Cluster 10 Descriptions and Overlap statements

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Advancing Therapeutics A (ATA)

The **Advancing Therapeutics A (ATA)** study section reviews applications that promote new therapeutic strategies for addressing neoplastic diseases (including solid tumors and leukemias) that extend foundational work by evaluating therapeutic efficacy and preclinical safety/toxicity in large or complex animal models. The major emphasis of this study section is to advance therapeutic strategies through preclinical development that exhibit potential for translation to the clinic.

Topics:

- Evaluation of gene and drug-delivery strategies (nonimmunological), including reformulation/combination of existing drugs or formulation development of evidence based new drugs
- Advanced preclinical drug toxicity and PK/PD studies in small, medium, large, patient-derived xenograft, or transgenic animal models, or human specimens for validation.
- Late-stage diversification and optimization of small molecule anti-cancer agents.
- Development of therapeutic strategies and rational combinations of cytotoxic drugs with novel agents including those targeting: growth factors, signaling, cell cycle regulation, angiogenic, and differentiation pathways.
- Early-stage, pilot clinical trials of novel anticancer therapeutic and drug-delivery strategies involving pharmacokinetic, pharmacodynamic, toxicologic, or pharmacogenomic endpoints.
- Development and application of mathematical and computational methods for the investigation of therapeutic strategies.

Shared Interests and Overlaps

There are shared interests in drug development with Drug Discovery and Molecular Pharmacology C (DMPC). Applications that emphasize late-stage drug development efforts are reviewed in ATA. Applications focused on early stages of drug discovery involving synthesis, validation/optimization of new anti-cancer therapeutic agents and in vivo evaluation of new drugs are reviewed in DMPC.

There are shared interests in nanotechnology related to nanomaterials for drug delivery with **Innovations in Nanosystems and Nanotechnology (INN)** study section. Applications that emphasize therapeutic efficacy or focus on the development therapeutic strategies as the endpoint are reviewed in ATA. Applications that focus on the disposition and toxicity of drugs, including mechanistic pathways involved in drug toxicity, are reviewed in INN.

There are shared interests in therapeutic bioavailability, toxicity, and efficacy with **Drug and Biologic Disposition and Toxicity (DBDT) Study Section**. Applications that focus on preclinical and pilot clinical studies on bioavailability, toxicity, and efficacy of cancer therapeutic agents are reviewed in ATA. Applications that focus primarily on drug or biologic bioavailability, biotransformation, and/or toxicity are reviewed in DBDT.

There are shared interests in the area of Gene and drug-delivery strategies with **Drug and Biologic Therapeutic Delivery (DBTD)**. Applications that focus efficacy, safety, or toxicity in animal models or pilot clinical trials are reviewed in ATA. Applications that focus on foundational technological advancements or are focused on bioengineering principles are reviewed in DBTD.

There are shared interests in nucleic-acid based drug development with **BBBT (81)**. Applications that emphasize late-stage drug development and advanced efficacy/safety studies are reviewed in ATA. Applications that emphasize disease-agnostic development of nucleic acid therapeutics are reviewed in BBBT (81).

There are shared interests on therapeutic strategies involving combinations of cytotoxic drugs with targeting agents with Mechanisms of Cancer Therapeutics-C (MCTC). Applications that focus on advanced animal experiments and pilot clinical trials may be reviewed in ATA. Applications that focus on mechanism of action of novel therapeutic combination strategies that include efficacy studies may be reviewed in MCTC.

There are shared interests on therapeutic strategies involving combinations of cytotoxic drugs with targeting agents with Mechanisms of Cancer Therapeutics-B (MCTB). Applications that focus on advanced animal experiments and pilot clinical trials may be reviewed in ATA. Applications that focus on mechanism of action of combination therapies and the effects of drug combination on key oncogenic signaling processes may be reviewed in MCTB.

There are shared interests in the therapeutic evaluation of the anti-cancer drug effect with Mechanisms of Cancer Therapeutics-A (MCTA). Applications that focus on the pre-clinical development and evaluation of novel anti-cancer therapeutics and rational combinations of cytotoxic drugs with novel agents may be reviewed in ATA. Applications that focus on the mechanism of action of novel anticancer agents and the impact of drug properties on anti-cancer drug function may be reviewed in MCTA.

There are shared interests in drug efficacies and toxicities with **Molecular Cancer Diagnosis and Combination (MCDC)**. Applications that focus on translational studies of novel/established antineoplastic agents and pre-clinical drug toxicity, pharmacokinetic/pharmacodynamic studies of anticancer agents may be reviewed in ATA. Applications that focus on the development of markers of responses and toxicity of established therapeutic agents are reviewed in MCDC.

There are shared interests in the areas of oncolytic virotherapy and chemoimmunotherapy with **Translational Immuno-oncology (TIO)**. Applications that are more focused on the non-immunological aspects such as gene therapy are reviewed in ATA. Applications that focus on the immunological aspects of virotherapy are reviewed in TIO.

There are shared interests in early-stage, pilot clinical trials **with Clinical Oncology (CONC)**. Applications that focus on the experimental therapy of neoplastic diseases in in vitro systems and in vivo model systems, including some pilot clinical trials are reviewed in ATA. Applications that focus on clinical trials with targeted therapy of small molecular inhibitors are reviewed in CONC.

There are shared interests in the areas of mathematical and computer modelling with Modeling and Analysis of Biological Systems (MABS). Applications which seek to apply the modeling for investigation of combination chemotherapy using small molecules and other modalities for cancer therapy are reviewed in ATA. Applications which focus on the early development of the modeling are reviewed in MABS.

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Advancing Therapeutics – ZRG1 MCST (81)

The **Advancing Therapeutics (ZRG1 MCST (81))** study section reviews applications that promote new therapeutic strategies for addressing non-cancer related diseases and extend foundational work by evaluating therapeutic efficacy and preclinical safety/toxicity in animal models and in pilot clinical trials. The major emphasis of this study section is to advance preclinical development of therapeutic strategies that exhibit potential for translation to the clinic. Studies include, but are not limited to, therapeutics for infectious diseases.

