Morning Session: Northwest Auditorium, Covel Commons

Breakfast, Foyer, Northwest Auditorium, Covel Commons

Welcome Remarks, Joseph Pisegna, Member of the Organizing Committee.

SESSION I: Clinical/Translational Session (Moderators: Lin Chang, MD and Dennis Jensen, MD)

Emeran Mayer, MD  
Professor, Physiology, Psychiatry and Biobehavioral Sciences, Vatche and Tamar Manoukian Division of Digestive Diseases, Department of Medicine, David Geffen School of Medicine at UCLA

“Clinical Implications of Brain Gut Microbiome Interactions”

Summary: Preclinical and clinical studies have demonstrated bidirectional interactions within the BGM axis. Gut microbes communicate to the central nervous system through at least three parallel and interacting channels involving nervous, endocrine, and immune signaling mechanisms. On the other hand the brain can affect the community structure and function of the gut microbiota through the autonomic nervous system, by modulating regional gut motility, intestinal transit and secretion, and gut permeability, and potentially through the luminal secretion of hormones which directly modulate microbial gene expression. A series of largely preclinical observations implicates alterations in BGM communication in the pathogenesis and pathophysiology of several common disorders including irritable bowel syndrome, obesity, and several psychiatric and neurological disorders. Even though the translational relevance of these findings and a potential causal role of gut microbial alterations in these disorders are not known, ongoing research efforts have the potential to develop novel diagnostic techniques, as well as dietary and other treatment strategies.

Genhong Cheng, PhD  
Professor, Department of Microbiology, Immunology and Molecular Genetics, David Geffen School of Medicine at UCLA

“Influenza infection in the lung affects microbiota in the gut through Type I interferon”

Summary: In addition to its well-known antiviral function, Type I interferon (IFN-I) also plays a very important role in anti-inflammatory responses through induction of anti-inflammatory genes such as IL-27 and IL-10, which protects host from cytokine storms during acute infections and also protects host from autoimmune diseases such as Experimental Allergic Encephalomyelitis (EAE) and inflammatory bowel disease. On the other hand, we found that strong or sustained activation of this IFN-I-mediated anti-inflammatory pathway may lead to acute infectious diseases such as post influenza secondary bacterial pneumonia and chronic
infectious diseases such as Mycobacterial Lepra. Most recently, we have demonstrated that influenza infection in the lung can strongly alter microbiota profile in the gut through the IFN-I-mediated anti-inflammatory gene program.

Break 9:35 am – 9:50 am
Break, Foyer, Northwest Auditorium

9:50 am - 10:50 am
SESSION II: Translational/ Basic Science Session (Moderators: Joseph Pisegna, MD and Charalabos Pothoulakis, MD)

9:50 am – 10:20 am
Thomas Vallim, MSci, PhD
Assistant Professor, Department of Cardiology, David Geffen Department of Medicine at UCLA

“Bile Acid Metabolism Pathways in Health and Disease”

Summary: Bile acids are detergents and important signaling molecules that activate the nuclear receptor FXR to control key metabolic processes, including those of bile acid and lipid metabolism. The master regulator of bile acid metabolism is the nuclear receptor FXR, which is activated by specific bile acids in different tissues, but particularly in liver and intestine. Synthetic FXR agonists are currently being evaluated to treat non-alcoholic fatty liver disease (NAFLD) which initiates with the accumulation of hepatic lipids. FXR activation counteracts lipid accumulation by lowering hepatic lipid levels, through mechanisms that are not fully elucidated. Using lipidomic analysis, we have identified novel molecular mechanisms utilized by FXR to lower hepatic lipid levels. We demonstrate that FXR activation selectively decreases lipid synthesis (de novo lipogenesis) by preferentially decreasing mono-unsaturated fatty acid containing lipid species, synthesized by the enzyme SCD1. Consistent with decreased mono-unsaturated fatty acids, FXR activation profoundly decreases SCD1 expression likely via a post-transcriptional mechanism. In addition, we also show that FXR activation reduces lipid absorption and increases fatty acid oxidation. Our studies demonstrate that FXR activation orchestrates complementary pathways that act in concert to reduce liver lipid levels.

10:20 am – 10:50 am
Martin G. Martin, MD
Professor, Department of Pediatrics, David Geffen School of Medicine at UCLA

“Building the Gut in Dish: Prospects for Modeling and Identifying New Therapies of GI Disorders”

Summary: The gastrointestinal tract undergoes dramatic changes throughout the developmental spectrum, and is significantly influenced by luminal nutrients and a dynamic microbiota and metabolome. Progress in recent years has led to the development of methods and tools to isolate and expand the human intestinal epithelium which has provided unprecedented opportunities to explore the mechanism underlying many acute and chronic disorders. We will examine various broad in situ and ex vivo therapeutic approaches for chronic disorders, and describe recent efforts to re-build the gut for purposes of modeling various conditions in a dish.

