HIGHEST PRIORITY CHALLENGE TOPICS
Note: Applicants are also encouraged to review the compilation of all NIH Institute and Center Challenge Topics:
http://grants.nih.gov/grants/funding/challenge_award/Omnibus.pdf

Topics in the table below that are marked with an asterisk (*) have been designated as the Institute, Center or Office's highest priority; however, applicants may apply to **any** of the topics listed in the Omnibus.

Broad Challenge Area	Specific Challenge Topic
(01) Behavior, Behavioral Change, and Prevention	**01-AA-101*** **Identifying Phenotypic Markers for Positive Behavior Change.** Identify reliable, robust intermediate phenotypic markers (using cognitive neuroscience and behavioral economics) that can be used to personalize approaches to support positive health behavior change in the near term. Examples include behavioral disinhibition, delay discounting, heart rate variability and implicit cognition. Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **01-AA-102*** **Functional Roles of Neuroimmune Factors in Mediating Behavior.** Neuroimmune factors significantly impact both normal brain functions and a variety of neurological and behavioral disorders. Emerging data suggest that physiological functions of neuroimmune factors, such as cytokines and chemokines, are not restricted to mediating neuroinflammatory responses but may be considered as a new class of neurotransmitter, neuromodulator, or neurohormone in the brain. This paradigm shift offers a new framework to understand the roles of neuroimmune factors in a variety of behavioral conditions such as excessive drinking, anxiety, depression, etc. Contact: Dr. Antonio Noronha, 301-443-7722, anoronha@mail.nih.gov **01-AA-103*** **Capturing Social Network Information for Groups at High Risk for Negative Health Behaviors.** Emerging evidence indicates that social networks influence health behaviors such as eating habits, alcohol consumption, and smoking. Research in this area is needed to enhance existing methodologies and/or devise novel methods that will capture social network information among groups at heightened risk for particular negative health behaviors. The ultimate public health goal is to use this information to influence behavioral choices and improve health outcomes. Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **01-GM-101*** **Individual-based model of social behavior.** Development of a robust and well-characterized individual-based model of social behavior that includes the dynamics of social interactions and that matches observed patterns of behavior. Contact: Dr. Irene Eckstrand, 301-594-0943, eckstrai@nigms.nih.gov **01-OD(OBSSR)-101*** **Tools for studying cultural phenomena.** Development of new tools for: the measurement of culturally-shared mental phenomena (e.g., representations, scripts, prejudices); studying mechanisms by which these phenomena are transferred and adapted across individuals; and advancing research on the distribution and transmission of cultural phenomena within populations. Contact: Dr. Christine Bachrach, 301-496-9485, cbachrach@nih.gov NIAAA Contact: Dr. Marcia Scott, 301-402-6328, mscott@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov; FIC Contact: Dr. Aron Primack, 301-496-1653, aron_primack@nih.gov

Broad Challenge Area	Specific Challenge Topic
	01-OD(OBSSR)-102* Methods for studying the interactions among behaviors, environments, and genetic/epigenetic processes. Research is needed to develop analytic methods, systems science approaches, or computational models designed to address the interactions among individual behaviors, social and physical environments and genetic/epigenetic processes during critical developmental periods and over time. This research is essential to incorporating the dynamic complexity of behavior and environments in the study of gene-environment interactions in health. Contact: Dr. Kay Wanke, 301-435-3718, wankek@od.nih.gov; NHLBI Contact: Dr. Peter Kaufmann, 301-435-2467, kaufmannp@nhlbi.nih.gov **01-OD-101* Test default options to promote healthier behaviors.** Exploration by behavioral economists and clinicians to develop and test default options (e.g., placement of fresh fruit displays in stores, the location of parking spaces at the workplace) to promote healthier behaviors. Contact: Dr. Jonathan King (NIA), 301-402-4156, kingjo@mail.nih.gov **01-TW-101* Novel strategies to improve health care access for stigma-related conditions**. Design and evaluate pilot interventions to improve access to health care for stigma-related health conditions, identify the qualitative characteristics of successful interventions, and demonstrate successful interventions that can be scaled up or generalized to other stigmatized public health problems and/or to other populations and cultures. Develop valid and reliable methods and measures for assessing stigma as an impediment to access to health care services that allow for comparisons over time and locations. Contact: Dr. Xingzhu Liu, 301-496-1653, liuxing@mail.nih.gov **01-TW-102* Improving health through ICT/mobile technologies: enhancing patient compliance**. Develop theory-based social and behavioral principles that influence the utility of evidence-based interventions using Information and Communication Technology (ICT) to effect patient compliance and adherence. Test effectiveness, feasibility and scalability of an ICT approach in real-world settings, including development and use of intermediate and end-point health outcomes measures. Contact: Dr. Xingzhu Liu, 301-496-1653, liuxing@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
(02) Bioethics	**02-HG-101* Informed consent and data access policies.** The creation of large databases that include genomic information on individual participants, coupled with the move to universal electronic medical records, makes it increasingly possible to identify individual research participants in databases, despite efforts to "de-identify" their data, and potentially to unearth an individual's private medical information. Research is urgently needed to address the implications of this for recruitment, informed consent, and data access policies in biomedical research. Contact: Dr. Jean McEwen, 301 402-7997, jm552n@mail.gov.nih; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIDA Contact: Dr. Marsha Lopez, 301-402-1846, lopezmar@nida.nih.gov **02-OD(OSP)-101* Unique Ethical Issues Posed by Emerging Technologies.** Advances in biotechnology and biomedical science raise novel ethical, legal, and social issues. Research in this area is needed to understand the unique ethical concerns related to emerging technologies (e.g. biotechnology, tissue engineering, nanomedicine, and synthetic biology). These include issues such as dual use research, privacy, safety, intellectual property, commercialization and conflict of interest, among others. Research is also needed to assess how these novel issues are addressed under current oversight and regulatory structures and identify where there may be gaps and/or need for revised or new oversight approaches. Contact: Abigail Rives, 301-594-1976, rivesa@od.nih.gov; NCCAM Contact: Dr. Jack Killen, 301-594-7103, killenj@mail.nih.gov; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIAID Contact: Dr. Liza Dawson, 301-496-6179, dawsonl@niaid.nih.gov; NCI Contact: Dr. Jerry Lee, 301-594-0255, leejerry@mail.nih.gov; NIDA Contact: Dr. Kathy Etz, 301-402-1749, ketz@nida.nih.gov; NIDCR Contact: Dr. Nadya Lumelsky, 301-594-7703, Nadya.Lumelsky@nih.gov; NIDDK Contact: Dr. Olivier Blondel, 301-451-7334, blondelol@niddk.nih.gov; NIBIB Contact: Dr. Belinda Seto, 301-451-6768, setob@mail.nih.gov; NIEHS Contact: Dr. David Balshaw, 919-541-2448, Balshaw@niehs.nih.gov; NIGMS Contact: Dr. Richard Anderson, 301-594-0943, andersor@nigms.nih.gov; NICHD Contact: Dr. James Hanson, 301-496-8535, hansonj@mail.nih.gov; NHGRI Contact: Dr. Joy Boyer, 301-402-7997, jb40m@nih.gov; NHLBI Contact: Dr. Gail Weinmann, 301-435-0233, weinmanng@nhlbi.nih.gov; NIMH Contact: Dr. Jean Noronha, 301-443-3367, jnoronha@mail.nih.gov; NINDS Contact: Dr. Joe Pancrazio, 301-496-1447, jp439m@nih.gov **02-OD(OSP)-102* Ethical Issues in Health Disparities and Access to Participation in Research.** Research is needed to assess the under-representation in biomedical and clinical research of U.S. minority populations, underserved populations, and populations who may be vulnerable to coercion or undue influence, to identify barriers to participation in research and to develop approaches for overcoming them. Additionally, studies are needed to assess the impact and ethical considerations of conducting biomedical and clinical research internationally in resource-limited countries. Contact: Abigail Rives, 301-594-1976, rivesa@od.nih.gov; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIAID Contact: Dr. Liza Dawson, 301-496-6179, dawsonl@niaid.nih.gov; NIAMS Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov; NCI Contacts: Dr. Alexis Bakos, 301-443-0542, bakosa@mail.nih.gov; Dr. Martha Hare, 301-594-1908, harem@mail.nih.gov; Dr. Shobha Srinivasan, 301-435-6614, Sriniva2@mail.nih.gov; NIDCR Contacts: Dr. Ruth Nowjack-Raymer, 301-594-5394, nowjackr@nidcr.nih.gov and Dr. Melissa Riddle, 301-451-3888, riddleme@mail.nih.gov; NIDDK Contact: Dr. Rebekah Rasooly, 301-594-6007, rasoolyr@EXTRA.NIDDK.NIH.GOV; NIEHS Contact: Contact: Mr. Liam O'Fallon, 919-541-7733, Ofallon@niehs.nih.gov; NICHD Contact: Dr. Regina James, 301-435-2692,

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	rjames@mail.nih.gov; NHGRI Contact: Dr. Jean McEwen, 301-402-4997, mcewenj@mail.nih.gov; NHLBI Contact: Dr. Patrice Desvigne-Nickens, 301-435-0515, desvignp@nhlbi.nih.gov; NCMHD Contact: Dr. Nathaniel Stinson, 301-402-1366, stinsonn@mail.nih.gov; NIMH Contact: Dr. Jean Noronha, 301-443-3367, jnoronha@mail.nih.gov; NINDS Contact: Dr. Salina Waddy, 301-496-3102, Salina.Waddy@nih.gov**;** FIC Contact: Dr. Barbara Sina, 301-402-9467, sinab@mail.nih.gov **02-OD(OSP)-103* Ethical Issues Associated with Electronic Sharing of Health Information.** The development of an electronic health information infrastructure and the sharing of health information for patient care and research offer enormous promise to improve health care and promote scientific advances. However, the broad sharing of such data raises numerous ethical issues that may benefit from additional studies (e.g. those related to privacy and confidentiality). Examples include studies to assess risks associated with health information technology and the broad sharing of health information for research, and novel approaches for mitigating them. Examination could also include analysis of current oversight paradigms and suggestions for enhancements, as well as assessments of how privacy risks may change in the future. Contact: Abigail Rives, 301-594-1976, rivesa@od.nih.gov; NIAAA Contact: Dr. Patricia Powell, 301-443-5106, ppowell@mail.nih.gov; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIAID Contact: Dr. Liza Dawson, 301-496-6179, dawsonl@niaid.nih.gov; NCCAM Contact: Dr. Jack Killen, 301-594-7103,killenj@mail.nih.gov; NCI Contacts: Dr. Chris Kinsinger, 301-436-1550, kinsingc@mail.nih.gov; Dr. Marsha Reichman, 301-534-7032, reichmam@mail.nih.gov; NIDCD Contact: Dr. Gordon Hughes, 301-435-4085, hughesg@nidcd.nih.gov; NIDCR Contact: Dr. Emily Harris, 301-594-4846, harrisel@nidcr.nih.gov; NIDDK Contact: Dr. Christine Hunter, 301-594-4728, hunterchristine@mail.nih.gov; NIBIB Contact: Dr. Belinda Seto, 301-451-6768, setob@mail.nih.gov; NHLBI Contact: Dr. Dina Paltoo, 301-435-0513, paltood@nhlbi.nih.gov; NLM Contact: Dr. Valerie Florance, 301-594-4882, florancev@mail.nih.gov; NIMH Contact: Dr. Jean Noronha, 301-443-3367, jnoronha@mail.nih.gov; NCRR Contact: Dr. Elaine Collier, 301-435-0794, colliere@mail.nih.gov **02-OD(OSP)-104* Ethical Issues in the Translation of Genetic Knowledge to Clinical Practice.** Genetics and genomics have great promise for the development of personalized medicine, yet the ethical, legal and social implications of both the research and application of genetic and genomic knowledge and technology are far reaching. Studies are needed to better understand the factors that influence the translation of genetic information to improved human health and the associated ethical issues. Examples of studies include those to address ethical issues related to broad sharing and use of new genetic information and technologies for research to improve human health, human subjects protection in genetic and genomic research, the identifiability of genetic/genomic information and how our understanding of identifiability is evolving, return of research results and incidental findings to subjects, alternative models of informed consent for broad data sharing for research, and the impact of intellectual property (IP) issues on development of new technologies. Contact: Abigail Rives, 301-594-1976, rivesa@od.nih.gov; NIAAA Contact: Dr. Patricia Powell, 301-443-5106, ppowell@mail.nih.gov; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIAID Contact: Dr. Liza Dawson, 301-496-6179, dawsonl@niaid.nih.gov; NIAMS Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov NCI Contacts: Dr. Mehdi Mesri, 301-496-1550, mesrim@mail.nih.gov; Dr. Leah Sansbury, 301-