Topics:

- Late-stage diversification and optimization of lead compounds for therapeutic efficacy
- Advanced preclinical drug toxicity and pharmacokinetic/pharmacodynamic studies in animal models
- Development of therapeutic strategies and rational combinations of existing drugs with novel agents
- Evaluation of gene- and drug-delivery strategies, including formulation development of new drugs and reformulation or combinations of existing drugs
- Early-stage clinical trials of novel therapeutic and drug-delivery strategies involving pharmacokinetic, pharmacodynamic, toxicologic, or pharmacogenomic endpoints
- Development and application of mathematical and computational methods for the investigation of therapeutic strategies

Shared Interests and Overlaps:

There are shared interests in drug development with **Drug Discovery and Molecular Pharmacology A, B (DMPA, DMPB) and DCAI (81)**. Applications that emphasize late-stage drug development efforts are reviewed in MCST (81). Applications that emphasize early-stage drug development, such as discovery of novel agents and characterization of mechanism of action are reviewed in DMPA and DCAI (81) (for infectious diseases) or DMPB (for all other diseases, excluding cancer).

There are shared interests in drug delivery nanomaterials with **Innovations in Nanosystems and Nanotechnology (INN)**. Applications that emphasize nanomaterial efficacy, safety, or toxicity in animal models or pilot clinical trials are reviewed in MCST (81). Applications that emphasize the design, synthesis, and development of nanomaterials are reviewed in INN.

There are shared interests in gene and drug-delivery strategies with **Drug and Biologic Therapeutic Delivery (DBTD).** Applications that emphasize treatment efficacy, safety, or toxicity in animal models or pilot clinical trials are reviewed in MCST (81). Applications that emphasize foundational technological advancements or are focused on bioengineering principles are reviewed in DBTD.

There are shared interests in nucleic acid-based therapeutics with **BBBT (81)**. Applications that emphasize efficacy, safety, or toxicity in animal models or pilot clinical trials are reviewed in MCST (81). Applications that emphasize fundamental design, delivery, and targeting of nucleic acid therapies are reviewed in BBBT (81).

There are shared interests in drug disposition and safety with **Drug and Biologic Disposition and Toxicity (DBDT)**. Applications that emphasize therapeutic efficacy or focus on the development of therapeutic strategies as the endpoint are reviewed in MCST (81). Applications that focus on the disposition and toxicity of drugs, including mechanistic pathways involved in drug toxicity, are reviewed in DBDT.

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Anti-Infective Resistance and Targets (AIRT)

The **Anti-Infective Resistance and Targets (AIRT)** study section reviews applications that focus on the mechanisms of drug resistance in bacterial, viral (excluding HIV), and eukaryotic pathogens. This study section also reviews applications focused on the discovery and initial characterization of novel anti-infective drug targets.

Topics:

- Mechanisms of the origin and spreading of anti-infective drug resistance ranging from molecular to population-level approaches
- Environmental regulators of drug resistance, including pathogen interactions with hosts, microbiomes, and biofilms
- Origin and spread of drug resistance through evolution, nature, ecology, agriculture, pathogen interactions, and infection control practices
- Identification and characterization of novel anti-infective drug targets, including assay development
- Strategies for preventing resistance, including identification of markers of drug resistance

Shared Interests and Overlaps:

There are shared interests in addressing the mechanism of action of antimicrobial drugs with **Drug Discovery and Molecular Pharmacology A (DMPA) and DCAI (81)**. Applications that emphasize the biology underlying drug resistance or that aim to establish novel drug targets are reviewed in AIRT. Applications that emphasize discovery of new drugs, including drug optimization are reviewed in DMPA and DCAI (81).

There are shared interests in biological studies of pathogens with study sections in the **Immunology and Infectious Diseases A and B (IIDA, IIDB) review branches.** Applications that focus on identifying novel drug targets are reviewed in AIRT. Applications that focus on the basic biology or pathogenesis of infectious agents are reviewed in the relevant pathogen-focused study section, including Bacterial Virulence (BV), Bacterial-Host Interactions (BHI), Molecular and Cellular Biology of Virus Infection (MCV), Viral Dynamics and Transmission (VDT), and Pathogenic Eukaryotes (PTHE).

There are shared interests in physiological studies of bacteria with **Prokaryotic Cell and Molecular Biology (PCMB)**. Applications that address the utility of a physiological process as a potential drug target are reviewed in AIRT. Applications that focus on understanding fundamental bacterial processes are reviewed in PCMB.

There are shared interests in pathogen evolution with **Genetic Variation and Evolution (GVE)**. Applications that emphasize drug resistance mechanisms are reviewed in AIRT. Applications that emphasize natural genetic variation in the context of pathogen physiology are reviewed in GVE.

There are shared interests in the spread of drug-resistant pathogens with **Etiology, Diagnostic, Intervention and Treatment of Infectious Diseases (EDIT)**. Applications that emphasize the pathogen physiology underlying resistance are reviewed in AIRT. Applications that focus on translational and applied research are reviewed in EDIT.

There are shared interests in population-level analyses of drug resistance with **Population-based Research in Infectious Disease (PRID)**. Applications that emphasize studies of microbe populations are reviewed in AIRT. Applications that focus on human populations are reviewed in PRID.

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Chemical Biology & Probes (CBP)

The **Chemical Biology & Probes (CBP)** study section reviews the applications that focus on the development and application of chemical and pharmacological methods to identify and manipulate biological targets relevant to human disease. The primary focus is on fundamental studies using chemical biology and probe development approaches to illuminate pathways, often relevant to the earliest stages drug discovery.

