ENQUIRE 2019 – Cluster 6 - Cardiac, Vascular and Hematologic Sciences

This report details the changes in scientific scope for study sections evaluated under the ENQUIRE process in 2019 as part of Cluster 6. 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

Atherosclerosis and Inflammation of the Cardiovascular System Study Section (AICS)

Cardiac Contractility, Hypertrophy, and Failure Study Section (CCHF)

Clinical and Integrative Cardiovascular Sciences Study Section (CICS)

Electrical Signaling, Ion Transport, and Arrhythmias Study Section (ESTA)

Hemostasis and Thrombosis Study Section (HT)

Hypertension and Microcirculation Study Section (HM)

Molecular and Cellular Hematology Study Section (MCH)

Myocardial Ischemia and Metabolism Study Section (MIM)

Vascular Cell and Molecular Biology Study Section (VCMB)
Transfusion Medicine Sep (ZRG1 VH-D 55)

Formed Study Sections

Basic Biology of Blood, Heart and Vasculature (BBHV)

Integrative Vascular Physiology and Pathology (IVPP)

Atherosclerosis and Vascular Inflammation (AVI)

Hemostasis, Thrombosis, Blood Cells and Transfusion Study Section (HTBT)

Integrative Myocardial Physiology/Pathophysiology A (MPPA)

Integrative Myocardial Physiology/Pathophysiology B (MPPB)

Therapeutic Development and Preclinical Studies (TDPS)

Clinical Integrative Cardiovascular and Hematological Sciences (CCHS)

Basic Biology of Blood, Heart and Vasculature - (BBHV)

The Basic Biology of Blood, Heart and Vasculature Study Section (BBHV) reviews applications focused on basic molecular and cellular mechanisms and physiology of blood, heart and vascular cells and tissues in normal and pathologic conditions. The applications in BBHV are focused on cells, tissues and experimental organisms. Cellular, biochemical, biophysical, immunological, genetic, pharmacological, and molecular biological approaches in experimental models are reviewed.

Topics

- Basic studies blood, heart and vascular cells and tissues: "Omics", stem cell biology and regenerative medicine (including hematopoiesis and cardiac differentiation), cell lineage and cell fate studies.
- Basic mechanisms for red blood cells or hemoglobin to carry oxygen, white blood cells and platelet adhesion, migration or interactions, platelet activation, shape change, release and aggregation.
- Gene therapy and gene editing technology: Transcriptional and posttranscriptional regulation of gene expression. Signaling, epigenetics, cell-cell interactions with adhesion molecules; chemokines, cytokines.
- Vascular cell development, differentiation and proliferation. Angiogenesis, apoptosis, and autophagy.
- Protein biochemistry and structural biology of components of the blood, heart and vasculature: Including cardiac and vascular ion channels, ion exchangers, and ion pumps.
- Intercellular communication of blood, vascular and heart cells. Exosomes, ectosomes, microvesicles, microparticles. Electrical propagation of cardiovascular cells. Cell fission and fusion.
- Cardiac myocytes: Contractile function and mechanical stress generation. Calcium regulation and signaling and involvement of the vasculature.
- Cardiac hypertrophy, heart failure and heart disease: Molecular and cellular mechanisms, Myocyte growth, proliferation, metabolism and apoptosis; receptor signaling; transcriptional pathways; inflammatory/ cytokine-mediatedprocesses.
    - Cellular mechanisms of arrhythmogenesis: genes and proteins involved.
    - Genetic cardiomyopathies: genotype-phenotype correlation; genomic and proteomic approaches.
    - Mechanisms for myocardial cell dysfunction, death (apoptosis/necrosis) and autophagy. Impact of diet, obesity or systemic metabolic disorders on myocardial metabolism mitochondrial function, or the response to ischemia/reperfusion.
    - Excitability, electrical propagation and repolarization in normal and diseased hearts; intercellular communication including gap junctions/connexins.

