ENQUIRE 2019 – Cluster 9 - GI, Renal, Endocrine Systems

This report details the changes in scientific scope for study sections evaluated under the ENQUIRE process in 2019 as part of Cluster 9. ENQUIRE integrates data and input from multiple stakeholders – the external scientific community, extramural programs at NIH, and CSR staff. An external panel of accomplished scientists, each with broad expertise and experience with multiple study sections was convened and asked to recommend changes necessary to facilitate the identification of high impact science, with special consideration of emerging science. Second, a panel of NIH extramural staff was convened and asked to focus on review process and concerns raised by the external recommendations. Additional input was provided by the CSR Advisory Council and by CSR staff in drafting of study section guidelines. Finally, to test the practicality of the recommended changes and the likely size of resulting study sections, CSR performed mock application referral using the new guidelines.

These changes will be implemented for grant applications submitted for Oct 2020 grant deadlines and beyond. New slates will be developed for each new standing panel to ensure expert review of the topics within each. Those who are members of currently existing panels with time remaining in their term will be to be asked to continue to serve, on one of the newly formed panels.

Evaluated Study Sections

Kidney Molecular Biology and Genitourinary Organ Development (KMBD)
Pathobiology of Kidney Disease (PBKD)
Urology and Urogynecology (ZRG1 DKUS 90)
Clinical, Integrative and Molecular Gastroenterology (CIMG)
Gastrointestinal Mucosal Pathobiology (GMPB)
Hepatobiliary Pathophysiology (HBPP)
Cellular Aspects of Diabetes and Obesity (CADO)
Clinical and Integrative Diabetes and Obesity (CIDO)
Integrative Physiology of Obesity and Diabetes (IPOD)
Integrative Nutrition and Metabolic Processes (INMP)
Molecular and Cellular Endocrinology (MCE)

Formed Study Sections

Kidney and Urological Systems Function and Dysfunction (KUFD)

Pathobiology of Kidney Disease (PBKD)

Hepatobiliary Pathophysiology (HBPP)

Digestive System Host Defense, Microbial Interactions and Immune and Inflammatory Disease (DHMI)

Digestive and Nutrient Physiology and Diseases (DNPD)

Basic Mechanisms of Diabetes and Metabolism (BMDM)

Pathophysiology of Obesity and Metabolic Disease (POMD)

Human Studies of Diabetes and Obesity (HSDO)

Nutrition and Metabolism in Health and Disease (NMHD)

Cell Signaling and Molecular Endocrinology (CSME)

Kidney and Urological Systems Function and Dysfunction - (KUFD)

The Kidney and Urological Systems Function and Dysfunction Study Section (KUFD) reviews applications that focus on the developmental mechanisms and function of the kidney and urinary tract, including the ureters, bladder and urethra; the male genital tract; and the visceral pelvis and pelvic floor musculature. Renal studies focus on basic and applied aspects of normal physiology, transport biology, obstructive diseases, and renal replacement including transplant and hemodialysis. Urology and urogynecology studies address both physiology and pathophysiology, including endocrine or neural influences; epidemiology, etiology and mechanisms of genitourinary disease; diagnostic strategies and biomarkers, bioengineering, and medical and surgical management, including clinical trials.

Topics:

