
National Institutes of Health SBA-Approved SBIR/STTR Topics for Awards over Statutory Budget Limitations

7/09/2020

NIH has received approval from SBA for the topics listed within for budgets greater than **\$256,580** for Phase I SBIR/STTR awards and greater than **\$1,710,531** for Phase II SBIR/STTR awards for 2020-2021. Applicants are **strongly encouraged** to contact NIH program officials prior to submitting any award budget in excess of these amounts. Applicants are also required to follow NIH Institute- and Center-specific budget guidance found in all SBIR and STTR funding opportunity announcements.

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NATIONAL CANCER INSTITUTE (NCI)

- A. Therapeutics (e.g. Small Molecules, Biologics, Radiomodulators, Cell-based Therapies and Drug Development- Related IT Tool and Algorithm Development)
- B. *In Vitro* and *In Vivo* Diagnostics (e.g. Companion Diagnostics, Prognostic Technologies, Treatment Monitoring and Diagnostic-Related IT Tool and Algorithm Development)
- C. Imaging Technologies (e.g. Agents, Devices, Software Tools, Algorithm Development, and Image-Guided Interventions)
- D. Devices for Cancer Therapy (e.g. Interventional Devices, Software Tools, Algorithm Development, Surgical, Radiation and Ablative Therapies)
- E. Agents for Cancer Prevention (e.g., Vaccines, but not “Technologies for Cancer Prevention”)
- F. Development of Low-Cost Technologies for Low-Resource Settings and Cancer Global Health
- G. Development of Digital Health Tools

NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES (NCATS)

- A. Innovative platforms for identification and prioritization of targets for therapeutic intervention with clear clinical impact.
- B. Technologies to determine alternative uses for existing therapeutic interventions.
- C. Tools and technologies to allow assaying of activities of compounds on currently “non-druggable” targets.
- D. Phenotypic assay development, including stem cell technology platforms for human “disease in a dish” applications and the evaluation of toxicity.
- E. Co-crystallization high-throughput screening techniques.
- F. Small molecule and biologics analytical characterization.
- G. Tools and technologies that increase the predictivity or efficiency of medicinal chemistry, biologic, or other intervention optimization.
- H. Accelerate bioengineering approaches to the development and clinical application of biomedical materials, devices, therapeutics, and/or diagnostics.
- I. Tools and technologies that increase the efficiency of human subjects research, including development of technologies that facilitate rapid diagnosis and/or clinical trial recruitment and subject tracking, IRB evaluation, and/or regulatory processes.
- J. Novel platforms, technologies and tools for: (1) enabling clinical and translational research, particularly those with mechanisms for inclusion of patient reported data and (2) integration of patient data collected from multiple devices and multiple/diverse clinical studies.
- K. Searchable access to information about researchers and their expertise, including but not limited to their publications, published data sets, methods, patents, clinical trials, partnerships, collaborators, and clinical specialty/expertise (if applicable).
- L. Tools for meaningful sharing of research data with low barrier for provision and user friendly access.
- M. Microphysiological Systems (MPS)/Tissue Chips.

NATIONAL CENTER FOR COMPLEMENTARY AND INTEGRATIVE HEALTH (NCCIH)

- A. Development and validation of biomarkers that correlate with efficacy of complementary health approaches.
- B. Formulation, development, and clinical testing of complementary health approaches and natural products that would permit FDA approval of a natural product for a specific indication.
- C. Identification and validation of biological targets associated with complementary health approaches.
- D. Development of innovative technologies and methods to assess natural product–drug interactions in humans.
- E. Studies of the mechanistic effects of mind and body interventions that will allow for optimization of the efficacy and safety of the mind and body approach for commercialization.
- F. Nontraditional phenotypic assay development for complex natural product mixtures.
- G. Integrated *in silico* tools for exploiting natural product bioactivity.
- H. Development and clinical testing of innovative technologies and methods for mind and body approaches. Examples include the use of mobile health technologies such as smartphone apps, sensors, online delivery, or phone-based delivery.
- I. Design, development, evaluation, and validation of devices or systems related to complementary health approaches.
- J. Utilizing biosynthetic engineering approaches to improve production of natural products in either native or heterologous hosts.

NATIONAL EYE INSTITUTE (NEI)

General Research and Development Topics

- A. New or improved ophthalmic or surgical instruments for diagnosis and treatment of eye disorders.
- B. Drug delivery systems; gene therapy, cell-based therapy or regenerative medicine.

Retinal Diseases

- A. New therapeutic approaches for inflammatory and degenerative diseases and for inhibition of abnormal angiogenesis in the retina and choroid.

Corneal Diseases

- A. New therapeutic approaches, artificial corneas, and drug delivery methods for the treatment of corneal injury, infection, dry eye, ocular pain, and other ocular surface disorders.

Lens and Cataract

- A. New approaches in the management of cataracts.

Glaucoma and Optic Neuropathies

- A. New therapeutic agents for treatment of glaucoma.

Visual Impairment and Blindness

- A. New or improved devices, systems, or programs that meet the rehabilitative and everyday living needs of blind or visually-impaired persons.

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI)

- A. Biomedical technologies (medical devices, instruments, pharmaceuticals, drugs, therapeutics, vaccines, diagnostics and biologics) for heart, lung, blood, and sleep related diseases and disorders requiring Federal regulatory approval (FDA) or clearance to be commercialized.
- B. Small and large animal testing of products of tissue engineering and regenerative medicine, drugs, medical devices, therapeutics, and biologics and studies involving *in vivo* animal experiments for heart, lung, blood, and sleep related diseases and disorders.
- C. Clinical trials and other experiments involving human subjects for heart, lung, blood, and sleep related diseases and disorders.
- D. Therapeutics (drugs, devices, or biologics) development for heart, lung, blood, and sleep related diseases and disorders.
- E. Device development for heart, lung, blood, and sleep related diseases and disorders
- F. Diagnostics development for heart, lung, blood, and sleep related diseases and disorders.
- G. Investigation of biomarkers and biosignatures of heart, lung, blood, and sleep related diseases and disorders.
- H. Technologies to enhance clinical research for heart, lung, blood, and sleep related diseases and disorders.
- I. Advanced instrumentation and high throughput tools for biomedical research in heart, lung, blood, and sleep related diseases and disorders.
- J. Tools and platforms to improve the dissemination and implementation of evidence-based interventions for heart, lung, blood, and sleep related diseases and disorders.

NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI)

- A. Development of novel or significant improvements for nucleic acid sequencing technology.
- B. Development of novel or significant improvements for functional genomics technology.
- C. Genomics tools ranging from new instruments to sophisticated molecular biology kits.
- D. Bioinformatics software for genomic, genetic and sequence data analysis, functional genomics, associations between genomic data and diseases or phenotypes, interpretation of variants, and genomic data integration.
- E. Databases and data management for genomics research and application including sequences, functional data, annotation of variants, and phenotypes.
- F. Incorporating genomic results into electronic medical records.
- G. Informatics tools that assist in delivering genomic medicine to patients.
- H. Development and application of methods for machine learning, pattern detection, and knowledge networks for genomics and translation to genomic medicine.
- I. Informatics methods and platforms to enhance privacy, data standards, and data exchange in genomics and translation to genomic medicine.
- J. Use of cloud and other computing models to improve scale, reproducibility, interoperability, cost-effectiveness, and utility of genomic and clinical data in genomics and translation to genomic medicine.
- K. Single cell genomic analysis.

NATIONAL INSTITUTE ON AGING (NIA)

Division of Neuroscience (DN)

The Division of Neuroscience (DN) fosters and supports extramural research and training to further the understanding of the dementias of old age, as well as neural and behavioral processes associated with the normally aging brain. An area of special emphasis is brain-behavior relationships. An important component of this Division is the support of basic, clinical, and epidemiological studies of AD and related dementias of aging.

