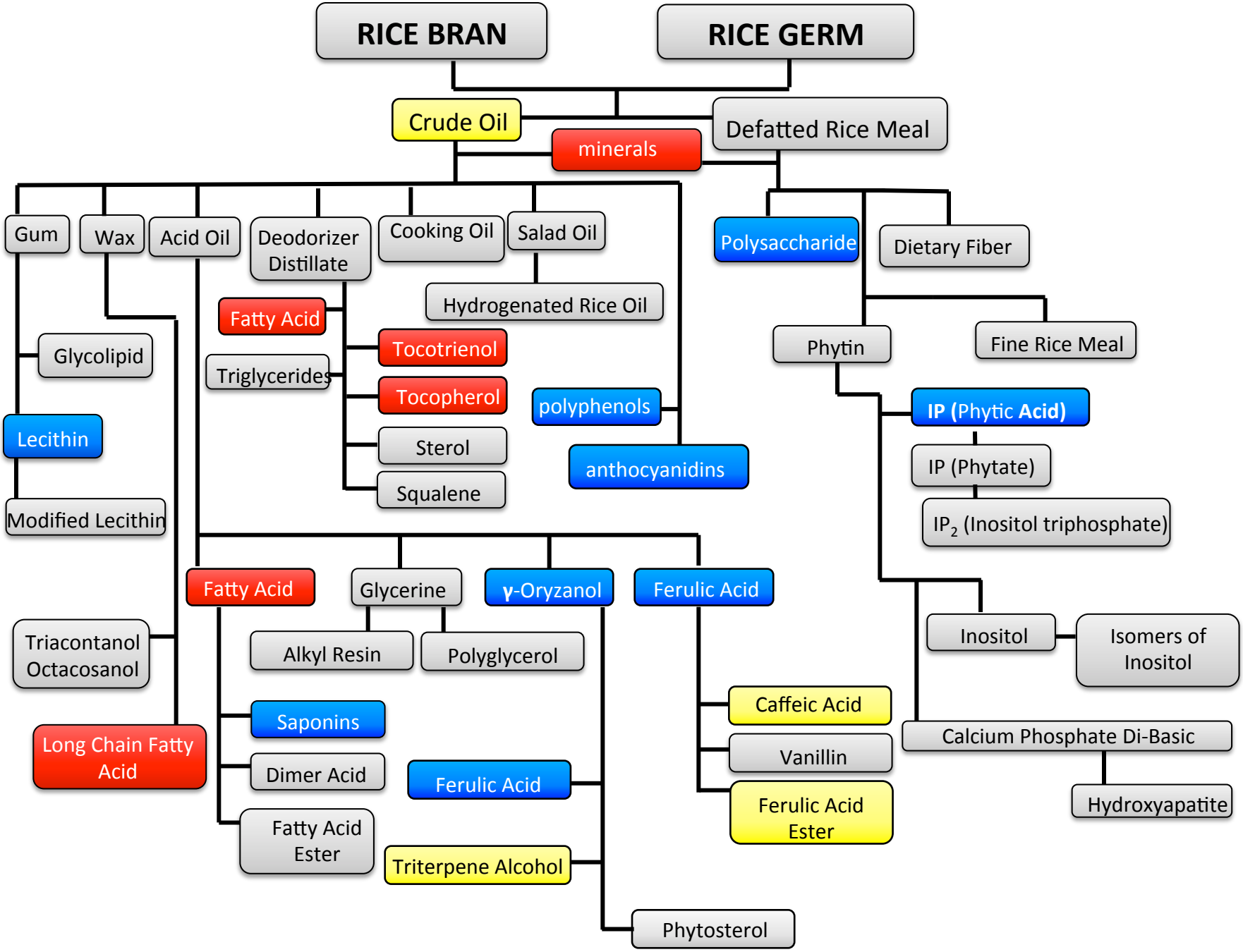
Dietary Fiber, Total (g)	0.21
Crude Fiber (g)	0.06
Sugar, Total (g)	0.01
Sucrose (g)	0.01

Ash (0.10g)

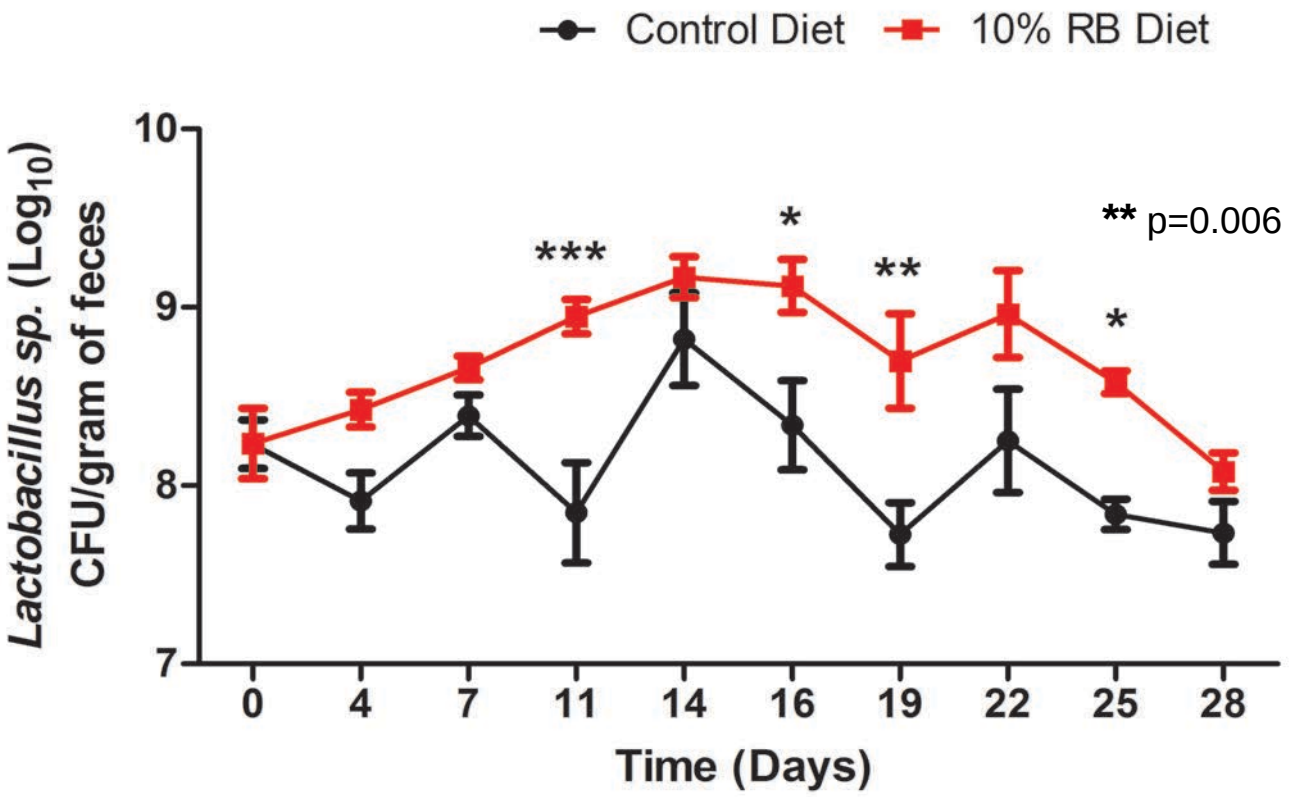
Sodium (mg)	0.05
Potassium (mg)	14.9
Phosphorus (mg)	16.8
Magnesium (mg)	7.81
Selenium (µg)	0.16
Calcium (mg)	0.57
Iron (mg)	0.19

Vitamins

Alpha-Tocopherol (mg)	0.05
Thiamin (mg)	0.03
Niacin (mg)	0.34
Pyridoxine (vitamin B6) (mg)	0.04
Folate (total) (µg)	0.63
Folate (DFE) (µg)	0.63
Pantothenic Acid (mg)	0.07
Vitamin K (µg)	0.02


RICE BRAN
RICE GERM
Crude Oil
Defatted Rice Meal
minerals
Gum
Wax
Acid Oil
Deodorizer Distillate
Cooking Oil
Salad Oil
Polysaccharide
Dietary Fiber
Hydrogenated Rice Oil
Fatty Acid
Tocotrienol
Tocopherol
Sterol
Squalene
Triglycerides
Glycolipid
Lecithin
Modified Lecithin
polyphenols
anthocyanidins
Phytin
Fine Rice Meal
IP (Phytic Acid)
IP (Phytate)
IP2 (Inositol triphosphate)
Fatty Acid
Glycerine
γ-Oryzanol
Ferulic Acid
Triacontanol Octacosanol
Alkyl Resin
Polyglycerol
Inositol
Isomers of Inositol
Saponins
Long Chain Fatty Acid
Dimer Acid
Fatty Acid Ester
Ferulic Acid
Triterpene Alcohol
Phytosterol
Caffeic Acid
Vanillin
Ferulic Acid Ester
Calcium Phosphate Di-Basic
Hydroxyapatite