- **Kidney epithelial and uroepithelial cell biology** including mechanisms of renal transport systems; hormonal and neural regulation of renal function; and other processes relevant to normal renal physiology.
- **Kidney transplantation and renal replacement therapies** including basic and clinical studies of uremia, and including dialysis, kidney ablation, artificial kidneys, chronic allograft nephropathy, and prevention and/or treatment of rejection.
- **Function of the bladder, ureter, and urethra and dysfunction of these and associated tissues** including conditions such as lower urinary tract symptoms (LUTS), interstitial cystitis/painful bladder and pelvic pain syndromes, overactive and underactive bladder, obstructive uropathy, diabetic uropathy and neurogenic and non-neurogenic incontinence.
- **Primary congenital and acquired kidney and urological conditions** affecting the kidney, bladder, ureters, urethra, and genital tracts, and secondary neurogenic conditions such as spina bifida including development, epidemiology, diagnosis and management.
- **Infection and inflammation in the urinary tract**, including studies of susceptibility, pathogenesis and treatment of bacterial, viral and fungal infections, and the role of the genitourinary microbiome in health and disease.
- **Urolithiasis and nephrolithiasis**, including studies of susceptibility, pathogenesis, and treatment of upper and lower urinary tract stones.
- **Function and dysfunction of the male and female genitourinary tract**. Studies of the prostate and associated non-cancerous conditions such as benign prostatic hyperplasia, physiology of penile erection and the pathophysiology and treatment of erectile dysfunction; pelvic floor tissues in health and disease, including the pathogenesis and treatment of pelvic floor weakness and prolapse with associated bladder and/or bowel incontinence.

Pathobiology of Kidney Disease - (PBKD)

The Pathobiology of Kidney Disease Study Section (PBKD) reviews grant applications involving renal tubular and glomerular cell pathophysiology and translational/clinical studies of kidney diseases including investigations of pathophysiology, diagnosis, and treatment of acute and chronic disorders of the kidney as well as the consequences of kidney disease and failure.

Topics:

- **Mechanisms of acute and chronic kidney injury and repair,** including acute renal failure and studies of the pathobiology of acute kidney injury transition to chronic kidney disease and renal fibrosis as well as toxic nephropathy.
- **Diabetic nephropathy** and aging nephropathy. Podocyte biology and its role in the pathogenesis of chronic kidney diseases including diabetic nephropathy, nephrotic syndrome, and proteinuria.
- **Polycystic kidney disease**, including ciliopathies and ciliary structure of the kidney tubules, and genetic models of polycystic kidney disease.
- **Renal tubular and glomerular pathophysiology**, renal hemodynamics, and disease resulting from disorders of fluid, electrolyte and acid-base homeostasis.
- **Disorders of tubular epithelial and endothelial cells** and the pharmacology of associated kidney disease.
- **Renal immunology** and immune glomerular diseases including lupus nephritis and IgA nephropathy.
- **Vascular biology** of the kidney and the role of renovasculature in blood pressure regulation and in the development of hypertension. Mechanisms of hypertensive renal injury.

Hepatobiliary Pathophysiology - (HBPP)

The Hepatobiliary Pathophysiology Study Section (HBPP) reviews applications involving pathophysiology and treatment of inherited and acquired viral and non-viral hepatobiliary diseases; molecular and genetic regulation of liver development and biochemical function under physiologic and pathophysiologic states; mechanisms of liver injury, repair, regeneration, fibrosis, cancer and transplantation; liver cell biology, immunology and inflammation; cholesterol and bile salt metabolism; hepatic fatty acid and triglyceride metabolism, insulin and hormone signaling, hepatobiliary transporters, hepatic protein metabolism, ion channels; and alcohol metabolism and disease. The HBPP study section focuses on both animal models and clinical work.

Topics:

- The use of isolated parenchymal and non-parenchymal cells of the liver including hepatocytes, stellate cells, Kupffer cells, endothelial cells, cholangiocytes and resident lymphocytes particularly as they relate to the pathogenesis of liver disease.
- Progenitor and stem cell therapies of genetic and acquired hepatobiliary diseases.
- Mechanisms of bile formation, bile salt synthesis hepatic cholesterol and lipid metabolism and their genetic and molecular regulation of cholestatic and gallstone disease.
- Molecular genetics and biochemical basis for NAFLD and NASH and approaches to intervention and reversal.
- Physiologic mechanisms of hepatobiliary transport including mechanisms of uptake and excretion of organic solutes, heavy metals, and ions.
- Inflammatory response of the liver to injury or infection, pro- and anti-inflammatory mediators, oxidative stress and ER stress, apoptosis and autophagy.
- Mechanism of hepatocyte injury including immune response, oxidative stress, apoptosis, pro- and anti-inflammatory mediators, including signal transduction pathways and neuromediators.
- Liver development, injury, repair, regeneration, growth, differentiation, development, and aging.
- Hepatocyte and cholangiocyte dysplasia and pre-neoplasia; mechanisms of transformation; cellular immortalization and mutagenesis.
- Liver cell and organ transplantation, liver ischemia-reperfusion injury and application of transplantation to the therapy of liver diseases.
- Regulation of splanchnic blood flow and endothelial vascular function as it pertains to mechanisms of portal hypertension.
- Cellular and molecular mechanisms of liver diseases, such as, fibrosis and cirrhosis including complications such as ascites and hepatic encephalopathy.
- Viral hepatitis as it relates to the pathogenesis of hepatobiliary disease.
- Pathogenesis of alcoholic liver injury, including the role of nutrient deficiencies and endotoxemia.

Digestive System Host Defense, Microbial Interactions and Immune and Inflammatory Disease - (DHMI)

The Digestive System Host Defense, Microbial Interactions and Immune and Inflammatory Disease Study Section (DHMI) reviews applications involving gastrointestinal innate and adaptive immunity, gut microbiota/microbiome, host-microbial interactions, intestinal infections, pathophysiology and immunobiology of inflammation including inflammatory bowel diseases, inflammatory processes in the exocrine pancreas, and epithelial cell biology as it relates to mucosal defense or repair. Approaches may utilize in vitro systems, animal models, or human samples and systems.

Topics:

- **GI mucosal immunology** including both innate and adaptive immunity, lymphocytes and myeloid cells, IgA and secretory immunity.
- **Host-microbe interactions in the GI tract** including commensal, pathogenic and microbial community interactions, maintenance of barrier function.
- **Intestinal infections,** including parasitic and viral host responses in the GI system
- **Inflammatory bowel diseases** including celiac and Crohn's disease, necrotizing enterocolitis (NEC), *C. difficile*, eosinophilic esophagitis
- **Nutritional immunology** including the use of pre- and pro-biotics in the treatment of inflammatory digestive diseases.
- **Pre-neoplasia** as a consequence of chronic GI infection or inflammation (e.g. colitis or H. pylori).
- **Regulation of gene expression as it relates to inflammatory processes, mucosal defense or repair**.

Digestive and Nutrient Physiology and Diseases - (DNPD)

The Digestive and Nutrient Physiology and Diseases study section reviews applications involving function and physiology of the GI tract with respect to the physiology or pathophysiology of digestion, nutrition and related functional disorders. Topics include GI development and growth differentiation control, GI dysplasia and pre-neoplasia not due to immune or host- microbe interactions, brain-gut interactions, enteric nervous system, motility disorders, acid secretion and acid related disease, GI hormones, pancreatic function and dysfunction, GI system nutrient absorption and malabsorption, diarrheal diseases.

Topics:

- **Epithelial biology** including barrier function, stem cells, development, regeneration and restitution throughout the GI tract
- **Epithelial metaplasia**, Barrett's esophagus, dysplasia and pre-neoplasia not due to immune or host-microbe interactions
- **Acid secretion and acid-related disease** including GERD.
- **Neurobiology of the GI system** including brain/gut interactions, IBS, enteric nervous system, visceral pain, influences and role of the microbiome in these processes.
- **GI motility and related disorders** including fecal incontinence, regulation of sphincters, esophageal motility, gastroparesis
- **Function and disease of the exocrine pancreas** including acute and chronic pancreatitis.
- **Physiology of digestion** including GI hormones, integrated responses to food intake, nutrient and vitamin transport and adsorption, fluid and electrolyte absorption and secretion, effects of pre and pro-biotics.
- **Genetic determinants** of digestive diseases including gene regulation, risk factors, and biomarkers.

