Table 1: Nutrients/bioactive food compounds of interest and putative biomarkers for bioavailability & bioactivity endpoints

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Biomarker for bioavailability</th>
<th>Molecules/Mechanism disturbed with deficiency</th>
<th>Health impact</th>
<th>Biomarkers of Health and Disease</th>
<th>Model Systems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary Fiber</td>
<td></td>
<td>Digestive health</td>
<td>Cancer, inflammation IBD Obesity Type II Diabetes</td>
<td>Short chain-fatty acids Gut permeability Mucus thickness</td>
<td>Rodent Humans</td>
</tr>
<tr>
<td>Calcium</td>
<td>Ca levels Ca kinetics Bone mineral turnover PTH hormone levels</td>
<td>PTH hormone levels Loss of bone Shifts in microbiota</td>
<td>Osteoporosis Kidney Failure</td>
<td>Bone density MicroCT (bone architecture)</td>
<td>Rodent Human</td>
</tr>
<tr>
<td>Potassium</td>
<td>K kinetics</td>
<td>Rise in blood pressure, Lower BMD Higher NAE</td>
<td>Hypertension</td>
<td>Blood pressure Bone density</td>
<td>Rodent Human</td>
</tr>
<tr>
<td>Iron</td>
<td>Hemoglobin, serum/plasma ferritin and soluble transferrin receptor, transferrin saturation, hepatic iron concentrations</td>
<td>Hemoglobin serum/plasma Ferritin, Soluble transferrin receptor, transferrin saturation,</td>
<td>Anemia, Risk of infection, immune competence, growth, neurodegeneration,</td>
<td>Hemoglobin, hematocrit, inflammatory cytokines, Hapcidin, acute phase proteins</td>
<td>Rodent Chicken Human Pig</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>Vitamin A levels Serum/plasma retinol</td>
<td>Night vision, plasma cholesterol, immune function</td>
<td>Obesity, CVD, blindness</td>
<td>Adiposity, atherosclerosis, function of the visual cycle</td>
<td>Rodent Human</td>
</tr>
<tr>
<td>Zinc</td>
<td>Zinc levels</td>
<td>Immune function DNA integrity microbiome Bone turnover balance</td>
<td>Infection susceptibility Inflammation Cancer Osteoporosis</td>
<td>Inflammatory markers/cytokines Oxidative stress DNA damage</td>
<td>In vitro Rodent Zebrafish Human Chicken</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Vitamin D3 levels 25(OH) vitamin D3</td>
<td>Ca homeostasis Loss of bone Bone turnover balance Albuminuria Bone turnover - release of Pb</td>
<td>Osteoporosis Kidney failure Higher circulating Pb concentrations, adverse birth outcome risk</td>
<td>Bone density MicroCT (bone architecture) Serum Pb concentrations</td>
<td>Rodent Human</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Vitamin E &amp; metabolite levels</td>
<td>Oxidative stress, inflammation, and systemic vitamin E trafficking</td>
<td>Nonalcoholic Steatohepatitis Cancer Vascular Dysfunction Osteoporosis</td>
<td>Oxidative stress Inflammation markers Fatty liver pathology Pharmacokinetics *studies done in animals and translational work in humans</td>
<td>In vitro digestion system Rodents Humans</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>Phyloquinone in plasma and lipoproteins</td>
<td>gamma-carboxylation of proteins, vascular calcification, bone mineralization</td>
<td>cardiovascular health, bone health</td>
<td>pharmacokinetic studies in humans; interaction of food matrix on bioavailability</td>
<td>Humans Rodents</td>
</tr>
<tr>
<td>Folate</td>
<td>C-14-folate &amp; metabolites Polymorphisms Homocysteine Methyl Pool Plasma and RBC folate</td>
<td>Epigenetic alterations Methylation changes DNA damage</td>
<td>Cancer Heart Disease NTD Anemia</td>
<td>Homocysteine accumulation Methyl-pool alterations DNA damage Increased cancer risk</td>
<td>In vitro Human</td>
</tr>
</tbody>
</table>
| B<sub>12</sub> | B<sub>12</sub> levels  
TCII saturation  
Methylmalonic acid | Epigenetic alterations  
Methylation changes  
DNA damage | Cancer  
Heart Disease  
Cognition  
Anemia  
Demyelination disease | Homocysteine  
accumulation  
Methyl-pool alterations  
DNA damage  
Increased cancer risk  
Memory tests | In vitro  
Human |
| --- | --- | --- | --- | --- | --- |
| Bioactive lipids | Lipid oxidative products,  
Bioaccessibility,  
sphingolipids | Oxidative stress,  
inflammation,  
adipogenesis | Inflammatory diseases,  
obesity | Inflammatory markers,  
total fat accumulation | In vitro,  
C. elegans,  
Drosophila,  
humans,  
rodents |
| Essential Amino Acids | Lysine,  
Methionine | Protein Biosynthesis | Protein deficiency | Cognition,  
disease resistance,  
Animal feeding for  
protein efficiency |
| Dietary exosomes and their RNA and protein cargos | Foreign RNAs in  
plasma; plasma and urine  
metabolites (purines); mixed  
lymphocyte reaction;  
activation of Toll-like receptors | Cognition (loss of  
learning, increased  
seizure activity); gut  
inflammation, fertility and  
postnatal growth | Cognition;  
fertility;  
inflammation | Plasma cytokines,  
plasma microRNAs,  
gut microbiome,  
cognitive performance,  
aberrant plasma and  
urine levels of purine  
metabolites | Humans,  
mice; gut bacteria |
| Soy isoflavones | Isoflavone metabolite levels | Estrogen metabolism  
Anti-inflammatory  
perturbations  
microbiota | Bone health  
Cancer  
Heart Disease | Bone density  
MicroCT (bone  
architecture)  
Inflammatory markers  
*studies done in  
animals and  
translational work in  
humans | Rodents  
Humans  
Chicken |
| Green tea catechins | Catechins and host- and  
microbiota-derived  
metabolites | Gut-liver inflammatory and  
oxidative stress responses; adipogenesis | Heart Disease  
Nonalcoholic  
Steatohepatitis  
Obesity  
Cancer  
Cognition  
Bone health | Inflammatory markers  
Oxidative stress  
Fatty liver pathology  
Cancer risk  
Lipid accumulation  
*studies done in  
animals and  
translational work in  
humans | Ex vivo  
fermentation,  
C. elegans,  
Rodents  
Humans  
Chicken |
| Isothiocyanates | Isothiocyanate &  
metabolite levels | Epigenetic alterations  
Altered detoxification  
Oxidative stress  
microbiota | Cancer  
Cancer  
Epigenetic changes  
Detoxification pathways  
Cancer risk/incidence  
Oxidative stress  
*studies done in cells,  
animals and  
translational work in  
humans | In vitro  
Rodent  
Human |
| Indole-3-carbinol | Metabolite | adipogenesis, immune  
regulation, gut  
permeability, microbiota | obesity,  
testinal inflammation, type 1  
diabetes | Total fat  
accumulation; intestinal  
permeability  
T cell differentiation,  
macrophage  
polarization, bacterial  
dysbiosis | C. elegans,  
Drosophila,  
Rodent |
| Stilbenoids | Resveratrol,  
piceatannol | Adipogenesis, aging,  
antioxidative responses | Obesity, aging | Total fat  
accumulation, lifespan | C. elegans |
| Anthocyanins and Phenolic acids | Levels of anthocyanins and  
metabolites | Inflammation, Oxidative Stress,  
inulin signaling pathways, adipocyte  
differentiation  
Angiogenesis  
Vascularization | Obesity  
Inflammation  
CVD  
cancer  
Acute and chronic  
wounds | Inflammation  
Oxidative stress  
Cardiovascular perturbations | In vitro  
Rodent  
Pigs  
Rabbits  
Chicken |
### Table 2: Active and Planned Collaborative Studies