Topics:

- Design, synthesis, and application of small molecule probes to explore biological systems
- Applications of biomolecules & mimetics (peptide, protein, oligonucleotide, carbohydrates) as tools to probe biological phenomena Target ID and validation (via chemical and combined chemical/genetic methods) – reverse screening
- Phenotypic and morphologic responses to chemical and genetic perturbations – forward screening
- 'Omic cataloging of responses to chemical and biological perturbations (proteomic, genomic, metabolomic, lipidomic, etc.) including developing new probes to drive such perturbations
- Connection of biochemical, cellular, and tissue responses driven by chemical probes and genetics (in vitro, in cells, in model organisms)
- Development and applications of bio-orthogonal labeling chemistry
- Imaging agents and radiochemistry to be used to study biological systems
- Early therapeutic lead validation via target identification system response characterization
- High-throughput (HTS) assay development and primary screen implementation relevant to drug discovery
- Optimization of chemical probes for use in vivo
- Medicinal chemistry focused on lead selection for disease-oriented programs
- Protein chemistry and protein engineering applied to potential therapeutic and tool development

Potential Overlaps:

- There are shared interests in synthetic methodologies with **Chemical Synthesis and Biosynthesis (CSB).** Applications involving medicinal chemistry, development of chemical probes, and protein chemistry and engineering are reviewed in CBP. Applications involving natural products, total synthesis, and peptide chemistry are reviewed in CSB.

- There are shared interests in drug development with **Drug and Biologic Disposition and Toxicity (DBDT)**. Applications that emphasize the early-stage development and characterization of novel compounds are reviewed in CBP. Applications focused on in vivo ADME/tox studies of candidate compounds already synthesized are reviewed in DBDT.

- There are shared interests in development of antibacterial, antiparasitic, antiviral, and antitumor therapeutics with **Drug Discovery and Molecular Pharmacology A, B, C (DMPA, DMPB, DMPC) and DCAI (81).** Applications that emphasize drug synthesis with limited biological assessments are reviewed in CBP. Applications that emphasize drug function and therapeutic potential are reviewed in DMPA, DMPB, DMPC or DCAI (81).

- There are shared interests in chemical and biochemical aspects of drug discovery and probe development with **Macromolecular Structure and Function A (MSFA)**. Applications that emphasize development and/or deployment of empirical synthetic and medicinal chemistry are reviewed in CBP. Applications that focus using elements of structure-based computational analysis and design/bioinorganic approaches to probe development are reviewed in MSFA.

- There are shared interests in chemical synthesis of reagents and probes for use with bioanalytical and biophysical technologies with **Enabling Bioanalytical and Imaging Technologies (EBIT)**. Applications that emphasize development of novel probes are reviewed in CBP. Applications that deploy well-established strategies while emphasizing customized adaptation to bioanalytical detection are reviewed in EBIT.

- There are shared interests in reviewing studies of effects of molecular probes or prospective therapeutic modifiers of prokaryotic or eukaryotic pathogens with **Prokaryotic Cell and Molecular Biology (PCMB), Bacterial-Host Interactions (BHI), Bacterial Virulence (BV) and Pathogenic Eukaryotes (PTHE).** Applications that emphasize development of novel synthetic or medicinal chemistry approaches are reviewed in CBP. Applications that use known or modestly modified drugs as probes are reviewed in PCMB, BHI, BV or PTHE.

- There are shared interests in reviewing studies of effects of molecular probes or prospective therapeutic modifiers of viral activity with **Molecular and Cellular Biology of Virus Infection (MCV), Viral Dynamics and Transmission (VDT), and Viral Pathogenesis and Immunity (VPI).** Applications that emphasize development of novel synthetic or medicinal chemistry approaches are reviewed in CBP. Applications that emphasize understanding fundamental viral processes or pathogenesis mechanisms using known or modestly modified drugs as probes are reviewed in MCV, VDT, VPI.

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Chemical Synthesis & Biosynthesis (CSB)

The **Chemical Synthesis & Biosynthesis (CSB)** study section reviews applications in the areas of fundamental methods and strategies for synthesis and biosynthesis of molecules that may contribute to advances in biology, medicine, and biotechnology. Areas broadly include synthetic methodology development, the chemistry of metals, nucleic acid, chemistry, and carbohydrate chemistry. Many objectives are relevant to early stages of drug development.

Topics:

- Methodologies of total synthesis and target-oriented synthesis of organic, organometallic, and inorganic compounds
- Isolation, synthesis, and biosynthesis/pathway bioengineering of complex natural products
- DNA encoded synthesis and associated methodologies
- Synthesis of nucleic acids, lipids, carbohydrates, and other biologically active molecules.
- Chemistry of peptides, proteins, and their mimetics.
- Secondary metabolism of biomolecules
- Synthesis of new supramolecular species and nanomaterials for drug discovery, including dendrimers and polymers
- Mechanisms of catalysis and biocatalysis
- Synthetic and biosynthetic methodologies in structure-based drug discovery
- Machine learning / AI driven development of synthesis methodologies

Potential Overlaps:

- There are shared interests in targeting biological systems with synthetic molecules with **Chemical Biology and Probes (CBP)**. Applications that emphasize development of synthetic methods are reviewed in CSB. Applications that emphasize strategic deployment in fundamental studies of biological system are reviewed in CBP.

- There are shared interests in natural product biosynthesis, metal catalysis, and computational methodology with **Macromolecular Structure and Function A (MSFA)**. Applications that use synthetic and coordination chemistry to design new metallo-reagents are reviewed in CSB. Applications that link metallo-centers to enzymatic catalysis and those examining molecular mechanisms of metal homeostasis are reviewed in MSFA. Applications that employ structural biology approaches to studying catalysis and biocatalysis are reviewed in MSFA. Applications that emphasize computational methodology not targeted specifically to synthesis are reviewed in MSFA.

- There are shared interests in development of polymeric, supramolecular and nanomaterials with **Innovations in Nanosystems and Nanotechnology (INN)** and **Drug and Biologic Therapeutic Delivery (DBTD)**. Applications that emphasize new basic synthetic chemistry strategies are reviewed in CSB. Applications that emphasize development of higher-level nanostructures, nanodevices, nano-biologics, or biomaterials customized for specific biomedical applications are reviewed in INN or DBTD.