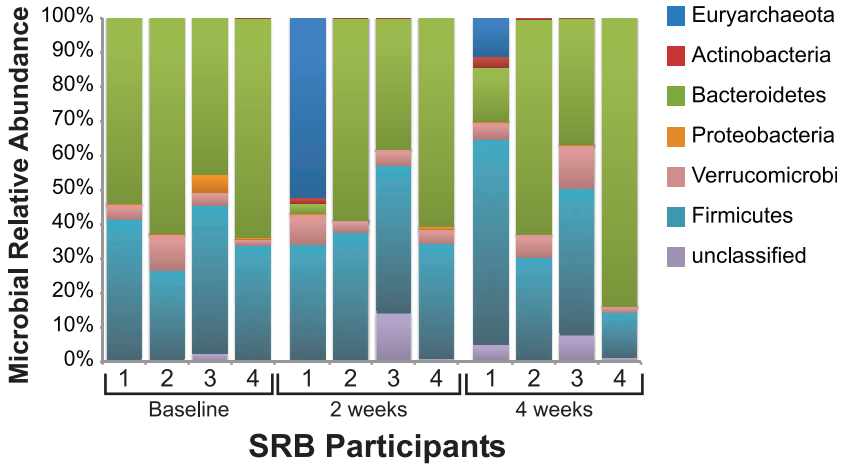
Rice Bran promotes Growth and Colonization of Fecal *Lactobacilli* in vivo

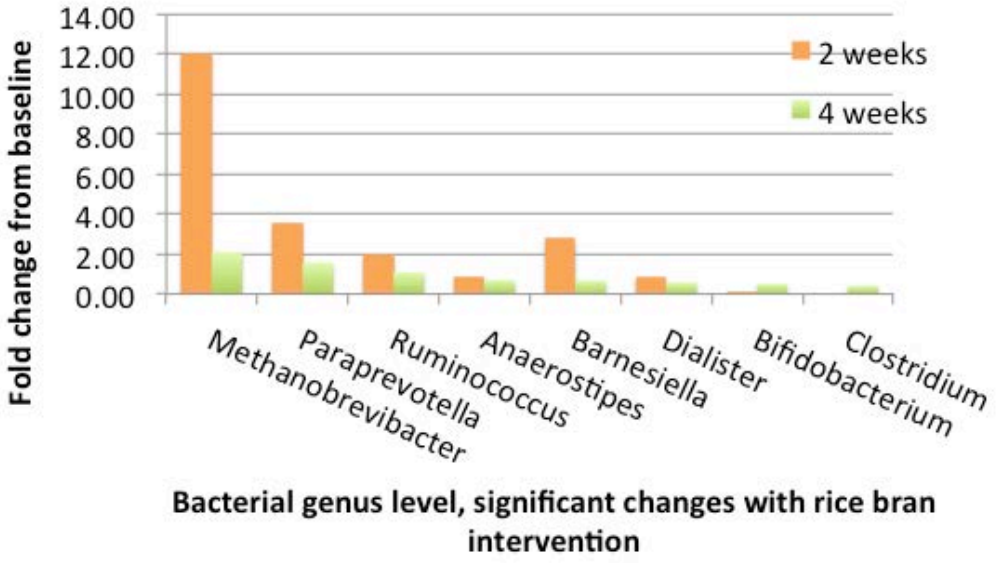


Henderson et. al. Journal of Medicinal Food. 2011
Kumar et. al. BMC Microbiology. 2012

Rice bran modulation of Gut microbes in healthy adults

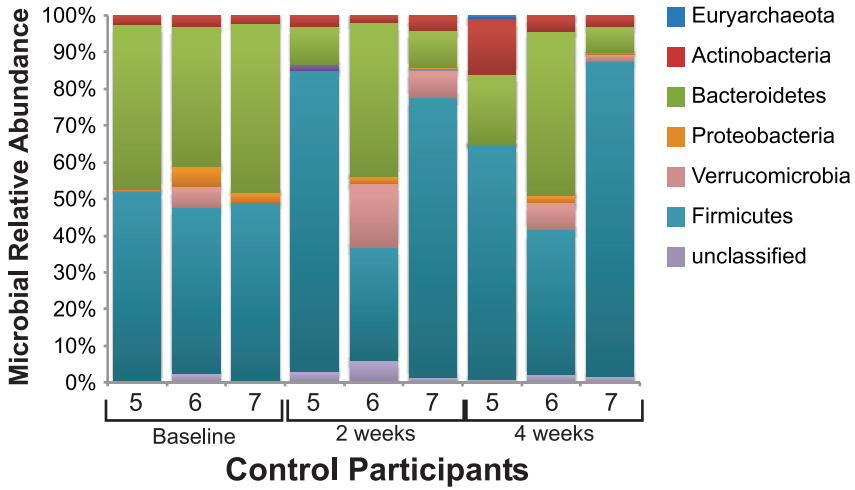
a)





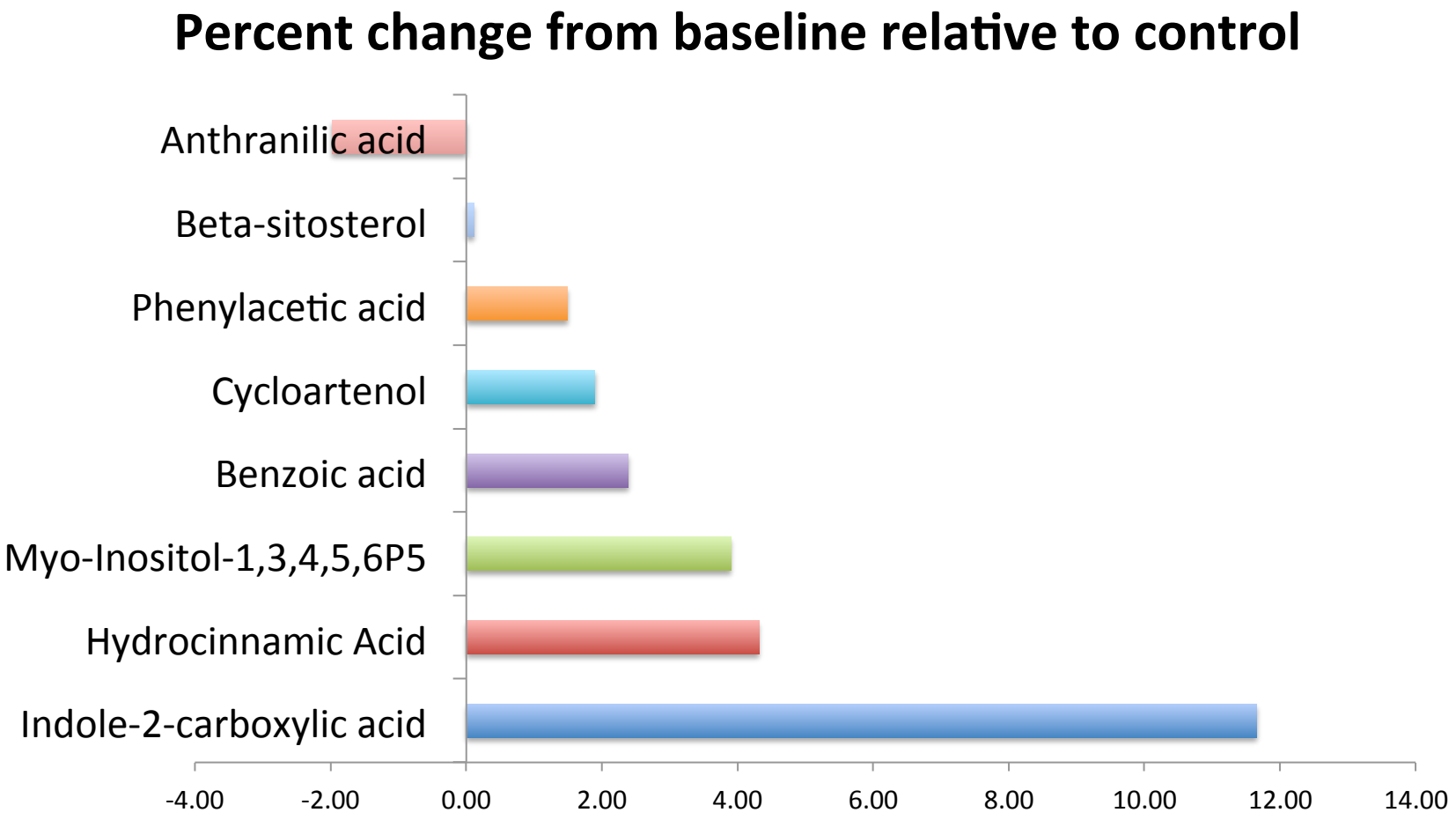
Bacterial genus level, significant changes with rice bran intervention

b)