Integrative Vascular Physiology and Pathology - (IVPP)

The Integrative Vascular Physiology and Pathology Study Section (IVPP) reviews applications focused on endothelial cells, blood vessels and lymphatics and their role in normal physiology and disease. Cellular, biochemical, biophysical, immunological, genetic, pharmacological, and molecular biological approaches are typical. Basic and applied aspects of cardiovascular regulation are reviewed that focus on the physiology of blood pressure regulation, the pathogenesis of hypertension and the microcirculation, biology of the endothelium and vascular smooth muscle cells and vascular homeostasis and dysfunction in experimental models.
Studies on cell surface receptors and signaling processes of various hormones, paracrines, and autocrines and their mechanisms of action as related to hypertension, integrated neural-humoral control of circulation, regional hemodynamics, lymphatic circulation, and microcirculation are also considered.

Topics

- Vascular cell and molecular biology of blood vessels ranging from major arteries to the microcirculation and sex-specific microvascular disease mechanisms.
- Neural and humoral control of the cardiovascular system in vertebrate animals including systems analysis of autonomic physiology involving central and peripheral mechanisms of cardiovascular regulation.
- Mechanisms that regulate vascular angiogenesis and rarefaction, cardiovascular stem cell functions and senescence.
- Hypertension (excluding pulmonary hypertension). Mechanisms that regulate arterial blood pressure, role of kidneys and other tissues/organs, nervous and endocrine systems, autocrine, paracrine factors. Pathogenesis of systemic hypertension.
- Vascular pathology in hypertension and co-morbidities, metabolic syndrome, chronic degenerative diseases (e.g. Alzheimer, retinopathy), stroke, cardiac microvascular dysfunctions, and aging.
- Vascular inflammation, immune regulation and dysregulation.
- Microcirculation and tissue transport processes, lymphatics, autonomic regulation. Capillary/vascular dynamics, mechanics and permeability, cellular and fluid mechanics and mechanotransduction .
- Vascular responses and changes due to environmental exposure, stress, metabolic disorders, aging and vascular drug toxicity.
- Pathogenesis of microvascular diseases related to diabetic vasculopathy, stroke, ischemia/reperfusion and chronic microvascular diseases such as Raynaud's disease. Propulsion of lymph, lymphatic tone, and pathogenesis oflymphedema.
- Mediators and modulators of vascular smooth muscle contractility: calcium homeostasis; calcium sensitive proteins; neural, redox, and transcriptional regulation of genes and proteins that modulate vascular excitability and contractility; regulation of ion channel function and expression.
- Injury/repair; remodeling; angioplasty; restenosis; grafts; stents; re- endothelialization; neointima hyperplasia; spasm; varicose; embolism; fistula; edema; stem cells.

Atherosclerosis and Vascular Inflammation and Aging - (AVI)

The Atherosclerosis and Vascular Inflammation and Aging Study Section (AVI) reviews applications involving inflammation of the vascular system with a focus on the pathobiology of the blood vessels leading to atherogenesis, its reversal and prevention. There is an emphasis on macrophage biology and hyperlipidemia, involving transport and metabolism of cholesterol, lipoproteins and their oxidation derivatives. The effects of major risk factors such as diabetes, liver disease, aging, and smoking on the vasculature are considered. Most studies use cell cultures and animal systems with some human subject approaches.

Topics:

- Lipoproteins in the vascular system and vascular disease: Function, metabolism, and oxidation. Cholesterol metabolism, and transport. Related gene expression and regulation, noncoding RNAs, post-translational modifications. Macrophage activation and regulation. Foam cell formation; plaque stability, plaque rupture and erosion. Cell-matrix interactions.
- Innate and adaptive immune mechanisms in vascular inflammation, atherosclerosis. Atheroprotection and vascular aging. Neutrophils, macrophages, monocyte subsets, T-cells and leukocytes. Cell migration, cell signaling, cytokines and chemokines, signal transduction.
- Endothelial and smooth muscle cell biology as related to atherosclerosis, vascular inflammation, plaque stability, or aneurysms. Lymphocyte-endothelial interactions and shear stress mechanotransduction mechanisms. Oxidative stress and endothelial dysfunction: Reactive oxygen species (ROS), reactive nitrogen species (RNS), nitric oxide (NO), and endothelial nitric oxide synthase (eNOS).
- Vascular disease and metabolic processes such as hyperlipidemia, abdominal aortic aneurysms, vascular calcification, adipose tissue inflammation, diabetes, atherothrombosis, vasculitis, autoimmune myocarditis.
- Effects of the environment on the vascular system. Exposure to toxins, drugs, nutritional components. The gut microbiome, lifestyle choices, diabetes and obesity. Sex specific and aging effects. Effects of turbulent blood flow, and arterial stiffening and vascular wall mechanics.
- Atherogenic mechanisms leading to myocardial infarction, stroke and peripheral artery disease.