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	435-4910, sansburl@mail.nih.gov; NIDCD Contact: Dr. Bracie Watson, Jr., 301-402-3458, watsonb@nidcd.nih.gov; NIDCR Contact: Dr. Emily Harris, 301-594-4846, harrisel@nidcr.nih.gov; NIDDK Contact: Dr. Rebekah Rasooly, 301-594-6007, rasoolyr@EXTRA.NIDDK.NIH.GOV; NIEHS Contact: Dr. Kimberly McAllister, 919-541-4528, mcalis2@niehs.nih.gov;NEI Contact: Dr. Grace Shen, 301-451-2020, sheng@mail.nih.gov; NICHD Contact: Dr. James Hanson, 301-496-8535, hansonj@mail.nih.gov; NHGRI Contact: Dr. Elizabeth Thomson, 301-402-4997, et22s@nih.gov NHLBI Contact: Dr. Dina Paltoo, 301-435-0513, paltood@nhlbi.nih.gov; NIMH Contact: Dr. Jean Noronha, 301-443-3367, jnoronha@mail.nih.gov; NINDS Contact: Dr. Danilo Tagle, 301-446-5748, dt39y@nih.gov **02-OD(OSP)-105* Ethical Issues Raised by the Blurring between Treatment and Research.** The distinction between clinical practice and research is growing less clear, a trend that may be more pronounced with respect to genetic information and medical records research. Studies are needed to better understand the ethical issues associated with this trend. Examples of studies include those to identify how this blurring in roles affects traditional human subjects protections, including, for example, essential practices such as informed consent, conceptions of the doctor/patient and investigator/subject relationship, and privacy protections. Contact: Abigail Rives, 301-594-1976, rivesa@od.nih.gov; NCCAM Contact: Dr. Jack Killen, 301-594-7103, killenj@mail.nih.gov; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIAID Contact: Dr. Liza Dawson, 301-496-6179, dawsonl@niaid.nih.gov NCI Contact: Dr. Paul Han, 301-594-6642, hanp@mail.nih.gov; NIDCD Contact: Dr. Gordon Hughes, 301-435-4085, hughesg@nidcd.nih.gov; NIDCR Contact: Dr. Jane Atkinson, 301-435-7908, Jane.Atkinson@nih.gov; NIDDK Contact: Dr. Rebekah Rasooly, 301-594-6007, rasoolyr@EXTRA.NIDDK.NIH.GOV; NIEHS Contact: Dr. Kim Gray, 919-541-0293, Gray6@niehs.nih.gov; NHGRI Contact: Dr. Elizabeth Thomson, 301-402-4997, et22s@nih.gov; NHLBI Contact: Dr. Carol Blaisdell, 301-435-0219, blaisdellcj@nhlbi.nih.gov NIMH Contact: Dr. Jean Noronha, 301-443-3367, jnoronha@mail.nih.gov; NINDS Contact: Dr. Brandy Fureman, 301-496-9135, bf103s@nih.gov**;** FIC Contact: Dr. Barbara Sina, 301-402-9467, sinab@mail.nih.gov. **02-RR-101* Recontact Issues in Genotype and Genome-Wide Association Studies.** Genotype and genome-wide association studies create challenging re-contact issues if subjects are later to be asked to return for clinical research including phenotyping. Applicants would propose 2-year awards for pilot programs that would be implemented at 3 or more affiliated sites to develop and apply IRB guidelines that addressed ethical barriers (e.g., re-contacting) in genotype – phenotype studies. This idea is submitted through NCRR on account of the ethics work underway at the Clinical and Translational Science Awards (CTSAs) and, if accepted, would be developed with NHGRI's ELSI Division. NCRR Contact: Dr. Andrea Sawczuk, 301-435-0792, sawczuka@mail.nih.gov; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIDA Contact: Dr. Louise Wideroff, 301-443-8663, wideroffl@nida.nih.gov; NHGRI Contact: Dr. Jean McEwen, 301-402-4997, mcewenj@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
(03) Biomarker Discovery and Validation	**03-AR-101*** **Biomarkers Of Persistent Damage After Acute Joint Injury.** Define early biochemical and structural changes that arise after joint injury, such as trauma or anterior cruciate ligament (ACL) tears, which would serve as indicators that could be analyzed in subsequent longitudinal studies to seek biomarkers for progression to early osteoarthritis (OA). These could be used for both preventive intervention, and as preliminary indications for pathways of disease pathogenesis to guide therapeutic development. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov; OD(ORWH) Contact: Dr. Lisa Begg, 301-402-1770, BeggL@od.nih.gov **03-AR-102*** **Develop Novel Imaging, Proteomic, Or Genomic Approaches To Identify Risk For Fragility Fractures.** Projects may use existing data sets to define and validate measures of bone quality that are more predictive than bone mineral density measurements. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov; OD(ORWH) Contact: Dr. Lisa Begg, 301-402-1770, BeggL@od.nih.gov **03-AT-101*** **Psychoneuroimmunology biomarkers of stress.** Identification of biomarkers to assess the impact of stress, both social and biological, on immune function. Contact: Dr. John Glowa, 301-496-0527, glowaj@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **03-AT-102*** **Antioxidant biomarkers**. Development and validation of biomarkers of oxidative stress that could be used to assess the antioxidant effects of dietary supplements *in vivo* and to examine their mechanisms of action, efficacy, and effectiveness with respect to human health. Contact: Dr. Laura Moen, 301-402-5867, moenl@mail.nih.gov **03-DA-101*** **Biomarkers for Pain.** Pain research has been greatly hampered by the unreliable nature of self-report based instruments. The establishment of objective, affordable and reliable pain biomarkers and measurements would advance our understanding of pain mechanisms, provide a basis for improved clinical management of pain, help assess an individual's risk for becoming addicted to opiate analgesics, and establish much needed objective measures of treatment success or failure. Contact: Dr. Yu Lin, 301-435-1318, ylin1@nida.nih.gov; OD(ORWH) Contact: Dr. Janine A. Clayton, 301-402-1770, Smithja2@od.nih.gov **03-DA-102*** **Novel Molecular Targets From Unexpected Sources.** The quiescent databases left behind by unsuccessful medication trials represent an incredibly rich resource with the potential to turn failure into success. Through the use of strategic alliances (e.g., with FDA Critical Path Initiative) and novel approaches, such as target deconvolution and network pharmacology, these databases, can be transformed into engines of discovery to dramatically increase our ability to recognize novel molecular targets that underlie robust biological responses such as liability to drug abuse. Contact: Dr. Elena Koustova, 301-496-8768, koustovae@mail.nih.gov **03-DA-103*** **Comprehensive biomolecular mass spectrometry** Current detection methodologies provide a narrow window into just 1% of the molecular universe. As a consequence, there is a strong need to develop new mass spectrometric technologies for the faster, more sensitive, more specific, and more comprehensive identification of

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	biomolecules (both charged and neutral proteins and lipids) in tissue samples and single cells. This initiative seeks to leverage the potential of cutting edge technologies in the areas of ion mobility and vacuum ultraviolet photofragmentation for developing molecular identification and quantitation instruments that could be deployed in the clinical as well as research environments. Contact: Dr. Christine Colvis, 301-443-6480, ccolvis@nida.nih.gov **03-DA-104*** **Biosignatures of Drug Exposure.** Chronic exposure to a pathogenic agent is one of the defining features of conditions such as infectious diseases and substance use disorders. This characteristic presents a unique opportunity to develop and harness the power of biosignatures that could reliably predict disease vulnerability, trajectory, and treatment outcome. This initiative is specifically designed to uncover and validate peripheral endogenous biomarkers in animal models exposed to chronic drug exposure, withdrawal, or relapse that may serve as surrogates for CNS changes in humans. The results are also likely to spur significant advances in a host of related disorders. Contacts: Dr. Ivan D. Montoya, 301-443-8639, Imontoya@mail.nih.gov; Dr. Jeffrey Schulden, 301-402-1526, schuldenj@nida.nih.gov; Dr. Elena Koustova, 301-496-8768, koustovae@mail.nih.gov **03-EY-101*** **Role of immunity in identifying relevant markers in ocular diseases.** Oxidative stress/injury and host immune response are postulated to be involved in many degenerative eye diseases such as age-related macular degeneration, diabetic retinopathy, uveitis, glaucoma, and keratoconus. Other disorders such as Sjögren's syndrome remain difficult to diagnose and treat. Characterizing the molecular events and the host immune response during disease progression, and the understanding of how genes and their products interplay between systemic inflammation, vascular disease and photoreceptor cell death will allow us to identify biomarkers for the diagnosis and treatment of these blinding diseases. Contact: Dr. Grace Shen, 301-451-2020, sheng@mail.nih.gov **03-HL-101*** **Identify and validate clinically relevant, quantifiable biomarkers of diagnostic and therapeutic responses for blood, vascular, cardiac, and respiratory tract dysfunction.** Treatment paradigms have evolved from studies of patients who, despite similar presentations, may have experienced disparate environmental exposures or clinical courses and may have varied underlying pathobiologies. As a result, patients who appear to be similar because of their clinical characteristics often demonstrate substantially different morbidity, mortality, and responses to drugs. Identification and validation of biomarkers from cell culture to animal models and human studies that can be efficiently and reproducibly quantified in a clinical setting could be used to determine the most effective care for individual patients and identify more precisely those who are most likely to benefit from specific interventions for prevention or treatment. Contact: Dr. James Kiley, 301-435-0233, kileyj@nhlbi.nih.gov **03-MH-101*** **Biomarkers in mental disorders.** Search for innovative approaches to identify candidate biomarkers for mental disorders that are suitable for subsequent validation efforts. Potential biomarkers would predict disease risk and course, prognosis, and/or treatment response. Techniques could include behavioral assessments, electrophysiology, neuroimaging, genomics, proteomics, metabolomics, or any combination thereof. Contact: Dr. Steven J. Zalcman, 301-443-1692, szalcman@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
	03-NS-101* Identification and validation of biomarkers for Proof of Concept (early Phase IIa) studies for Nervous System Disorders. For many neurological disorders, moving potential therapies from promising studies in animal models to clinical trials that demonstrate effectiveness in patients remains a major hurdle. Identifying and validating biomarkers that associate with a beneficial response to treatment in the human (or in the animal model) which can also be measured in patients would help overcome this hurdle. These biomarkers could be used in Phase IIa Proof of Concept studies to determine whether a therapeutic intervention has engaged the intended biologic target. Contact: Dr. Ursula Utz, 301-496-1431, utzu@ninds.nih.gov **03-OD(OBSSR)-101* Developing high-throughput biomarker assays from finger-stick dried blood spots.** Develop, using finger-stick dried blood spots, novel high-throughput biomarker assays, to identify lipids, proteins, metabolites, and genetic information to expand the array of available biomarkers for use in large community-based biosocial surveys. OD(OBSSR)Contact: Dr. Kay Wanke, 301-435-3718, wankek@od.nih.gov NIAAA Contact: Dr. Marcia Scott, 301-402-6328, mscott@mail.nih.gov; NIEHS Contact: Dr. Daniel Shaughnessy 919-541-2506, Shaughn1@niehs.nih.gov; NHLBI Contact: Dr. Catherine Stoney, 301-435-6670, stoneyc@nhlbi.nih.gov **03-OD(ORDR)-101* Validating biomarkers for functional outcomes in rare diseases.** This initiative will provide a program of an expert consultative group to work with research investigators in the design to validate biomarkers and collect the data necessary to relate the biomarker with functional outcome in rare diseases. This program will be designed to stimulate development of new treatment trials. Contact: Dr. Rashmi Gopal-Srivastava, 301-402-4336, gopalr@mail.nih.gov NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
(04) Clinical Research	**04-AA-101* Medication Development for Hepatic Fibrosis.** Alcohol and infectious disease induced hepatic fibrosis affects millions of patients worldwide and remains an unresolved challenge for clinicians. Given the morbidity/mortality associated with this disease, there is an urgent need for translation of emerging antifibrotic molecules into effective therapies. Expediting clinical trials for compounds that have successfully undergone preclinical studies has the potential to make much needed medications available and reduce the need for liver transplantation. Contact: Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **04-AG-101* Therapeutic algorithms for older patients with multiple conditions: data analyses and pilot testing.** Analysis of existing medical record data sets (e.g., from the VA or HMOs) to identify problems associated with the combination of therapies for two or more specific conditions in older patients with multiple conditions. This information could be used to develop new therapeutic algorithms or refine existing algorithms to address problems related to the use of multiple algorithms in older clinically complex patients and to inform short-term intervention studies to assess their efficacy and practicality. Contact: Dr. Susan Nayfield, 301-496-6949, nayfiels@mail.nih.gov; NIAMS Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **04-AI-101* Develop novel methods and address key questions in mucosal immunology:** Human mucosal immunology has been an extremely difficult area of study, despite its importance for developing interventions for immunologic and infectious diseases of the airway, GI, and vaginal tract, and for improving human vaccine responses. Greater understanding of the immunology of the mucosa will also be important in the design and development of topical microbicides and a variety of immune-based therapies. Furthermore, immunizations of the mucosa are likely to be more relevant, simpler, and less expensive than systemic immunizations. Contact: Dr. Annette Rothermel, 301-496-5429, arothermel@mail.nih.gov **04-AI-102* The human immune response to infection and immunization – Profiling via modern immunological methods and systems biology.** Challenge grants in this area will capitalize on recent advances in immune profiling and systems biology to understand the diversity of human immune responses to vaccination and generate profiles of protective as well as ineffective immune responses. This effort will rely on existing, phenotypically well-characterized cohorts (e.g., human microbiome project, various longitudinal birth cohorts, etc.) and apply a variety of modern analytic tools, including transcriptional, cytokine, and proteomic profiling, and analysis of leukocyte subsets and functional status. Parallel efforts will focus on development of a wide range of human sample-sparing assays. The resulting challenge grants will expand ongoing NIAID-sponsored efforts in immune profiling and accelerate a planned expansion of these activities. The results of these studies will have immediate implications for rational design and development of safe and effective vaccines and improved immunization schedules. Contact: Dr. Dan Rotrosen, 301-496-1886, drotrosen@mail.nih.gov **04-AR-101* Autoimmunity For Diseases Of The Skin, Joints, Muscle And Other Tissues.** Develop reagents and analytic methods to identify, characterize, track, and inhibit human B and T cells specific for defined self-antigens, and antigen-presenting cells