Sheflin et. al, 2015. Pilot Dietary Intervention with Heat-Stabilized Rice Bran Modulates Stool Microbiota and Metabolites in Healthy Adults . Nutrients 7, 1282-1300

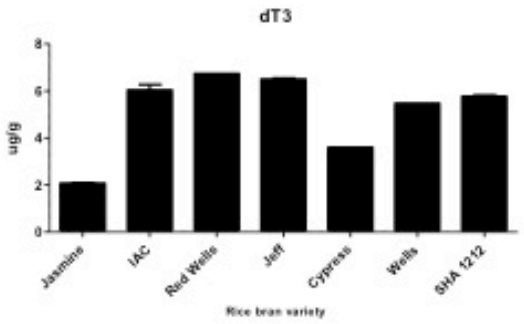
Changes in the Stool Metabolome Following 30g/day of Rice Bran Intake

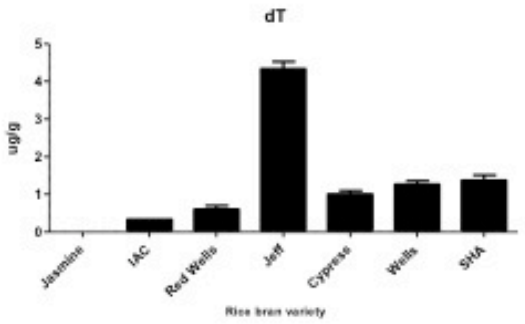


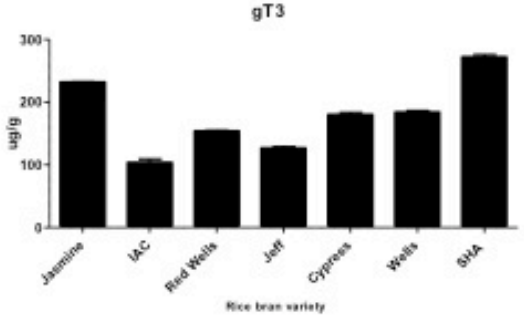
Sheflin et. al, 2015. Pilot Dietary Intervention with Heat-Stabilized Rice Bran Modulates Stool Microbiota and Metabolites in Healthy Adults . Nutrients 7, 1282-1300

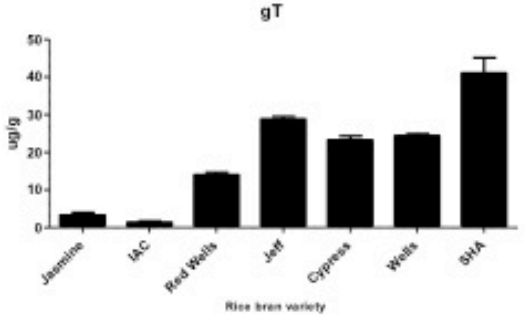
Ryan EP, Bioactive Food Components in Rice Bran, JAVMA 2011

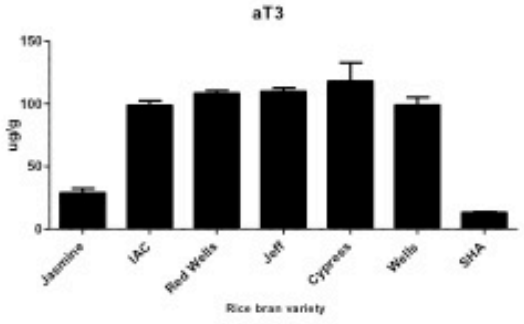
Rice Varietal Differences in Tocotrienol and Tocopherol Contents

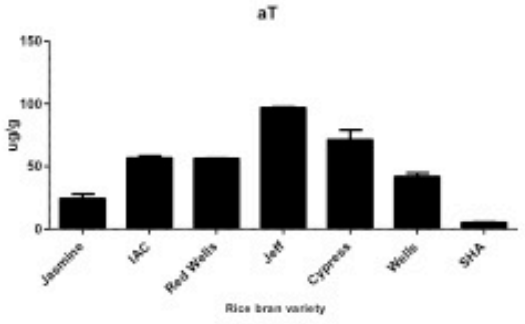






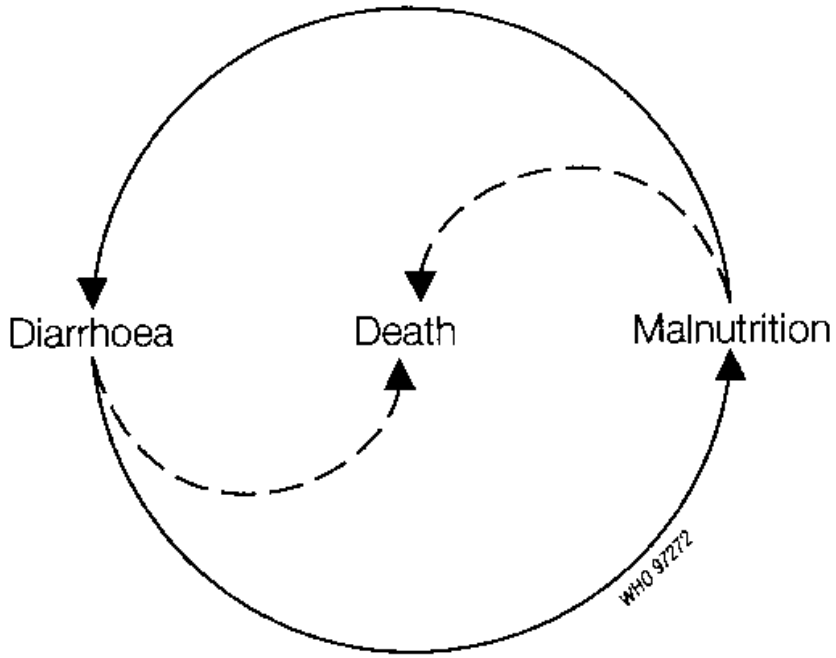






Forster GM, Raina K, Kumar A, Kumar S, Agarwal R, Chen MH, Bauer JE, McClung AM, **Ryan EP. Rice varietal differences in bioactive bran components for inhibition of colorectal cancer cell growth.** Food Chemistry 2013 Nov 15;141(2):1545-5

The Vicious Cycle Between Enteric/Diarrheal Disease and Malnutrition



The need for novel and rapidly achievable intervention strategies remains high, and should address enteric dysfunction, impaired gut mucosal immunity AND malnutrition.