- There are shared interests in natural product isolation with **Enabling Bioanalytical and Imaging Technologies (EBIT)**. Applications that emphasize overall chemistry of end products or their derivatives are reviewed in CSB. Applications that focus on developing new analytical/bioanalytical tools isolation and identification are reviewed in EBIT.

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Drug and Biologic Disposition and Toxicity (DBDT)

The **Drug and Biologic Disposition and Toxicity (DBDT)** study section reviews applications related to the disposition and safety of therapeutic agents including small molecule drugs and pro-drugs, biological products such as therapeutic proteins and gene therapies, and phytochemicals/botanicals. The panel reviews studies on how the body's transporter, enzymatic and other biological processes affect the pharmacokinetic properties and toxicological profiles of drugs and therapeutic biologics. Additionally, this panel reviews applications focused on the development of in vitro, in vivo, and mathematical models for use in understanding and predicting therapeutic agent disposition and safety. Further, studies of how formulation can alter safety and efficacy are within the scope of this panel. It also examines mechanisms of therapeutic agent-induced toxicity as well as how pharmacogenetics and biological processes may impact the action and/or pharmacokinetics of drugs and biologics. Applications reviewed by this panel may have a focus on any cell type, tissue, organ, organ system, or anatomical compartment.

Topics:

- Mechanistic, preclinical, and clinical studies related to the disposition and safety of therapeutic agents (drugs and biologics) including processes of absorption, biotransformation, distribution, excretion and toxicity.
- Studies investigating mechanisms of nanoparticle toxicity and/or immunogenicity, as well as mechanisms of action of xenobiotics, non-nutrient chemicals and nutrients, including pharmacological effects across multiple organ systems.
- Toxicity and off target effects of gene therapies.
- Optimization of lead compounds for absorption, biotransformation, distribution, excretion, and toxicity. Studies may include structure-function relationships for enzymes/transporters/receptors involved in nutrient, non-nutrient chemicals and/or xenobiotic disposition and their toxic effects.
- Impact of genetics on disposition including pharmacogenetics/pharmacogenomics and toxicogenetics/toxicogenomics.
- Theoretical, mechanistic, and/or physiologically based modeling of pharmacokinetics, pharmacodynamics, toxicokinetics and toxicodynamics including the development of in vitro and in vivo model systems to study drug and/or biologic disposition and safety.
- Interactions between therapeutic agents that impact disposition, toxicity, and efficacy such as interactions among xenobiotics (e.g., drug-drug interactions, nutrient-drug interactions, alcohol-drug interactions) involving disposition and response processes.
- Environmental factors and agents that impact drug and/or biologic disposition including bioavailability, metabolism, pharmacokinetics, and toxicokinetics, including the effect of the microbiome on bioavailability, metabolism and pharmacokinetics of drugs and xenobiotics.
- Studies of the influence of formulation on disposition, safety, and efficacy.

Potential Overlaps:

- There are shared interests in the pharmacology, metabolism and disposition of xenobiotics with **Environmental Determinants of Disease (EDD).** Applications that emphasize disposition or metabolism and pharmacology of xenobiotics and supraphysiologic levels of nutrient and non-nutrient chemicals (not environmental toxicants) are reviewed in **DBDT.** Applications that involve environmental toxicants/toxins are reviewed in **EDD**.

- There are shared interests in studies of drug or biologic bioavailability, biotransformation, and/or toxicity with **Advancing Therapeutics A (ATA)** and **MCST (81)**. Applications that primarily focused on those areas are reviewed in **DBDT**. Applications that emphasize pilot studies of drug or biologic bioavailability, biotransformation, and/or toxicity as part of the larger proposal are reviewed in **ATA** or **MCST (81).**

- There are shared interests in involving agents for therapeutic delivery with **Drug and Biologic Therapeutic Delivery (DBTD)**. Applications that focus on the disposition and safety of delivery agents are reviewed in **DBDT**.

Applications that involve fundamental aspects of therapeutic delivery, including controlled or triggered release, intraorgan/intracellular delivery, delivery vehicle development, or targeting strategies are reviewed in **DBTD**.

- There are shared interests in nanosystem/nanotechnology development with **Innovations in Nanosystems and Nanotechnology (INN)**. Applications that emphasize the disposition, safety and toxicity of delivery agents are reviewed in **DBDT.** Applications that focus on novel nanotechnology development are reviewed in **INN**.

- There are shared interests in therapeutic systems for nucleic acid delivery with **BBBT (81)**. Applications that emphasize the disposition, safety and toxicity of delivery agents are reviewed in **DBDT.** Applications that focus on fundamental aspects of nucleic acid delivery are reviewed in **BBBT (81)**.

- There are shared interests in the effects of nutrients on the disposition of drugs and xenobiotics with **Nutrition and Metabolism in Health and Disease (NMHD)**. Applications that investigate the disposition of supraphysiologic levels of nutrients are reviewed in **DBDT**. Applications that emphasize the integrated effects of nutrients on physiological functions and their influence on disease are reviewed in **NMHD**.

- There are shared interests in drug development with **Chemical Biology and Probes (CBP)**. Applications that focus on ADME/tox studies of candidate compounds already synthesized are reviewed in **DBDT.** Applications that focus on the early-stage development and characterization of novel compounds are reviewed in **CBP**.

- There are shared interests in hepatobiliary transport, liver injury and alcohol liver disease with **Hepatobiliary Pathophysiology (HBPP)**. Applications that investigate alcohol-drug interactions and the contributions of alcohol to pharmacological-induced injury in the liver are reviewed in **DBDT**. Applications that focus on the pathogenesis of alcoholic liver injury and other liver diseases are reviewed in **HBPP**.

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Drug and Biologic Therapeutic Delivery (DBTD) Study Section

The **Drug and Biologic Therapeutic Delivery (DBTD)** study section reviews applications that focus on the fundamental aspects of preclinical therapeutic gene and drug delivery, delivery vehicle development, targeting strategies, mechanisms, and the consideration of biological barriers. Applications are typically focused on bioengineering principles of small molecules and biologics and their mode of delivery and may not be hypothesis driven.