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	in diseases of the skin, joints, and other tissues. Define mechanisms by which autoreactive lymphocytes contribute to tissue damage. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov; ORWH Contact: Dr. Janine A. Clayton, 301-402-1770, Smithja2@od.nih.gov **04-DC-101*** **Prevention of Otitis Media.** Otitis media, or middle ear infection, is a major public health problem in young children. Resistance of bacterial pathogens to traditional antibiotic therapy is making this approach to treating this disorder increasingly problematic. The Challenge is to develop and utilize knowledge of the basic biology underlying bacterial colonization and infection of the middle ear to create new approaches to preventing infection. Contact: Dr. Bracie Watson 301-402-3458, watsonb@nidcd.nih.gov **04-DK-101*** **Role of the human gut microbiome in NIDDK diseases.** This effort would support metagenomic studies aimed at understanding the role of the human microbiome in contributing to NIDDK diseases and conditions. Studies are needed that would evaluate appropriate sampling techniques, high throughput platforms, and analytic techniques that would provide sufficient data to serve as the foundation for further hypothesis driven studies in the disease or condition of interest. Contact: Dr. Robert Karp, 301-451-8875, karpr@mail.nih.gov **04-GM-101*** **Personalized drug response and toxicity.** Application of pharmacogenetics and pharmacogenomics, quantitative and systems pharmacology (this could be part of a larger grouping to include systems biology and systems genetics), ADMET pharmacology, preclinical models, and new technologies and approaches to complement pharmacogenomic studies to enhance signal-to-noise ratios and aid mechanistic studies, and consensus standards for normal and altered phenotypes in drug response and toxicity. Contact: Dr. Rochelle Long, 301-594-3827, longr@nigms.nih.gov; Dr. Richard Okita, 301-594-3827, okitar@nigms.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **04-HD-101*** **Identify the Factors that Place Women at Risk for Preterm Birth**. Over 12 percent of births happen prematurely, and the rate is rising--increasing the risk of adverse outcomes for babies and mothers. However, most of these births occur in women who do not have any of the few known risk factors for preterm birth. New approaches and technologies (such as fetal imaging, fetal EKG, blood or urine tests, or response to maternal position or exercise) are urgently needed to improve physicians' ability to identify women at increased risk for preterm birth, so that preventive interventions can be developed. Contact: Dr. Catherine Spong, 301-435-6894, spongc@mail.nih.gov; ORWH Contact: Dr. Indira Jevaji, MD, 301-402-1770, jevajiip@od.nih.gov **04-HD-102*** **Development of Pediatric Medical Devices**. Currently, many cardiovascular, surgical, prosthetic, and diagnostic devices originally designed for adults are also being adapted for use in young children, without having demonstrated that they are safe, effective, and appropriately sized. Pediatric medical devices need to be developed that are properly designed for children, with safety and effectiveness demonstrated rather than presumed, and with accurate risk assessments. Contact: Dr. Steven Hirschfeld, 301-496-0044, hirschfs@mail.nih.gov. **04-MD-101*** **Development of effective approaches to increase minority recruitment and retention into clinical trials.** NCMHD will focus on research activities

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	that reduce barriers to diversity and participation in clinical trials and on initiatives that build partnerships and utilize new and non-traditional recruitment approaches. Specific health disparity diseases/conditions of concern include but are not limited to diabetes, obesity, cardiovascular disease, infant mortality, cancer, substance abuse, mental health, and HIV/AIDS. Contact: Dr. Derrick Tabor, 301-402-1366, tabord@mail.nih.gov **04-MH-101*** **Autism: Addressing the challenge.** Target research gap areas identified by the Inter-Agency Autism Coordinating Committee (IACC) Strategic Plan for Autism Spectrum Disorder Research, including biomarkers, novel interventions, and new tools for screening, among other topics. Contact: Dr. Ann E. Wagner, 301-443-5944, awagner@mail.nih.gov **04-NR-101*** **Integrating Cost-Effectiveness Analysis into Clinical Research** This initiative calls for the inclusion of rigorous cost-effectiveness analysis in the design and testing of new and innovative interventions as well as existing interventions with demonstrated effectiveness. Cost-effectiveness research will provide accurate and objective information to guide future policies that support the allocation of health resources for the treatment of acute and chronic diseases across the lifespan. Contact: Dr. Linda Weglicki, 301-594-6908, weglickils@mail.nih.gov; NIAAA Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **04-NR-102*** **Methods to Enhance Palliative Care and End-of-Life Research** This initiative will develop and test interventions to enhance the quality of care for persons with a life-threatening illness. This research will provide the foundation for the development of evidenced-based guidelines to standardize palliative and end-of-life care. Contact: Dr. Josephine Boyington, 919-316-4560, boyingtonje@mail.nih.gov **04-NR-103*** **Improving Quality of Life of Patients and Family Following a War-Related Traumatic Injury.** This initiative will develop and test personalized interventions to prevent complications in persons with war-related traumatic injuries during the post hospitalization transition period, with the ultimate goal of improving the health and quality of life of individuals and families following a war-related traumatic injury. Contact: Dr. Karen Huss, 301-496-9558, hussk@mail.nih.gov **04-OD-101*** **Develop and validate behavioral metrics to measure the impact of chronic pain.** Standardized and validated measures of behaviors commonly associated with spontaneous pain in human chronic pain conditions are needed. These metrics can provide a basis for understanding the role and potential therapeutic impact of behavior in initiating and modulating chronic pain. Contact: Dr. Linda Porter (NINDS), 301-496-9964, porterl@mail.nih.gov **04-TW-101*** **Examining the clinical and mechanistic link between diabetes mellitus and cardiovascular disease in low- and middle-income countries.** The rising epidemic of obesity, insulin resistance, and type 2 diabetes has placed societies at dramatically elevated risks for atherosclerotic disease. Epidemiologic studies involving global populations exposed to different environmental and genetic risk will improve understanding of the complex clinical and mechanistic links between diabetes and heart disease, and help create the next generation of control measures. Contact: Dr. Aron Primack, 301-496-1653, aron_primack@nih.gov; NHLBI Contact: Dr. Cristina Rabadan-Diehl, 301-435-0550, rabadanc@nhlbi.nih.gov

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(05) Comparative Effectiveness Research	**05-AA-101* Innovative Analyses of Existing Clinical Datasets.** Typically secondary analyses of administrative and clinical data have been utilized for multiple objectives that include estimating incidence and prevalence of alcohol use and alcohol disorders, estimating treatment needs, developing health policy, testing clinical hypotheses, and performing meta-analyses that may contribute insights on the comparative effectiveness of behavioral and pharmacological therapies. Under this Challenge Grant initiative, researchers are encouraged to use secondary data analyses in methodologically innovative ways. An example is the use of cross-design synthesis to standardize and compare clinical data collected by different methods, thereby expanding the scope of knowledge on comparative treatment effectiveness. Another example is evaluation of the impact of new statistical models and methods on treatment effectiveness outcomes, for instance, comparing the relative impact of linear models and dynamic models on clinical trial outcomes. Both clinical and health services research proposals based on secondary analyses are invited under this initiative. NIAAA Contact: Dr. Mark Willenbring, 301-443-1208, mwillenb@mail.nih.gov **05-AA-102* Adaptive Designs and Person-Centered Data Analysis for Alcohol Treatment Research.** Simple trials comparing two treatments, or a treatment and a control condition, are essential in determining the efficacy of various treatments. However, such studies often do not answer questions of particular import to clinicians, who have to make a series of decisions in the same patient based upon response to initial and subsequent treatment. Adaptive designs offer a potential solution, but they are methodologically complex, are difficult to implement and require large numbers of subjects. Similarly, statistical analyses using variable-centered approaches (e.g., comparison of means) may miss important variability in outcomes, especially since statistical assumptions (e.g. normality) are routinely violated. Person-centered approaches such as trajectory analysis may offer an alternative that better captures differences in outcomes and also is more clinically intuitive. Research and development are needed to further develop such approaches and especially to make them easier to use. Also, additional new approaches are needed in order to speed the process of comparing effectiveness of different treatments. NIAAA Contact: Dr. Mark Willenbring, 301-443-1208, mwillenb@mail.nih.gov **05-AA-103* Use of Innovative Technologies in Alcohol Treatment Research**. Although progress has been made to standardize methods for measuring alcohol consumption in research on treatment of heavy drinkers, the best methods currently available still rely on retrospective accounts. Recent research comparing these interview methods with interactive voice response (IVR) has demonstrated that the interviews have reasonable validity for overall consumption, but day-to-day variability does not adequately characterize true consumption. More research is needed on the best type of technologies to use (IVR, pagers, etc.) and how best to integrate it into clinical trials. A related challenge has been standardizing behavioral interventions through the use of extensive training, monitoring and supervision. However, substantial variability exists with regard to the outcome of individual therapists. In addition, these therapies are not feasible to implement in community settings. Research is needed to develop and validate computerized behavioral interventions that can be used in clinical trials, especially for pharmacotherapy trials, and that offer easy adoption in the community. NIAAA Contact: Dr. Mark Willenbring, 301-443-1208, mwillenb@mail.nih.gov **05-AG-101* Data Infrastructure for Post-Marketing Comparative Effectiveness Studies.** The challenge is to create the data infrastructure that will enable comparisons of particular therapies, prescribing patterns, and benefit designs on health outcomes. Problems with currently available studies include omission of key patient groups (such as

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	the elderly in nursing homes), lack of information on adherence and outcomes in polypharmacy, lack of information on outcomes across different insurance benefit designs, and lack of information on actual prescribing patterns and outcomes across regions and over time. Responsive projects could include: (1) Data linkages to allow studies of diffusion of therapies and comparisons of their effects on outcomes, health care utilization and expenditures across hospital referral regions, hospitals, and physician practices; (2) Linkage of Medicaid administrative data and Medicare Part D claims data for comparative research on prescribing patterns and patient outcomes in the nursing-home population; (3) Linkage of prescription drug data to data banks such as those maintained by the Alzheimer's Disease Neuroimaging Initiative to allow comparative research on outcomes in defined patient populations; (4) Supplements to longitudinal data sets and ongoing clinical trials to allow comparisons of the effects of alternative benefit designs on adherence, patient outcomes and health care expenditures; (5) Analyses of how context (geographic region, hospitals, insurance) affects comparative effectiveness studies of two or more interventions; (6) Data linking features of health and prescription drug insurance (public or private) to utilization of health services and health outcomes; and (7) Planning grants for comparative effectiveness research using and building the data infrastructure on these topics. NIA Contacts: Dr. John Haaga, 301-496-3131, haagaj@nia.nih.gov; and Dr. John Phillips, 301-496-3138, PhillipJ@nia.nih.gov **05-AG-102*** **Prevention and Risk Factor Reduction Strategies for Disabilities.** A variety of risk factors contribute to disabilities in activities of daily living and instrumental activities of daily living in older persons. Reduction in the number of individuals' risk factors has been shown to reduce risks of certain causes of disabilities, such as falls. However, effective risk-factor reduction strategies require a high degree of coordination of care across diverse health services and settings. Alternative strategies to achieve this coordination in risk-reduction interventions could be tested in two-year studies. In addition, planning grants could develop protocols for clinical trials to compare the effectiveness of different pharmacologic (e.g. analgesic) and lifestyle (e.g. physical activity) interventions to prevent a variety of disability outcomes, such as loss of walking ability and cognitive disability, for which current data do not provide a clear basis for comparison. Secondary analyses of existing clinical trial data and expanded data collection on ongoing trials could also address these issues. NIA Contacts: Dr. Sergei Romashkan, 301-435-3047, romashks@nia.nih.gov and Ms. Georgeanne Patmios, 301-496-3138, patmiosg@nia.nih.gov **05-AG-103*** **Imaging and Fluid Biomarkers for Early Diagnosis and Progression of Aging-related Diseases and Conditions including Neurodegenerative Diseases.** Diseases and conditions of aging have a huge public health burden, and the ability to diagnose these early and follow their course would greatly help in treating and managing them. Various imaging modalities and fluid biomarkers have been proposed as being useful for early diagnosis and following the course of diseases and conditions of aging including neurodegenerative diseases such as Alzheimer's disease. However, most studies have not compared multiple imaging and/or fluid biomarkers in the same study with the same study participants to evaluate their comparative effectiveness at being able to provide for the early diagnosis or for following the progression of disease. Two-year grants could be used to analyze data from available studies which include multiple imaging and fluid biomarker measures (e.g. MRI and PET imaging; blood, urine, or cerebrospinal measures of disease-associated molecules) or to plan or implement new studies which would incorporate multiple imaging and/or fluid biomarker modalities for early diagnosis and/or progression of conditions and diseases of aging including neurodegenerative