- A. Development of new and/or validation of existing sensitive, specific, and standardized tests for diagnostic screening and the development of biomarkers.
- B. Target discovery and validation through the application of systems biology and systems pharmacology approaches of MCI, AD, ADRD, or other dysfunctions of the central nervous system.
- C. Preclinical and/or clinical discovery, development, and/or evaluation of drug, nutritional, behavioral, cognitive, sensory, environmental, or other types of interventions to remediate age-related cognitive decline and/or other dysfunctions of the central nervous system.
- D. Development of new technologies for in-home use or for coordination or delivery of services to sustain in-home living for individuals with MCI, AD, ADRD, or that may prolong functional independence when there are dysfunctions of the central nervous system.
- E. Development of biosensors and prosthetic devices, technologies, and related software development to aid in the assessment, diagnosis, and remediation of age-related cognitive decline and/or other dysfunctions of the central nervous system.
- F. Development of technology and analysis tools to examine genetic, epigenetic, transcriptomic, proteomic, metabolomic, and cell stress pathways in neurons and glia of the aging and AD/ADRD brain.
- G. Improvement of technology to analyze structural and functional brain connectivity at the cell, neural circuitry, and global-network levels to define the normal trajectory of brain structure and function over the adult lifespan.
- H. Development of technology, including non-invasive methods and novel probes, to monitor and manipulate the plasticity of neural circuits in the adult and aged nervous system.
- I. Development of novel markers of neural stem cell function and novel approaches for analysis of next-generation sequence data.

Division of Aging Biology (DAB)

The Division of Aging Biology promotes and supports research and training on the molecular, cellular, genetic, and physiological mechanisms underlying normal aging and age-related pathologies. The objective of DAB-funded research is to elucidate the basic biochemical, genetic, and physiological mechanisms underlying the process of aging and age-related changes in humans and in animal models of human aging. This includes investigations of the gradual or programmed alterations of structure and function that characterize normal aging and investigations of how these adverse changes become risk factors for, or accompany, age-related conditions and disease states.

- A. Development of interventions to 1) reduce oxidative or other stresses and aging-related diseases; 2) improve the immune response to foreign molecules or reduce the response to self or suppress age-induced inflammation; 3) enhance longevity or slow aging and may affect other age-related conditions or diseases; 4) reduce the level of damage to nucleic acids, proteins and lipids and the macromolecular complexes formed from these molecules, and improve the damage surveillance and repair potential of cells.
- B. Development of minimally-perturbing techniques for collecting blood old non-human animals and the development of non-invasive research and test methods for use in non-human animals.
- C. Development of novel strategies for treating age-related renal, pulmonary, urology, reproductive disorders, and age-related changes in hormone production and function.
- D. Development of novel methodology for treating osteoarthritis, including devices, processes and pharmacological agents with the potential to: (1) slow the rate of joint deterioration, (2) promote the remodeling of damaged joints, (3) reduce the likelihood of progression to osteoarthritis, and/or (4) improve outcomes for patients with active osteoarthritis.
- E. Development of tools and resources in genetics and genomics to study molecular mechanisms of normal aging or aging-related diseases.
- F. Development of novel methodology for treating chronic wound healing, including devices, processes and pharmacological agents with the potential to: (1) improve the rate and or quality of wound healing, and/or (2) improve outcomes for patients with chronic wounds.
- G. Development of biomarkers for prognosis, diagnosis, or treatment monitoring of aging or aging-related diseases; and analysis or integration of large data sets for developing biomarkers or biomarker signatures of aging or age-related diseases.

Division of Behavioral and Social Science (DBSR)

- A. Behavioral-economics approaches (incentives or disincentives) to motivate sustainable behavior change to improve health and well-being.
- B. Social, behavioral, environmental and or/technical interventions (including robotics) on the individual, institutional, family, or community level to promote older adult independence, increase well-being and prevent disease and/or disability (across home, work and institutional settings), including age-related cognitive impairment.
- C. Evidence-based methods, technologies, and interventions to reduce the burden of caregiving for persons with Alzheimer's disease and AD-related dementia, including training materials/resources appropriate for use by informal caregivers, or professional caregivers within health-care systems or community-based organizations.
- D. New sampling and data-collection methodologies for use in large population-based household surveys and behavioral interventions of relevance to aging, including blood-spot technology for biological data collection, genetics and Genome Wide Association approaches and survey and archiving/database-support technology and resources for integrating big data and utilizing artificial intelligence and machine learning for assessing/diagnosing aging-related illnesses.
- E. Risk-reduction programs for improving the health of older workers, lowering the rate of health-care utilization, and improving the cost effectiveness of employer-based insurance plans.

Division of Geriatrics and Clinical Gerontology (DGCG)

- A. Development and validation of human aging mechanistic markers predictive for various age-related conditions or responses to interventions. Products of interest include the development and validation of commercial assays which could be used in clinical/epidemiologic research to assess mechanisms of aging (e.g., cell senescence, autophagy, DNA damage and repair) in human blood, tissues or cells and markers of age-related chronic inflammation. This may involve refinement of existing assays (e.g., conversion of lab assay to high-throughput screening) and/or de novo assay development for use in clinical research. Novel molecular imaging techniques (in vitro and in vivo) to study aging mechanisms in humans are also encouraged.
- B. Potential new therapeutics and/or interventions targeting fundamental mechanisms of aging and that influence the risk or progression of multiple age-related conditions. This may include identification of new therapeutic targets or repurposing of existing FDA-approved medications.
- C. Development of high throughput drug screening platforms to identify small molecules for enhancing the functions of protective genetic/metabolic factors associated with exceptional longevity or health span in humans.
- D. Development of clinical decision-support tools able to broadly integrate into the electronic health record to help physicians/providers caring for patients with multiple (3 or more) chronic conditions prioritize, coordinate, and deliver the interventions that are most beneficial and relevant within the context of these patients' lives and the health-care-delivery system.
- E. Development of assistive technologies/robotics to enable and support older persons to live independently and safely at home; socially-assistive robots; robots for caregiver and mobility assistance; robots for exercise and rehabilitation assistance.
- F. Development of technologies/robotics/sensors to assist in the improvement of physical function and mobility in older persons prior to (pre-habilitation) or following (rehabilitation) elective/planned surgery.
- G. Development and validation of improved approaches for evaluation, monitoring or treatment of diastolic dysfunction in older adults.
- H. Development of improved instrumentation/ imaging and sensor technology for measuring ambulation and biomechanics of movement including balance, sway, gait, and postural control to identify stable and unstable patterns of movement during activities of daily living.
- I. Development of methods and technology to accurately determine the renal glomerular filtration rate (GFR) in older persons and patients with chronic kidney disease; new methods and technology should accommodate the effects of age-related changes in muscle mass, levels of serum creatinine, renal blood flow and renal concentrating ability.
- J. Development and validation of non-invasive methods of examining bone quality (density, architecture, and strength of bone).
- K. Development and validation of instruments and/or methods to evaluate fatigability—the level of fatigue related to the intensity, duration, and/or frequency of activity (in contrast to measures of fatigue), particularly in adults with or at-risk of developing age-related conditions or diseases leading to physical disability.

- L. Development and validation of innovative approaches to pain control that considers age-related physiologic changes such as gastrointestinal absorption, cutaneous integrity, and musculoskeletal structure and function.
- M. Development and validation of new technology such as non-invasive methods to examine blood-flow velocity in arteries, individual coronary arteries, renal arteries, and cerebral arteries.
- N. Development of clinical decision support tools that help physicians caring for patients with multiple chronic conditions to prioritize the interventions that are most beneficial and relevant within the context of these patients' lives; or tools for patient self-management of multiple chronic conditions. Development of patient-focused tools for prioritizing and making decisions about the most significant health concerns to help select and order their self-management behaviors related to 3 or more chronic conditions.
- O. Development of new therapeutic interventions to promote wound healing, including improved post-surgical treatments/technologies promoting wound healing, prevention of chronic wounds, or reduced scar formation.
- P. Development of vaccines and other agents for preventing and treating infections in older persons, including development of new vaccines or preventive interventions, and new methods using currently available vaccines or preventive medications. Improve vaccine response/immune function, and for physical functional problems in old age.
- Q. Development of devices and/or techniques for preventing or treating urinary incontinence.
- R. Development and effectiveness testing of innovative, practical, cost-effective technologies, data collection and extraction systems and devices that could enhance the participation in clinical trials of older vulnerable people who are typically under-represented in clinical trials.
- S. Development of new diagnostic tests to predict adverse and/or costly, or favorable, health outcomes with aging or in the setting of chronic diseases, injuries, surgery, hospitalization, or other health-related conditions.