Enteric Pathogens Implicated in Diarrheal Disease

Small bowel and colonic pathogens

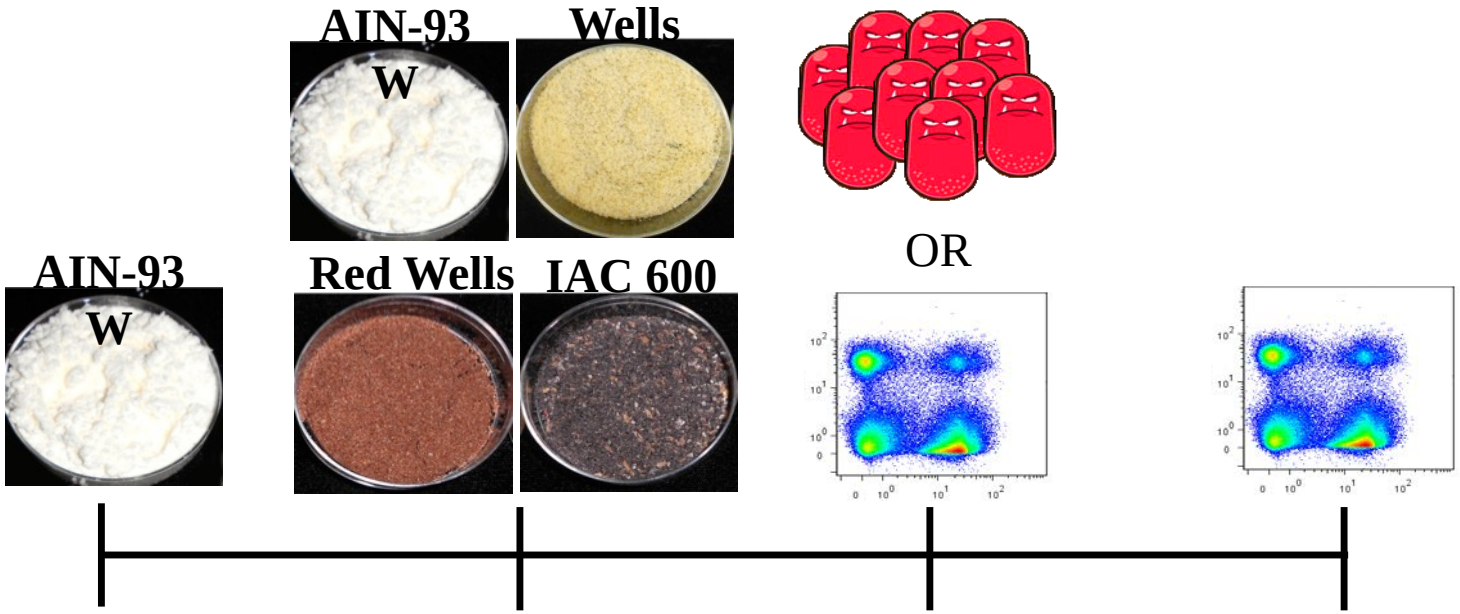
Pathogen	Small bowel	Colon
Bacteria	Salmonella Escherichia coli Clostridium perfringens Staphylococcus aureus Aeromonas hydrophila Bacillus cereus Vibrio cholerae	Campylobacter Shigella Clostridium difficile Yersinia Vibrio parahaemolyticus Enteroinvasive E. coli Klebsiella oxytoca (rare)
Virus	Rotavirus Norovirus	Cytomegalovirus Adenovirus Herpes simplex virus
Protozoa	Cryptosporidium Microsporidium Isospora Cyclospora Giardia lamblia	Entamoeba histolytica

Overarching Hypothesis:

Rice bran contains bioactive phytochemicals that when converted during digestion by gastrointestinal microflora, modulate gut mucosal immunity for protection against gut pathogens.

Rice Bran phytochemical contents differ in health properties and efficacy varies across genetically diverse cultivars

Experimental Design to Assess Dietary Rice Bran Effects on Gut Mucosal Immunity and Salmonella Fecal Shedding in mice



Day -14
All 129SvEv mice fed AIN-93 W control diet.

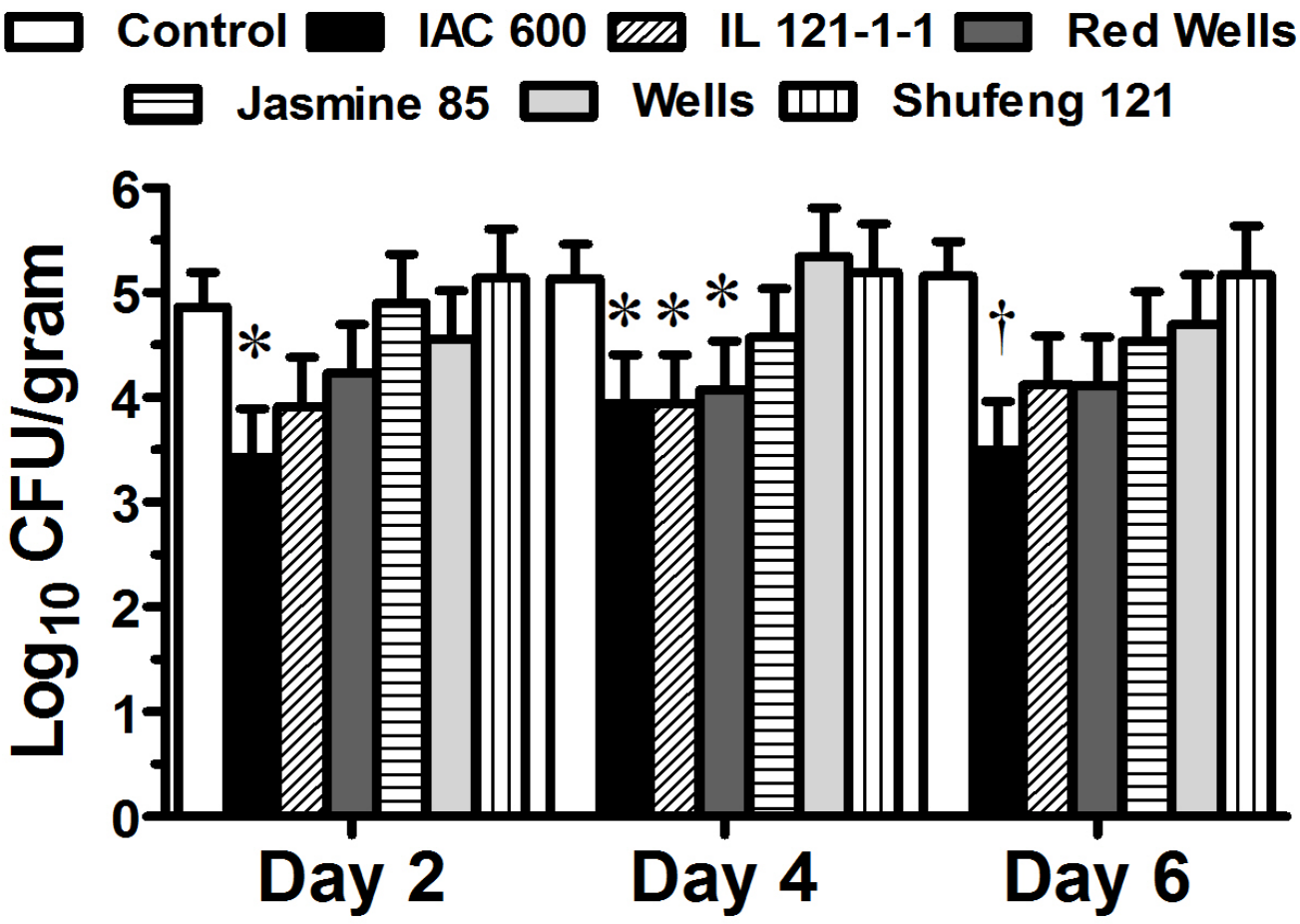
Day -7
10% rice bran (Wells, Red Wells or IAC 600 variety) or left as AIN-93 W control diet.

Day 0
Infect mice orally with 2×10^7 CFU *Salmonella enterica* 14028s.

