W-3122: ***Beneficial and Adverse Effects of Natural, Bioactive Dietary Chemicals on Human Health and Food Safety***

Minutes of the 2014 – Annual Meeting, October 9th -10th 2014, Monterey, CA

Participants in Attendance:

Administrative Advisor:

H. Michael Harrington (Colorado)

Committee Members:

Abby Benninghoff	(Utah State University)
Roger Coulombe	(Utah State University)
Bill Helferich	(University of Illinois)
Prathiba Nerurkar	(University of Hawaii),
Marie-Louise Ricketts	(University of Nevada Reno)
Nancy Turner	(Texas A&M University)
Tiffany Weir	(Colorado State University)
Dave Williams	(Oregon State University)
Meijun Zhu	(Washington State University)

Brief Summary of Minutes of the Annual Meeting

Dr. Marie-Louise Ricketts opened the meeting at 8:30 on October 9th and welcomed everyone.

Dr. Michael Harrington opened the discussions with an update on the federal research and funding environment. He stated the national priorities have not changed but that NIFA has published an action plan/road map for future work. There are a few changes in AFRI, with fewer new programs that focus heavily on collaborations and integrated teams. There is no longer a match requirement in the 2014 Farm Bill. Mandatory programs were renewed and the specialty crop program is now a permanent part of the program. The Foundation for Food and Ag Research was also authorized by the new bill, and for some programs it will not require matching funds. The USDA regions have changed; for example, the northern and southern plains regions have been combined. USDA wants to increase capacity (formula) and competitive funds because the ROI on those funds have been very good over the last 40 years. Overall funds for NIFA in Extension and Research have declined, but those for 1890 and 1994 institutions have remained flat. The proposed AFRI budget for 2015 is 325M. The water initiative is a key problem/resolution focus near term. We should review the NRC report "Spurring innovation in food and agriculture" that describes the AFRI program. He is going to submit the W3122 program again for the Multistate Research Excellence Award, which means he will need updated competitive funding in the near term. Impact reporting is critical to continued success of all programs. There is a National Impact Reporting Project that provides content on Multistate Projects. There is now training for how to make impacts clearer (Prezi.com/lmiicky_liuu/research-reporting-why-it-matterns-and-how-to-do-it-well/). Everyone should review this presentation to get tips for how to increase success in impact statements.

Technical Reports of Committee Members:

Abby Benninghoff – Utah State University

Dr. Benninghoff presented an update on 3 projects: 1) The ability of green tea to combat the promotion of colon carcinogenesis induced by the Total Western Diet; 2) The impact of micronutrient profiles in the Total Western Diet on tumor development in an AOM/DSS model of inflammation associated colon cancer; and 3) The impact of the total western diet and diet-induced obesity in colon carcinogenesis using the APC min mouse model. She described two new projects that will address questions concerning the impact of: 1) diet in a multigenerational experiment, and 2) a new Total Western Diet prepared using food ingredients, instead of a purified diet. Some of this work will be conducted using their humanized mouse gut microbiota model.

Roger Coulombe – Utah State University

Dr. Coulombe reported on a project in which he is using probiotics as chemopreventive agents. He found that the probiotics were able to reduce aflatoxin adducts. The data suggest the bacteria may bind aflatoxin on their cell walls, and thereby decrease absorption by the host. The LGG strain of probiotics both restored body weight and reduced adducts in turkey chicks exposed to aflatoxin. RNAseq data showed changes in cell adhesion and cytotoxicity functional groups induced by probiotics, relative to the controls. Probiotics alone downregulated several genes associated with cytotoxicity and bacterial surveillance. He is continuing to pursue this area of work.

Bill Helferich – University of Illinois

Dr. Helferich provided an update on the long-term effect of consuming soy-derived products. He is proposing to look at people living with cancer – most are prostate, breast and colon cancer subjects. In his animal models, he reported that lower doses of GEN produce longer latency periods for tumors to develop, but when GEN is removed tumors do not regress as much as when either estrogen is the treatment or when GEN is given at higher doses. With a low dose soy protein isolate, tumors take about 30 weeks to grow and when the estrogenic components are removed, the tumors continue to grow. So long term consumption of low doses elicits changes that create less treatable tumor types. However, soy flour is more similar to negative control, even when the soy flour diet provides similar blood levels of estrogenic activity. The mixed isoflavones treatment was more like estrogen treatment. Therefore, there is something in the soy flour that negates the promotive effect derived from the individual isoflavones.

Pratibha Nerurkar – University of Hawaii

Dr. Nerurkar reported on her projects targeting adipose and gut inflammation for management of obesity-associated T2Diabetes. Obesity induced chronic inflammation in target tissues – including liver inflammation leading to insulin resistance. Bitter melon (BM) reduces TNF-α and Il-1ß. This reduces insulin signaling and inhibits insulin resistance – being mediated by activation of the inflammasome. She is now testing the impact of BM in high fat mouse studies, and has found that BM reduced fat content and fasting glucose. BM reduced macrophage infiltration into adipose tissue. BM reduced TLR4 and NF-κB in circulation. Leptin, MCP-2 and TNF-α were reduced (protein levels). PGE2 and COX-2 were reduced to normal levels with BM in the gut – may be

associated with increases in AMPK1 and reduction in TLR4. Lactobacillales in cecum was elevated by BM. Demonstrated improvements in insulin signaling with BM.