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

- A. Treatment of alcohol use disorder.
 - Pharmacological discovery, strategies, and development
 - Innovative therapeutic approaches
 - Prevention strategies
 - Therapies for co-morbid conditions, including organ damage
- B. Technology development to support screening, brief intervention, and referral to treatment for alcohol-involved patients in medical settings.
- C. Development of novel technologies, methods or applications.
 - To detect the effects of alcohol on CNS structure and activities
 - To prevent harmful drinking during pregnancy, to identify prenatal alcohol exposure, and to enhance outcomes of individuals with Fetal Alcohol Spectrum Disorder
 - Tools for alcohol-related laboratory studies, such as animal strains, cell lines, stem cells, in vitro techniques, neuroimaging, ligands, in vivo detection of neuromodulators, or computational tools
 - Stem cell generation, dissemination, and model development
 - Voice technology, cell phones, and other
 - To assist investigators in conducting research in alcohol field (i.e., application development, electronic data management system, etc)
- D. Development of Biomolecular Signatures of Alcohol Exposure and Alcohol-induced Tissue Injury.
- E. Development, Optimization, and Validation of Novel Tools and Technologies for Neuroscience Research.
- F. Design, Development, and Improvement of Alcohol Biosensors.
- G. Investigational New Drug (IND)-enabling Development of Medications or Devices to Treat Alcohol Use Disorder and Alcohol-related Disorders.
- H. Genotyping of DNA samples from subjects with addiction and substance use disorders.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)

Division of AIDS (DAIDS)

- A. Development of anti-HIV agents directed at new viral or cellular targets, including development and *in vivo* evaluation of sustained release formulations for treatment and prevention of HIV infection.
- B. Development and evaluation of therapeutic vaccines and other immune-based therapies to attenuate HIV disease progression or reduce HIV infectiousness.
- C. Development of therapeutic strategies for curing HIV infection or effecting a sustained remission in the absence of daily antiretroviral drug therapy.
- D. Development of methods for detecting and quantifying persistent reservoirs of replication competent latent HIV in blood and tissues, including bio-imaging.
- E. Development and evaluation of practical and affordable tests (e.g., viral load, drug toxicities, drug resistance) to monitor populations infected with HIV and associated infectious agents. Development of tests to detect early infection or viral rebound in HIV-infected individuals and to determine HIV incidence (HIV infection before seroconversion).
- F. Development of long-acting (minimum 30 days) sustained/extended release pre-exposure prophylaxis (PrEP), post-exposure prophylaxis (PEP), and multipurpose prevention technologies (MPT) products that can provide systemic protection from HIV infection.
- G. Development of rapid tests for the detection of antiretroviral drugs in various human matrices (e.g., blood, urine, hair).
- H. Support novel technologies for HIV incidence detection; biomarkers of infection and prevention engagement; social media approaches to increase HIV prevention initiation/promote adherence; mathematical modeling of prevention strategies; and approaches to identify and retain key populations for HIV prevention research.
- I. Development of processes suitable for HIV-1 vaccine product design, development and cGMP manufacturing, formulation, analytics and characterization of (a) HIV Env immunogens and related constructs/products; (b) fabrication, and development of nanoparticle-based delivery modalities, such as self-assembling proteins, surface conjugated/adsorbed nanoparticles, synthetic, lipid and polymer-based nanoparticles; (c) antigen-adjuvant formulations and/or combination-adjuvant(s) and dosage forms (e.g., suspension, lyophilized and aerosolized) for co-delivery/co-administration, , (d) production of monoclonal antibodies (neutralizing and/or non-neutralizing); (e) delivery of antibodies as vectored or by nucleic acid technologies), (f) VLPs and viral vectors, and (g) DNA and RNA vaccine platforms.
- J. Improving cell line development process (transient, stable pools, stable clones, etc.) by using existing and novel cell lines, cultures, and supporting/customized technologies to expedite and increase Env expression, production, quality, and yield, novel chromatography purification platforms for viral vectors and Env proteins for HIV vaccine manufacturing.
- K. Development of formulation and dosage form technologies to prevent or treat HIV and HIV-associated co-infections.

Division of Allergy, Immunology, and Transplantation (DAIT)

- A. **Allergy, Asthma and Airway Biology Branch** will consider preclinical and clinical research for conditions of interest: asthma, food allergy, eosinophilic esophagitis and gastroenteritis in relation to food allergy, atopic dermatitis, urticaria, rhinitis, rhinosinusitis, drug allergy, and sepsis. This includes but is not limited to the development of methodologies to manage, and analyze clinical and epidemiologic research in the above conditions and the development of biomarkers as diagnostic markers, markers of disease severity, predictive markers for treatment effectiveness, particularly of

immunologic interventions such as allergen immunotherapy for food and respiratory allergy; novel approaches for detecting infants at risk for developing asthma and other allergic diseases; immune targets for asthma and allergic disease interventions; development of immunotherapies to prevent or treat allergic diseases.

- B. **Basic Immunology Branch** will consider preclinical and clinical research to study the origin, maturation, and interactions of immune cells, immune cell receptors, ligands, cytokine biology, molecular basis of activation, antigen recognition, immune tolerance, immune response regulation, hematopoiesis and stem cell biology, enhancement of vaccine effectiveness in neonates and adults, and basic immunology of vaccines and immunotherapeutics as medical countermeasures for biodefense. This research includes but is not limited to development of novel vaccine adjuvants; single cell assays to isolate and study antigen-specific lymphocytes; immunotherapeutic antibodies; biomarkers of host immune defense; single cell and other sample-sparing assays for study of human immunology.
- C. **Autoimmunity and Mucosal Immunology Branch** will consider preclinical and clinical research to develop and improve therapies for the treatment of autoimmune diseases and primary immune deficiencies (not HIV), basic research of autoimmune disease mechanisms, and biomarkers, immunotherapy of disease processes, disorders mediated by lymphocyte products, and mucosal immunity. This includes but is not limited to innovative treatments for autoimmune diseases; standardized validated diagnostic criteria and outcome measures for autoimmune diseases correlated with disease activity; high throughput assay of T-cell activity in autoimmune diseases; biomarkers to measure risk, disease activity, and therapeutic response in autoimmune diseases; innovative treatments for autoimmune diseases; mucosal immunity.
- D. **Transplantation Branch** will consider preclinical and clinical research in organ, vascularized composite tissue and cellular transplantation: acute and chronic graft rejection, allogeneic and xenogeneic transplantation, development of immunomodulatory agents to prevent and treat graft rejection and to promote acute and long term graft acceptance and immunologic tolerance, genomics of the alloimmune response, graft versus host disease for hematopoietic stem cell transplantation, minor histocompatibility antigens, complications of immunosuppression in transplantation, and major histocompatibility complex (MHC) region genomics and technologies for MHC typing. This includes but is not limited to methods and analysis tools to facilitate high throughput, high-resolution MHC typing in humans and non-human primates.
- E. **Radiation Countermeasures Program** will consider preclinical research to support specific product development activities leading to creation of IND or IDE packages to be submitted to FDA. These IND/IDE-enabling activities could include: efficacy studies to optimize formulation, dose, and dose schedule; drug product stability studies, drug product GMP manufacturing scale-up, GLP toxicology and pharmacology safety studies, pharmacokinetic and metabolism studies, development of GLP analytical methods for efficacy studies and product characterization (including using chip technology to determine tissue-specific efficacy of a lead drug candidate), mechanism of action studies and completion of IND or IDE package for FDA submission. Product development efforts will advance new medical countermeasures towards Phase I clinical safety studies, GLP animal pivotal efficacy studies, and licensure/approval/clearance by the FDA.