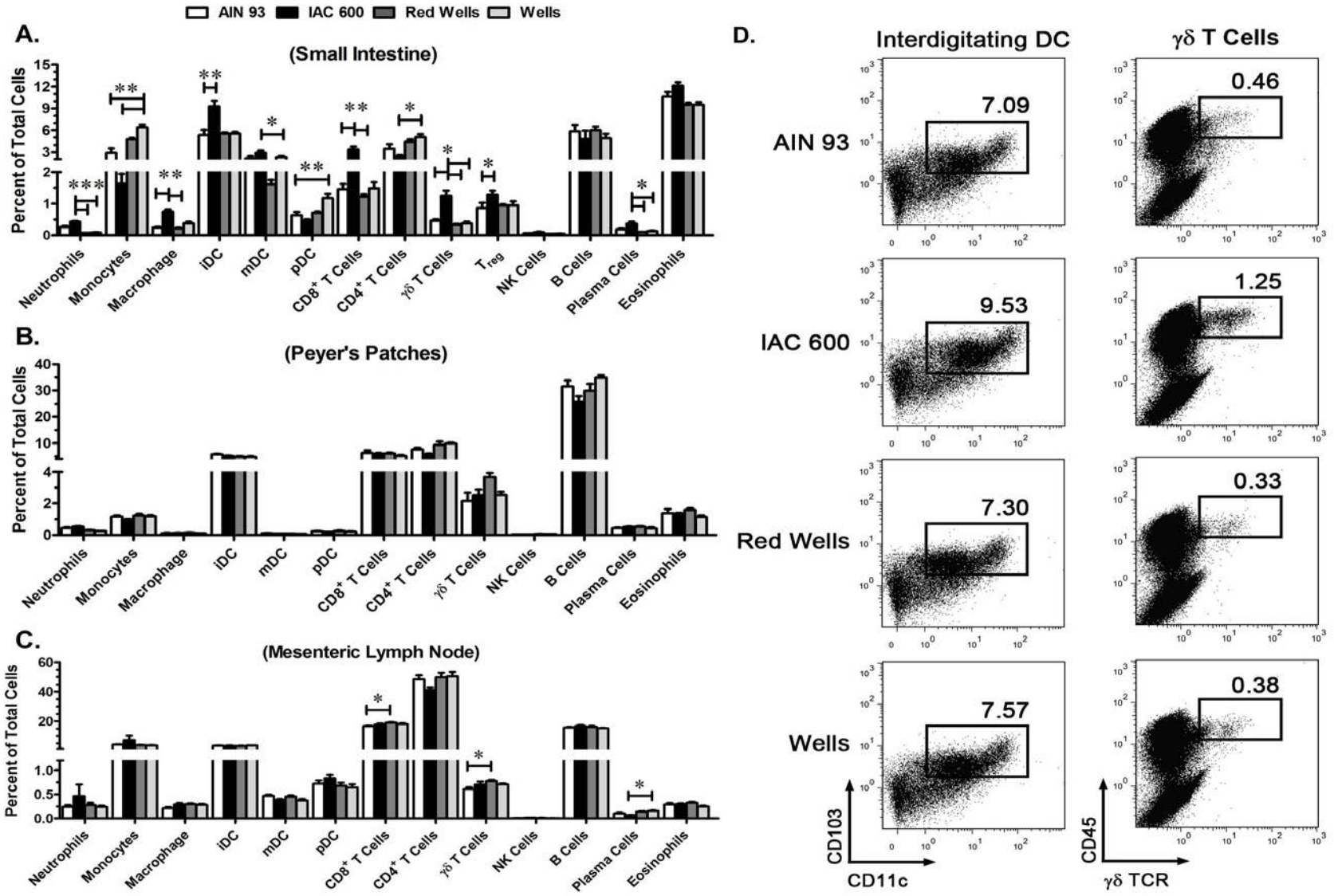
Measure diet changes and induction of immune response.

Day 7
Euthanize mice for analysis of immune response to *S. enterica* infection.

Effect of dietary rice bran varieties on *Salmonella* fecal shedding



2015. Goodyear et. al. Journal of Functional Foods



Rice bran consumption maintains intestinal immune populations despite *S. enterica* infection.

2015. Goodyear et. al. Journal of Functional Foods

LTH rice bran inhibits salmonella entry and intracellular replication in intestinal epithelial cells better than SHZ rice bran

Table 2. Number of metabolites detected in sub-pathways of lipid metabolism

	LTH	SHZ
Fatty acid amide	4	4
Fatty acid conjugate	1	1
Fatty acid ester	2	2
Fatty acid, Amino	0	1
Fatty acid, Dicarboxylate	11	11
Free fatty acid	31	31
*Galactolipids	13	8
Glycerolipids	33	33
Oxylipins	5	5
*Phospholipids	57	47
Sphingolipid	3	2
Sterols	3	3
Total	163	148

In preparation

Correlations between rice bran metabolite profiles and *Salmonella* fecal shedding

Fiber

Component	r	p-value
Organic Matter	-0.94	0.02 *
Total Fiber	0.31	0.56
Soluble Fiber	-0.8	0.03 *
Insoluble Fiber	0.54	0.3

Phenolics

Component	r	p-value
GAE	-0.83	0.06 §

Antioxidants

Component	r	p-value
γ-oryzanol	0.09	0.92

Vitamin E

Component	r	p-value
α-tocopherols	-0.89	0.03 *
γ-tocopherols	0.6	0.24
δ-tocopherols	0.4	0.52
α-tocotrienol	-0.54	0.3
γ-tocotrienol	0.94	0.02 *
δ-tocotrienol	-0.54	0.3
Total Vitamin E	0.14	0.8

Fatty Acids

Component	r	p-value
Myristic acid (14:0)	-0.41	0.42
Palmitic acid (16:0)	0.49	0.36
Palmitoleic acid (16:1)	0.06	0.92
Stearic acid (18:0)	-0.94	0.02 *
Oleic acid (18:1n9)	0.03	1
Vaccenic acid (18:1 n7)	0.37	0.5
Linoleic acid (18:2 n6)	-0.14	0.8
α-linolenic acid (18:3n3)	0.84	0.06 §
Arachidonic acid (20:0)	-0.03	1
Gadoleic acid (20:1)	0.37	0.5
Behenic acid (22:0)	-0.81	0.06 §
Lignoceric acid (24:0)	-0.94	0.02 *

Elements

Component	r	p-value
Boron	-0.89	0.03 *
Calcium	-0.6	0.24
Cobalt	0.43	0.42
Copper	-0.03	1
Iron	-0.09	0.92
Potassium	0.2	0.71
Magnesium	0.26	0.66
Manganese	0.43	0.42
Molybdenum	-0.26	0.66
Nickel	-0.77	0.1
Phosphorus	-0.09	0.92
Sulfur	-0.43	0.42
Zinc	-0.54	0.3

- An approach directed towards understanding the ratios and distinct stochiometry of components required for protection against Salmonella
- A process that may be useful to inform rice crop improvement for diarrheal disease protective/health traits

2015. Goodyear et. al. Journal of Functional Foods

Rice Bran protects gnotobiotic neonatal pigs against human rotavirus induced diarrhea

Treatments	n	Clinical signs				Fecal virus shedding (ELISA)			Fecal virus shedding (CCIF)
		% with diarrhea*, a	Mean days to onset**	Mean duration days**	Mean cumulative scores**, b	% shedding virus*	Mean days to onset**	Mean duration days**	Peak virus titer (FFU/ml)
RB+LGG+EcN	6	0^{B}	8 $(0^{c})^{A}$	0 $(0)^{B}$	6.2 $(0.5)^{C}$	100^{A}	2.8 $(0.3)^{A}$	5.2 $(0.3)^{C}$	$6.0x10^{2\,B}$
LGG+EcN	6	50^{B}	5.2 $(1.3)^{A}$	0.7 $(0.3)^{B}$	8.9 $(0.6)^{B}$	100^{A}	1.2 $(0.2)^{B}$	6.8 $(0.2)^{A}$	$1.3x10^{5\,A}$
RB only	5	20^{B}	7.2 $(0.8)^{A}$	0.2 $(0.2)^{B}$	4.4 $(1.6)^{C}$	100^{A}	1.6 $(0.2)^{B}$	6.2 $(0.2)^{B}$	ND
Mock	9	100^{A}	1.4 $(0.2)^{B}$	5.6 $(0.3)^{A}$	14.4 $(1.0)^{A}$	100^{A}	2.0 $(0.3)^{AB}$	4.7 $(0.7)^{BC}$	ND

- **Rice bran or Lactobacillus (LGG)+ Ecoli Nissle (EcN) alone reduced HRV diarrhea**
- **Addition of RB to LGG+EcN colonized pigs completely protected against HRV diarrhea and can prevent the increase of HRV shedding in the LGG+EcN fed pigs**

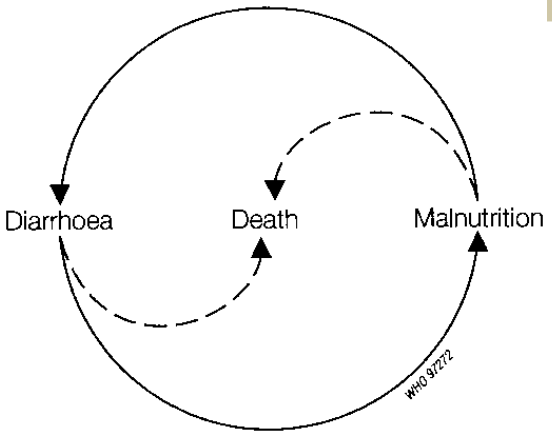
Yang et. al. Clinical and Vaccine Immunology (2014) and Scientific Reports (2015)

Multidisciplinary Efforts to reduce diarrheal disease, malnutrition, and growth stunting

Locally grown

Provide nutritionally dense foods to at-risk infants

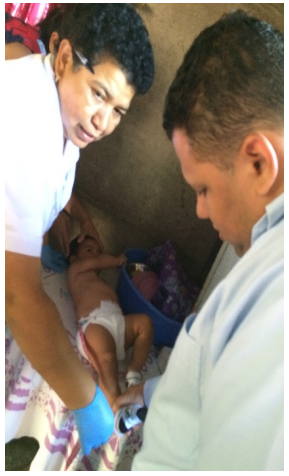
Community-based dietary interventions & clinical trials