Marie-Louise Ricketts – University of Nevada, Reno
Dr. Ricketts reported findings from her studies using grape seed procyanidins (GSPE) to identify naturally occurring gene-selective bile acid receptor modulators. She started by explaining the regulators involved in conversion of cholesterol to bile acids (FXR, SHP, Cyp7A1), bile acid transport and reabsorption (ASBT). GSPE reduces ASBT expression when FXR is present, but not in FXR KO mice. GSPE is repressing expression of IFABP1, which is shutting down transport of bile acids. This reduces serum bile acids in WT mice, but there is no change in FXR KO mice. GSPE increases HMG CoA synthase and reductase. All together this reduces enterohepatic BA recirculation. New studies are trying to figure out if GSPE is also regulating glucose metabolism. May act as an insulinomimetic by stimulating Akt and MAPK pathways to increase glucose uptake, or may change GLUT4 expression/translocation. Might be making more CDCA and LCA in the gut because of changes in cholesterol metabolic pathway targeted by GSPE. TGR5 is the bile acid membrane receptor that prefers LCA. TGR5 activity increases levels of cAMP and subsequent activation of GLP-1.

Nancy Turner – Texas A&M University
Dr. Turner reported on projects studying the impact of dietary bioactives and other environmental inputs on colon microbiota and how these impact colon and systemic health. She gave an update on the impact of a condensed tannin rich sorghum bran on colon microbiota, plasma metabolites, and microbial metabolites in overweight human subjects. She indicated that metabolites reflective of metabolic syndrome were improved with the sorghum bran intervention and the changes in circulating metabolites of polyphenols were, in part, reflected by changes in the concentration of those molecules in fecal samples. She is also studying the impact of these sorghum polyphenols on serum lipoproteins. She reported on a new study using dried plums, in which the levels of early lesions of colon cancer were reduced by 50% in rats consuming the plum diet. She is sequencing fecal microbial samples and will be studying epigenetic regulation of colon epithelial cell gene expression with samples from this study. She also reported the impact of microgravity and radiation on fecal microbial populations. She will be continuing this work to understand how radiation suppresses apoptosis in colon adult stem cells through epigenetic mechanisms regulated by microbial metabolites.

Tiffany Weir – Colorado State University
Dr. Weir reported on her work to develop biological markers to improve assessment of nutrition education programs. The project will use global metabolomic profiling to detect true intake of fruits and vegetables. Goal is to identify those biomarkers that not only reflect intake but also is associated with health markers (e.g., insulin sensitivity). Stool metabolites obtained from the BENEFIT study were used to segment people into food intake patterns, compared to reported intake patterns. Using OPLS-DA analytical approach, she was able to discriminate between tertiles of intake. Found some metabolites that were reflective of intake patterns. Currently conducting an intervention study to demonstrate the biomarkers are indicative of intake in a controlled feeding study.

Primary outcome is to validate OPLS-DA model and to identify other markers in urine. Secondary measures will be plasma biomarkers (alpha-hydroxybutyrate), stool microbiome analysis, dried blood spot methods development for alternative of plasma collection (alpha-hydroxybutyrate). She has other projects that are exploring the impacts of artificial sweeteners, phytoestrogen supplementation, as well as diet and genetic factors on the intestinal microbiome.

David Williams – Oregon State University
Dr. Williams reported on his studies to understand the epigenetic mechanisms of chemoprevention in a transplacental model because there are several transplacental carcinogens. Her is currently working to understand why a humanized Cyp1B1 mouse model is not responsive to dibenochrysene (DBC) induction of T-ALL. Cyp1B1 is important for adduct formation in spleen. He found that adducts in fetal lung is as high as the maternal lung adduct levels. Indole-3-carbinol did not affect adduct formation, but Chlorophyllin was able to reduce circulating aflatoxin. He is doing a human study to evaluate the pharmacokinetics of BaP at the zemptomole level (not hazardous). Other work is evaluating the epigenetic effects of DNA Methyltransferases and HDAC (Lys) inhibitors in newborns. I3C brings global DNA methylation back to normal levels, even when faced with PAH administration. Is also evaluating Nrf-2 and maternal dietary SFN effect in newborns (Nrf-2 KO animals). Initial observations show only a few deaths (T-ALL), but they were with the DBC/SFN diet.

Meijun Zhu – Washington State University
Dr. Zhu provided an update on her work to determine the impact of bioactives on inflammatory bowel disease and gut microbiota. Her work has shown a grape seed extract (GSE) decreases intestinal permeability in IL-10 deficient mice. The GSE was associated with elevated intestinal AOX levels and reduced serum TNF-alpha levels. Now studying goji berry –has high AOX activity, polyphenols and other beneficial compounds. Uses IL-10 KO mice and DSS-induced colitis. Body weight loss with DSS occurs with goji-berry, but not as much as with control diet. Goji-berry improved disease scores, but there were no changes in AOX or AOX-markers in colon. SCFA were altered by goji-berry; acetic is down but butyrate and isovaleric acid are elevated. Butyrate producing bacteria and butyrate gene expression were increased with goji-berry. No real differences in bacterial groups associated with IBD, but Actinobacteria and Bifidobacteria levels were elevated by goji-berry. There was a reduction in IL-17A, INF-gamma and TGF-beta expression with goji-berry. Results suggest the goji-berry improvement in IBD is from changes in bacterial groups.

Business meeting:
Marie-Louise Ricketts collected the registration fee ($110) for the 2014 meeting. The date for the 2015 business meeting was set for October 8-9 in Calistoga, CA. Meijun Zhu was elected to serve as Secretary. Abby Benninghoff will serve as Chair of the 2015 meeting and Nancy Turner will serve as the Chair-Elect of the meeting.