Topics

- Delivery of therapeutic-based molecules, biologics, hybrids, drug combinations, vaccines (non-mRNA), novel viruses, VLPs (Virus Like Particles), antibiotics, antivirals, antigens, and cell therapies.
- Studies utilizing controlled or triggered release, intraorgan, and intracellular delivery.
- Targeted strategies using peptides, lipids, carbohydrates. Delivery strategies including light and physical methods, antibiotics, and antivirals.
- Delivery vehicles including viruses, liposomes, micelles, vesicles, nanoparticles, biomaterials, and cells.
- Studies of the biological barriers to delivery (e.g., membrane, tissue, cellular, trafficking, physical). Including the blood-brain barrier.
- Studies of the interactions of delivery vehicles, devices, and/or payloads with the immune system and host-tissue.
- AI & ML approaches in preclinical drug delivery.

Shared Interests and Overlaps

- There are shared interests in nanomaterials and nanosystems towards biomedical applications with **Innovations in Nanosystems and Nanotechnology (INN)**. Applications that focus on the targeted delivery, use as vehicles, and controlled release, of these nanostructures as therapeutic strategies are reviewed in DBTD**.** Applications that focus on the design, synthesis, and development of nanostructures, engineered exosomes, protein-based materials, and theranostics are reviewed in INN.

- There are shared interests in gene and drug delivery with **Biomaterials and Biointerfaces (BMBI)**. Applications that focus more on the design and development of novel delivery vehicles, vectors, or payloads are reviewed in DBTD. Applications that focus on biocompatibility of delivery vehicles or delivery from implants are reviewed in BMBI.

- There are shared interests in delivery with **BBBT (81)**. Applications that focus on fundamental aspects of therapeutic delivery of cargoes of synthetic and biologic nature except nucleic acids are reviewed in DBTD. Applications that focus on fundamental aspects of nucleic acid delivery, including intracellular delivery, delivery vehicle development, targeting strategies, and overcoming biological barriers are reviewed in BBBT (81).

- There are shared interests in gene and drug-delivery strategies with **Advancing Therapeutics A (ATA)**. Applications that focus on foundational technological advancements, preclinical evaluation of gene and drug delivery strategies or are focused on bioengineering principles may be assigned to DBTD. Applications that focus on efficacy, safety, or toxicity in animal models, or pilot clinical trials for neoplastic diseases may be assigned to ATA.

- There are shared interests in gene and drug-delivery strategies for non-cancer related diseases with **MCST (81)**. Applications that focus on foundational technological advancements, preclinical evaluation of gene and drug delivery strategies or are focused on bioengineering principles may be assigned to DBTD. Applications that

emphasize treatment efficacy, safety, or toxicity in animal models or pilot clinical trials for non-cancer related are reviewed in MCST (81).

- There are shared interests in development of polymeric, supramolecular and nanomaterials with **Chemical Synthesis & Biosynthesis (CSB)**. Applications that emphasize development of higher-level nanostructures, nanodevices, nano-biologics, or biomaterials customized for specific drug or biologic agent delivery are reviewed in DBTD. Applications that emphasize new basic synthetic chemistry strategies are reviewed in CSB.

- There are shared interests in involving agents for therapeutic delivery with **Drug and Biologic Disposition and Toxicity (DBDT)**. Applications that involve fundamental aspects of therapeutic delivery, including controlled or triggered release, intraorgan/intracellular delivery, delivery vehicle development, or targeting strategies are reviewed in DBTD. Applications that focus on the disposition and safety of delivery agents are reviewed in DBDT.

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Drug Discovery and Molecular Pharmacology A (DMPA)

The **Drug Discovery and Molecular Pharmacology A (DMPA)** study section reviews applications that are concerned with the identification of novel antibacterial, antiparasitic, and antifungal agents for the prevention and treatment of infectious diseases using biochemical, pharmacological, structural, cell-based, and animal model approaches.

Topics:

- Discovery of novel antimicrobial agents including small molecule inhibitors, natural products, antimicrobial peptides, antibodies, adjunct therapeutics, drug combination regimens, repurposed drugs, CRISPR-based antimicrobial technologies, phage therapy, and probiotic/microbiota-based approaches
- Molecular characterization of antimicrobial agents, including mechanism of action, structural characterization, and confirmation of target engagement
- Optimization of antimicrobial agents, including structure-guided drug design, medicinal chemistry, hit-to-lead optimization, adjunct therapeutics, and combination regimens
- Discovery of novel agents for host-directed therapies, including immunotherapies, to counter infections
- Development of novel assays and models to test drug efficacy, including cellular, organoid, and animal model systems

Shared Interests and Overlaps:

There are shared interests in drug development with **MCST (81)**. Applications that emphasize early-stage drug development, such as discovery of novel agents and characterization of mechanism of action are reviewed in DMPA. Applications that emphasize late-stage drug development efforts are reviewed in MCST (81).

There are shared interests in addressing the mechanism of action of anti-infective drugs with **Anti-Infective Resistance and Targets (AIRT)**. Applications that emphasize discovery and optimization of new drugs are reviewed in DMPA. Applications that emphasize the biology underlying drug resistance or that aim to establish novel drug targets are reviewed in AIRT.

There are shared interests in drug design with **Chemical Biology & Probes (CBP)**. Applications that emphasize drug function and antimicrobial potential are reviewed in DMPA. Applications that emphasize drug synthesis with limited biological assessments are reviewed in CBP.

There are shared interests in pathogen physiology with **Prokaryotic Cell and Molecular Biology (PCMB), Bacterial-Host Interactions (BHI), Bacterial Virulence (BV), and Pathogenic Eukaryotes (PTHE)**. Applications that emphasize developing new antimicrobial drugs are reviewed in DMPA. Applications that emphasize understanding fundamental processes or pathogenesis mechanisms, or that use known drugs as probes are reviewed in PCMB, BHI, BV, or PTHE.