Hemostasis, Thrombosis, Blood Cells and Transfusion - (HTBT)

The Hemostasis, Thrombosis, Blood Cells and Transfusion Study Section (HTBT) reviews applications involving basic and applied aspects of hemostasis, thrombosis, hematopoiesis, red blood cells, white blood cells, platelets, and transfusion. Studies using cellular, biochemical, biophysical, immunological, genetic, pharmacological and molecular biological approaches to define normal and pathological processes are reviewed. Applied aspects of normal and abnormal hematopoiesis, as well as applied aspects of the formed elements of the blood are also reviewed.
Additional areas of review include hematopoietic stem cells, hematopoietic growth factors and their receptors, iron and heme metabolism, blood cell cytoskeleton biology, myeloid biology, transfusion medicine and gene therapy. HTBT does not review applications related to leukemia. These will typically be reviewed in the OBT/ OTC IRGS.

Topics

- Mechanisms of hemostasis, thrombosis and blood coagulation.
- Hematopoiesis, including hematopoietic stem and progenitor cells and epigenetic regulation of gene expression.
- "Omics" of blood cells and plasma proteins related to hematologic diseases.
- Thrombolysis/fibrinolysis, Plasminogen activation, sepsis, proteases and their receptors.
- Platelet and Megakaryocyte biology, congenital and acquired platelet/bleeding disorders and their gene therapy.
- Pathogenesis and pathophysiology of thromboembolism, thrombophilia, thromboembolism and related diseases. Thrombogenesis and coagulation in inflammation/immune response and cancer/uncontrolled tissue growth, acquired coagulopathies.
- Transfusion medicine, blood substitutes; blood banking; development of globin gene regulation, immunohematology.
- Inherited or acquired anemias including sickle cell anemia, sideroblastic anemias, hemolytic anemias, anemia of chronic disease and anemias of bone marrow failure. Inherited or acquired bleeding and thrombotic disorders, including hemophilia. Iron and heme metabolism and iron overload states.
- Thrombocytopenia due to aplastic anemia, lymphoma, Wiskott-Aldrich or May- Hegglin syndrome, viral infection and chemotherapy or radiation treatments.
- Leukocyte biology and diseases (not including leukemia): Leukocyte adhesion, migration and release of bioactive factors and related roles in capillary permeability, vasomotor response, blood clotting, inflammation, tissue repair and remodeling, fibroblast activation and scar formation.
- Myelopoiesis, erythropoiesis, leukopoiesis and thrombopoiesis.

Integrative Myocardial Physiology/Pathophysiology A - (MPPA)

The Integrative Myocardial Physiology/Pathophysiology A Study Section (MPPA) reviews basic and applied/translational applications focused on mechanisms which regulate normal and pathologic myocardial function, with an emphasis on myocardial contractility, heart failure, cardiotoxicity, inflammation and immune influences. Topics include metabolism and energetics related to myocardial function and pathology, including but not limited to contractile dysfunction, hypertrophy and heart failure; differences related to sex and age are appreciated. Representative methods and experimental strategies may include electrophysiology, stem cells/bioengineered tissue, genetics, genomics and proteomics.