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	diseases. NIA Contact: Dr. Neil Buckholtz, 301-496-9350, buckholn@gw.nih.gov **05-AG-104* Planning Grants and Pilot Studies for Comparisons of Management Strategies for Older Patients with Multiple Coexisting Conditions.** The majority older individuals suffer from multiple coexisting conditions. This poses challenges for medical management in regard to factors such as adverse interactions of drugs used for different conditions, and conflicting recommendations from treatment guidelines for different individual conditions. Different treatment strategies to optimize health and quality-of-life outcomes need to be compared to identify strategies that provide the best risk-benefit ratios for such older patients. Two-year planning grants, and pilot feasibility testing for different management strategies could contribute to this goal. Although many clinical trials testing pharmacological, behavioral, or community-level interventions to remediate or prevent aging-related disorders or declines in function have established the efficacy of specific interventions, we know much less, however, about the comparative effectiveness of these approaches. Two-year planning grants to develop protocols for clinical trials directly testing the comparative effectiveness of these different intervention types would be appropriate, as would comparative effectiveness analyses of data from existing clinical trials data. Specific examples of target domains that could benefit from either further analysis or planning activities include the following: (1) The comparison of different types of interventions (e.g., different anti-inflammatories and behavioral interventions) for the prevention of Alzheimer's disease; (2) The comparison of efficacious treatments (e.g., physical exercise vs. cognitive training) for the remediation of age-related cognitive decline exclusive of dementia. NIA Contact: Dr. Sergei Romashkan, 301-435-3047, romashks@nia.nih.gov **05-AG-105* Comparative Intervention Trials for Diseases and Syndromes of Aging Including Neurodegenerative Diseases.** Although many clinical trials testing pharmacological, behavioral, or community-level interventions to remediate or prevent aging-related disorders or declines in function have established the efficacy of specific interventions, we know much less, however, about the comparative effectiveness of these approaches. Two-year planning grants to develop protocols for clinical trials directly testing the comparative effectiveness of these different intervention types would be appropriate, as would comparative effectiveness analyses of data from existing clinical trials data. Specific examples of target domains that could benefit from either further analysis or planning activities include the following: (1) The comparison of different types of interventions (e.g., different anti-inflammatories and behavioral interventions) for the prevention of Alzheimer's disease; (2) The comparison of efficacious treatments (e.g., physical exercise vs. cognitive training) for the remediation of age-related cognitive decline exclusive of dementia; and (3) Comparisons of interventions for "geriatric syndromes", such as urinary incontinence and involuntary weight loss. NIA Contacts: Dr. Laurie Ryan, 301-496-9350, ryanl@nia.nih.gov; Dr. Jon King, 301-402-4156, kingjo@nia.nih.gov; Dr. Molly Wagster, 301-496-9350, wagsterm@gw.nia.nih.gov; and Dr. Sergei Romashkan, 301-435-3047, romashks@nia.nih.gov **05-AI-101* Accelerated Aging in Treated vs. Untreated HIV/AIDS.** There is increasing evidence that suggests that HIV-1 infected individuals experience similar immunologic changes as the uninfected elderly. This may be due to the continuous highly productive viral replication which persistently stimulates immune cells. It is not clear whether antiretroviral therapy can reverse this process. This program will aim to compare the effectiveness of different treatment regimens in reversing or preventing accelerated aging as manifested in the immune and other body systems. Contact: Dr. Robin Huebner,

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	301-402-4239, rhuebner@mail.nih.gov **05-AI-102*** **Comparative-effectiveness of ART.** Challenge grants in this area would focus on collection of additional HIV/AIDS epidemiologic data and subsequent analysis of comparative-effectiveness of different regimens of ART in highly representative populations in the US. Contact: Dr. Carolyn Williams, 301-402-2305, cwilliams@niaid.nih.gov **05-AI-103*** **Clinical Research to Reduce the Risk of Antimicrobial Resistance.** Support research to preserve antimicrobial effectiveness by targeting infectious disease areas experiencing the greatest antimicrobial selective pressure, and within these areas, develop strategies that test the safety and effectiveness of different therapeutic approaches/regimens that reduce the probability of the emergence of drug resistance by minimizing unnecessary drug exposure. Contact: Dr. Dennis Dixon, 301-435-2858, dmdixon@niaid.nih.gov **05-AR-101*** **Comparative Effectiveness (CE) of Biologics in Autoimmune Rheumatic and Skin Diseases**. Create a research structure to study clinical and cost-effectiveness of biologics to determine the best therapy for individual patients. Disease- and treatment-specific methodologies could include: systematic review of existing research; analysis of effectiveness from large dateset, construction of medical registries for clinical and laboratory data related to efficacy, safety, and health care utilization rates data to evaluate cost-effectiveness; and computer-based modeling of clinical trials to predict the efficacy, safety and cost effectiveness. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **05-AR-102*** **Comparative Effectiveness (CE) of Treatments for Chronic Childhood Arthritis and Musculoskeletal (MSK) and Skin Disease.** Create a research structure to study clinical and cost-effectiveness of pediatric rheumatic and MSK disease treatments. A number of resources exist to support the rapid implementation of this project, including networks of physicians and researchers (The Childhood Arthritis and Rheumatology Research Alliance; Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers) that have already developed preliminary protocols to evaluate efficacy, effectiveness, and safety of pediatric therapies for specific disease. Examples of CE studies utilizing these approaches could include a registry of all children receiving biologic therapy for JIA, to evaluate comparative clinical and cost-effectiveness, and long-term safety; A randomized, controlled trial to evaluate the efficacy and cost effectiveness of laser surgery and other non surgical approaches in the treatment of infantile hemangiomas;.CE of agents that target interleukin 1 pathways in NOMID; CE of steroid therapies and steroid administration regimens in children with DMD. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **05-AR-103*** **Comparative Effectiveness of Therapies to Treat Fibromyalgia** Several drugs have been approved to treat fibromyalgia, a chronic musculoskeletal pain condition. Chronic pain, and its adverse impact on patient functioning and quality of life, will become even more of an economic and societal burden in the United States as the population ages. The purpose of this proposal is to compare recently approved drugs with differing mechanisms of action, i.e., serotonin and norepinephrine reuptake inhibitors, with tricyclic antidepressants1, and biopsychosocial approaches, such as cognitive behavioral therapy. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov

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	05-AT-101* Comparative Effectiveness Studies of Non-Pharmacological Treatments for Chronic Low Back Pain. Observational studies or secondary data analyses to compare the effectiveness of: non-pharmacological treatments or integrative health care approaches for chronic low back pain when used in addition to and/or as an alternative to standard conventional care. Contact: Dr. Partap Khalsa, 301-594-3462, khalsap@mail.nih.gov **05-AT-102* Comparative Effectiveness Studies of Complementary and Alternative Medicine.** Observational studies or secondary data analyses to compare the effectiveness or cost-effectiveness of: 1) CAM used in addition to standard conventional care; 2) CAM or integrative health care versus standard conventional care; OR 3) one CAM therapy to another. Contact: Dr. Richard Nahin, 301-496-7801, nahinr@mail.nih.gov **05-CA-101* Comparative Effectiveness Research in Cancer Primary Prevention.** A number of chemoprevention agents have been shown to be potentially effectiveness for the prevention of common cancers. But dissemination of chemoprevention remains low and controversy remains about the side effects associated with these agents. Comparative effectiveness research in this area would have the following aims: to document the level of dissemination of chemoprevention agents and the examine the physician, patient and health system factors that either facilitate or retard this dissemination; to conduct head to head studies of alternative chemoprevention agents and or approaches (e.g. risk stratification) to determine the relative clinical risk and benefits and economic cost of these alternatives. These studies could be conducted as adjuncts to existing controlled trials, as retrospective analysis of health system data or as prospective studies of cohorts of patients and physicians within the context of various healthcare delivery systems. Contact: Dr. Martin Brown, 301-496-5716, brownm@dcpcepn.nci.nih.gov **05-CA-102* Comparative Effectiveness Research on Cancer Screening.** The effectiveness of cancer screening has been established through randomized trials and other evidence for breast, colorectal and cervical cancer. However since screening for these cancers were initially introduced, there has been rapid and substantial innovation in new early detection technologies. Many of these technologies have disseminated into the practice of screening but without sufficient evidence as to their comparative effectiveness relative to earlier established technologies. In addition newer technologies may influence how the earlier technologies are most effectively used. Comparative effectiveness research in this area would augment evidence from controlled screening trials with: data from observational studies in defined populations of screening, intermediate and final outcomes; head-to-head studies of the technical performance characteristics, physician and patient acceptability and cost of alternative screening technologies, and decision models designed to project the costs and benefits of different screening technologies and strategies over the long-term at the individual, program and policy level. Contact: Dr. Martin Brown, 301-496-5716, brownm@dcpcepn.nci.nih.gov **05-CA-103* Cost-Effectiveness of Patient Navigation.** Patient navigation is currently being tested to determine if this approach has an impact on the timeliness of diagnostic testing and treatment. While the cost-effectiveness of patient navigation is being modeled by investigators in NCI's Patient Navigation Research Program (PNRP), studies comparing the costs associated with navigation as compared to usual care are still needed. The purpose of this pilot project would be to *implement* a cost effectiveness model that has been developed within PNRP to understand and quantify the costs associated with

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	implementing and maintaining a patient navigation program, and to determine if this model can be applied to varied patient navigation projects (i.e., screening, diagnosis, treatment). Results would help to determine whether patient navigation is providing both clinically sound and cost-effective service. This initiative would involve supplements to current Patient Navigation Research Programs (PNRP). Using data from the nine funded PNRPs, successful applicants will work collaboratively with the other PNRP PIs, CRCHD Project Scientists, and the PNRP evaluator to test the cost-effectiveness model. The results will form a basis for cost-effectiveness studies in future patient navigation research. Contacts: Dr. Martha L Hare, 301-594-1908, Martha.hare@nih.gov and Dr. Mary Ann Van Duyn, 301-451-4284, vanduynm@mail.nih.gov **05-CA-104*** **Comparative Effectiveness Research on Cancer Treatment.** The results of controlled clinical trials guide recommendations for many initial cancer treatments. But cancer treatments are also prevalent for cancers for which the evidence base in-complete, not applicable to the patient population (e.g. older patients) or non-existent. Prostate cancer is a prime, but not the only example, of this situation. Comparative effectiveness research in this area would use retrospective data and/or prospective interviews with patients, physicians and policy makers to assess the clinical benefits, risks and economic costs of commonly used treatment approaches and assess patient, physician and health system factors that effect dissemination of these treatment approaches. Contact: Dr. Martin Brown, 301-496-5716, brownm@dcpcepn.nci.nih.gov **05-CA-105*** **CISNET.** The Cancer Intervention and Surveillance Modeling Network (CISNET http://cisnet.cancer.gov/) is a consortium of NCI-sponsored investigators whose focus is to use modeling to extrapolate evidence from RCT's, epidemiologic, and observational studies to help determine the best strategies for implementing prevention, screening, and treatment strategies in the population and clinical practice. CISNET models could be applied to three areas: evaluation of competing early detection technologies, such as MRI vs digital mammography for breast cancer ; evaluation of competing diagnostic technologies, such as PET scans; evaluation of competing treatments, such as aggressive vs. conservative treatment for early stage prostate cancer. NCI Contact: Dr. Eric Feuer, 301-496-5029, feuerr@dcpcepn.nci.nih.gov **05-DA-101*** **Behavioral and Medication Interventions To Treat Drug Abuse Disorders in Non-Specialty Care Settings.** Treatment for substance use disorders has most commonly been provided in specialty care settings such as residential therapeutic communities, methadone maintenance treatment clinics, and dedicated inpatient or outpatient substance abuse treatment programs. One way to broaden access to substance abuse treatment would be to expand care in non-specialty care settings (i.e., primary care settings such as emergency departments, general medicine and public health clinics), and the criminal justice system. Research is needed on the comparative effectiveness of treatment interventions delivered in non-specialty care settings compared to those in traditional settings. Contact: Dr. Redonna Chandler, 301-443-8768, rc274k@nih.gov and Dr. Will Aklin, 301-4433207, aklinwm@nida.nih.gov **05-DA-102*** **Treatment of Substance Abuse and Related Health Consequences Using Web-Based Technologies.** Evidence-based behavioral therapies are not routinely integrated in substance abuse treatment programs because of financial constraints or inadequate provider training. Technology is increasingly being harnessed as a low-cost option for teaching behavioral skills to substance users, thereby broadening their availability. Research is needed to compare the effectiveness of already developed web-