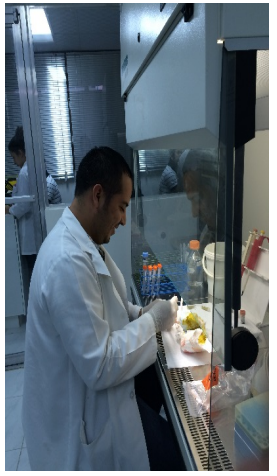


Nicaragua/Mali RB Project Overview

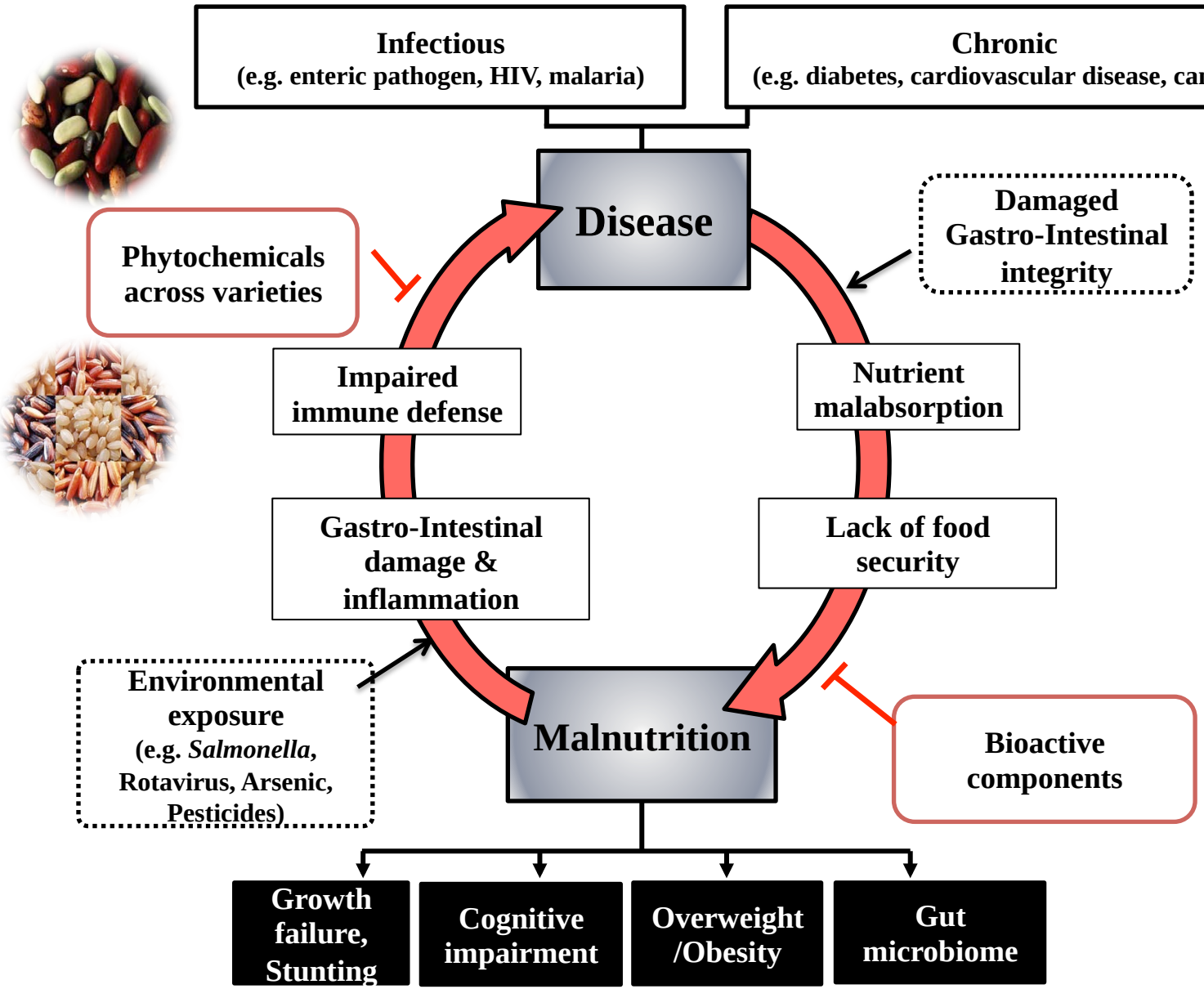
- Objective: To assess feasibility of rice bran consumption in healthy weaning children for enteric/diarrheal disease prevention.
  - Is it realistic for mothers to feed 6 -12 month old children heat-stabilized dietary rice bran daily in their diet?
  - Does heat-stabilized dietary rice bran consumption modulate the stool microbiome/metabolome?
  - Can daily consumption of heat-stabilized rice bran prevent diarrheal disease episodes and indicators of malnutrition?







Rice bran for health, nutrition and disease prevention



EC Borresen & EP Ryan (2014). Rice Bran: A Food Ingredient with Global Public Health Opportunities. In RR Watson, VR Preedy, & Sherma Zibadi (eds.), Wheat and Rice in Disease Prevention and Health: Benefits, risks, and mechanisms of whole grains in health promotion (pp. 301-311) Oxford, UK: Elsevier.

Legumes

Soybeans
Peanuts

Pulses
Peas, lentils, chickpeas, and dry beans.

Fresh Peas & Beans

Current Recommendations for Cancer Prevention

1. Be as lean as possible without becoming underweight.
2. Be physically active for at least 30 minutes every day.
3. Avoid sugary drinks. Limit consumption of energy-dense foods.
4. Eat more of a variety of vegetables, fruits, whole grains and legumes such as beans.
5. Limit consumption of red meats and avoid processed meats.
6. If consumed at all, limit alcoholic drinks to 2 for men and 1 for women per day.
7. Limit consumption of salty foods and foods processed with salt (sodium).
8. Don't use supplements to protect against cancer.
9. *It is best for mother breastfeed exclusively for up to 6 months and then add other liquids and foods.
10. *After treatment, cancer survivors should follow the recommendations for cancer prevention.

*Special population recommendations.

11. *do not smoke or chew tobacco.*

Following these recommendations, one third of total cancers could be prevented. Combined with eliminating tobacco use, one half of total cancers could be prevented. (AICR, 2012)

Health Promoting Properties of Dry Beans (*Phaseolus vulgaris* L.)

1. **Dry cooked beans have unique nutrient profiles compared to corn and cereal grains.**
2. **Consumption of common beans has been shown to alter chronic disease processes and risk factors.**
   Reduce inflammation
   Promote weight loss *(>50% of dogs are overweight)*
   Inhibit tumor growth *(one in four dogs get cancer)*
   Alter tumor metabolism
   Reduce serum cholesterol

3. Common dry beans are a promising staple food for chronic disease prevention.

- Finley, J. W., Burrell, J. B., Reeves, P. G., **Pinto bean consumption changes SCFA profiles in fecal fermentations, bacterial populations of the lower bowel, and lipid profiles in blood of humans.** *J Nutr* 2007, *137*, 2391-2398.
- Lanza, E., Hartman, T. J., Albert, P. S., Shields, R.*, et al.*, **High dry bean intake and reduced risk of advanced colorectal adenoma recurrence among participants in the polyp prevention trial**. *J Nutr* 2006, *136*, 1896-1903.
- Birketvedt, G. S., Travis, A., Langbakk, B., Florholmen, J. R., **Dietary supplementation with bean extract improves lipid profile in overweight and obese subjects.** *Nutrition* 2002, *18*, 729-733.