Topics

- Mediators and modulators of cardiac and vascular smooth muscle contractility: calcium homeostasis; calcium sensitive proteins; neural, redox, and transcriptional regulation of genes and proteins that modulate cardiac and vascular excitability and contractility; regulation of ion channel function and expression.
- Cardiac myocyte contractile function: sarcomeric proteins; calcium regulation and signaling; calcium-force relationship; excitability, excitation contraction coupling.
- Systolic and diastolic function/dysfunction: adaptation to abnormal hemodynamic load and ventricular mechanics; mechanical signal transduction; stress-strain relationships; effects of therapeutic interventions such as pacing, ventricular assist devices and others; valvular heart disease.
- Cardiac hypertrophy and heart failure: basic molecular and cellular mechanisms; myocyte growth, proliferation, metabolism and apoptosis; receptor signaling; transcriptional pathways; inflammatory/ cytokine-mediated processes. Mechanisms of remodeling and heart failure resulting from arrhythmia.
- Genetic cardiomyopathies: genotype-phenotype correlation; genomic and proteomic approaches to cardiac hypertrophy and failure.
- Cardiac repair to address issues of remodeling and contractility deficit: strategies may include cell-based, gene therapy and the evaluation of bioengineered cells and tissues; capillary density. Topics include those related to heart transplantation, changes in ventricular and cellular function, myocardial inflammation & repair processes, recovery of cardiac function in the presence of cardiac assist devices and by tissue engineering approaches.
- Metabolism and energetics associated with heart disease: impact of diet, obesity or systemic metabolic disorders, including diabetes, obesity and hypercholesterolemia, associated with cardiac health and dysfunction; inclusion of age and sex in disease process. Issues contributing to cardiac-related metabolic dysfunction, lifestyle; diet, exercise, nutrition, environmental science; influences of age and sex in disease process.
- Cardiotoxicology: Effects of toxicants, including environmental and chemotherapeutic agents, on cardiac health and function.

Integrative Myocardial Physiology/Pathophysiology B - (MPPB)

The Integrative Myocardial Physiology/Pathophysiology B Study Section (MPPB) reviews basic and applied/translational applications focused on mechanisms which regulate normal and pathologic myocardial function, with an emphasis on myocardial infarction, ischemia-reperfusion injury, remodeling, arrhythmia and drug induced myocardial toxicity. Topics include metabolic dysfunction, particularly associated with myocardial infarction and ischemia-reperfusion injury; differences related to sex and age are appreciated. Proposed research may involve approaches which include the use of bioengineering/stem cell technologies, computational and systems biology and mathematical modeling.

Topics

- Mechanisms of ischemia/reperfusion tissue injury and post injury responses: myocardial stunning, infarction, hibernation, early post-ischemic cardiac remodeling, cellular and molecular mechanisms that govern the biology of stem cells in ischemic heart disease. Myocardial remodeling and fibrosis: extracellular matrix reorganization and collagen metabolism; cytoskeleton.
- Metabolic dysfunction, mechanisms of myocardial cell death (apoptosis/necrosis) mitochondrial dysfunction and autophagy. Influence of metabolic dysfunction related to both health and disease, including impact of lifestyle (diet, exercise, nutrition, environmental science), age and sex in disease process.
- Control of coronary blood flow: post-ischemic coronary vascular abnormalities, coronary endothelial function, angiogenesis, collateral circulation;hypertension.
- Novel methods for cardiac imaging: approaches to assess myocardial metabolism, injury, and fibrosis.
- Signal transduction: mechanisms related to myocardial ischemia/reperfusion injury, including preconditioning, postconditioning. Mechanical signal transduction; stress-strain relationships; effects of therapeutic interventions such as pacing and ventricular assist devices.
- Drug-induced cardiovascular toxicity: including pathology developed during or following treatment for disorders such as myocardial dysfunction, ischemia, hypotension, hypertension, QT-interval prolongation, arrhythmias and thromboembolism.
- Cardioprotection, cardiac repair and regeneration: cardiac repair/regeneration following ischemic injury, cardiac bioengineering, including strategies to support stem cell therapy, gene therapy and the use of bioengineered cells andtissues.
- Electrophysiological consequences of acquired heart diseases: including those related to ischemia, hypertension, diabetes, obesity, heart failure, hypertrophy, and heart transplant; mechanisms and therapy of cardiac arrhythmias and ion channel dysfunction.
- Cellular mechanisms of arrhythmogenesis: identification of genes and proteins that modulate electrical activity; electrophysiological consequences ofacquired

heart diseases including ischemia, hypertension, diabetes, obesity, heart failure, hypertrophy, and heart transplant.

