

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

1/1/2018

NIH has received approval from SBA for the topics listed within for budgets greater than \$225,000 for Phase I SBIR/STTR awards and greater than \$1,500,000 for Phase II SBIR/STTR awards for 2018-2019. 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.

## Table of Contents

National Cancer Institute (NCI) .....	3
National Center For Advancing Translational Sciences (NCATS) .....	4
National Center for Complementary and Integrative Health (NCCIH).....	5
National Eye Institute (NEI).....	6
National Heart, Lung, and Blood Institute (NHLBI) .....	7
National Human Genome Research Institute (NHGRI) .....	8
National Institute on Aging (NIA) .....	9
National Institute on Alcohol Abuse and Alcoholism (NIAAA).....	16
National Institute of Allergy and Infectious Diseases (NIAID) .....	17
National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).....	19
National Institute of Biomedical Imaging and Bioengineering (NIBIB).....	20
<i>Eunice Kennedy Shriver</i> National Institute of Child Health and Human Development (NICHD).....	22
National Institute on Deafness and Other Communication Disorders (NIDCD) .....	24
National Institute of Dental and Craniofacial Research (NIDCR) .....	25
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).....	27
National Institute on Drug Abuse (NIDA).....	28
National Institute of Environmental Health Sciences (NIEHS) .....	29
National Institute of General Medical Sciences (NIGMS) .....	30
National Institute of Mental Health (NIMH) .....	32
National Institute on Minority Health and Health Disparities (NIMHD).....	36
National Institute of Neurological Disorders and Stroke (NINDS) .....	37
National Institute of Nursing Research (NINR) .....	39
National Library of Medicine (NLM) .....	40
Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), Office of Research Infrastructure Programs (ORIP) .....	41

## **NATIONAL CANCER INSTITUTE (NCI)**

- A. Therapeutics (e.g. Small Molecules, Biologics, Radiomodulators, and Cell-based Therapies)
- B. *In Vitro* and *In Vivo* Diagnostics (e.g. Companion Diagnostics and Prognostic Technologies)
- C. Imaging Technologies (e.g. Agents, Devices, and Image-Guided Interventions)
- D. Devices for Cancer Therapy (e.g. Interventional Devices, 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 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 which 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 innovated 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. Non-traditional phenotypic assay development for complex natural product mixtures.
- G. Integrated *in silico* tools for exploiting natural product bioactivity.

# **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 Behavioral and Social Science (DBSR)**

- A. Development and translation of behavioral-economics approaches (incentives or disincentives) to motivate sustainable behavior change to improve health and well-being:
  - 1. Increase levels of physical activity or promote treatment adherence or social connectedness;
  - 2. Address biases such as loss aversion, errors in affective forecasting, present bias, ambiguity effect, base-rate neglect, and susceptibility to framing effects in health and financial decision making;
  - 3. Use information, or the mode of data presentation, to improve decision-making (e.g., through “nudges,” policies, or practices that constrain choices);
  - 4. Integrate behavioral economics techniques with retail Electronic Health Records (EHRs) to produce low cost interventions designed to improve physician adherence to recommended treatment guidelines without overruling physician autonomy.
- B. Development of robotics applications to aid elderly:
  - 1. Develop socially-assistive robots to enhance the capabilities of older Americans to preserve their independence and remain in their homes. NIA envisions these robotics applications supporting machine cognition, language understanding and production, human-robot interaction (cognition, perception, action control, linguistics, and developmental science), and perception;
  - 2. Use of robots to promote social interaction and engagement and reduce loneliness among the elderly;
  - 3. Use of robots to motivate elderly to exercise.
- C. Development of cognitive training applications/intervention to improve cognitive function in elderly:
  - 1. Rapidly develop novel, engaging computer-based cognitive training programs that are based on efficacious approaches and that use cognitive training to target a specific neural system/functional domain;
  - 2. Augment existing computerized cognitive interventions to be personalized, engaging, adaptive, sufficiently challenging, and optimal for maximizing real world functional improvements;
- D. Development of blood-spot technology for biological data collection:
  - 1. Develop multiple and reliable assays for limited blood-spot specimens for large surveys.
- E. Development of social, behavioral, environmental and or/technical interventions on the individual, institutional, family, community or national level intended to maintain older adult independence or functioning, increase well-being and prevent disease and/or disability:
  - 1. Devise interventions that promote a safe home environment, including technological innovations to improve monitoring and communication;
  - 2. Devise interventions addressing self-management of chronic diseases among the elderly, including behavioral change and compliance;
  - 3. Devise interventions to promote self-awareness and attention to health and well-being in caregivers; including interventions focusing on stress management, maintaining a healthy diet, creating and maintaining contact with a supportive social network, and attending to one’s own physical health;
  - 4. Devise interventions to promote productive and effective communication with health-care providers, interventions that enhance understanding and communication of changes in

symptomology, promote transparency of care needs, increase receipt of family-centered optimal care, make informed health-care decisions, and for informed advance-care planning and directives;