Whole grains and dry beans consumption across socioeconomic groups

Percentages of adults' that meet minimum recommended consumption levels

Group	Dry beans & peas	Total Grains	Whole grains
All Adults	3.5 ± 0.6	58.9 ± 1.4	0.8 ± 0.2
Lowest, poverty income ratio (≤1.30)	4.8 ± 1.0	53.9 ± 2.4	0.3 ± 0.1
Middle , poverty income ratio (1.31-1.85)	6.1 ± 1.3	55.4 ± 3.2	0.3 ± 0.1
Highest , poverty income ratio (≥1.86)	2.7 ± 0.7	61.0 ± 1.5	1.0 ± 0.2
Non-Hispanic white	2.2 ± 0.7	59.9 ± 1.6	0.9 ± 0.2
Non-Hispanic black	1.7 ± 0.9	45.0 ± 1.9	0.4 ± 0.1
Mexican American	20 ± 2.6	70.5 ± 2.5	0.2 ± 0.1

Kirkpatrick *et al*. J Acad Nutr Diet 2012

Community-Academic Partnerships in Northern Colorado

Kendall Anderson Nutrition Center

Medical Center of the Rockies
UNIVERSITY OF COLORADO HEALTH

Poudre Valley Hospital
UNIVERSITY OF COLORADO HEALTH

Harmony Surgery Center

Colorado School of PUBLIC HEALTH

Healthy Hearts

- Improve limetabolism in children at risk for hypercholestermia with dietary interventions

Beans/Bran Enriching Nutritional Eating For Intestinal health Trial

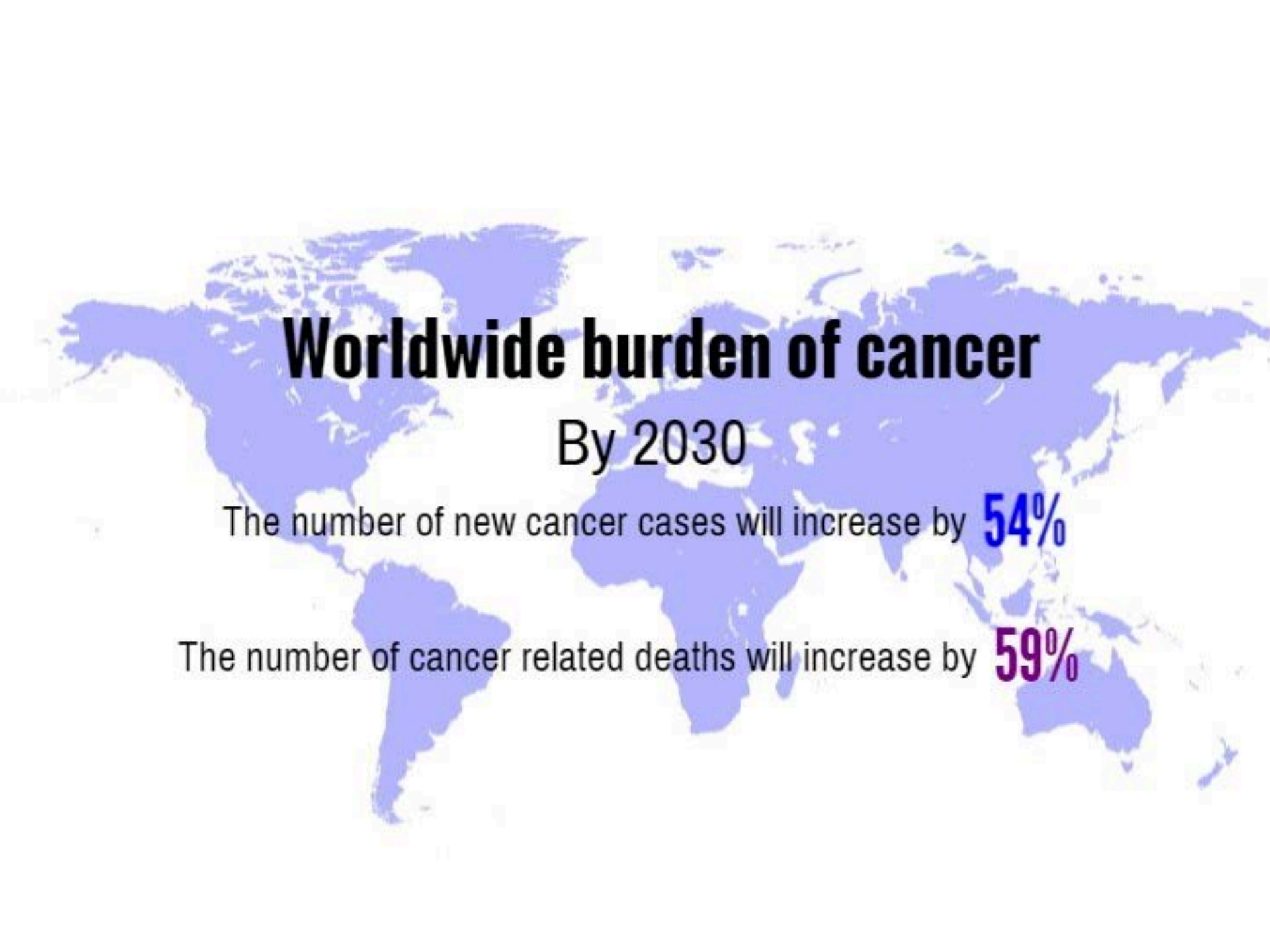
- Enhance gut & immune health in cancer survivors

Colorectal cancer control & chemoprevention

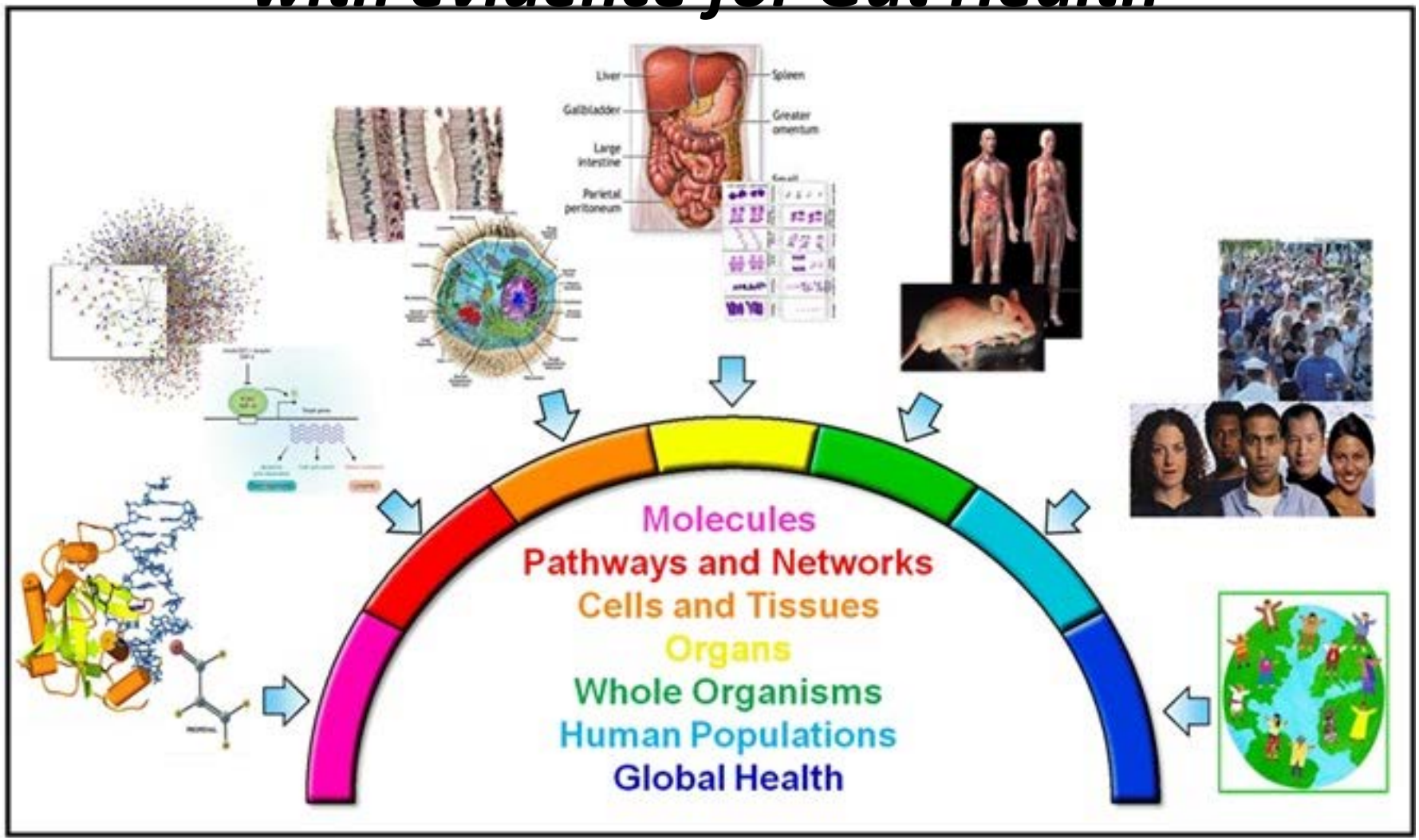
- Establish biomarkers for reduced gut inflammation and colorectal cancer prevention