Division of Microbiology and Infectious Diseases (DMID)

- A. Identify and qualify infectious disease-related biomarkers, including:
 - 1. Biomarkers to predict susceptibility to infection and/or diagnose an infectious disease.
 - 2. Biomarkers to predict or monitor a subject's response to therapeutics or vaccinations.
 - 3. Biomarkers from natural history studies that could be used to assess disease progression in acute and chronic diseases.

- B. Development of rapid, highly sensitive and specific clinical diagnostics, including point-of-care diagnostics, that are easy to use, cost-effective and can diagnose individuals infected with pathogens or individuals that have been exposed to toxins.
- C. Discovery and development of vaccines or other immunoprophylaxis tools for infectious diseases.
- D. Development of vaccine enhancement and formulation technologies with the goal of providing protection against infectious disease agents, providing accelerated immune responses (more rapid schedules or reduced number of immunizations), increasing ease of administration (i.e., self-administration), increasing product stability to minimize cold chain requirements, and enhancing cost-effectiveness of vaccine manufacturing.
- E. Discovery and development of therapeutics for infectious diseases.
- F. Development of technologies or approaches that address arthropod vector monitoring, management, and control to prevent transmission of vector-borne pathogens to humans.

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES (NIAMS)

- A. Research and development of new therapies using small molecules or biologics for arthritis, musculoskeletal and skin diseases.
- B. Research and development of novel biomedical devices or tissue engineered products for arthritis, musculoskeletal and skin diseases.
- C. Research and development of new biomarkers or novel imaging technologies for arthritis, musculoskeletal and skin diseases.
- D. Research and development of innovative internet-based technologies to manage arthritis, musculoskeletal and skin diseases.

NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING (NIBIB)

- A. **Connected Health-Mobile Health and Telehealth.** Development of enabling technologies that emphasize the integration of wireless technologies with human and biological interfaces. This program includes the development of software and hardware for telehealth and mobile health studies. This program includes the input and delivery of healthcare information digitally for the analysis or monitoring of health or disease status. The emphasis is on developing mobile health technologies driven by clinical needs and integrating these technologies in healthcare delivery, wellness, and daily living.
- B. **Engineered Cells.** Development of engineered cells to elicit a broadly applied biomedically relevant effect across a spectrum of diagnostic, therapeutic, imaging, and interventional applications. Emphasis is on engineering functionality and issues surrounding biocompatibility of engineered cells. Functionality could be derived from controlling natural or artificial attributes of an engineered cell and based on biochemical, optical, and/or mechanical properties, for example.
- C. **Engineered Tissues.** Development of technologies to enable the *in vivo* and *in vitro* engineering of human tissue constructs for biomedical applications. Emphasis is on the design and construction of tools for analyzing and controlling the function of engineered human tissues. Outcomes include but are not limited to: real-time, non-invasive monitoring of tissue function and cell-environment interactions; control of spatiotemporal tissue growth through cell viability, guiding, differentiation, and migration; design, 3D printing, and assembly of human tissues for and biomedical applications; preservation of biological specimens, from protein solutions and cell suspensions to tissues and organs, for a variety of biomedical applications, including transplantation.
- D. **Image-Guided Interventions.** Development of novel image-directed technologies for guidance, navigation, tissue differentiation, and disease identification for reaching specified targets during therapeutic procedures, which may range along the continuum from non-invasive to minimally invasive to open surgical interventions. These technologies may range from molecular to macroscopic scale levels. In addition, emphasis includes technologies that expand needed procedural access for individuals otherwise excluded by disease characteristics, co-morbidities, and other parameters.
- E. **Magnetic Resonance Imaging.** Development of *in vivo* MR imaging and MR spectroscopy, for both animal and human research and potential clinical applications. The emphasis is on the development of MRI hardware and methodologies, including image acquisition and reconstruction techniques, that would improve the speed, spatial resolution, information content, efficiency, robustness, quality, patient experience, and safety. The emphasis should be on technological development rather than detailed applications to specific diseases or organs.
- F. **Mathematical Modeling, Simulation and Analysis.** Development of novel mathematical modeling, simulation and analysis tools that can be broadly applied across a wide spectrum of diagnostic, therapeutic, imaging, and interventional applications. Emphasis is on engineering solutions for theory-driven, physics-based, physiologically realistic, virtual representations of biomedical systems, with a particular weight on multiscale modeling. Interests include, but are not limited to: multiscale modeling, predictive modeling frameworks, non-standard methodologies, and methods to address model credibility, reproducibility, and reuse.
- G. **Nuclear Medicine.** Research and development of technologies that create images out of the gamma-ray or positron emissions from radioactive agents that are injected, inhaled, or ingested into the body. The emphasis is on: simulation and development of new detectors, collimators, and

readout methods that enhance the signal quality of detecting isotope emissions; designs of novel camera geometries; and correction methods that compensate for the radiation physics properties to improve the clinical reliability of the image. Of interest are improvements and corrections for interaction events in PET detectors and enhancement to time of flight (TOF) image generation methods (reconstruction algorithms); as well as new collimator and camera designs for SPECT.

- H. **Optical Imaging and Spectroscopy.** Development and application of optical imaging, microscopy, and spectroscopy techniques for improving disease prevention, diagnosis, and treatment in the medical office, at the bedside, or in the operating room. Examples of research areas include fluorescence imaging, bioluminescence imaging, OCT, SHG, IR imaging, diffuse optical tomography, optical microscopy and spectroscopy, confocal microscopy, and multiphoton microscopy. The emphasis is on development of cost effective, portable, safe, and non-invasive or minimally invasive devices, systems, and technologies.
- I. **Technologies for Tissue Chips.** Development of technologies to enable the engineering of tissue chips/microphysiological systems for biomedical applications. Emphasis is on the design and construction of in vitro tools for analyzing and controlling the function of engineered human tissues. Examples include but are not limited to: microfluidics to control spatiotemporal tissue growth, 3D bioprinting systems for tissue assembly, high-throughput assays and instruments to reduce the cost, time, and complexity of tissue engineering, and bioreactors to produce tissues at scale.
- J. **Therapeutic Medical Devices.** Design and development of non-imaging devices intended for therapeutic interventions. Emphasis is on engineering non-imaging devices, components, and control systems for in vivo therapeutic interventions directed toward overcoming a technological challenge that limits biomedical application. Devices may be, but are not limited to: rehabilitative or curative; assistive; or preventative.
- K. **Ultrasound: Diagnostic and Interventional.** Improvement of technologies for diagnostic or therapeutic uses of ultrasound. The diagnostic ultrasound program includes, but is not limited to the design, development and construction of transducers, transducer arrays, and transducer materials, innovative image acquisition and display methods, innovative signal processing methods and devices, and optoacoustic and thermoacoustic technology. It also includes the development of image-enhancement devices and methods, such as contrast agents, image and data presentation and mapping methods, such as functional imaging and image fusion. The therapeutic ultrasound program includes, but is not limited to the design, development, and construction of transducers, transducer arrays, interventional technologies, adjunct enhancement of non-ultrasound therapy applications, high-intensity focused ultrasound (HIFU), or hyperthermia applications. It also includes non-invasive or minimally invasive interventional surgical or therapy tools, ultrasound contrast agents for therapy, targeted drug delivery, neuromodulation, and biopsy.
- L. **X-ray, Electron, and Ion Beam.** Simulation, design and development of new detector systems; new readout methods that enhance the signal quality for x-ray image generation; designs of novel imaging geometries; algorithms that compensate for the physical properties of the detection system to improve the clinical reliability of the image (reconstruction algorithms); and approaches to radiation dose reduction, especially in CT. Of interest are diagnostic image enhancements via photon counting, dual energy, and new applications of cone-beam tomography.

EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD)

Child Development and Behavior Branch

- A. Real time Human Interactive Data Acquisition and Analysis Technologies for Research and Telehealth Needs: Development and research testing of new or adaptation of existing devices and innovative technologies to improve virtual/remote data collection, to facilitate child and parenting intervention and/or healthcare (telehealth) delivery platforms with integrated collection, analysis, and automated coding, including audio and video recordings in real world settings (e.g., homes, childcare centers, schools, and primary care offices) over prolonged periods of time (i.e., days, weeks, or longer) to allow for (1) rapid analysis of interactions, including those involving one or more languages, and (2) simultaneous analysis of nonverbal and verbal behaviors during interactions. Incorporation of data from sensors capable of simultaneously recording real time physiological signals (e.g., pulse, heart rate, skin conductance response, temperature, accelerometer, etc.) time-locked to audio and video data and analyses is also highly desired.

Contraception Research Branch

- A. Development of innovative contraceptive approaches for both males and females.

Developmental Biology and Structural Variation Branch

- A. Software development to facilitate the collection, mining, and analyses of genomic and phenotypic data from children affected with structural birth defects, and cross-analysis with model organism data
- B. Innovative technologies for validation and functional characterization of human structural birth defects-associated genetic variants in model systems
- C. Development of user-friendly software for biomedical researchers with limited knowledge of computational biology to analyze large-scale human genomic and other datasets associated with structural birth defects
- D. Creation of software platforms for assembly and display of predictive interactive computational models for complex gene regulatory networks coordinating embryogenesis

Fertility and Infertility Branch

- A. Development of novel techniques for assessment of gamete quality
- B. Development of Apps to monitor male and female reproductive health
- C. Over-the-Counter devices for in-home monitoring of ovarian follicle growth and ovulation
- D. Novel techniques for preservation of gametes and whole ovary and testes
- E. Development of techniques for use of non-embryonic stem cells for fertility preservation in cancer survivors
- F. Diagnostic tools for PCOS detection
- G. Development of smart phone-based semen assay
- H. Tools and technology for single cell analysis of gonadal and reproductive tract tissues

Gynecologic Health and Disease Branch

- A. Development of marketable novel or improved methods, devices, and technologies for the diagnosis, monitoring, and therapy of uterine fibroids, endometriosis, adenomyosis, benign ovarian cysts, abnormal menstrual cyclicality, reproductive tract abnormalities (including congenital structural abnormalities and complications from female genital cutting), female pelvic floor disorders (including drugs and devices used for treatment of pelvic organ prolapse, urinary incontinence, fecal incontinence, and other female pelvic floor disorders), and gynecologic pain disorders (including chronic pelvic pain, vulvodynia, and dysmenorrhea).

Intellectual and Developmental Disabilities Branch

- A. Technology development to improve screening, diagnosis, treatment, and management of intellectual and developmental disabilities.

Maternal and Pediatric Infectious Disease Branch

- A. New technologies relevant to resource-limited countries for screening, diagnosis, and management of HIV and other infectious diseases, including tuberculosis, viral hepatitis, other congenital infections such as cytomegalovirus, respiratory infections, etc., in infants, children and pregnant/breastfeeding women.
- B. Development and evaluation of vaccines relevant to HIV and other infectious diseases for infants, children, and pregnant/breastfeeding women.

Obstetric and Pediatric Pharmacology and Therapeutics Branch

- A. Development of devices to help diagnose or treat pediatric and pregnancy associated disorders.

Pediatric Growth and Nutrition Branch

- A. Isolation, purification, and synthesis of human milk components with biological activity.
- B. Develop rapid and reliable methods to determine components (both nutritive and non-nutritive) in human milk.

Pediatric Trauma and Critical Illness Branch

- A. The development of devices, innovative therapeutic technologies, and behavioral interventions to improve pediatric patient outcomes and minimize the negative sequelae of trauma, injury or critical illness.

Population Dynamics Branch

- A. Developing tools and methods to accurately and reliably measure head circumference in infants and children
- B. Technological innovations or inventions to improve collection of biomarker and anthropometric data in large population-representative surveys
- C. Hardware or software to improve collection of accurate cause of death information in large population-representative surveys or in administrative data sets
- D. Innovative methods to add new reproductive and gynecologic questions and/or sampling frameworks to existing large cohorts and/or longitudinal studies

Pregnancy and Perinatology Branch

- A. Devices, instruments, and tools to minimize health-care associated infection risks.
- B. Methods to reduce pain in all of perinatal care (in newborn infants, in mothers in labor, during the postpartum period and after spontaneous delivery and cesarean section
- C. Novel methods to predict, assess, monitor, or treat (when feasible) fetal health, fetal growth, preterm birth, and preeclampsia.

National Center for Medical Rehabilitation Research

- A. Development of medical rehabilitation interventions and biomedical technologies to improve rehabilitation treatment for restoration of function.

NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS (NIDCD)

- A. Research and development for biomedical technologies (medical devices, diagnostic instruments, pharmaceuticals, drugs, therapeutics, vaccines, and biologics) that require clearance by the FDA as a regulated product before commercial distribution.
- B. Development of novel open design hardware and software that facilitate rapid dissemination, reconfiguration, and enhancement to enable research beyond what can be performed with existing tools.
- C. Projects proposing clinical trials with a large number of participants.

NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH (NIDCR)

Infectious Diseases and Immunity

- A. Develop oral topical formulations with combined microbicidal, analgesic, and anti-inflammatory activities to enhance oral mucosal defenses and prevent and/or control oral infections and lesions in HIV-infected and/or immunosuppressed subjects.
- B. Develop safe and effective targeted diagnostic and therapeutic technologies in response to endemic and pandemic infections

Preclinical Research

- A. Preclinical research and development activities for dental, oral and craniofacial technologies (including devices, diagnostic instruments, reconstructive materials, pharmaceuticals, therapeutics, vaccines and biologics) that require review and approval by the FDA as a regulated product before commercial distribution.**

Clinical Research

- A. Develop improved methods to detect and predict progression of dental caries, periodontal disease, reversible and irreversible pulpitis.
- B. Develop new or improve methods or materials to enhance oral and craniofacial surgery. This would include both intraoral and extraoral surgery.
- C. Develop improved methods or materials to mechanically and/or biologically repair or treat tooth structure damaged by dental caries or periodontal disease.
- D. Develop safe and efficacious methods to diagnose caries, pulp vitality and / or periodontal diseases utilizing non-ionizing radiation.
- E. Develop technologies for local delivery of drugs to treat oral and craniofacial diseases or disorders.
- F. Develop novel non-opioid pharmacological medications for management of acute dental pain.
- G. Develop safe and efficacious methods or medications to manage complications of head and neck cancer treatment.

Oral, Oropharyngeal and Salivary Gland Cancers

- A. Develop imaging techniques for the early detection, diagnosis and prognosis of pre-malignant lesions.
- B. Develop genetic animal models of oral cancer premalignancy and oral cancer progression that mimic human oral cancers, including HPV associated oropharyngeal cancers.

Temporomandibular Disorder and Orofacial Pain

- A. Identify and develop novel pharmacologic or biologic agents, including but not limited to small molecules, peptides, recombinant proteins and nucleic acids to prevent, control, and/or treat orofacial pain.

Saliva, Salivary Diagnostics, and Salivary Gland Diseases

- A. Develop viral, non-viral and gene therapy-based approaches to address compromised salivary gland function. Develop cell and tissue-based strategies and technologies for restoration of damaged or destroyed salivary gland function.
- B. Develop novel compounds or materials that protect and preserve salivary glands from head and neck cancer irradiation therapy.
- C. Development of non-invasive methods for the determination of efficacy and safety of artificial saliva, sialogogues, and of their delivery vehicles used in addressing the diminution or lack of saliva (xerostomia) due to Sjögren's Syndrome or head and neck cancer irradiation therapy.
- D. Develop biomarker-based technologies for the identification of Sjögren's Syndrome using blood or saliva as body fluids.