5. Devise interventions and/or assistive devices to promote independence outside of the home, including but not limited to such activities as driving, wayfinding, and navigation;
6. Develop evidence-based methods, technologies, and behavioral interventions to reduce the burden of caregiving for AD caregivers. In addition, development should yield training materials/resources appropriate for use by either health-care organizations or community-based organizations.

F. Development of genetics and Genome Wide Association Approaches (GWAS):

1. Develop online genetic counseling for users to interface with professionals regarding issues that may have arisen after learning about genetic risk for disease;
2. Create smartphone applications that are capable of crowd sourcing new phenotype information from participants who have been genotyped.

G. Development of new sampling and data-collection methodologies for use in large population-based household surveys and behavioral interventions of relevance to aging. These include:

1. Develop methods and/or devices to conduct experience-sampling and other real-time collection of data, particularly for recording and analyzing social interactions;
2. Develop, test, and market assays to analyze bio-specimens collected as part of large longitudinal studies of aging.

H. Development of survey and archiving/database-support technology and resources:

1. Develop new databases and database-support infrastructure to satisfy data and research needs in aging;
2. Develop innovative data archives to make current statistical and epidemiological data more accessible per NIH rigor/reproducibility policy;
2. Develop data-extraction web and archiving tools for public-use databases;
3. Develop innovative methods and software to provide improved access to complex longitudinal studies or surveys that preserve confidentiality;
4. Develop innovative methods and software to facilitate analysis of personal data linked to geocoded data, biological, cognitive or genetic measures, with improved protection for confidentiality of respondents;
5. Develop data infrastructure and tools for assessing the economic impact of federally-funded research;
6. Develop and enhance existing NIA-supported longitudinal surveys/studies by creating longitudinal data files and corresponding codebooks (similar to the Rand Health Retirement Survey files and codebook);
7. Test, validate, process, and analyze biospecimens collected as part of large longitudinal studies of aging;
8. Develop remote data-enclave infrastructure to enable researchers to share and analyze restricted data (e.g. CMS claims records and other sensitive data).

- I. Develop risk-reduction programs (also referred to as health-promotion, health-management, demand-management, and disease-prevention programs) among those aged 45-64 years. The goal of these interventions would be to improve the health of older workers, lower the rate of health-care utilization, and improve the cost effectiveness of employer-based insurance plans.
- J. Integrate technology, big data, artificial intelligence (AI) and machine learning for early diagnosis of aging-related illnesses;
- K. Develop technology and innovative statistical methods (e.g., machine learning, development of artificial intelligence algorithms) to analyze Big Data (including, for example, time-intensive, multi-source data) to provide a better understanding of mechanisms underlying aging in formal or institutional treatment settings (e.g. early diagnosis of aging related disease such as dementia, and multiple co-morbidities in using EHR data) and in naturalistic settings (e.g. home assessment using technology to mine and integrate Big Data to predict early diagnosis of aging-related diseases).
- L. Develop new and/or validate existing sensitive, specific, and standardized tests for diagnostic screening of Mild Cognitive Impairment (MCI) to distinguish it from normative age-related cognitive change. Such development could include the creation of novel technology and/or methods or the validation of existing measures/methods/ technology for the early detection of cognitive impairment and MCI. Examples of such technology include biosensors, prosthetic devices, and software development targeting the assessment, diagnosis, and remediation of age-related cognitive decline.
- M. Discover, develop, and evaluate behavioral methods to remediate age-related cognitive decline, and to treat the cognitive impairment and/or behavioral symptoms associated with MCI, as well as to slow and/or reverse the course of cognitive decline or to prevent it entirely.