<table>
<thead>
<tr>
<th>Collaborative Studies</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absorption and metabolism modeling</td>
<td>NE, OH, OR, IA, IN, AZ, NY</td>
</tr>
<tr>
<td>Biomarker discovery, assessment measurements and validation</td>
<td>AZ, IL, OR, OH, OR, CA-B, IA, NY, CA-D, OK</td>
</tr>
<tr>
<td>Development of novel technological approaches and their applications</td>
<td>HI, IL, KS, MA, NE, OR, OH, MT, NJ, MO, IA, IN, FL, NY, ME</td>
</tr>
<tr>
<td>Model organisms</td>
<td>KS, NE, OR, CAB, AZ, NY, HI, OK</td>
</tr>
<tr>
<td>Animal models</td>
<td>HI, IL, MA, KS, NE, OR, OH, CA-B, CT, CA-D, PA*, AZ, IN, NY, ME</td>
</tr>
<tr>
<td>Human and population-based studies</td>
<td>IL, KS, NE, OR, OH, CA-B, OK, MT, IA, IN, FL, CT, AZ, RI</td>
</tr>
<tr>
<td>Microbiome studies/gut health</td>
<td>NE, OR, OH, IN, AZ, IN, MT, NY, CA-D, OK, CT</td>
</tr>
<tr>
<td>Susceptibility factors (age, sex, race, disease, environment, gene interactions)</td>
<td>OR, OH, CA-B, OK, IA, IN, RI, AZ, CA-D, CT</td>
</tr>
<tr>
<td>Obesity</td>
<td>CT, ME, AZ, IL, OH, HI, OR, OK</td>
</tr>
<tr>
<td>Maternal Obesity</td>
<td>NE, OK</td>
</tr>
</tbody>
</table>