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	based technologies (e.g., cognitive behavioral therapy; community reinforcement; HIV risk reduction) with traditional modes of treatment delivery (e.g., counselors, physicians, etc.) in order to optimize use of the web for expanding delivery of science-based behavioral treatment, with fidelity, and in a manner that reduces cost and staff burden. Contact: Dr. Cecilia Spitznas, 301-4021488, spitznasc@mail.nih.gov **05-DA-103* Integrated vs. Separate Treatment of Substance Abuse and Comorbid Conditions.** Comorbid psychiatric disorders as well as other serious medical conditions such as infectious diseases (e.g., HIV/AIDS) and chronic pain commonly co-occur with substance use disorders. Additionally, people addicted to one substance are frequently addicted to others. Comparative effectiveness research could fill a knowledge gap regarding the benefits of treating conditions in an integrated manner versus separately, pointing treatment providers and physicians toward the most effective intervention strategies for multiple disorders, identifying optimal methods of coordinating and delivering treatment while ensuring its quality and access, reducing costs, preventing further illness and disability, and improving community functioning and integration. Contact: Dr. Shoshana Kohana, 301-443-2261, kahanas@mail.nih.gov **05-DA-104* Comparing Drug Treatment Effectiveness in Ethnic Minority Populations.** Research suggests that treatment response can vary among different minority populations due to genetic, environmental and cultural factors. Still, it is unknown which treatments work best for which ethnicities. Comparative effectiveness studies in ethnic minorities would test pharmacotherapies and behavioral treatments for substance abuse that have already shown efficacy in some populations. Results could reveal optimal treatment types for various populations, many of which are currently under-studied or under-served in terms of treatment need, including African Americans, Native Americans, and Hispanics. Contacts: Dr. Mary Ellen Michel, 301-443-6697, michelm1@nida.nih.gov and Dr. Lula Beatty, 301-443-0441, Lb75x@nih.gov **05-DA-105* Comparing Episodic and Continuous Care for Drug Abuse Treatment**. Concerns have been raised over the mismatch between usual drug abuse treatment, which follows an acute care model, and emergent perspectives that addiction is a chronic illness. To treat drug abuse and addiction as a chronic illness implies that treatment providers should follow acute care with long-term monitoring and interventions to prevent a recurrence of drug use and to re-engage relapsed patients in treatment in order to minimize the consequences of the relapse. Research is needed on the comparative effectiveness of usual drug abuse treatment with drug treatment based on a model of continuing chronic illness care. Contacts: Dr. Shoshana Kohana, 301-443-2261, kahanas@mail.nih.gov and Dr. Bennett Fletcher, 301-443-2274, bf31v@nih.gov **05-DE-101* Validating dental caries risk assessment guidelines.** Traditionally, dental caries is prevented and managed with surgical restoration of damaged teeth and by recalling patients at regular six-month intervals. New strategies propose tailoring dental caries management to the individual's risk for dental disease. However, proposed caries risk assessment approaches have not been validated extensively. Projects that answer this challenge could include planning projects for large-scale definitive clinical trials or sophisticated analyses of existing datasets or records. NIDCR Contact: Dr. Ruth Nowjack-Raymer, 301-594-5394, nowjackr@nidcr.nih.gov **05-DE-102* Treatment of tobacco and drug dependence in dental settings.** Use of tobacco and other drugs is a major culprit in oral diseases. The dental office provides a

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	potentially important entry point for supporting drug-abusing patients in cessation efforts. However, busy dental practices may have difficulty finding the resources, staff, training time, and patient acceptance to incorporate comprehensive drug abuse treatment into clinical practice. Approaches that involve Screening for drug use, Brief Intervention, and Referral to Treatment (SBIRT) provide a promising, practical solution. Studies in other busy clinical settings have found that simple provider-delivered and computer-assisted SBIRT approaches increase identification of drug use, and importantly, increase cessation rates. Similar studies are needed in the dental setting comparing provider-delivered substance abuse SBIRT to computer-assisted SBIRT for tobacco use, or abuse of alcohol or other drugs. Projects that answer this challenge could include proposals to design and pilot a randomized clinical trial comparing different therapies in the dental setting. Applicants would need to submit a future NIDCR Clinical Trial Implementation grant for support of any proposed clinical trials, which could be considered for support through regular NIDCR appropriated funds. NIDCR Contact: Dr. Melissa Riddle, 301-451-3888, riddleme@nidcr.nih.gov **05-DE-103* Treatment and Outcomes Cleft Palate/Cleft Lip Anomalies.** Cleft lip and/or palate are among the most common of all birth defects, occurring once in every 600 to 800 births. The care of affected infants is complex and requires coordination with surgeons, orthodontists, dentists, surgical support staff, speech therapists, audiologists, and other specialists. Surveys of care centers in the United States and Europe demonstrate that there are enormous variations in timing and type of reconstruction procedures. Practices associated with best outcomes need to be identified. Projects that answer this challenge could address: (1) Presurgical appliances, whether to use and what type (NAM or Latham); (2) Surgical timing, at what age to repair unilateral and bilateral cleft lip and with what technique; (3) Use of lip adhesion and indication for its use; (4) Cleft palate repair technique and timing of repair. Investigators could compare existing approaches to repair of cleft lip and cleft palate, evaluating efficacy, cost effectiveness, speech outcomes and quality of life measures. Approaches could include: 1) establishment of observational patient registries to follow outcomes and identify best practices; or 2) planning grants for a definitive RCT or practical trial to address a significant issue. Applicants would need to submit a future NIDCR Clinical Trial Implementation grant for support of any proposed clinical trials, which could be considered for support through regular NIDCR appropriated funds. Contact: Dr. Holli Hamilton, 301-451-3852, hamiltonho@nidcr.nih.gov **05-DE-104* Adjunctive techniques for detection of oral premalignant and malignant lesions.** Approximately 35,000 Americans are diagnosed each year with oral cancer, and early detection, usually during a regular dental check-up, is critical to successful treatment of this disease. Adjunctive techniques have been developed to enhance visual detection of oral premalignant and malignant lesions. Overall, there is insufficient evidence to support their effectiveness. Projects that answer this challenge could include planning for randomized clinical trials that compare visual and tactile oral mucosal examination with adjunct-assisted examination in dental settings. Projects responsive to this challenge could estimate the effectiveness of existing adjunctive techniques for detection of oral premalignant and malignant lesions from available datasets or records, including cost effectiveness analyses. Applicants would need to submit a future NIDCR Clinical Trial Implementation grant for support of any proposed clinical trials, which could be considered for support through regular NIDCR appropriated funds. Contact: Dr. Jane Atkinson, 301-435-7908, jatkinso@nidcr.nih.gov

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	05-DE-105* Infrastructure for Comparative Effectiveness Studies in Oral Health and Craniofacial Conditions. There is a limited evidence base to support common interventions in dental care and management options in craniofacial disorders. Having adequate infrastructure for evaluating effectiveness in oral health and craniofacial conditions, as distinguished from effectiveness in medical care, is critical because much of oral health care is delivered outside of medical care (e.g., dental offices) or fragmented to address the complex needs of individuals with certain conditions affecting oral/craniofacial structures (e.g., birth defects such as cleft lip and palate, ectodermal dysplasias, or conditions resulting in hypodontia). Projects that answer this challenge could support planning grants to develop infrastructure as well as feasibility studies to assess existing infrastructure. Support for planning grants to develop infrastructure will be provided, as well as support for feasibility studies to assess existing infrastructure. Successful two-year projects may lead to applications to: implement and assess infrastructure (e.g. development of datasets or registries); enhance and re-assess existing infrastructure; or conduct comparativeness effectiveness studies. Contact: Dr. Emily Harris, 301-594-4846, harrisel@nidcr.nih.gov. **05-DK-101* Selecting the Optimal Initial Treatment Regimen for Patients With Newly Discovered Type 2 Diabetes.** The natural history of type 2 diabetes, treated by widely used current regimens, is marked by gradual increases in glucose levels, loss of insulin secretion, progressive increases in drug therapy, and frequent development of chronic complications. Clinical trial data suggests that aggressive early therapy attempting to keep glucose levels near normal is associated with a more benign long-term course. The optimal treatment regimen (effectiveness and avoidance of hypoglycemia) is not known, but current drugs provide options for multiple treatment approaches. In view of the numerous options, pilot studies are needed to assess the short-term effectiveness of common treatment strategies. Studies of treatments comparing different drugs and levels of glucose control or studies to use insulin sparing versus Insulin-intensive regimens will help to define the most effective short-term therapy. Impact of the approaches at one and two years can be assessed. These studies can measure effects on glucose control, hormone responses, adverse events, and cost of therapies, providing crucial data for designing future clinical trials to assess the long-term clinical effectiveness and cost of the most promising therapeutic approaches. Contact: Dr. Peter Savage, 301-594-8858, savagep@niddk.nih.gov **05-DK-102* Understanding the Effects of Bariatric Surgery on Type 2 Diabetes and Cardiovascular Risk Factors.** Interest has been building in the scientific and medical communities regarding the risks and benefits of the different types of bariatric surgery in obese patients, with type 2 diabetes, particularly in those with lesser degrees of obesity. A randomized clinical trial to compare the impact of various types of bariatric surgery versus intensive medical weight loss treatment on type 2 diabetes is needed to understand the balance of risks and benefits of the different approaches. This is critically necessary given the increasing numbers of bariatric surgeries being performed and the lack of well-controlled studies to inform clinicians in selecting the best approach for a given patient and health care payors in their decision to cover specific procedures. Investigators could compare the impact of bariatric surgery compared with intensive medical weight loss treatment on insulin resistance, beta cell function, and resolution of type 2 diabetes in adults with type 2 diabetes and BMI between 30 and 40. Pilot and feasibility projects to explore different study designs and test feasibility of methods and implementation could be conducted using short term funding (~2 years). Evidence of feasibility in pilot studies would be expected to lead to a larger multi-site trial to determine long-term (3-5 year)

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	impact of bariatric surgery on type 2 diabetes. Contact: Dr. Myrlene Staten, 301-402-78896, statenm@mail.nih.gov **05-DK-103* Antihypertensive Drugs and Level of Blood Pressure Control in Hemodialysis Patients.** End-stage renal disease requiring dialysis is a burdensome, expensive medical and public health problem. Hypertension, present in nearly all dialysis patients, is a prime risk factor for cardiovascular disease (CVD) death and complications. Commonly used anti-hypertensive drugs including renin-angiotensin-aldosterone system (RAAS) inhibitors and non-RAAS agents (i.e., beta-blockers) improve survival in other populations, but it is not known whether a specific class of drug or level of blood pressure control can significantly reduce CVD morbidity and mortality in vulnerable hemodialysis patients. Projects that address these challenges could include planning or feasibility studies for a randomized trial of a representative subset of hemodialysis patients to better inform choices of anti-hypertensive therapy (RAAS vs. non-RAAS) and blood pressure targets. Short-term funding could be used for 1) meta-analysis of existing datasets or registries (for example, the United States Renal Data System), 2) planning grants for a randomized controlled trial, or 3) pilot studies of recruitment feasibility or implementation strategies. The NIDDK could fund a more definitive randomized clinical trial in subsequent years from its base. Contact: Dr. Catherine Meyers, 301-451-4901, meyersc@amil.nih.gov **05-DK-104* Fascial Versus Mid-Urethral Sling Surgery in Stress Urinary Incontinence Treatment Failures**. Urinary incontinence affects 17-50% of all U.S. women, is increasing as the population ages, and is associated with diminished quality of life. Approximately 30% of women with urinary incontinence treated surgically undergo repeat procedures for recurrent stress urinary incontinence (SUI). Fascial sling surgery and mid-urethral sling surgery are used commonly in women with recurrent SUI who failed initial surgical treatment; however, it is not clear which strategy is better for improving continence, quality of life, and for reducing costs of health care. Short-term funds could be used for 1) planning grants for a RCT, or 2) pilot feasibility studies of recruitment or other implementation strategies. The NIDDK could fund a full randomized clinical trial in subsequent years from its base. Contact: Dr. Debuene Chang, 301-594-7717, changtd@mail.nih.gov **05-DK-105* Medical Treatment of Calcium Stones: Calcium Stone Trial** Urolithiasis affects approximately 10 to 15 percent of the United States population, with a cost of at least $2.1 billion per year. The lifetime recurrence rate is 50 percent. After initial treatment, patients are commonly treated with potassium citrate or thiazide diuretics. However, the relative efficacy and durability of these two strategies has not been determined. Projects that address these challenges include planning or feasibility studies of a randomized trial of a representative sample of recurrent stone formers stratified by initial therapy, then randomized to receive potassium citrate or a thiazide diuretic to measure treatment durability, stone formation and passage, quality-of-life, and cost. Short-term funds could be used for 1) meta-analysis of existing datasets or registries (for example, *Urologic Diseases in America*), 2) planning grants for a randomized clinical trial, or 3) pilot studies of recruitment feasibility or implementation strategies. The NIDDK could fund a full randomized clinical trial in subsequent years from its base. Contact: Dr. Debuene Chang, 301-594-7717, changtd@mail.nih.gov and Dr. Paul Kimmel, 301-594-7713, kimmelp@mail.nih.gov