### **Division of Aging Biology**

- A. Development of anti-oxidants or other interventions to reduce oxidative or other stresses and aging-related diseases, including interventions that address how metabolic regulation influences longevity.
- B. Development of minimally-perturbing techniques for collecting blood from mice, rats, and other animals several times a day in sufficient quantities for measurement of hormone levels and other circulating factors in young and old non-human animals, or development of non-invasive research and test methods for use in non-human animals.
- C. Development of interventions that improve the immune response to foreign molecules or reduce the response to self or suppress age-induced inflammation.
- D. Validation and further development of candidate interventions which have been found to enhance longevity or slow aging and may affect other age-related conditions or diseases.
- E. Development of novel strategies for treating age-related renal, pulmonary, urology, reproductive disorders, and age-related changes in hormone production and function, including devices, pharmacological targets and their validation, small molecules and other approaches to treat these disorders in the elderly; early-stage pharmacological validation of novel targets and accompanying pre-therapeutic leads for these age-related diseases are encouraged.
- F. 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.

- G. Development of interventions that 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.
- H. Development of tools and resources in genetics and genomics to study molecular mechanisms of normal aging or aging-related diseases.
- I. 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.
- J. Development of biomarkers for prognosis, diagnosis, or treatment monitoring of aging or aging-related diseases.
- K. Analysis and integration of large data sets for developing biomarkers or biomarker signatures of aging or age-related diseases.

### **Division of Geriatrics and Clinical Gerontology**

- A. 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.
- B. 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.
- C. 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.
- D. Development and validation of improved approaches for evaluation, monitoring or treatment of diastolic dysfunction in older adults.
- E. 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.
- F. 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.
- G. Development and validation of non-invasive methods of examining bone quality (density, architecture, and strength of bone).
- H. 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.

- I. 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.
- J. 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.
- K. 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.
- L. 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.
- M. 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.
- N. Development of devices and/or techniques for preventing or treating urinary incontinence.
- O. 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.
- P. Development and validation of novel, practical, cost-effective and reliable assays of multiple markers of age-related chronic inflammation, designed for use in comprehensive geriatric assessment and for research purposes.
- Q. 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.
- R. Development of new therapeutic interventions targeting putative aging mechanisms that influence the risk or progression of multiple age-related conditions.

#### **Division of Neuroscience (DN)**

- A. Development of new and/or validation of existing sensitive, specific, and standardized tests for diagnostic screening of Mild Cognitive Impairment (MCI), Alzheimer's disease (AD), and Alzheimer's disease related dementias (ADRD), which includes but is not limited to the development of minimally-invasive biomarkers that can be used for screening in the general populations and in a community setting, biomarkers that could serve as surrogate measures for disease progression in MCI, AD and ADRD, novel neuropsychological, biochemical, and neuroimaging technology and/or methods or the validation of existing measures/methods/technology for the early detection of cognitive impairment and MCI and the early diagnosis of AD and ADRD and development of new technology and tests for detection of pre-clinical AD and other dementias of aging.
- B. Discovery, development, and/or evaluation of compounds, drugs, biological or natural products, including central-nervous-system delivery systems to remediate age-related cognitive decline, and to

treat the cognitive impairment and/or behavioral symptoms associated with MCI, AD, and ADRD as well as to slow and/or reverse the course of the disease or to prevent it entirely. Development of therapies that might prevent, slow or reverse the course of AD and ADRD, through the application of system biology and systems pharmacology approaches.

- C. 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 other dementias. Examples include systems and devices to: evaluate, monitor and improve or adapt to changes in cognition; to improve health-service delivery; to prolong functional independence; to support independent living and performance of tasks of everyday life; to provide information to health-care providers and family members to enable them to evaluate the need for intervention; and to promote communication and interaction between individuals living in the community or in institutional settings and their health-care providers, friends, and family members.
- D. Testing in clinical trials of drug, nutritional, behavioral, cognitive or other types of interventions to remediate age-related cognitive decline, and to treat cognitive impairment and/or behavioral symptoms associated with MCI, AD, ADRD, and other dementias of aging as well as to prevent the onset of disease or to slow and/or reverse the course of disease.
- E. Development of manuals for existing evidence-based interventions that reduce the burden of caregiving for AD caregivers so that the manuals and training materials can be used by community-based agencies or health care organizations.
- F. Development of a predictive platform or tool that would enable Medicare Advantage managed care providers to estimate future costs for care of patients with AD, ADRD, and other forms of dementia. The predictive tool would use Medicare claims data, particularly incidence and cost data. In addition, the predictive tool would allow for adjustments to reflect variable plans and kinds and levels of coverage associated with diverse patient demographics and risk profiles.
- G. Development of behavioral, environmental, pharmacological, & nutritional interventions to prevent and/or remediate brain biochemical and/or neurophysiological changes caused by neurodegenerative diseases, including age-related sensory dysfunction, motor dysfunction or age-related decrements in balance & postural control, gait performance, and mobility.
- H. Development of biosensors and prosthetic devices, technologies, and related software development to aid in the assessment, diagnosis, and remediation of age-related cognitive decline or sensory dysfunction (including pain, age-related vision loss, and age-related hearing loss), motor dysfunction (including Parkinson's disease and other motor disorders of aging), or age-related changes in balance, postural control, and gait.
- I. Development of novel markers of normal age-dependent cognitive decline or sensory and/or motor system changes at the molecular cellular, circuitry, physiological or behavioral level in humans or relevant animal models.
- J. 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 brain. Development of molecular imaging technology and/or chip-based technology for the in-vitro and in-vivo analysis of gene, epigenome, proteostasis, lipidomics and metabolomics and metabolic function in the normal aging brain and in AD.
- K. 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.
- L. 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.