Break 10:50 am – 11:05 am
Break, Foyer, Northwest Auditorium

11:05 am – 12:30 pm
Remarks and the John H. Walsh Memorial Lecturer
Eric Esrailian, MD, MPH, Co-Chief, Vatche and Tamar Manoukian Division of Digestive Diseases, David Geffen Department of Medicine at UCLA

Enrique Rozengurt, DVM, PhD, AGAF Director, CURE: Digestive Diseases Research Center, State of CURE

John H. Walsh Memorial Lecture: Roger Liddle MD, Professor of Medicine, Duke University School of Medicine.

“The gut connectome and implications for disease”

Summary: Enteroendocrine cells (EECs) are sensory cells of the gastrointestinal tract and secrete hormones in response to eating. Despite being electrically excitable, enteroendocrine cells are generally thought to communicate indirectly with nerves through hormone secretion and not through direct cell-nerve contact. However, we recently uncovered a connection between EECs and neurons that comprise a neural circuit connecting the lumen of the gut with the nervous system. This lecture will describe the EEC-neural circuit and its implications for diseases of the gastrointestinal tract and nervous system.

Elizabeth Marcus, MD
Assistant Professor, Department of Pediatrics, David Geffen School of Medicine at UCLA

“Helicobacter pylori and gastric injury”

Summary: Helicobacter pylori colonizes the normal acid secreting human stomach and infects 50% of the world’s population. 100% of those infected will develop gastritis, yet only a fraction will ultimately develop gastric or duodenal ulcers or gastric cancer. It is unknown who will develop advanced disease. H. pylori is known to interfere with epithelial cell junctions, which is a possible mechanism of gastric injury. One potential target of H. pylori is the Na,K-ATPase, an important cell adhesion molecule in epithelial cells, where it functions to stabilize junctional complexes in addition to its transporter role. The presence of H. pylori leads to a decrease in membrane associated and total Na,K-ATPase in gastric epithelial cells with a corresponding increase in endoplasmic reticulum forms, suggesting ER retention. This effect is dependent on new protein synthesis and is independent of transcription. ER chaperones BiP and GRP94 have decreased association with the Na,K-ATPase in the presence of H. pylori while total cellular levels do not change. H. pylori infection decreases the level of the Na,K-ATPase by interfering with the association of its α1 and β1 subunits with ER chaperones, leading to decreased pump delivery to the membrane, resulting in loss of epithelial integrity. Further investigation into mechanisms of progression to advanced disease will be critical for improving treatment options and gastric protective strategies.
“The role of long non-coding RNA’s in Inflammatory Bowel Disease”

Summary: Inflammatory bowel disease (IBD) is associated with significant morbidity for many patients. Currently, the etiology of IBD is thought to be multifactorial with recent work being directed on genetic and epigenetic aspects of IBD. A new area of research is now looking at aspects of gene regulation from previously uninvestigated portions of the genome, namely long noncoding RNAs (lncRNAs). These new players have been implicated in a variety of cell processes including cell-cycle control, embryonic development, and inflammation. However, their role in inflammatory bowel disease has yet to be determined. Using a combination of in vitro cell assays, mouse models of colitis, and human clinical samples, we aim to investigate the role of a recently identified clinically-validated lncRNAs such as IFNG-AS1 and CDKN2B-AS1, in the pathogenesis of IBD. Both of these lncRNAs have been implicated in inflammatory processes and epithelial biology and serves as an interesting and significant target for developing new therapeutic and diagnostic tools to tackle IBD.

“Brain signatures in Obesity”

Summary: Neuroimaging studies have identified the role of the brain in the pathophysiology of obesity and an imbalance between homeostatic and reward aspects of ingestive behavior may contribute to overeating and “food addiction”. Early life adversity, by contribution to this imbalance increases the risk for later obesity. However, a crucial issue remains that treatments in obesity remain suboptimal, and one barrier to progress is related to the inconsistent consideration of sex differences in the underlying mechanisms. Even though obesity is more prevalent in women, the mechanism underlying this sex difference is not known. Therefore, this presentation will focus on 1. Identifying the brain reward signatures associated with obesity, 2. Identifying sex differences in brain reward signatures related to obesity, and 3. How early life adversity increases vulnerability to hedonic eating, obesity, and decreased quality of life later in life. This has implications for future treatments and will help to devise and implement more personalized and precise treatments for obese individuals with increased hedonic ingestion.