Wound closure

IBD (UC)

Adipocyte growth/differentiation
Insulin resistance
Impaired glucose tolerance
Gut barrier function
Bacterial dysbiosis
Mucosal immunity

Nitrate and nitrite
Nitric oxide, nitrosothiols, nitroalkenes, nitroamines
Vascular function, blood pressure, efficiency of muscle contraction
CVD risk, chronic kidney disease risk, cognition
Endothelial dysfunction, increased blood pressure, reduced endurance upon physical exertion
Rodents, Zebrafish

Ellagitannins and ellagic acid
Urolithins via gut microbial hydrolysis
Inflammation, oxidative stress, vascular function, blood pressure, efficiency of muscle contraction
CVD, obesity and cancer risk, cognition
Inflammatory markers, oxidative stress
Zebrafish

Egg and Dairy Proteins
N/A
Inflammation, oxidative stress, vascular function, blood pressure
CVD, diabetes, metabolic syndrome, gut health
Brachial artery flow-mediated dilation, oxidative stress, inflammation, cardiometabolic indices
Humans

Carotenoids
Carotenoid levels
Vision, plasma cholesterol, oxidative stress
age-related macular degeneration, CVD, mitochondrial function, inflammation, NAFLD
visual impairment, atherosclerosis, Rodents
Humans

Bean protein
Cellular biomarkers
Diabetes,
Diabetes, inflammation
Inflammatory markers, oxidative stress, lipid metabolism
Rodents
In vitro (Cell culture)

Fatty acids
Serum fatty acid concentrations
Bone turnover - release of Pb
Higher circulating Pb concentrations, adverse birth outcome risk
Serum Pb concentrations
Humans