- M. Development of novel markers of neural stem cell function (proliferation, migration, and differentiation) as well as methods to assess the integration and function of stem cells in the nervous system.
- N. Development of novel approaches for analysis of next-generation sequence data.

## **NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)**

- A. Treatment of alcoholism.
  - 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 or methods.
  - 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
  
- 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 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 and engraftment 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 on the identification and evaluation of medical countermeasures (MCMs) for public health emergencies involving ionizing radiation, through: 1) development of mitigators and therapeutics for acute radiation syndrome, delayed effects of acute radiation exposure, and/or radiation combined injury; 2) advancement of radionuclide-specific therapies, including chelating, blocking, or other novel decorporation agents; 3) improved methods of accurate, high-throughput radiation biodosimetry; 4) identification of biomarkers of organ-specific radiation injury; and 5) assessment of biomarkers of radiation injury in special populations and formulation of MCMs for administration to these affected groups.

### **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 that are easy to use, cost-effective and can diagnose individuals infected with pathogens or individuals that have been exposed to toxins.
- C. Development of vaccines 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), increase ease of administration (i.e., self-administration), and increase product stability to minimize cold chain requirements.
- 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.

#### **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 in seropositive HIV-infected individuals and to determine HIV incidence (HIV infection before seroconversion).
- F. Discovery and development of agents or strategies for sustained release protection (>30 days) from HIV infection in the genital and gastrointestinal tracts of men and women for Pre-exposure prophylaxis (PrEP) and Multipurpose Prevention Technologies (MPT).
- G. Development of rapid tests for the detection of ARTs in various human matrices (e.g. blood, urine, hair).
- H. Characterization, process development, formulation and manufacturing of HIV Env immunogens and novel HIV vaccines including RNA vaccines.
- I. Research on HIV vaccine adjuvants, analytics, formulations and immune responses.
- J. Development of formulation technologies to prevent or treat HIV and HIV-associated co-infections.