Sooper Staples

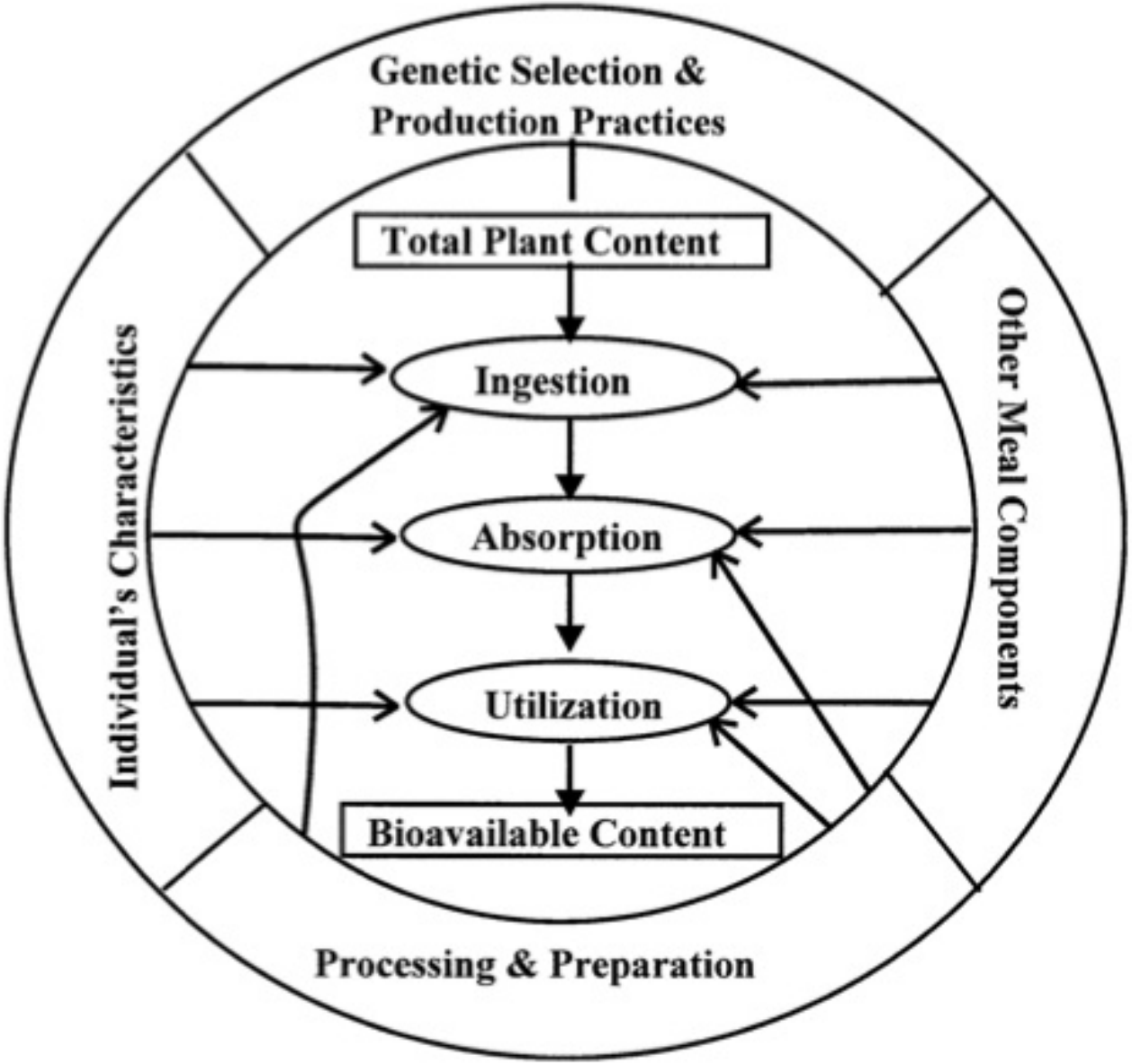
- Educate & empower community on whole grains and legumes at point of purchase


Worldwide burden of cancer
By 2030
The number of new cancer cases will increase by 54%
The number of cancer related deaths will increase by 59%

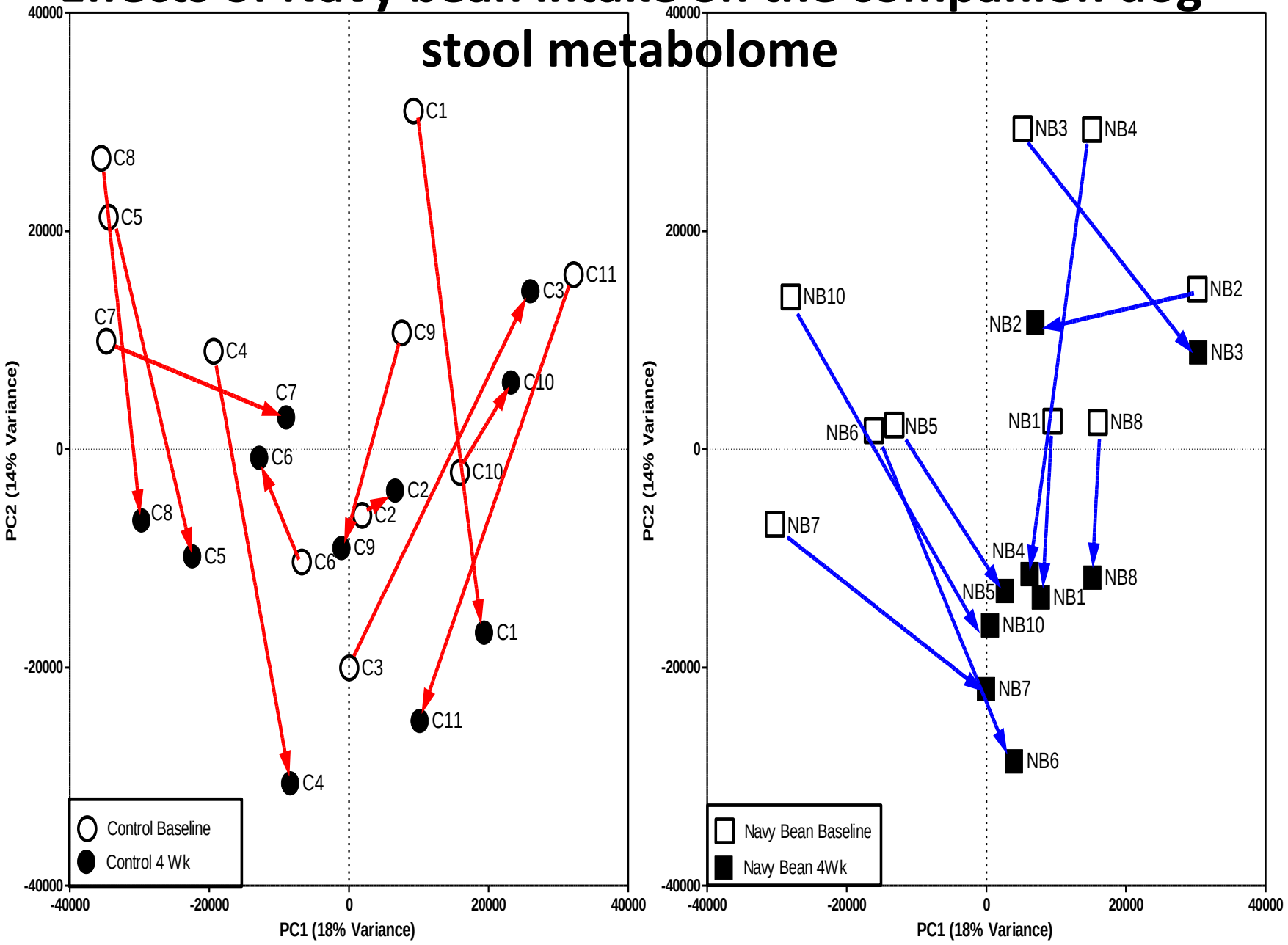
Building Partnerships in Research, Training, Education and Outreach on Sustainable Foods with evidence for Gut Health



Complex Interactions to determine the health benefits of whole grains



Effects of Navy bean intake on the companion dog stool metabolome



Forster et. al. Current Metabolomics 2015

A Simple, Sustainable Goal

Achieve Health benefits from a general increase in whole grain and legume consumption across the lifespan