Biotechnology, Biomaterials, and Applications for Regeneration and Restoration of Oral, Dental and Craniofacial Tissues

- A. Develop methods, materials, and devices for orthodontic, prosthetic, periodontic, endodontic and craniofacial applications including those that can be used for craniofacial bone distraction, reconstruction, hard and soft craniofacial tissue healing and regeneration, and scarless craniofacial tissue repair.
- B. Develop imaging diagnostics to accelerate clinical implementation of reliable, reproducible, highly specific and sensitive diagnostic instruments for various applications, including but not limited to dental caries, cracked teeth, pulp vitality, bone quality, and periodontal disease.
- C. Develop safe and effective biosensors, monitoring devices and systems, data driven and computational tools for automated detection, diagnosis and treatment of dental, oral and craniofacial disease.

Clinical and Behavioral Research

- A. Develop and test for safety, efficacy, and/or effectiveness of measures or materials for diagnosing, preventing, or treating oral, dental, and craniofacial conditions and disorders.

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES (NIDDK)

NIDDK supports the topics below as they pertain to *Diabetes* (Type 1 and Type 2 Diabetes, Metabolic Disorders, and Endocrine Disorders), *Digestive Diseases* (Gastrointestinal Diseases, Liver and Pancreatic Diseases, Obesity, Nutrition, and related diseases), and *Kidney Diseases* (Kidney Diseases, Urologic Diseases, and Hematologic Diseases).

- A. Development or evaluation of pharmacological agents (i.e., drugs, therapeutics), gene therapies, novel formulations, cell-based or other biological technologies for intervention in or prevention of *Diabetes and Digestive and Kidney Diseases*.
- B. Development or evaluation of biomedical devices, tools, techniques, or instrumentation for intervention in or prevention of *Diabetes and Digestive and Kidney Diseases*.
- C. Development of biomarkers, assays, techniques, diagnostic technologies or associated reagents for assessing state or function in normal, developing, or diseased cells or tissues affected by *Diabetes and Digestive and Kidney Diseases*.
- D. Development or evaluation of imaging, screening, or evaluation techniques or technologies for assessing state or function in normal, developing, or diseased cells or tissues affected by *Diabetes and Digestive and Kidney Diseases*.
- E. Development or evaluation of animal or cell models for studying *Diabetes and Digestive and Kidney Diseases*.
- F. Development or evaluation of novel materials or material treatments (e.g., sterilization, coating, etc.) for use in devices or other tools or methods used to prevent, diagnose, or treat *Diabetes and Digestive and Kidney Diseases*.
- G. Development of cell- or data-banks for the biomedical research community.
- H. Development or evaluation of technologies, including software applications, for improving patient adherence in *Diabetes and Digestive and Kidney Diseases*.
- I. Development or evaluation of technologies for improving clinical research in *Diabetes and Digestive and Kidney Diseases*, including technologies for improving data collection and reporting of patient outcomes.
- J. Development or evaluation of –omics, informatics, or internet-based technologies for biomedical research or clinical applications in diagnosing or managing *Diabetes and Digestive and Kidney Diseases*.
- K. Development or evaluation of technologies to prevent or avert cell or tissue injury during other disease states or surgical procedures.

NATIONAL INSTITUTE ON DRUG ABUSE (NIDA)

NIDA will allow the increase in budget for the applications in two specific technical/scientific areas: (1) Substance Use Disorders (SUD) Drug Discovery and Development; (2) FDA-regulated Medical Devices for SUD.

Area 1 research will lead to the submission of an Investigational New Drug (IND) application, New Drug Application (NDA) and/or Biological License Application (BLA) to the U.S. Food and Drug Administration (FDA). Area 2 research will lead to regulatory submissions to the FDA for pre-market clearance / approval.

Area 1. SUD Drug Discovery and Development

Projects proposed under Area 1 include application of emerging and existing technologies and platforms for SUD medication development with the focus on products with the potential to minimize drug seeking, compulsive behavior, overdose prevention and reversal:

- A. Early therapeutic discovery activities ranging from target identification and validation through lead development.
- B. Preclinical and/or clinical drug development.
- C. Technologies or formulations to improve medication delivery, longer-acting formulations of existing addiction medications.

Area 2. FDA-regulated Medical Devices for SUD

Projects proposed under Area 2 include pre-clinical and clinical studies in support of FDA pre-market clearance / approval (510(k), DeNovo, Pre-Market Approval) for the following categories of medical devices:

- A. Imaging devices for investigating brain function and enhancing disease diagnosis and treatment of SUD;
- B. Devices that directly diagnose and/or reduce craving and withdrawal symptoms;
- C. Devices that identify and treat neonatal opioid withdrawal syndrome (NOWS), also referred to as neonatal abstinence syndrome (NAS);
- D. Digital health therapeutics (e.g., Software as Medical Device, Software in Medical Device) focused on behavioral health interventions to alleviate the burden of SUD;
- E. Therapeutic (e.g., neuromodulation) devices and other advanced methods to improve SUD treatment outcomes and relapse prevention;
- F. Devices used to diagnose and treat opioid-induced respiratory depression;
- G. FDA-regulated devices for physiological monitoring, including remote detection (e.g., wearable sensors, health monitoring/emergency notification systems), specifically tailored to patients with SUD.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)

NIEHS will accept only Phase IIB SBIR Competing Renewal grant applications in response to specific RFAs focused on the validation of environmental exposure assessment sensor technologies.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS)

Division of Biophysics, Biomedical Technology, and Computational Biosciences

- A. Development of reagents and methods for detecting in real time, analyzing, and separating biologically important compounds, macromolecules, and their interactions.
- B. Development of new methods and materials directed toward the solution of biological macromolecule structures, including membrane proteins, assemblies and complexes by, but not limited to, x-ray diffraction, electron diffraction, cryo-EM, NMR and mass spectroscopy.
- C. Imaging probes and sensors, other reagents and methods, instrumentation, software for microscopy, spectroscopy, and single molecule analysis of molecules, cells, tissues, embryos and small model organisms. Technologies for applications of microscopy, spectroscopy and single molecule analysis in basic biomedical research, including but not limited to light, electron, X-ray, cryo-electron, and scanning probe microscopy and fluorescence, magnetic and electron paramagnetic spectroscopy. NOT included are small animal and preclinical imaging.
- D. Development of instrumentation and devices for detection, analysis, separation and/or manipulation of biologically important molecules, cellular components or cells.
- E. Development of instrumentation and devices for elucidating interactions of biologically important molecules *in vitro*, *in vivo*, within cells.
- F. Development of probes for detection of genetic polymorphisms, including disease genes.
- G. Development of valid animal models for genetic diseases and birth defects.
- H. Improvement of methodology (technology) for genetic analysis (e.g., gene expression, probes).
- I. Development of tools and technologies to detect and monitor complex phenotypes or traits.
- J. Development or improvement of methods for high throughput detection of epigenomic changes.
- K. Development of improved technology, reagents and tools to derive, grow, isolate, differentiate and characterize cells.
- L. Development or improvement of methods for characterizing and studying complex communities of microorganisms, including interactions with host organisms.
- M. Development of non-mammalian model systems.
- N. Development of tools and methods for the modeling, simulation, and/or analysis of complex biological systems.
- O. Development and/or enhancement of computational tools and methods to collect, store, interpret, analyze and/or visualize biomedical data.
- P. Development of software and hardware for improving the effectiveness of computational approaches in biomedical research.
- Q. Development of high-throughput and/or computational methods and strategies to define/characterize the function, inhibition, and/or interactions of biological macromolecules and cells.

Division of Pharmacology, Physiology, and Biological Chemistry

- A. Methods for isolation, characterization, and production of natural and bio-engineered products.
- B. Development of methodology to improve the efficiency of discovery, development, and production of bio-medically relevant compounds.

- C. Isolation, characterization, and development of factors and strategies, methods, or treatments involved in critical illness and injury including tissue repair, wound healing, sepsis and associated pain management. Research may involve emergency, peri-operative, and/or critical care conditions.
- D. Research to improve drug design and delivery.
- E. Development of technologies, instrumentation, software, reagents, and methods for the study of carbohydrates and for determining carbohydrate structure and biological function.
- F. Development of tools to study oxidative stress and/or mitochondrial function.
- G. Sepsis diagnostics and therapeutics.

Division of Training, Workforce Development, and Diversity

- A. Development of products or services to enhance diversity of the scientific workforce.