## **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. **Image-Guided Interventions.** Research on use of images for guidance, navigation and orientation in minimally invasive procedures to reach specified targets. Examples include image-guided interventions for minimally invasive therapies such as surgery and radiation treatment, for biopsies, and for the delivery of drugs, genes and therapeutic devices.
- B. **Magnetic Resonance Imaging and Spectroscopy.** Development of MR imaging and MR spectroscopic imaging, for both animal and human research, and potential clinical applications. Examples include (but are not restricted to) fast imaging, high field imaging, design of novel RF and gradient coils, novel pulse sequences, design of novel contrast mechanisms, imaging informatics, *in vivo* EPR imaging, molecular imaging, etc. The emphasis should be on technological development rather than detailed applications to specific diseases or organs.
- C. **Medical Devices and Implant Science.** Design, development, evaluation and validation of medical devices and implants. This includes exploratory research on next generation concepts for diagnostic and therapeutic devices; development of tools for assessing host-implant interactions; studies to prevent adverse events; development of predictive models and methods to assess the useful life of devices; explant analysis; improved *in vitro* and animal models for device testing and validation.
- D. **Micro- and Nano-Systems, Platform Technologies.** Development of BioMEMS, microfluidics and nanoscale technologies, including micro-total analysis systems, arrays, and biochips, for detection and quantitation of clinically relevant analytes in complex matrices. Application areas include biomedical research, clinical laboratory diagnostics, biodefense, high-throughput screening, drug delivery, tissue engineering, and implantable devices, among others.
- E. **Optical Imaging and Spectroscopy.** Development and application of optical imaging, microscopy, and spectroscopy techniques; and development and application of optical imaging contrasts. Examples of research areas include fluorescence imaging, bioluminescence imaging, OCT, SHG, IR imaging, diffuse optical tomography, optical microscopy and spectroscopy, confocal microscopy, multiphoton microscopy, flow cytometry, development of innovative light sources and fiber optic imaging devices.
- F. **Telehealth.** Development of software and hardware for telehealth studies that have broad applications as well as early stage development of telehealth technologies that may have specific focus areas. Research that is supported includes methods to address usability and implementation issues in remote settings, and methods to develop technology for standardizing and incorporating state of the art security protocols for verifying user identities and preserving patient confidentiality across remote access.
- G. **Tissue Engineering and Regenerative Medicine.** Development of enabling technologies including real-time, non-invasive tools for assessing the function of engineered tissues; real-time assays that monitor the interaction of cells and their environment at the molecular and organelle level; predictive computational models for engineering function 3D tissues; high-throughput assays and instruments to reduce the cost, time, and complexity of tissue engineering; novel bioreactor techniques for expanding stem cells and growing tissues and organs on a large scale; and strategies for preserving, sterilizing, packaging, and transporting living-tissue products. The program also supports applications of rational engineering design principles to functional engineered tissues; the development of novel biomaterials for use as tissue scaffolds that mimic the extracellular matrix and support multiple cell types in defined spatial orientation; and engineering approaches to study how biomaterials interact with cells and guide cell growth, differentiation, and migration.
- H. **Ultrasound.** Improvement of technologies for diagnostic, interventional and 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 interventional ultrasound program includes the use of ultrasound for therapeutic use, or as an adjunct for enhancement of non-ultrasound therapy applications. Examples include, but are not limited to, high-intensity focused ultrasound (HIFU) as a non-invasive or minimally invasive interventional surgical or therapy tool, and as an adjunct interventional tool. It also includes the use of ultrasound contrast agents for therapy and for targeted drug delivery, and the use of ultrasound for image-guided surgery, biopsy, and other interventions.

# **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: Development and research testing of new or adaptation of existing devices and innovative technologies to improve the collection, analysis, and automated coding of 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. Innovative technologies for imaging developmental processes and gene expression; technologies for gene manipulations and perturbations; and *in vivo* tools for quantitative measurement of physical properties of cells and tissues contributing to embryonic morphogenesis.

## **Fertility and Infertility Branch**

- A. Development of novel techniques for assessment of gamete quality.

## **Gynecologic Health and Disease Branch**

- A. Development of innovative technologies for the treatment of endometriosis, uterine fibroids, or pelvic floor dysfunction, the latter including pelvic organ prolapse, urinary incontinence or fecal incontinence.

## **Intellectual and Developmental Disabilities Branch**

- A. Technology development to improve screening, diagnosis and treatment 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 oligosaccharides and peptides with antimicrobial activity.
- B. Develop rapid and reliable methods to test human milk components for antimicrobial activity.

#### **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

#### **Pregnancy and Perinatology Branch**

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



# **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.

## **Preclinical Research**

- A. Preclinical research and development activities for dental 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.

## **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.

#### **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, Cystic Fibrosis, 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)**

### **1. Drug (Medication) discovery and development-enabling activities for Substance Use Disorders (SUDs).**

- Innovative in vitro, in situ, or in vivo tools for the analysis of the central nervous system, normal and/or diseased.
- Technologies, including molecular imaging, gene expression profiling, and genotyping and sequencing approaches designed to better inform SUD diagnosis and treatment.
- Assay development (e.g., biochemical, functional) and validation, especially, hiPSC-based assays, human organoid, or 3-D culture systems with the intention of developing medium to high-throughput assays.
- Tools to simplify the design and preclinical development of medications for SUDs.
- Discovery of SUD-related biomarkers (BMs) (e.g., BMs of chronic drug exposure, pharmacodynamic, toxicological/safety; BM assay development and validation), and BM-associated device development.
- Development of BM known to be associated with a health (salutary) outcome, which are quantitatively affected by reduction in drug use are particularly welcome
- Predictors of clinical outcomes in SUDs, e.g. physiological, electroencephalographic, cognitive tests, and biochemical, epigenetic, and genetic assays.
- Point of care monitoring systems to improve quantitative assessment of subject adherence to clinical trial protocols
- Tools that could be used as quantitative direct (e.g. plasma, saliva, or urine) measures or indirect (e.g. physiological, facial, motor, pupillometry) BMs of drug intoxication.