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Drug Discovery and Molecular Pharmacology – ZRG1 DCAI (81)

The **Drug Discovery and Molecular Pharmacology (ZRG1 DCAI (81))** study section reviews applications that are concerned with the identification of novel antiviral (excluding HIV) agents for the prevention and treatment of infectious diseases using biochemical, pharmacological, structural, cell-based, and animal model approaches.

Topics:

- Discovery of novel antiviral agents including small molecule inhibitors, natural products, antiviral peptides, antibodies, DNA and RNA-based therapeutics, receptor decoys, adjunct therapeutics, drug combination regimens, repurposed drugs, and CRISPR-based antiviral technologies
- Molecular characterization of antiviral agents, including mechanism of action, structural characterization, and confirmation of target engagement
- Optimization of antiviral agents, including structure-guided drug design, medicinal chemistry, hit-to-lead optimization, adjunct therapeutics, and combination regimens
- Discovery of novel agents for host-directed therapies, including immunotherapies, to counter viral infections
- Development of novel assays and models to test drug efficacy, including cellular, organoid, and animal model systems

Shared Interests and Overlaps:

There are shared interests in drug development with **MCST (81)**. Applications that emphasize early-stage antiviral drug development, such as discovery of novel agents and characterization of mechanism of action are reviewed in DCAI (81). Applications that emphasize late-stage drug development efforts are reviewed in MCST (81).

There are shared interests in addressing the mechanism of action of antiviral drugs with **Anti-Infective Resistance and Targets (AIRT)**. Applications that emphasize discovery and optimization of new antiviral drugs are reviewed in DCAI (81). Applications that emphasize the biology underlying drug resistance or that aim to establish novel drug targets are reviewed in AIRT.

There are shared interests in drug design with **Chemical Biology & Probes (CBP)**. Applications that emphasize drug function and antiviral potential are reviewed in DCAI (81). Applications that emphasize drug synthesis with limited biological assessments are reviewed in CBP.

There are shared interests in drug target characterization with **Molecular and Cellular Biology of Virus Infection (MCV), Viral Dynamics and Transmission (VDT),** and **Viral Pathogenesis and Immunity (VPI)**. Applications that emphasize developing new antiviral drugs are reviewed in DCAI (81). Applications that emphasize understanding fundamental viral processes or pathogenesis mechanisms using known drugs as probes are reviewed in **MCV**, **VDT**, or **VPI**.

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Drug Discovery and Molecular Pharmacology C (DMPC)

The **Drug Discovery and Molecular Pharmacology C (DMPC)** study section reviews cancer-related applications focused on the discovery, design, identification, isolation, development of new molecular agents that are potentially useful in cancer therapy of solid tumors and leukemias. Agents may combat cancer by slowing cancer cell growth, hastening cancer cell death, sensitizing cancer cells to other therapies, inhibiting metastasis or angiogenesis, or ameliorating side effects.

Topics:

- Discovery of novel anti-cancer agents including small molecule inhibitors, natural products, peptides/proteins/peptidomimetics, repurposed drugs, immunomodulators, and combination regimens.
- Molecular characterization of new anti-cancer agents, including mechanism of action, structural characterization of enzyme-inhibitor complexes, and confirmation of target engagement.
- Optimization and preclinical studies of anti-cancer agents, including medicinal chemistry, hit-to-lead optimization; combination regimens, and early- stage toxicity and PK/PD studies in cellular and animal models.
- Design and development of new molecular entities/ vehicles for targeted delivery of anti- cancer therapeutics (eg, polymers, micelles and nanoparticles)
- Development of methods to test drug efficacy, including cellular, organoids, and animals.

Shared Interests and Overlaps

There are shared interests in drug development with **Advancing Therapeutics A (ATA)**. Applications focused on early stages of drug discovery involving synthesis, validation/optimization of new anti-cancer therapeutic agents and in vivo evaluation of new drugs are reviewed in **DMPC**. Applications focused on preclinical safety/toxicity that also involve limited late-stage optimization of anti-cancer agents are reviewed in **ATA.**

There are shared interests in drug design with **Chemical Biology & Probes (CBP)**. Applications that emphasize drug function and anticancer therapeutic potential are reviewed in DMPC. Applications that emphasize drug synthesis with limited biological assessments are reviewed in CBP.

There are shared interests in developing conventional and molecularly targeted agents with **Mechanisms of Cancer Therapeutics-A (MCTA)**. Applications that focus on early stages of drug discovery involving synthesis, validation/ optimization of new anti-cancer therapeutic agents and in vivo evaluation of new drugs are reviewed in DMPC. Applications that focus on mechanistic validation of novel agents at the molecular, cellular, or target tissue level are reviewed in MCTA.

There are shared interests in developing conventional and molecularly targeted agents with **Mechanisms of Cancer Therapeutics-B (MCTB)**. Applications that focus on chemical modification of existing compounds are reviewed in DMPC. Applications that focus on mechanism of action of these compounds at the molecular, cellular, or target tissue level are reviewed in MCTB.

There are shared interests in developing conventional and molecularly targeted agents with **Mechanisms of Cancer Therapeutics-C (MCTC)**. Applications that focus on chemical modification of existing compounds are reviewed in DMPC. Applications that focus on mechanism of action of these compounds at the molecular, cellular, or target tissue level are reviewed in MCTC.

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Drug Discovery and Molecular Pharmacology B (DMPB)

The **Drug Discovery and Molecular Pharmacology B (DMPB)** study section reviews applications proposing preclinical work aimed at discovering new pharmacotherapeutic and immunotherapeutic agents for treating or preventing disorders of the nervous system, including drug abuse; analgesics, anti-inflammatories, cardiovascular agents, and other treatments for the human body that exclude cancer and infectious disease.