<table>
<thead>
<tr>
<th>Nitrate and nitrite</th>
<th>Nitric oxide, nitrosothiols, nitroalkenes, nitroamines</th>
<th>Vascular function, blood pressure, efficiency of muscle contraction</th>
<th>CVD risk, chronic kidney disease risk, cognition</th>
<th>Endothelial dysfunction, increased blood pressure, reduced endurance upon physical exertion</th>
<th>Rodents, Zebrafish</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ellagitannins and ellagic acid</td>
<td>Urolithins via gut microbial hydrolysis</td>
<td>Inflammation, oxidative stress, vascular function, blood pressure, efficiency of muscle contraction</td>
<td>CVD, obesity and cancer risk, cognition</td>
<td>Inflammatory markers, oxidative stress</td>
<td>Zebrafish</td>
</tr>
<tr>
<td>Egg and Dairy Proteins</td>
<td>N/A</td>
<td>Inflammation, oxidative stress, vascular function, blood pressure</td>
<td>CVD, diabetes, metabolic syndrome, gut health</td>
<td>Brachial artery flow-mediated dilation, oxidative stress, inflammation, cardiometabolic indices</td>
<td>Humans</td>
</tr>
</tbody>
</table>
| Carotenoids | Carotenoid levels | Vision, plasma cholesterol, oxidative stress | age-related macular degeneration, CVD, mitochondrial function, inflammation, NAFLD | visual impairment, atherosclerosis | Rodents
Humans |
| Bean protein | Cellular biomarkers | Diabetes | Diabetes, inflammation | Inflammatory markers, oxidative stress, lipid metabolism | Rodents
In vitro (Cell culture) |
<p>| Fatty acids | Serum fatty acid concentrations | Bone turnover - release of Pb | Higher circulating Pb concentrations, adverse birth outcome risk | Serum Pb concentrations | Humans |</p>
<table>
<thead>
<tr>
<th>Station</th>
<th>PI</th>
<th>Special Research Capability</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZ</td>
<td>Teske, Jennifer Duca, Frank</td>
<td>Animal models, body composition, behavioral measures of sleep, physical activity, energy expenditure, feeding, brain site-specific microinfusion, molecular biology, qPCR, EEG and EMG, radiotelemetry. Environmental and genetic interactions in altering the gut microbiota and nutrient-sensing pathways of the intestine in obesity and diabetes.</td>
</tr>
<tr>
<td>CA-B</td>
<td>Shane, Barry</td>
<td>molecular biology, genomics, genetic variation, animal models, cellular and <em>in vitro</em> systems, human studies</td>
</tr>
<tr>
<td>CA-D</td>
<td>Ehrlich, Allison Liu, Yanhong Ji, Peng</td>
<td>Gnotobiotic mouse models, mucosal immunology (T cell differentiation, macrophage polarization), gut health, dietary indoles and aryl hydrocarbon receptor activation Antimicrobial resistance of food-borne bacteria, alternatives to antibiotics, feed-based health technologies to improve animal health. Micronutrient deficiency and excess and dietary bioactive compounds on neurodevelopment, gut health and host resilience to infections</td>
</tr>
<tr>
<td>CT</td>
<td>Lee, Ji-young Blesso, Christopher</td>
<td>Dysregulation of energy metabolism, chronic inflammation and dyslipidemia, lipid metabolism and inflammatory signaling pathways, molecular targets for liver fibrosis and fibrogenic pathway, epigenetic regulations Lipid metabolism and chronic inflammation, lipoprotein particle functionality, phospholipid/sphingolipid metabolism, cardiovascular disease, human studies, rodent models of disease</td>
</tr>
<tr>
<td>FL</td>
<td>Andrade, Juan</td>
<td>Sensors for biological and food matrices, nutrient and bioactive analysis, bioavailability and bioefficacy of nutrients, food product development, food fortification, encapsulation technologies, global food and nutrition security</td>
</tr>
<tr>
<td>HI</td>
<td>Ho, Kacie Yang, Jinzeng</td>
<td>Effect of pre-harvest conditions and processing on bioavailability of carotenoids, minerals, and polyphenols, colloidal emulsion-based delivery systems for enhancing carotenoid or polyphenol bioavailability Control of blood glucose in prediabetes models by papaya leaf and seaweed juice.</td>
</tr>
<tr>
<td>IL</td>
<td>Amengual, Jaume DeMejia, Elvira</td>
<td>Role of vitamin A, carotenoids, and other bioactive products in cardiovascular disease and obesity. Inflammation and immune function and its relationship with atherosclerosis. Bioactive peptides and proteins in foods, inflammation, markers of type 2 diabetes, cancer, and cardiovascular disease risk</td>
</tr>
<tr>
<td>IN</td>
<td>Reddivari, Lavanya</td>
<td>Bioavailability and bioactivity of dietary fibers and flavonoids (anthocyanins); structure function relationships; interaction of fibers, flavonoids and gut bacteria; complexification of fibers and flavonoids; intestinal inflammation (IBD); chemical-induced and genetic models of ulcerative colitis; germ-free and gnotobiotic mice models.</td>
</tr>
<tr>
<td>IA</td>
<td>White, Wendy S</td>
<td>Bioavailability and metabolism of carotenoids, including beta-carotene and lutein, use of stable isotopic tracers to measure bioefficacy of beta-carotene in humans, nutritional genomics, biofortification to combat vitamin A malnutrition.</td>
</tr>
<tr>
<td>KS</td>
<td>Lindshield, Brian</td>
<td>Micronutrient bioavailability, protein quality, food aid development and assessment, international agricultural development nutrition and health assessment</td>
</tr>
<tr>
<td>ME</td>
<td>Klimis-Zacas, Dorothy</td>
<td>Nutritional Physiology and Biochemistry, Nutrition and Vascular Function and Metabolism, Berry bioactives and their role on chronic disease (Cardiovascular, Hypertension, Metabolic Syndrome, Wounds). Development of transdermal nanocarriers for bioactive compound delivery.</td>
</tr>
</tbody>
</table>