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	05-EB-101* **Comparative Effectiveness of Advanced Imaging Procedures** – Medical imaging is the fastest growing component of medical spending in the United States. This is due to increases in both the cost and utilization of advanced imaging procedures. The NIH invites applications that explore the comparative effectiveness of advanced imaging procedures in providing optimal clinical treatment. Evaluation of hybrid imaging such as combined PET-CT is particularly encouraged. Contact: Dr. Alan McLaughlin, 301-496-9321, mclaugal@mail.nih.gov **05-EB-102*** **Screening Methodologies for Breast Cancer** – Phase II trials suggest that dedicated breast CT approaches can detect earlier stage cancer (i.e., smaller lesions) than mammography. Comparative effectiveness studies are invited to determine if the information obtained from earlier detection can be used to better treat breast cancer, and improve clinical outcome in terms of survival and quality of life. Contact: Dr. Alan McLaughlin, 301-496-9321, mclaugal@mail.nih.gov **05-EB-103*** **Comparative Effectiveness of Non-Invasive Ultrasound Techniques** – Non-invasive High Intensity Focused Ultrasound (HIFU) techniques have the potential to destroy tumors without the need for invasive surgery. Comparison of non-invasive HIFU approaches with invasive or minimally-invasive surgical procedures are encouraged. Comparison of technologies for assessing the level and extent of non-invasive tissue ablation are also encouraged. Contact: Dr. Victor Lopez, 301 451-4775; lopezh@mail.nih.gov. **05-EB-104*** **Comparative Effectiveness of Robotic Surgery -** Compared to standard invasive surgical procedures, minimally-invasive robotic surgical procedures have the potential to provide a safer and more precise treatment for a variety of conditions including prostate cancer. Comparison of robotic procedures with standard invasive treatments should demonstrate the comparative effectiveness and comparative cost of robotic interventions for the clinical treatment of disease**.** Contact: Dr. John Haller, 301 451-3009; hallerj@mail.nih.gov **05-EB-105*** **Comparative Effectiveness of Medical Implants**. The utilization of medical implants such as artificial hips varies significantly between different locations and between different countries. Proposals are invited that would make use of this utilization variability to assess the comparative effectiveness of medical implants. Contact: Dr. Christine Kelley, 301-451-4778, Kelleyc@mail.noh.gov **05-EY-101*** **Treatment of Age Related Macular Degeneration and Diabetic Eye Diseases and Disorders.** Age Related Macular Degeneration and Diabetic Eye Disease are leading causes of blindness among American adults. Commonly used treatment strategies include various combinations of drug and/or laser treatments but it is not clear how these agents or their combinations compare with each other for preventing visual loss, improving quality of life, and reducing health care costs. Projects that answer this challenge include studies that will compare agents to prevent the development and progression of age related macular degeneration or diabetic eye diseases and conditions. Contact: Dr. Don Everett, 301-451-2020, deverett@nei.nih.gov **05-EY-102*** **Treatment of Pediatric Eye Diseases and Disorders.** There are a variety of eye diseases and disorders that lead to visual impairments and blindness among children. Eye Care Professionals can treat these disorders with certain medications, surgery, or optical instruments or devices. However, it is unclear how the strategies compare with each other for improving and maintaining vision, quality of life, and reducing

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	health care costs. Projects that answer this challenge could include the planning and conducting of trials or analyses of existing data. Contact: Dr. Don Everett, 301-451-2020, deverett@nei.nih.gov **05-EY-103*** **Eye and Vision Systematic Reviews**. There are a variety of eye diseases and disorders that lead to visual impairments and blindness. Eye Care Professionals are treating these disorders with certain medications, surgery, or optical instruments or devices. However, in many instances it is unclear how the strategies compare with each other for improving and maintaining vision, quality of life, and reducing health care costs. Projects that answer this challenge would help health care providers and patients make well-informed decisions about healthcare. Contact: Dr. Don Everett, 301-451-2020, deverett@nei.nih.gov **05-GM-101*** **Anesthesiology Clinical Pharmacology Sepsis Trauma, Burn, and Peri-operative Injury Wound Healing.** NIGMS supports clinical research in the areas of anesthesiology, clinical pharmacology, sepsis, injury (trauma, burn and peri-operative) and wound healing. Within these general clinical areas are opportunities for rigorous comparative evaluation of the impact of different treatment options or standards of care in a variety of clinical conditions, settings and/or situations. Possible opportunities include but are not limited to comparisons of drugs, devices, and/or protocols Sophisticated analyses of existing data sets/registries, planning projects for subsequent larger scale clinical studies, or other activities that would provide comparative evaluations in these areas are appropriate. Applications that address the following topics are encouraged: o genetic basis of variable drug responses, both therapeutic and adverse o resuscitation strategies o therapies that influence stabilization and recovery following trauma and burn injury o post-injury nutrition management o studies of the methods, roles and predictive value of monitoring in critically ill patients o effective drug treatments for multi-organ failure o use of sedatives, analgesics and anesthetics in critically ill patients o responses related to gender or population-based differences o therapies that accelerate wound healing, that induce healing in a nonhealing wound or that reduce/eliminate scarring NIGMS Contact: Dr. Michael Rogers, 301-594-3827, rogersm@nigms.nih.gov **05-HL-101*** **Treatment of atrial fibrillation.** Atrial fibrillation, the most common acquired arrhythmia in adults, substantially increases risk for stroke and premature death. Percutaneous pulmonary vein ablation and the surgical Cox Maze procedure have been shown to be effective in eliminating arrhythmias, but it is not clear how they compare to standard therapies, such as anticoagulation combined with rate control drugs, with respect to their effect on quality and length of life and health care costs. Projects that address this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries. Contact: Dr. Michael Lauer, 301-435-0422, lauerm@nhlbi.nih.gov **05-HL-102*** **Treatment of obstructive sleep apnea.** Obstructive sleep apnea is becoming increasingly common as the nation experiences an obesity epidemic. Patients with obstructive sleep apnea are at increased risk for poor quality of life, myocardial infarction, and stroke. Physicians can treat obstructive sleep apnea with certain medications, surgery, or mechanical devices (continuous positive airway pressure), but it is not clear how the strategies compare with one another with respect to their effect on

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	quality and length of life and health care costs. Projects that answer this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries. Contact: Dr. Michael Twery, 301-435-0199, twerym@nhlbi.nih.gov **05-HL-103*** **Treatment of mild persistent asthma in children**. Physicians currently choose among three alternative approaches to initiate daily, long term therapy for children with asthma that is not well controlled by intermittent therapy alone; namely, low dose inhaled corticosteroids, combination therapy of inhaled corticosteroids and long acting beta-agonists, and leukotriene receptor antagonist. Yet little data are available to inform the physician's decisions: randomized controlled efficacy trials in children have focused on comparing each drug to placebo rather than directly comparing the three options in children, especially children less than 12 years of age. Large scale, efficient studies are urgently needed to assist physicians in understanding the comparative advantages of the treatments with respect to benefits, risks, and costs. Projects that address this challenge would use existing data bases, e.g., administrative and electronic health records, and distributive data networks to conduct direct comparisons of the three treatments. Contact: Dr. Virginia Taggart, 301-435-0202, taggartv@nhlbi.nih.gov **05-HL-104*** **Reducing cardiovascular risk in moderate-risk and asymptomatic patients**. Evidence-based treatment guidelines exist for patients at high risk for a cardiovascular event due to existing clinical disease or risk factors including hypertension, dyslipidemia, obesity, and smoking. Nearly half of all life-threatening cardiovascular disease events occur in previously asymptomatic people, who may have undetected subclinical disease. In addition, many people are at elevated risk for whom evidence-based treatments are not clear; these include people with moderate elevations of multiple risk conditions as in the Metabolic Syndrome. Various technologies exist to detect asymptomatic subclinical disease and predict risk, including global risk scores, inflammatory biomarkers, specific genotypes, and imaging tests. Many intervention strategies to reduce risk also exist, including lifestyle interventions, various medications, combinations of medications, and combinations of lifestyle and medication. However, it is not clear how the existing technologies compare with each other or could be combined or sequenced, or what intensity of intervention is needed, to reduce disease risk. Projects are needed to address this challenge by comparing effectiveness, risks, and cost-effectiveness of various strategies for screening and treatment of moderate-risk and asymptomatic patients. Projects that address this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries Contact: Dr. Simons-Morton, 301-435-0384, simonsd@nhlbi.nih.gov **05-HL-105*** **Optimizing of anti-platelet treatment after revascularization procedures**. The long-term effectiveness of revascularization procedures to treat ischemic cardiovascular disease is limited by the risk for thrombotic complications, which may necessitate a second costly procedure, sometimes under emergency conditions, and may even be fatal. Anti-platelet therapy i to offer effective protection against thrombotic complications, though at the cost of increased risk for serious bleeding events, including (potentially fatal) cerebral hemorrhage. Comparative effectiveness trials are needed to determine the best regimens for achieving maximal benefit with minimal risk. Personalized approaches for tailoring the optimal regimen to the particular patient may be of value. Projects that answer this challenge could include planning grants for clinical trials comparing alternative strategies for optimizing anti-platelet therapy in this setting. Contact:

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	Dr. David Gordon, 301-435-0466, gordond@nhlbi.nih.gov **05-LM-101* Effect of "Information Prescriptions" on Improving Care by Increasing Compliance with Medication Protocol Given to Discharged Emergency Department Patients.** A significant fraction of patients who are given a set of prescriptions, such as when they leave a physician office or the Emergency Department, are known to disregard or curtail recommended medications. Individually tailored information about risks, benefits, costs and treatment options are given by some clinicians as "information prescriptions", but the effectiveness of "information prescriptions" is not known. Studies in this area should determine value of such "information prescriptions" in improving patient compliance as contrasted to current discharge advice systems or standard office practices. Contact: Dr. Valerie Florance, 301-594-4882, florancev@mail.nih.gov **05-LM-102* Ability of Decision Tools in an Electronic Health Care System to Increase Use of Generic Drugs**. Although generic drugs are much less expensive than "brand name", clinicians commonly prescribe "brand name" drugs for a plethora of reasons often not related to belief that "brand name" drugs are more effective. Evaluation studies are needed to determine whether a Decision Support Tool that feeds information about generic options, presented to physicians prescribing "brand-name" drugs through a Computerized Physician Order Entry System (CPOE), would increase physician selection of less-expensive generic drugs. Studies should compare the use of such pre-decision feedback to situations where no feedback about generic options is provided. Contact: Dr. Hua-Chuan Sim, 301-594-4882, simh@mail.nih.gov **05-LM-103* Improving Compliance of School Children with Immunization Schedules**. An increasing problem in inner city and some rural school systems is failure of pre-school children to complete immunization schedules for common illnesses as required by the school system. Some of the problem is caused by the discontinuity of record-keeping systems, and the absence of reminder systems in physician offices and clinics where students receive immunizations. Evaluation studies should compare completion of immunization schedules where clinics and physicians use tools specifically designed to record, share and manage progress of immunization for each child with completion rates of children where such tools are not used. Contact: Dr. Hua-Chuan Sim, 301-594-4882, simh@mail.nih.gov **05-LM-104* Value of "Virtual Reality" Interaction in Improving Compliance with Diabetic Regimen.** Despite often intensive educational efforts, patients with diabetes commonly mismanage or undermanage their illness despite the known ability of optimal management to reduce complications and morbidity. Interactions between avatars in virtual reality environments such as Second Life are known to influence behavior. Studies should explore the effectiveness of periodic physician/nurse interaction with diabetic patients via a virtual reality environment in improving diabetic control, as compared to standard practice. Contact: Dr. Milton Corn, 301-496-4621, cornm@mail.nih.gov **05-MD-101* Social Determinants of Health**. There is a growing research that reveals the important role of social determinants of health in addressing and understanding health disparities. Social determinants of health are the economic and social conditions under which people live which determine their health. We propose research that investigates