- Excitability, electrical propagation and repolarization in normal and diseased hearts: structure and function of cardiac ion channels, ion exchangers, and ion pumps; impulse propagation; excitation contraction coupling; conduction system; intercellular communication including gap junctions/connexins; molecular and genetic evaluations of ion channels.
- Computational and systems modeling to predict arrhythmias: mathematical modeling of ion channels, myocytes, multi-cellular tissue and the whole heart; development and evaluation of interventions and biomedical devices to diagnose and treat cardiac rhythm disorders.

Therapeutic Development and Preclinical Studies - (TDPS)

The Therapeutic Development and Preclinical Studies Study Section (TDPS) will review applications on preclinical work in animal models, where research efforts are focused on the generation/development of novel therapies within fields such as cardiac, vascular systems and related regulatory organ systems including hemostasis and thrombosis. Proposed research may involve efforts to develop new understanding/perspectives associated with cardiac, vascular or blood-related dysfunction/toxicology. Aims may focus on device optimization, therapeutic target development and drug discovery programs.

Topics

- Preclinical studies: including proof of concept (POC) and mechanism-of-action (MOA) studies, those providing insight toward the development of novel therapeutic strategies;
- Resuscitation studies evaluated in animal model systems;
- Dosing studies in pre-clinical models: large and small animal systems. Studies may involve varied proposed therapeutic approaches including small molecule, cell- based, viral, peptide, antibody as well as the evaluation of microbiome/microbiota- based strategies;
- Target development: including efforts to discover and/or characterize potential therapeutic targets;
- Preclinical and population "-omic" studies: those involving genomic, transcriptomic, metabolomic, etc.
- Preclinical device development and safety studies in animal models: proposed research may involve assist devices, bioengineered technologies, stem-cell based treatments;
- Development and evaluation of interventions and biomedical devices: those aimed at diagnosing and/or treating cardiac, vascular and hematologic disorders.

Clinical Integrative Cardiovascular and Hematological Sciences - (CCHS)

The Clinical Integrative Cardiovascular and Hematological Sciences Study Section (CCHS) reviews patient-oriented research related to cardiac, vascular and hematological systems as well as related regulatory organ systems, including hemostasis. Applications reviewed in CCHS typically focus on studies which investigate cardiovascular physiology of humans, including studies related to autonomic regulation, exercise, and aging, as well as pathology associated with cardiovascular and hematological dysfunction, including thrombosis. Applications may include studies involving genetics, pharmacology, transfusion medicine, surgical procedures, toxicity, and environmental stressors. Proposed clinical trials which focus on mechanisms of health and/or disease may be reviewed in CCHS.

Topics

- Human clinical studies, including pediatric populations, cardiovascular imaging, mechanisms and consequences of disease. Investigations may include physiology, pharmacology, electrophysiology, regional circulation, transfusion medicine, blood cell abnormalities, hemodynamics, cardiac mechanics, biomarker discovery, and genetic considerations in cardiovascular studies.
- Disease states may include cardiac and vascular ischemia, heart failure/cardiomyopathy, metabolic syndrome, atherosclerosis, stroke, dyslipidemia, hypertension, obesity, diabetes, thyroid disease, general inflammation, hypercholesterolemia, and hematologic disorders such as sickle cell disease and hemophilia.
- Modulation of cardiac/cardiovascular responses and adaptations including influence of sex, aging, pregnancy, and acute/chronic exercise on metabolic function and cardiac, vascular smooth muscle, and vascular endothelial function(s).
- Neural control of the cardiovascular system including central and peripheral autonomic physiology, pharmacology, and receptor mechanisms in healthy and diseased populations.
- Clinical studies investigating the responses of the cardiovascular system to trauma or surgery including arrhythmias associated with cardiac surgery or cardiopulmonary bypass, cardiac sudden death, resuscitation, stenting, pacemakers, cardiovascular injury and repair, and myocardial ischemia/reperfusion injury.
- Environmental stresses, cardiovascular toxicity, and modifying conditions/stimuli including smoking, altitude, microgravity, heat, cold, bed rest/deconditioning, and environmental pollution in patients.