Topics:

- Discovery of novel agents to target disorders of the nervous system, cardiovascular system, immune system, anti-inflammatories, anti-ulcer, and other diseases such metabolic and respiratory diseases including small molecule inhibitors, natural products, peptides, proteins, and combination regimens.
- Molecular characterization of therapeutic agents, including mechanism of action, structural characterization of enzyme-inhibitor complexes, and confirmation of target engagement.
- Optimization and preclinical studies of therapeutic agents, including medicinal chemistry, hit-to-lead optimization; adjunct therapeutics and combination regimens, cellular and animal models.
- Targeted delivery of therapeutics to biological targets (e.g., antibody-based; T-cell-based)
- Development of novel models to test drug efficacy, including cellular, organoids, and animals.

Shared Interests:

There are shared interests in new drug development and production with **Drug and Biologic Disposition and Toxicity (DBDT)**. Applications that involve new molecular agents that are potentially useful in disease therapy, other than cancer and anti-infectious agents, are reviewed in DMPB**.** Applications that investigate the metabolism, pharmacokinetics and mechanism of action of drugs are reviewed in DBDT.

There are shared interests in drug development with **MCST (81).** Applications that emphasize early-stage drug development for systems other than infectious diseases or cancer, such as discovery of novel agents and characterization of mechanism of action are reviewed in DMPB. Applications that emphasize late-stage drug development efforts are reviewed in MCST (81).

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Environmental Determinants of Disease (EDD) Study Section

The **Environmental Determinants of Disease (EDD)** study section reviews applications related to the pharmacological and toxicological mechanisms of adverse outcomes that can occur in individuals and populations exposed to toxicants, xenobiotics, and toxins, as well as the role of environmental factors in the etiology and outcome of diseases. The focus includes studying gene-environment interactions, identifying the molecular mechanisms and physiological processes by which environmental toxicants/toxins/xenobiotics initiate or promote disease progression, the molecular basis of susceptibility to environmentally induced disease, and the identification of biomarkers of exposure, susceptibility, and effect. Applications reviewed by this panel may involve any species, cell type, tissue, organ, organ system, or anatomical compartment.

Topics:

- Environmental toxicants, toxins, and emerging pollutants.
- Development of animal and human tissue/organoid model systems for the purpose of studying environmental toxicant-induced systemic effects.
- Modifiers of toxic/toxicant exposures and outcomes such as the identification of modifiable risk factors (e.g., diet or lifestyle) or the study of molecular mechanisms that affect the outcome of exposures (e.g., genes that affect the phenotypic and/or molecular expression of other genes).
- Identification and validation of biomarkers of environmental toxicant-induced injury in animals and humans.
- Exposure biology and the use of transitional epidemiology studies to develop and use biomarkers of exposure, susceptibility, and effect.
- Molecular basis for susceptibility to environmental and pharmacological induced toxicity and disease (e.g., pharmacogenomics and toxicogenomics) including alterations in microbiota.
- Gene-environment interactions including the molecular basis for the impact of an environmental exposure on disease risk on individuals or populations with different genotypes.
- Mechanisms whereby environmental toxicant exposures contribute to disease pathogenesis (e.g., carcinogenesis) in model systems and humans, resulting in toxicological, pharmacological, and epigenetic manifestations.
- Analysis of the exposome and how contact with environmental factors effects the human body to determine the types, levels, and combinations of exposures people experience and how those exposures affect human health and disease across the lifespan.

Potential Overlaps:

- There are shared interests in the disposition and/or metabolism of xenobiotics with **Drug and Biologic Disposition and Toxicity (DBDT).** Applications that focus on environmental toxicants/toxins are reviewed in **EDD**. Applications that emphasize disposition (metabolism) and pharmacology of xenobiotics (not environmental toxicants) and supraphysiologic levels of nutrient and non-nutrient chemicals are reviewed in **DBDT**.

- There are here are shared interests in the epidemiology of toxicant exposures with **Social and Environmental Determinants of Health (SEDH)**. Applications that focus on the pharmacological and toxicological mechanisms by which environmental toxicant exposures affect human disease pathogenesis, including studies employing animal models, are reviewed in **EDD**. Applications that focus on characterizing the relationship between environmental exposures and human health outcomes at the population level are reviewed in **SEDH**.

- There are shared interests in lung injury with **Lung Injury, Repair and Remodeling (LIRR).** Applications that emphasize lung toxicology (such as particulate air pollutants, tobacco, cannabis, and/or vaping) are reviewed in **EDD**. Applications that address adverse effects of environmental or other toxicants on the lung in the context of lung development, lung injury/repair, emphysema, and interstitial lung diseases such as sarcoidosis and asbestosis are reviewed in **LIRR**.

- There are shared interests in the effects of toxicants (e.g., organophosphates, heavy metals) that effect the nervous system with **Neurotoxicology and Alcohol (NAL)**. Applications that focus on the effects of environmental toxicants outside the central nervous system are reviewed in **EDD**. Applications that emphasize

neurotoxicology in model systems or that address the effects of environmental toxicants or alcohol on the central nervous system in animal models and humans are reviewed in **NAL**.

- There are shared interests in endocrine disruptors with **Cellular, Molecular and Integrative Reproduction (CMIR)**. Applications that emphasize the contribution of environmental toxicants to the etiology or progression of reproductive pathologies are reviewed in **EDD**. Applications that emphasize the use of xenobiotics/toxicants to alter molecular, cellular, genomic, endocrine, and physiological aspects of reproductive biology in both mammalian and model organism systems are reviewed in **CMIR**.

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Innovations in Nanosystems and Nanotechnology (INN)

The **Innovations in Nanosystems and Nanotechnology (INN)** study section reviews applications focused on the fundamental development of new enabling materials that take advantage of the unique properties of nanomaterials towards biomedical applications. These materials may exhibit novel advances in chemistry, biology, materials, or physics that advance gene and drug delivery, imaging/diagnostic approaches, or technology development. Novel nanotechnology development may overcome challenges in therapeutic delivery, diagnosis, biodistribution, or overcoming biological barriers.