Basic Mechanisms of Diabetes and Metabolism - (BMDM)

The Basic Mechanisms of Diabetes and Metabolism Study Section (BMDM) reviews applications concerned with the cellular regulation of metabolic homeostasis, genetics and pathobiology of diabetes (both, type 1 and type 2) and obesity, relying on cellular, in vitro and in vivo experimental settings (i.e., human cells/tissues, model systems, and animal models).

Topics:

- Adipocyte biology, adipogenesis, tissue plasticity (e.g., beiging/browning of white adipose tissue).
- Signaling pathways involved in integration of thermogenic processes at cellular level.
- Stem cell biology, cell-based regenerative and tissue engineering approaches for thermogenic adipose tissue.
- Pancreatic islet cell biology, islet cell plasticity (e.g., fate switching of cells in the pancreatic islet).
- Islet cell replication, stem cell biology, cell-based regenerative and tissue engineering approaches to replace islet cell function.
- Insulin action, insulin resistance, and mechanisms of glucose transport in metabolic tissues.
- Extracellular cell matrix-parenchymal cell signaling in metabolic tissues.
- Paracrine signaling/feedback loops.
- Role of inflammatory pathways in metabolic tissues.
- Pathobiology of type 1 diabetes.
- Genetics of obesity and diabetes; analysis of the functional consequences of specific genetic alterations concerning obesity and/or diabetes.

Pathophysiology of Obesity and Metabolic Disease - (POMD)

The Pathophysiology of Obesity and Metabolic Disease Study Section (POMD) reviews applications on pathogenesis and treatment of metabolic disease associated with obesity and diabetes. POMD reviews applications with emphasis on integrative systems, involving neurobiological, neuroendocrinology, system biology, nutritional, metabolic and physiological studies predominantly in animal models and model organisms.

Topics:

- Analysis of circuits in the central nervous system (CNS), and the action of gut hormonal and other peripheral endocrine signaling pathways and nutrients in the CNS that regulate metabolism, energy balance and food behavior; studies to elucidate how dysregulation of these circuits and pathways contribute to the pathogenesis of metabolic disease.
- Studies focusing on the regulation of peripheral metabolism, food intake and pathophysiology of metabolic disease by the autonomic nervous system (ANS).
- Analysis of hypoglycemia and counter regulatory responses, including glucose sensing and neural control of counter regulatory mechanisms; glucoregulation of neuronal activity in CNS areas involved in metabolic and energy control.
- Developmental processes in the CNS and ANS that regulate predisposition to offspring obesity and metabolic disorders. Perinatal diet and intrauterine environment effect on metabolic processes, tissues and disease in mother and offspring.
- Integration between circadian/sleep central and peripheral regulatory pathways and metabolic disease.
- Effects of diet and caloric excess in microbiota and impact on metabolic tissues and the development of metabolic disease.
- Mechanistic studies related to the effects of bariatric surgery, diet and exercise on metabolic tissues including adipose, liver, skeletal muscle and the central and peripheral nervous system.
- Analysis of endocrine signaling among the pancreas, adipose tissue, liver and skeletal muscle; nutrient storage and release and communication among these tissues; insulin action in adipose, liver, muscle and neural processes; and analysis of whole-body insulin resistance (including integration between tissues).
- Investigation of intermediary metabolic pathways and mitochondrial function in metabolic tissues related to diabetes and obesity; and physiologic integration of thermogenic processes and energy homeostasis.
- Inflammatory regulation of metabolism and energy balance, including the analysis of cellular and molecular responses to cytokine and adipokine levels and the role of immune cells.

Human Studies of Diabetes and Obesity - (HSDO)

The Human Studies of Diabetes and Obesity Study Section (HSDO) primarily reviews applications related to clinical and translational research associated with prevention and treatment of diabetes and obesity. Interventions may include lifestyle, diet, exercise, pharmacotherapies, behaviors, and surgery. Approaches may include human studies and clinical trials.