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	interventions that address these social determinants (e.g., employment training, school readiness programs, food stamp programs, and adequate and affordable housing programs) their relationship to health outcomes for health disparity populations. Contact: Dr. Kyu Rhee, 301-402-1366, rheekb@mail.nih.gov **05-MD-102*** **Prevention of Chronic Diseases in Disparity Populations.** Approximately 70-80% of all current health care costs are connected with the treatment of chronic diseases. Chronic diseases compose a large majority of health disparity conditions, such as asthma, obesity, oral health, diabetes, HIV/AIDS, heart disease, mental health, chronic pain, and substance abuse. We propose research to examine and inform the clinical and cost effectiveness of prevention efforts, including medical devices, behavioral interventions, care management approaches (e.g., incorporation of nontraditional members of the healthcare team such as community health workers, pharmacists), pharmaceuticals, surgery, and other interventions for the prevention of chronic disease. Contact: Dr. Kyu Rhee, 301-402-1366, rheekb@mail.nih.gov **05-MD-103*** **Limited English Proficiency (LEP)**. Limited English Proficiency populations continue to grow and are a significant health disparity population. We propose conducting comparative effectiveness research studies on current health services delivery for LEP populations (medical interpreter, telephone language line, bilingual professional, translated educational aides) and the cost impacts of effective, cultural competent healthcare interventions for LEP populations (e.g. reductions in ER visits, diagnostic tests, hospital stay, disability and improved functional health status). Contact: Dr. Irene Dankwa-Mullan, 301-402-1366, dankwamullani@mail.nih.gov **05-MD-104*** **Screening of Health Disparity Conditions.** Comparing different screening approaches for diseases with increased prevalence in disparity groups with the goal to inform and determine the most effective modality that will result in reduced morbidity and mortality and improved survival rates in different disparity groups. Contact: Dr. Irene Dankwa-Mullan, 301-402-1366, dankwamullani@mail.nih.gov **05-MD-105*** **Health Literacy.** Research has shown that over 90 million individuals in the United States are unable to read a prescription bottle. Health literacy is the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions. We propose research that investigates interventions that address health literacy issues (e.g., technology tools, literacy aides or other community health workers, language-appropriate labels for prescription and over-the-counter medications) and their relationship to health outcomes for health disparity populations. Contact: Dr. Irene Dankwa-Mullan, 301-402-1366, dankwamullani@mail.nih.gov **05-MH-101*** **Leveraging Existing Healthcare Networks for Comparative Effectiveness Research on Mental Disorders and Autism.** Existing large integrated healthcare networks are needed to more efficiently conduct large-scale effectiveness trials in “real-world” patient settings. The NIMH solicits individual or collaborative, linked grant applications from researchers with experience conducting studies within large integrated healthcare delivery systems to develop and test infrastructure to efficiently conduct trials on the effectiveness of treatment, preventive and services interventions to improve care for people with mental disorders and autism. Applicants can propose studies to 1)

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	demonstrate the ability to identify, recruit and enroll large patient populations into clinical trials, 2) harmonize electronic medical record data across multiple integrated systems for research use, 3) pool data for common analyses, and 4) build capacity for the collection and storage of biologic material. Contact: Dr, David Chambers, 301-443-3747, dchamber@mail.nih.gov **05-MH-102* Cost Effectiveness of Mental Health Interventions.** Information on the cost effectiveness of promising mental health interventions is needed to ensure widespread uptake by payers and health systems. NIMH is interested in adding/extending cost-effectiveness components to randomized controlled trials of treatment, preventive and services interventions through two-year grants. Investigators should prioritize the calculation of the cost/QALY ratio by the most advanced available methodologies to ensure that findings from these projects can contribute to improving the efficiency of mental health care financing. In addition, researchers can conduct analyses of existing databases for systematic cost-effectiveness, cost-benefit, benefit/harm analyses or to compare interventions on "real life outcomes" such as level of functioning or acceptability, using meta-analytic methods. Contact: Dr. Agnes Rupp, 301-443-3364, arupp@mail.nih.gov **05-MH-103* Collaboration with AHRQ Comparative Effectiveness Research Program.** In FY09 and FY10 AHRQ plans to support research grants (PA-09-070) on comparative effectiveness of clinical treatments and services as authorized in the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) Section 1013. MMA section 1013 mandates two mental health categories: Depression and other mental health disorders; and Developmental delays, attention deficit hyperactivity disorder and autism. NIMH is interested in funding ancillary studies including but not limited to: 1) studies on the comparative effectiveness of important new or existing technologies; and 2) assessment of the comparative effectiveness of treatments that are commonly administered to children but have been evaluated for safety and effectiveness in adult populations. Two year studies will contribute to successfully implement the mental disorders components of MMA Section 1013 by utilizing AHRQ networks (e.g. EPCs, DEcIDE, CERTs, PBRN, ACTION, etc) to generate information for health care decision-making. Contact: Dr. Agnes Rupp, 301-443-3364, arupp@mail.nih.gov **05-MH-104* Building ASD Registries for Use in Comparative Effectiveness Research.** Given the low base-rate and high variability of phenotypes among people with autism, comparative effectiveness trials of treatments for autism spectrum disorders (ASD) provide significant recruitment challenges to include well-phenotyped samples. Autism registries are needed to more efficiently conduct large-scale effectiveness trials in "real-world" service systems. The NIMH solicits grant applications from researchers with experience in diagnosis of ASD and database registry creation to develop and test infrastructure to efficiently identify populations to include within registries for use in future ASD comparative effectiveness trials. Grants applications to optimize current registries and leverage existing databases are encouraged. Applicants can propose studies to 1) demonstrate the ability to identify and collect relevant clinical, environmental, and genetic data from large populations with autism within multiple service settings, 2) Improve consensus on "caseness" within samples, given variability in phenotypes 3) harmonize data systems across multiple integrated systems serving populations with autism (e.g. health care, special education, Medicaid) for research use, 4) pool data for common analyses, and 5) build capacity for the collection and storage of biologic material. Contact:

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	Dr. Lisa Gilotty, 301-443-3825, gilottyl@mail.nih.gov **05-NS-101* Consortia Building for Comparative Effectiveness Research in Clinical Neuroscience.** The development of evidence-based medicine to inform health decisions in neurology, neurosurgery and neurorehabilitation requires analysis of high quality, risk-stratified, data collection from "real world" practice. The challenge is to develop multi-center consortia that effectively utilize modern electronic data collection systems to standardize, collect and analyze high quality data in order to compare the effectiveness of alternative methods of prevention, diagnosis, or treatment in groups of patients with specific types/subtypes of neurological disorders. NINDS Contact: Dr. Walter J. Koroshetz, 301-496-3167, koroshetzw@ninds.nih.gov **05-NS-102* Technologies to Enable Comparative Effectiveness Research in Clinical Neuroscience** High per patient costs limit the number of patients studied in RCTs as well as the rate at which important questions can be tested by RCTs. High per patient costs make it prohibitively expensive to study the comparative effectiveness of a treatment, prevention or diagnostic regimen as it transitions from clinical trial to the larger venue of clinical practice. The challenge is to develop new technologies that can obtain clinically significant outcomes in larger numbers of patients at lower cost. The performance characteristics of such technologies in providing high quality outcome measures could be tested by comparing to standard outcome measures in the context of an ongoing RCT. NINDS Contact: Dr. Walter J. Koroshetz, 301-496-3167, koroshetzw@ninds.nih.gov **05-NS-103* Validating NIH's New Clinical Tools in Populations With Neurological Disorders** The NIH Blueprint for neuroscience is developing a variety of standardized tests in the domains of cognition, emotion, sensation, and motor function as part of the NIH Toolbox project. The NINDS is supporting the development of quality of life outcomes in neurological disorders. The NIH Roadmap project has developed the patient reported outcomes measurement information system (PROMIS). Each of these tools utilizes computerized adaptive testing methods to obtain important clinical outcome data and will be tested in large groups of normal individuals across the lifespan. The challenge is to assess the performance and research utility of these new tools in well described patient populations for future comparative effectiveness research projects. NINDS Contact: Dr. Claudia Moy, 301-496-2789, moyc@ninds.nih.gov **05-NS-104* Intervention vs. Best Medical Therapy in Asymptomatic Persons With Identified Vascular Abnormalities**. A variety of vascular/cardiac abnormalities cause stroke but are treated by a surgical or endovascular intervention that itself carries risk of stroke and death, i.e. carotid stenosis, vertebral origin stenosis, berry aneurysm, arteriovenous malformation, cerebral artery dissection, patent foramen ovale, etc. In many of these conditions the risk of stroke due to the vascular abnormality is significantly lower in asymptomatic patients as compared to those who present with symptoms. Without a means to accurately stratify risk, such asymptomatic patients are faced with very difficult health decisions. The challenge to be completed over a two year period could include one or all of the following: 1) meta-analysis of existing datasets or registries (for example, Medicare, HMO, or Insurance company data to develop an evidence base for clinical-decision making. 2) pilot grants for an RCT, and 3) validation of selection criteria to stratify stroke risk in asymptomatic patients with defined anatomic abnormalities. NINDS Contact: Dr. Walter J. Koroshetz, 301-496-3167, koroshetzw@ninds.nih.gov

Broad Challenge Area	Specific Challenge Topic
	05-RR-101* **Build CER Capacity Through Education**. Build capacity for subject recruitment, IRB and regulatory compliance, and data management for comparative effectiveness research conducted in community environments. Applicants could propose educational experiences and resources for study coordinators, medical auxiliaries, and data managers that would build capacity for the conduct of comparative effectiveness research in community settings. Where appropriate, these applications could develop links with existing clinical research infrastructure resources. Contact: Dr. Anthony Hayward, 301-435-0791, haywarda@mail.nih.gov **05-RR-102*** **Support Pilot CER Projects in Community Settings**. Pilot/demonstration projects using collaborations between academic health centers and community-based organizations or community-based research networks that bring CER into community settings. Contact: Dr. Anthony Hayward, 301-435-0791, haywarda@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
(06) Enabling Technologies	**06-AG-101* Neuroscience Blueprint: Development of non-invasive imaging approaches or technologies that directly assess neural activity.** This could include research on imaging neuronal electrical currents, neurotransmitter changes and/or neuronal/glial cell responses to brain circuit activation. This scientific area could be advanced by improvements/refinements in existing imaging technology or use of emerging technology that could be developed in two years. The outcome of this challenge could have high impact by connecting the system-level, large population view afforded by fMRI with the cellular processes and responses that contribute to the BOLD-fMRI signal. Two-year challenge projects could stimulate the development of human brain imaging techniques that link cell activity underlying neural communication to the structure and function of brain circuits, and could complement other brain connectivity imaging modalities. Contact: Dr. Bradley Wise, 301-496-9350, wiseb@nia.nih.gov; NIAAA Contact: Dr. Antonio Noronha, 301-443-7722, anoronha@mail.nih.gov; NIBIB Contact: Dr. Yantian Zhang, 301-402-1373, yzhang@mail.nih.gov; NIMH Contact: Dr. Michael F. Huerta, 301-443-1815, Mhuert1@mail.nih.gov; NINDS Contact: Dr. Randy Stewart, 301-496-1917, rs416y@nih.gov **06-AT-101* Imaging correlates of brain states.** Exploration of brain imaging technologies to provide insight into higher-order states such as awareness of self, focused attention, stress, meditative states, calm and other emotional states; utilize brain imaging to develop objective measures and rigorous, quantitative evaluation of subjective states. Contact: Dr. Partap Khalsa, 301-594-3462, khalsap@mail.nih.gov; NIDA Contact: Dr. Steven Grant, 301-443-4877, sgrant@nida.nih.gov **06-DC-101* Develop Improved Hearing Devices.** Approximately 36 million American adults report some degree of hearing loss and would benefit from hearing aid use. However, only approximately 20% of potential hearing aid candidates actually use these devices, owing to concerns about stigma, cosmesis, sound quality, and affordability. The Challenge is to develop improved hearing aids, both worn and implantable, for individuals with hearing loss. Contacts: Dr. Dan Sklare, 301-496-1804, sklared@nidcd.nih.gov); Dr. Gordon Hughes, 301-496-5061, hughesg@nidcd.nih.gov). **06-DC-102* Develop and Validate Methods for Delivery of Drugs and Molecules to the Inner Ear.** In order to capitalize on the new knowledge of the molecular basis for hearing impairment, better methods to deliver drugs and molecules to the inner ear need to be developed and validated. The Challenge is to identify methods of delivery that are robust, long lasting, and minimally toxic to the sensitive structures in the inner ear. Contacts: Dr. Nancy Freeman, 301-402-3458, freemann@nidcd.nih.gov; Dr. Amy Donahue, 301-402-3458, donahuea@nidcd.nih.gov. **06-DC-103* Understanding the Neural Mechanisms Responsible for Tinnitus.** Millions of Americans suffer from chronic tinnitus, or the percept of ringing in one or both ears. The numerous mechanisms that underlie tinnitus are very poorly understood, and as a consequence, the known intervention strategies are ineffective for most affected individuals. The Challenge is to understand the specific neural mechanisms giving rise to tinnitus and to develop novel intervention strategies. Contact: Dr. Roger Miller, 301-402-3458, millerr@nidcd.nih.gov.