Topics:

- Design, synthesis, and development of novel nanostructures, nanodevices, nanobiologics, and nanosystems for biomedical applications.
- Multifunctional nanoparticles in imaging, sensing, targeted drug/gene delivery and theranostics.
- Biomaterials and/or bioengineered materials, such as extracellular vesicles, engineered exosomes, and recombinant protein-based materials.
- Mathematical or computational approaches for the advancement of nanotechnology in biomedical applications.
- Studies of the unique properties of nanomaterials for biomedical applications.
- Biocompatibility and toxicities associated with nanomaterials.

Shared Interests and Overlaps:

- There are shared interests in nano-therapeutics with **Drug and Biologic Therapeutic Delivery (DBTD) and BBBT(81)**. Applications focused on unique features of multifunctional nanoparticles, nanobiomaterials, DNA scaffolds, liposomes, micelles, vesicles, and biomimetic membranes as delivery and targeting platforms as well as their synthesis, engineering, chemical properties, and/or cellular processing are reviewed in INN. Applications that focus on biological delivery and targeting issues involving the use of nanocarriers for small molecules and biologics are reviewed in DBTD or for nucleic acids are reviewed in BBBT (81).

- There are shared interests in nanosystem/nanotechnology development with **Drug and Biological Disposition and Toxicity (DBDT**). Applications that focus on the development of novel nanotechnology are reviewed in INN. Applications that focus on the disposition, safety and toxicity of delivery agents are reviewed in DBDT.

- There are shared interests in nanobiomaterials with **Biomaterials and Biointerfaces Study Section (BMBI)**. Applications that focus on the biocompatibility and toxicities associated with nanomaterials are reviewed in INN. Applications that address the use of nanomaterial-based approaches for tissue engineering are reviewed in BMBI.

- There are shared interests in biosensing development with **Instrumentation and Systems Development (ISD).** Applications that emphasize developing biosensing or technologies involving the development of novel nanostructures or functionalize nanoparticles are reviewed in INN. Applications that emphasize developing biosensing or technologies that are more device-based are reviewed in ISD.

- There are shared interests in area of drug delivery using nanomaterials with **Advancing Therapeutics A (ATA) and MCST (81)**. Applications that focus on the fundamental development, engineering, and rational design of new classes of multifunctional nanoparticle systems and combination therapy using novel nanoparticles are reviewed in INN. Applications that emphasize late-stage preclinical development of therapeutic nanoparticles are reviewed in ATA for cancer or MCST (81) for other biological systems.

- There are shared interests in nanomaterials with **Cellular and Molecular Technologies (CMT)**. Applications that focus on material development and characterization are reviewed in INN. Applications that focus on the use of nanomaterials to address cellular and molecular processes are reviewed in CMT.

- There are shared interests in development of polymeric, supramolecular and nanomaterial entities with **Chemical Synthesis & Biosynthesis (CSB)**. Applications that emphasize the development of higher-level nanostructures, nanodevices, nano-biologics, or biomaterials customized for specific biomedical applications are reviewed in INN. Applications that propose new basic synthetic chemistry strategies are reviewed in CSB.

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Nucleic Acid Therapeutic Delivery – ZRG1 BBBT (81)

The **Nucleic Acid Therapeutic Delivery (ZRG1 BBBT (81))** study section reviews applications focused on fundamental aspects of nucleic acid delivery, including intracellular delivery, delivery vehicle development, targeting strategies, and overcoming biological barriers. Applications are typically focused on bioengineering principles and may not be hypothesis driven.

Topics:

- Delivery of therapeutics based on nucleic acid delivery, including siRNA, mRNA, DNA, oligonucleotide therapies.
- Studies developing mRNA Vaccines
- Delivery vehicles including plasmids, viruses, liposomes, micelles, vesicles, nanoparticles, biomaterials, polycationic polymers and lipids, and cells.
- Targeting strategies via aptamers.
- Delivery strategies including light and physical methods (optical caging, Electroporation, Ultrasound)
- Study of the biological barriers to nucleic acid delivery (e.g., membrane, tissue, cellular, trafficking, physical).
- Studies of the interactions of delivery vehicles, devices, and/or payloads with the immune system and host tissue related to nucleic acid therapeutic delivery.

Potential Overlaps:

- There are shared interests in drug discovery with **Drug and Biologic Therapeutic Delivery (DBTD)**. Applications that focus on fundamental aspects of nucleic acid delivery, including intracellular delivery, delivery vehicle development, targeting strategies, and overcoming biological barriers are reviewed in BBBT (81). Applications that emphasize fundamental aspects of therapeutic delivery of cargoes of synthetic and biologic nature except nucleic acids are reviewed in DBTD.

- There are shared interests in nano-therapeutics with **Innovations in Nanosystems and Nanotechnology (INN)**. Applications that focus on biological delivery and targeting issues involving the use of nanocarriers for nucleic acids are reviewed in BBBT (81). Applications that focus on unique features of multifunctional nanoparticles, nanobiomaterials, DNA scaffolds, and delivery and targeting platforms as well as their chemical properties and synthesis are reviewed in INN.

- There are shared interests in therapeutic delivery with **Advancing Therapeutics A (ATA)**. Applications that focus on vehicle development and targeting strategies for nucleic acid, small molecules and biologics are reviewed in BBBT (81). Applications that focus on vehicle development and targeting strategies for preclinical cancer therapeutic studies are reviewed in ATA.

- There are shared interests in nucleic acid-based therapeutics with **MCST (81)**. Applications that emphasize fundamental design, delivery, and targeting of nucleic acid therapies are reviewed in BBBT (81). Applications that emphasize efficacy, safety, or toxicity in animal models or pilot clinical trials are reviewed in MCST (81).

- There are shared interests in therapeutic systems and nuclei acid delivery with the **Drug and Biologic Disposition and Toxicity (DBDT)**. Applications that examine the fundamental aspects of nucleic acid delivery, are reviewed in BBBT (81). Mechanistic and preclinical applications that focus on the disposition and safety and toxicity of delivery agents are reviewed in DBDT.

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