### **2. Drug (Medication) discovery and development activities.**

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:

- Early therapeutic discovery activities ranging from Target ID and validation through lead development
- Preclinical and/or clinical drug development
- Technologies or formulations to improve medication delivery

## **NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)**

- A. Development and validation of alternative test methods to protect human and animal health while reducing, refining, or replacing animal tests.

# **NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS)**

## **Division of Cell Biology and Biophysics**

- 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, 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 and high throughput platforms for diagnostic and clinical applications.
- D. 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 Genetics and Developmental Biology**

- A. Development of probes for detection of genetic polymorphisms, including disease genes.
- B. Development of valid animal models for genetic diseases and birth defects.
- C. Improvement of methodology (technology) for genetic analysis (e.g., gene expression, probes).
- D. Development of tools and technologies to detect and monitor complex phenotypes or traits.
- E. Development or improvement of methods for high throughput detection of epigenomic changes.
- F. Development of improved technology, reagents and tools to derive, grow, isolate, differentiate and characterize cells.
- G. Development or improvement of methods for characterizing and studying complex communities of microorganisms, including interactions with host organisms.
- H. Development of non-mammalian model systems.

## **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 tissue repair, wound healing, sepsis, and traumatic injury, emergency, peri-operative, or critical care conditions, and associated pain management.
- D. Research to improve drug design and delivery.
- E. Development of technologies, including instrumentation, reagents, and methods for -omics, including but not limited to robotics, sample preparation and pre-fractionation, analytical

separations, mass spectrometry, intelligent automated data acquisition, and improved informatics technologies.

- F. Development of technologies, including instrumentation, software, reagents, and methods for the study of carbohydrates, including but not limited to development of: specific glycan structural databases, methodologies for synthesis of robust glycan libraries, glycan labeling reagents and glyco-enzyme inhibitors, and analytical tools for determining carbohydrate structure and biological function.
- G. Development of tools to study oxidative stress and/or mitochondrial function.

#### **Division of Biomedical Technology, Bioinformatics, and Computational Biology**

- A. Development of instrumentation and devices for detection, analysis, separation and/or manipulation of biologically important molecules, cellular components or cells.
- B. Development of instrumentation and devices for elucidating interactions of biologically important molecules *in vitro*, *in vivo*, within cells, or in fluid or solid-state conditions.
- C. Development of tools and methods for the modeling, simulation, and/or analysis of complex biological systems.
- D. Development and/or enhancement of computational tools and methods to collect, store, interpret, analyze and/or visualize biomedical data.
- E. Development of software and hardware for improving the effectiveness of computational approaches in biomedical research.

#### **Division of Training, Workforce Development, and Diversity**

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

#### **Center 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.

#### **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.

1. 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.
2. Clinical and Rehabilitation Tools, including intraoperative technologies for neurosurgeons, rehabilitation devices and programs for neurological disorders, and brain monitoring systems
3. 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 technologies or devices requiring extensive engineering. Some examples include mobility assistive devices, POC monitors, or monitors of gait or other physiological measures. This does not include projects utilizing only mHealth technology.
- B. Projects proposing large (hundreds of participants) clinical trials.
- C. Technologies to facilitate delivery of prevention interventions across the lifespan.
- D. Innovative web-based information and communication technologies for addressing clinical care and advance care planning specific to hospice and palliative care symptoms, and for those in need of care to improve the effectiveness and efficiency of patient report data and integration into appropriate hospice/palliative health care systems.
- E. Use and integration of Health Information technology within/across “big data” systems, e.g., electronic health records for data collection, management and care integration. Of particular interest is technology that can be used across the spectrum of hospice and palliative care services/health systems.
- F. IT implementation across the spectrum of palliative and hospice settings that highlight the potential of informatics to improve the metrics and standards of palliative and hospice care.

## NATIONAL LIBRARY OF MEDICINE (NLM)

- A. Technology development and applications to improve storage, retrieval, access, management and use of biomedical knowledge
- B. Computational representation of biomedical knowledge
- C. Enhancement of human intellectual capacities through virtual reality, artificial intelligence, and machine learning
- D. *In silico* science
- E. Natural language understanding
- F. Support for health decisions
- G. Integration, organization and retrieval in very large databases, disparate forms of knowledge, and multiple datasets
- H. Investigations of topics relevant to health information science, computational modeling, and management of information during disasters



## **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 to rapidly phenotype large number 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, gametes, and their predecessors.
- G. Development of technologies and devices for the effective monitoring of frozen and cryopreserved cells, biological materials/tissues and laboratory animal embryos, gametes, and their predecessors.
- H. Development of improved reagents, techniques, 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 damaged by injury or disease.