*The member at PA moved to Purdue University (IN)*

Table 3. Resources
<table>
<thead>
<tr>
<th>MO</th>
<th>Gruen, Ingolf U</th>
<th>Analytical chemistry with applications in food composition, flavor chemistry and the influence of food ingredients on quality attributes of foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>MT</td>
<td>Giroux, Michael</td>
<td>Plant breeding and cereal quality expertise. Bread, pasta, noodles, production and quality testing. Subject preference testing.</td>
</tr>
</tbody>
</table>
| NE  | Natarajan, Sathish Kumar Yu, Jiuju Zempleni, Janos | Maternal obesity-induced Complications, Placental Lipid Metabolism, Bioactive Lipids, Bioactive Nutrients  
Dietary exosome-like nanoparticles, chronic inflammation, NLRP3 inflammasome, obesity-related diseases  
Bioavailability studies, drug delivery, exosome biology, gut microbiome, molecular biology, RNA biology, transgenic models, human studies |
| NY  | Tako, Elad | Specialty fields: Fe and Zn bioavailability, Dietary bioactives, Animal models, Molecular biology, intestinal morphology, energetic status, microbiome. Essential micronutrients and dietary bioactives (including discovery) assessment by using a unique dual in vivo (Gallus gallus) system. Effects of dietary bioactives and physiological status (as obesity, mineral deficiencies) on intestinal functionality, morphology and microbiome, in vivo. |
| OH  | Bruno, Richard | In vitro and animal models, flavonoids, polyphenols, vitamin E (alpha- and gamma-tocopherol) and metabolites, carotenoids, oxidative stress, inflammation, cardiometabolic disorders (metabolic syndrome, (pre)diabetes, nonalcoholic steatohepatitis, vascular endothelial function), human intervention studies |
| OK  | Lin, Dingbo | Food biochemistry, egg lutein, egg xanthophylls, food bioactive compounds and chronic disease prevention - inflammation, diabetes, obesity, vitamin A and inflammation, maternal obesity and offspring health risk, epigenetics, precision nutrition and carotenoids metabolism, mitochondrial function and immunoregulation |
| OR  | Ho, Emily Dallas, David Iwaniec, Urszula | Molecular biology, epigenetics, signal transduction, chemoprevention studies in cell culture, animal models (mouse, zebrafish), and humans; mineral metabolism and gene regulation (humans), nutrient/gene/epigene interactions, nutrient/environment interactions  
Examine survival of pathogen-specific human milk immunoglobulins in the infant gut, toxic metabolites and gut inflammation, digestion and putrefaction via peptidomics, metabolomics, microbial sequencing and inflammatory protein analysis  
Imaging (dual energy absorptiometry, microcomputed tomography, histomorphometry), animal models (mice, rats, monkeys), mineral metabolism, bone metabolism, adipose tissue, osteoimmunology, cancer metastasis |
| RI  | Oaks, Brietta | Maternal micronutrient deficiencies, nutrient/environment interactions, human studies, dietary intake, multivariate modeling |