Division for Research Capacity Building

- A. Development of efficient, user-friendly, and culturally appropriate resources to enhance health science literacy

NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)

All Divisions:

- A. Preclinical drug/device development studies, including pharmacology, efficacy and toxicology.
- B. Completion of studies as required by the Food and Drug Administration (FDA) for Investigational New Drug (IND) or Radioactive Drug Research Committee (RDRC) application.
- C. Studies in normal healthy volunteers to determine a drug's safety profile, metabolism, etc.
- D. Clinical studies in patient/disease population to assess the drug's effectiveness.
- E. Assessment of devices with regard to performance standards related to the FDA approval process.
- F. Safety and effectiveness studies of novel medical devices.
- G. Evaluation of novel imaging approaches for diagnostic purposes.
- H. Clinical studies in support of Pre-Market Approval for biomarkers/medical devices by the FDA.
- I. Rapidly develop novel, engaging computer-based cognitive training programs that are based on efficacious neurotherapeutic approaches and which use cognitive training to target a specific neural system/functional domain.
- J. Augment existing computerized cognitive interventions to be personalized, engaging, adaptive, sufficiently challenging, and optimal for maximizing real world functional improvements.
- K. Test the feasibility, efficacy and potential adverse effects of these programs utilizing measures of functional outcomes in an identified clinical population, particularly those with neuropsychiatric disorders, ASD, and/or HAND, at a specified developmental stage, including measurement of the duration of treatment effects.
- L. Rapid development and evaluation of mobile based platforms and applications.

Division of Neuroscience and Basic Behavioral Science (DNBBS)

- A. Novel imaging probes to study brain structure and function at all levels, from the molecular to the whole organ, using any imaging modality (PET, fMRI, optical, etc.).
- B. Drug discovery/drug development of novel compounds which act on molecular pathways (receptors, enzymes, second messengers, etc.) that are not typically targeted with currently available psychiatric drugs, and that have a strong biological justification as a novel mechanism for treatment of psychiatric disorders.
- C. Novel screening assays for high throughput acquisition and analysis of data about behavior and the brain, from the level of genes to the level of behavior.
- D. Novel technologies that would enable researchers to study how populations of neural cells work together within and between brain regions, in order to understand how changes in neural activity contributes to mental disorders.
- E. Complex instrumentation for neuroscience research
- F. Complex brain or cellular imaging or analysis.

- G. Tools to facilitate the detailed analysis of complex circuits and provide insights into cellular interactions that underlie brain function.
- H. Proof-of-concept testing and development of new technologies and novel approaches for large scale recording and manipulation of neural activity, at or near cellular resolution, at multiple spatial and/or temporal scales, in any region and throughout the entire depth of the brain
- I. Iterative refinement of such tools and technologies with the end-user community with an end-goal of scaling manufacture towards reliable, broad, sustainable dissemination and incorporation into regular neuroscience practice.
- J. Novel informatics tools to facilitate the sharing of complex data sets between laboratories.
- K. Novel tools for investigating brain-derived GPCRs in mental health research.
- L. Educational tools/technologies for neuroscience and mental health.
- M. Technologies to support the goals of the BRAIN Initiative: <http://www.braininitiative.nih.gov/>

Division of Translational Research (DTR)

- A. Develop, test and validate reliable and stable biomarkers that can identify at-risk individuals prior to disease onset, improve diagnosis, predict treatment response, or measure disease progression. Biomarkers are also needed in clinical trials to identify dose ranges, to identify a specific subpopulation of subjects to enroll in a treatment trial, or to measure efficacy or toxicity/side effects.
- B. Develop novel and targeted interventions (pharmacological, cognitive, behavioral, computer, or device-based) that affect particular neural circuits and signaling pathways relevant to the developmental trajectory of the disease.
- C. Conduct early stage, proof of concept clinical trials to advance the development of novel therapeutics. The clinical trials are expected to include biological/behavioral data to assess target engagement and to help determine potential success or failure of the compound before moving on to larger clinical trials (see NOT-MH-11-015 <http://grants.nih.gov/grants/guide/notice-files/NOT-MH-11-015.html>).
- D. Based on expanded knowledge of neurobehavioral trajectories, develop novel objective assessment tools that can identify early signs of risk or onset of recurrence of particular mental disorders or in domains of functioning (see MH's RDoC project: <http://www.nimh.nih.gov/research-funding/rdoc/index.shtml>) for pediatric populations.
- E. Develop computational biological/behavioral assessment tools that can be used across ages, species, and cultures to evaluate dysfunction in domains relevant to mental disorders (e.g., mood dysregulation, deficits in executive function).
- F. Develop computational platforms to enable the integration and sharing of data characterizing typical and atypical developmental trajectories in humans and non-human animals.
- G. Clinical research tools.
- H. Develop valid measures of the various constructs in the Research Domain Criteria (RDoC) matrix (see <http://www.nimh.nih.gov/research-funding/rdoc/index.shtml>), e.g., neurocognitive tasks,

psychometrically sophisticated questionnaires, measures of behavior, and biomarkers, into a commercial product.

- I. Develop clinical risk assessment instruments that encompass multiple domains (e.g., genetic, neurobiological, and environmental), are sensitive to developmental stage, and have high predictive power for the onset or recurrence of mental illness.
- J. Developing clinical risk assessment instruments for developing particular benefits or harms during treatment for mental disorders, and communicating such probabilistic information to patients and their families in a readily understandable manner.
- K. Develop electronic sensors, monitoring devices and systems, and data analysis software for automated detection and diagnosis of mental disorders and key transdiagnostic dimensions of psychopathology.

Division of AIDS Research (DAR)

- A. Develop and test novel, non-invasive diagnostic approaches (instrumentation, imaging, biomarkers, central nervous system [CNS] cell-based *in vitro* models) to detect neurocognitive dysfunction associated with HIV-1 infection and innovative technologies to study the mechanisms involved in HIV-1 associated neuropathogenesis and persistence of HIV-1 in the CNS or strategies to prevent viral resurgence in the CNS upon cessation of anti-retroviral therapy.
- B. Design and test novel therapeutic strategies aimed at amelioration of HIV-1 induced CNS dysfunction and/or eradication of HIV-1 from CNS reservoirs or strategies to prevent viral resurgence in the CNS upon cessation of anti-retroviral therapy.
- C. Discover and develop innovative technologies for targeting therapies to the brain, including antiretroviral drugs, nanotechnology, imaging tools to study HIV-aging interactions or HIV-related neurodegeneration and neuroprotective strategies with improved capability to cross the blood-brain barrier for amelioration of HAND.
- D. Develop evidence-based interventions to reduce risk for HIV among at-risk individuals or improve outcomes along the HIV care continuum for individuals living with HIV which are delivered through mobile devices or other technologies.
- E. Develop technologies, instruments and tools to aid in improving uptake, adherence, and persistence to biomedical HIV prevention and treatment regimens; Increasing regular HIV testing among those most at risk of acquiring HIV and translating findings from basic behavioral and social science research into processes to improve engagement in HIV care.
- F. Develop new tools/ techniques to aid in deciphering the complex neuro-immune interactions at a molecular and cellular level in the context of HIV.
- G. Build and optimize multimodal domain based informatics tools to aid in analyzing and characterizing the phenotype of CNS disease modalities associated with HIV by using machine learning, big data and systems biology-based approaches.

Division of Services and Intervention Research (DSIR)

- A. Randomized clinical trials evaluating the effectiveness of known efficacious interventions.
- B. Analyses of naturalistic databases to evaluate the effectiveness of known efficacious interventions.

- C. Identifying moderators and mediators of intervention effects as a step to design and test personalized interventions.
- D. Evaluating the combined or sequential use of interventions.
- E. Determining the optimal length of intervention, establishing the utility of continuation or maintenance treatment (that is, for prevention of relapse or recurrence).
- F. Evaluating the long-term impact of efficacious interventions on symptoms, functioning, and quality of life.
- G. Developing novel information technology tools designed to improve the delivery and dissemination of evidence-based interventions and assist healthcare providers in identifying, adopting, and implementing proven prevention and treatment interventions.