Topics:

- Clinical trials across the life span to evaluate the efficacy of lifestyle (e.g. diet,physical activity, sleep), pharmacologic, biologic, or surgical interventions for prevention or treatment of diabetes and obesity and their metabolic complications.
- Translational studies to understand the mechanisms of interventions for preventing or treating diabetes and obesity.
- Human studies to understand the pathogenic mechanisms of diabetes and obesity, including retrospective studies, secondary data analysis.
- Studies to validate applications of genomics, phenotyping, technologies, and biomarkers or other new outcome measures for therapeutic purpose for diabetes and obesity.
- Studies to investigate the effects of gestational diabetes or maternal obesity on mother/ offspring metabolic health, and the effects of interventions on the metabolic outcomes.
- Effects of central nervous system and behavioral interventions on prevention or treatment of diabetes and obesity.

Nutrition and Metabolism in Health and Disease - (NMHD)

The Nutrition and Metabolism in Health and Disease Study Section (NMHD) reviews applications concerned with mechanisms of macro- and micro-nutrient transport and processing and impacts on metabolism and physiological and pathophysiological pathways and outcomes. Emphasis spans relevant research performed in vitro and in animal models and human subjects, including clinical trials.

Topics:

- Nutrient sensing of dietary patterns, components and metabolites (including carbohydrates, amino acids, fatty acids, bile acids and other substrates) and impacts on metabolic regulation.
- Nutrient (including prebiotic) effects on microbiota community structure and function and impacts on host metabolism and disease etiology.
- Effects of maternal and postnatal nutrition on fetal and postnatal metabolic programing, development and health.
- Sterol, lipid and lipoprotein transport and metabolism in physiological and pathophysiological processes, including nonalcoholic fatty liver disease (NAFLD) and related aspects of cardiometabolic syndrome.
- Vitamin and mineral requirements, absorption, utilization, metabolism and function, including genetics affecting these processes.
- Physiologic and pathophysiologic mechanisms of chronic and intermittent micro- and macronutrient excess, deficiency and restriction, including impacts on brain development, cognition, immune function, and metabolic homeostasis; identification and assessment of biomarkers of food and nutrient exposures.
- The role of phytochemicals and food additives, including non-caloric artificial sweeteners, on metabolism, oxidative stress, inflammation and other cellular and physiologic and pathophysiologic processes.

The Cell Signaling and Molecular Endocrinology - (CSME)

The Cell Signaling and Molecular Endocrinology Study Section review applications addressing molecular and cellular aspects of endocrine organs and their products in normal and pathological states. Areas covered include structural and molecular studies, receptor-mediated cell signaling mechanisms of hormones, growth factors, polypeptides and lipid-based ligands and regulation of gene expression. In vitro studies as well as in vivo models are included.

Topics:

- Molecular pathways involved in the synthesis, processing, folding, trafficking and secretion of local and circulating peptides and hormones (including insulin, steroid and thyroid).
- Nuclear Receptors: regulation, biochemistry and molecular mechanisms of action of androgen and estrogen receptors.
- Regulation, biochemistry and molecular mechanisms of action of glucocorticoids and other nuclear receptors (*e.g.* thyroid, PPARs, RXRs).
- Structural, biological and biophysical interactions of G-protein-coupled, nuclear and peptide hormone receptors.
- Hormonal regulation of gene expression: Epigenetics, chromatin structure, transcriptional regulators (*e.g.* DNA-binding proteins, coactivators/ corepressors), nuclear and mitochondrial transcription factors.
- Cell signaling and metabolic regulation of endocrine organs (thyroid, adrenal, parathyroid, endocrine pancreas, pituitary, bone); energy homeostasis (e.g. mitochondria).
- Hormone regulation of non-malignant cell growth and differentiation events.
- Cell signaling and epigenetic mechanisms controlling cell function, and gene expression in metabolic tissues (liver, adipocytes, skeletal muscle).
- Signaling mechanisms and epigenetic regulation of pancreatic islets cells growth and function.