Services research covers all mental health services research issues across the lifespan and disorders, including but not limited to:

- A. Services organization, delivery (process and receipt of care), and related health economics at the individual, clinical, program, community and systems levels in specialty mental health, general health, and other delivery settings (such as the workplace).
- B. Interventions to improve the quality and outcomes of care.
- C. Enhanced capacity for conducting services research.
- D. The clinical epidemiology of mental disorders across all clinical and service settings.
- E. The dissemination and implementation of evidence-based interventions into service settings.

NATIONAL INSTITUTE ON MINORITY HEALTH AND HEALTH DISPARITIES (NIMHD)

- A. Telehealth, telemedicine, and mobile health technologies (e.g., smart phone apps, web-enabled wearable sensors) to improve remote access to prompt diagnosis, early treatment, and clinical management for adult and pediatric patients in minority and health disparity populations, and to improve access to specialty care that would otherwise be inaccessible due to high cost or transportation barriers (e.g., by linking academic tertiary care-oriented health centers with community-based primary care settings).
- B. Products, technologies or services designed to improve accessibility or uptake of existing technologies (e.g., mobile phones, tablets, free WiFi, diabetic glucometers, blood pressure monitors, etc.) within disadvantaged communities and medically underserved areas (including urban, rural, remote, or island regions) to promote healthy lifestyles, enhance patient-clinician communication, provide patient education for self-management of chronic diseases/conditions, or enhance surveillance of communicable and non-communicable diseases in minority and health disparity populations.
- C. Products, technologies or services that take advantage of existing or emerging technologies (e.g., electronic health record systems, biomedical informatics platforms, big data resources and analytics, precision medicine) to improve health services delivery and quality of care, including but not limited to coordination of primary and specialty care, integration of behavioral health services into primary care settings, enhancement of provider-patient communication, and reduction of health literacy barriers in minority and health disparity populations.
- D. Products, technologies or services to enhance early detection of diseases, pre-disease states, or adverse health conditions in minority and health disparity populations through analysis of novel or validated biomarkers in saliva, breath, blood, and other tissues or specimens, including microbiota.
- E. Groundbreaking products or technologies to monitor real-time or cumulative exposures to physical, social and environmental risk factors acting at multiple levels across the life course (“exposome”) to improve understanding and situational awareness of factors that may significantly contribute to population health disparities, and/or to empower individuals or communities to take steps to avoid or mitigate the effects of such exposures.

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE (NINDS)

The NINDS accepts a broad range of small business applications that are significant, innovative, and relevant to its mission. Examples of research topics within the mission of NINDS are shown below. This list is not all inclusive and some research areas fall into multiple categories.

- A. Therapeutics and Diagnostics Development for Neurological Disorders, including biomarker and diagnostic assays, therapeutics (drugs, biologics, and/or devices) for treatment of neurological disorders, and technologies/methodologies to deliver therapeutics to the nervous system.
- B. Clinical and Rehabilitation Tools, including intraoperative technologies for neurosurgeons, rehabilitation devices and programs for neurological disorders, and brain monitoring systems
- C. Technology and Tools, including technologies to image the nervous system, neural interfaces technologies, and tools for neuroscience research and drug development.

Within these research topics, the following research may require additional funds above the hard budget caps:

- A. *In vivo* animal testing required for therapeutics and diagnostics development.
- B. Drug and biologics preclinical discovery and development activities for regulatory submission, such as lead identification/optimization, preclinical efficacy testing, IND-enabling studies, and manufacturing for clinical trials.
- C. Device preclinical discovery and development activities for regulatory submission, such as hardware prototyping, device/software verification, biocompatibility/sterilization testing, pre-clinical efficacy testing, large animal GLP safety testing, and preparing material/devices for human testing.
- D. Clinical testing of therapeutics (drugs, devices, or biologics), diagnostics, clinical and rehabilitation tools (i.e. intraoperative technologies, rehabilitation devices and programs, and brain monitoring systems), and technologies for clinical research. This would include clinical research studies to test scientific hypothesis that are not feasible or practical to conduct in animal models but would inform a final device design.
- E. *In vivo* animal testing of technologies for animal research and development of animal models for drug development and neuroscience research.
- F. Research that requires special facilities to contain hazardous or infectious materials.

Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative

The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative is a Presidential project aimed at revolutionizing our understanding of the human brain. NIH is one of several federal agencies involved in the BRAIN Initiative. Planning for the NIH component of the BRAIN Initiative is guided by the long-term scientific plan, "BRAIN 2025: A Scientific Vision," which details seven high-priority research areas. This report, as well as a list of the specific BRAIN Initiative funding opportunities, can be found at <http://braininitiative.nih.gov/>.

Based on priority areas identified by the BRAIN 2025, technology areas were identified to be appropriate for commercial development and may require additional funds above the hard budget caps:

- A. Development of research tools and technologies to understand the dynamic activity of neural circuits.
- B. Development of novel tools and technologies to facilitate the detailed analysis of complex circuits to provide insights into cellular interactions that underlie brain function.

- C. Development of invasive and non-invasive devices for recording and modulation in the human central nervous system.

NATIONAL INSTITUTE OF NURSING RESEARCH (NINR)

- A. Development of digital health technologies or services
- B. Development of health information/integration technologies or services
- C. Development and/or implementation of medical robotic systems
- D. Development of medical devices
- E. Projects proposing clinical trials with a large number of participants.

NATIONAL LIBRARY OF MEDICINE (NLM)

- A. Development and applications to improve storage, retrieval, access, management, representation, and use of biomedical knowledge
- B. Development of tools and methods for visualization, modeling, simulation, or analysis of complex biological systems and clinical processes
- C. Innovative approaches for data security and privacy, and technical issues related to other ethical, legal, and social implications of personal health data
- D. Methods for data integration to support discovery, learning, and health care
- E. Informatics tools that assist in delivering precision medicine to patients, or health decisions

DIVISION OF PROGRAM COORDINATION, PLANNING, AND STRATEGIC INITIATIVES (DPCPSI), OFFICE OF RESEARCH INFRASTRUCTURE PROGRAMS (ORIP)

RESEARCH AND DEVELOPMENT IN THE DIVISIONS OF COMPARATIVE MEDICINE AND OF CONSTRUCTION AND INSTRUMENTS

- A. Development of new technologies for rapid characterization and deep phenotyping of large numbers of animals.
- B. Development of technologies to identify biomarkers for clinical diagnostics in well validated disease models.
- C. Development of vaccines and new therapeutic agents to prevent and/or control selected laboratory animal diseases. One high priority need is to develop methods to control and prevent Herpes virus B in nonhuman primates.
- D. Design of specialized equipment and caging for laboratory animals to permit optimal environmental control and operational efficiency, including improvements in caging, identification/tagging of animals and remote monitoring in animal facilities.
- E. Identification, development, and characterization of spontaneous and engineered vertebrate animal models for studies of various human diseases, excluding most random mutagenesis projects performed on rodents.
- F. Development and refinement of high throughput technologies and devices for the effective cryopreservation, long-term maintenance of cells, tissues, and laboratory animal embryos, and gametes.
- G. Development of technologies and devices for the effective monitoring of frozen and cryopreserved cells, biological materials/tissues and laboratory animal embryos, and gametes.
- H. Development of improved reagents, artificial intelligence/machine learning technologies, devices and high throughput technology to perform, analyze, capture and process data gathered in “omics” studies (genomics, transcriptomics, phenomics, proteomics, glycomics, epigenomics, metabolomics, among others) in normal disease and intervention conditions in animal/biological models.
- I. Development of biological tools and reagents for reconstruction, remodeling, repair and regeneration of tissues damaged by injury or disease. Development of the technologies and procedures to test efficacy and safety of these experiments in animal models. Approaches to detect and track the implanted cells and tissues *in vivo*.
- J. Development of acellular biomaterials, biosensors and reagents to promote, detect and track reconstruction, remodeling, repair and regeneration of tissues and organs damaged by injury or disease.