Broad Challenge Area	Specific Challenge Topic
	06-DK-101* **Development of cell-specific delivery systems for therapy and imaging.** Develop non-viral strategies for cell-specific delivery of pathway-interactors and molecular probes. These new molecular complexes could allow delivery of cell-penetrating agents for the study of disease pathways, the imaging of tissue mass and disease progression, or the development of tissue-specific therapeutics. Contact: Dr. Olivier Blondel, 301-451-7334, blondelol@mail.nih.gov; NIAAA Contact: Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov; Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **06-DK-102*** **Mechanisms and measurement of human thermogenesis**. The unique mechanisms that alter the efficiency of energy utilization in various organ beds—white and brown fat, skeletal muscle, liver, gut—remain largely unknown. New technologies are needed that can quantify organ specific energy production, utilization and heat production in human subjects. Contact: Dr. Maren Laughlin, 301-594-8802, laughlinm@mail.nih.gov **06-EB-101*** **Development of minimally invasive image-guided systems.** Target areas include (1) improving the accuracy of biopsy sampling / staging of disease such as in the evaluation for prostate cancer, (2) reducing the incidence of complications such as in improving prostate nerve bundle sparing, (3) reducing recovery time such as in thoracic cancer resection and (4) improving the safety of interventional procedures such as in lead placement in deep brain stimulation. Contact: Dr. John Haller; 301 451-3009; hallerj@mail.nih.gov **06-EB-102*** **Development of biomedical technologies and systems.** Focus areas include: (1) providing immediate diagnostic information for multiple conditions at the point-of-care; (2) a robust, consistently accurate glucose sensor with extended functional lifetime, improved accuracy and low variability of readings; or (3) low cost diagnostic or therapeutic systems. Also, development of such devices engineered to work in low resource settings. Contact: Dr. William Heetderks, 301 451-6771, heetderw@mail.nih.gov **06-ES-101*** **Measuring the body burden of emerging contaminants: Biosensors and lab "on-chip" technology for measuring *in vivo* environmental agents** New advances in biosensors and lab-on-chip technology create novel ways to measure the body burden and sub-clinical health effects of emerging contaminants in the environment in large study populations. Additional research funds would support field testing of the most promising sensors and analysis techniques through collaboration with existing epidemiologic studies taking advantage of both new and banked tissue specimens. Contact: Dr. David Balshaw, 919-541-2448, Balshaw@niehs.nih.gov **06-ES-102*** **3-D or virtual models to reduce use of animals in research: Creation of miniature multi-cellular organs for high throughput screening for chemical toxicity testing.** Development of novel micro-scale systems of multiple cell types that replicate the macro-scale structure and function of major organ systems in response to environmental stressors linked with development of computational models of organ system function can accelerate testing of the multitude of chemicals in our environment for toxicity. Research which furthers the generation of 3-D biological models will provide new assays for rapid screening of toxicity in organs such as the lung and liver. Cell types, such as human stem cells, used in these systems would reduce the use of animals and improve our assessment of chemical hazards in the environment. Contact: Dr. David Balshaw, 919-541-2448, Balshaw@niehs.nih.gov

Broad Challenge Area	Specific Challenge Topic
	06-GM-101* **Structural analysis of macromolecular complexes.** Development of new approaches, technologies, and reagents that would facilitate functional and/or structural analysis of macromolecular complexes. Contacts: Dr. Ravi Basavappa, 301-594-0828, basavapr@nigms.nih.gov; Dr. Laurie Tompkins, 301-594-0943, tompkinl@nigms.nih.gov **06-GM-102*** **Chemist/biologist collaborations facilitating tool development.** Development of chemical probes, imaging agents, radiochemicals, and other tools for understanding biology through collaborations between a chemist(s) and a biologist(s). Contacts: Dr. James Deatherage, 301-594-0828, deatherj@nigms.nih.gov; Dr. Michael Rogers, 301-594-3827, rogersm@nigms.nih.gov **06-GM-103*** **Development of predictive methods for molecular structure, recognition, and ligand interaction.** Studies to more precisely predict molecular structure and interactions between molecules and ligands to lay the foundation for a new generation of therapeutics and drug design. Powerful predictive methods will require the acquisition of experimentally derived constraints and breakthrough computational methods. Reliable, high-throughput predictive methods would create a more comprehensive resource for understanding molecular interaction that would eventually replace the use of slower, empirical determinations. Contacts: Dr. Peter Preusch, 301-594-0828, preuschp@nigms.nih.gov; Dr. Warren Jones, 301-594-3827, jonesw@nigms.nih.gov **06-HD-101*** **Improved interfaces for prostheses to improve rehabilitation outcomes.** Mechanical design and control algorithms for prosthetic limbs have seen remarkable advances recently. Still lacking, however, are robust interfaces for these limbs to both the brain and the skeleton. The foci of this challenge will be to improve functional rehabilitation outcomes by 1) developing or refining control interfaces that can utilize signals from cerebral cortex to drive the latest generation of arm prostheses; 2) developing or refining methods for anchoring prosthetic arms directly into residual bone without risk of infection; and 3) incorporating these technologies into standard rehabilitation practices to improve patient quality of life. These improvements in prosthetic limbs could potentially provide enhanced functionality for recipients while reducing the time and cost of rehabilitation efforts. Contact: Dr. Michael Weinrich, 301-402-0832, weinricm@mail.nih.gov. **06-HG-101*** **New computational and statistical methods for the analysis of large data sets from next-generation sequencing technologies.** The introduction of new methods for DNA sequencing has opened new avenues, including large-scale sequencing studies, metagenomics, transcriptomics, genetic network analysis, and determination of the relationship of sequence variation and phenotypes to disease, to address heretofore unapproachable problems in biomedical research. However, since the large amounts (terabases) of data generated overwhelm existing computational resources and analytic methods, urgent action is needed to enable the translation of this rich new source of genomic information into medical benefit. Contact: Dr. Lisa Brooks, 301 496-7531, brooksl@mail.nih.gov **06-HG-102*** **Technologies for obtaining genomic, proteomic, and metabolomic data from individual viable cells in complex tissues.** Most existing technologies can only measure the properties of a population of cells and not the properties of individual cells. Technologies that are able to use one or a small number of cells are needed to generate data to understand the molecular phenotype, or state, of a particular cell type and

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	the role it plays in tissue and organ function in health and disease. Contact: Dr. Brad Ozenberger, 301-496-7531, bozenberger@mail.nih.gov **06-HG-103* Methods to sequence highly variable, repeat-rich regions of complex genomes.** Variants in complex genomic regions, e.g. the MHC region, have implications for infectious and autoimmune diseases, yet these and many other highly repetitive and highly variable loci are often poorly represented in sequence assemblies using data from newer "short read" sequencing platforms, and are too expensive to sequence with older, Sanger-based platforms. Technology development is needed to sequence and assemble these regions efficiently and accurately or they will continue to be unexamined in large medical genomics studies. Contact: Dr. Adam Felsenfeld, 301 496-7531, felsenfa@mail.nih.gov **06-LM-101* Intelligent Search Tool for Answering Clinical Questions.** Develop new computational approaches to information retrieval that would allow a clinician or clinical researcher to pose a single query that would result in search of multiple data sources to produce a coherent response that highlights key relevant information which may signal new insights for clinical research or patient care. Information that could help a clinician diagnose or manage a health condition, or help a clinical researcher explore the significance of issues that arise during a clinical trial, is scattered across many different types of resources, such as paper or electronic charts, trial protocols, published biomedical articles, or best-practice guidelines for care. Develop artificial intelligence and information retrieval approaches that allow a clinician or researcher confronting complex patient problems to pose a single query that will result in a search that appears to "understand" the question, a search that inspects multiple databases and brings findings together into a useful answer. Contact: Dr. Valerie Florance, 301-594-4882, florancev@mail.nih.gov **06-LM-102* Self-documenting encounters**. Develop technologies, tools, and processes to achieve rapid and comprehensive electronic documentation of encounters with patients/research subjects. Clinicians & clinical researchers spend considerable time and effort in documenting clinical encounters (including using text to describe findings that are seen or heard) - often after the fact and with little immediate benefit to care of patients and clinical research subjects. Technologies and tools that could fully automate the capture of encounters and update electronic health records in real-time would support more effective and efficient health care and clinical research. Contact: Dr. Hua-Chuan Sim, 301-594-4882, simh@mail.nih.gov **06-MD-101* Development of Telehealth Tools to Promote Health and Connect At-Risk Youth to the Health System via Low-Cost, Mobile, and Wireless Technologies.** NCMHD is interested in the development of telehealth messages utilizing various forms of technology, aimed at high-risk youth as well as innovative culturally and linguistically appropriate media strategies for connecting at-risk youth with the healthcare system. Contact: Dr. Kyu Rhee, 301-402-1366, rheekb@mail.nih.gov; NIAAA Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov; NIDA Contact: Dr. Jacqueline Lloyd, 301-443-8892, lloydj2@nida.nih.gov **06-OD(OBSSR)-101* Using new technologies to improve or measure adherence.** New and innovative technologies to improve and/or measure patient adherence to prescribed medical regimens and utilization of adherence-enhancing strategies in clinical practice would greatly enhance the health impact of efficacious treatments and preventive

Broad Challenge Area	Specific Challenge Topic
	regimens. This challenge invites the development of new technologies to measure or improve patient adherence. Contact: Dr. Lynn Bosco, 301-451-4286, boscol@od.nih.gov; NIAAA Contact: Dr. Marcia Scott, 301-402-6328, mscott@mail.nih.gov; NHLBI Contact: Dr. Susan Czajkowski, 301-435-0406, czajkowskis@nhlbi.nih.gov; FIC Contact: Dr. Xingzhu Liu, 301-496-1653, liuxing@mail.nih.gov **06-OD-101*** **Development of new tools and technologies to interrogate human mitochondrial function *in vivo.*** These tools would include methods to manipulate human mitochondrial structure and activity, as well as novel imaging techniques to monitor and measure human mitochondrial function or dysfunction in healthy and diseased tissues. Contact: Dr. Phil Smith (NIDDK), 301-594-8816, smithp@mail.nih.gov; NIAAA Contact Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov **06-RR-101*** **Virtual environments for multidisciplinary and translational research.** Virtual networking environments like Science Commons, Facebook, and Second Life, create platforms that can eliminate many barriers in scientific collaborations. These environments integrate fragmented information sources, enable "one-click" access to research resources, and assist in re-use of scientific workflows. Funded projects would develop and implement virtual collaborative environments to facilitate biomedical and translational research, e.g. addressing issues of privacy, technology transfers, and sharing resources. Contact: Dr. Olga Brazhnik, 301-435-0758, brazhnik@mail.nih.gov; NIDA Contact: Dr. David Thomas, 301-435-1313, dthomas1@nida.nih.gov **06-RR-102*** **Infrastructure for biomedical knowledge discovery.** Biomedical research depends on heterogeneous data of varying reliability that are increasingly multimedia and high-dimensional. Recent advances in web technologies enable discovery and aggregation of disparate data on specified topics, visualization and navigation of complex and abundant data, extraction of concepts from text, and detection of associations. Funded projects would coalesce the most effective information technologies with domain specific knowledge structures and data processing and to create computational infrastructures for integrated, customizable access to biomedical data. Contact: Dr. Olga Brazhnik, 301-435-0758, brazhnik@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
(07) Enhancing Clinical Trials	**07-CA-101*** **Novel Agents for Cancer Treatment.** Initiate early phase clinical trials of novel agents in three areas: 1) targeting the tumor stem cell by evaluating the sonic hedgehog smoothened antagonist, GDC-0449, and the pan-notch inhibitor, RO4929097, in collaboration with Genentech and Roche, respectively, in trials of breast, lung, colon, leukemia and ovarian cancer; 2) testing Anti-IGFR-1 Monoclonal Antibody IMC-A12 (ImClone) in pediatric tumors such as rhabdomyosarcoma, osteosarcoma, and neuroblastoma, as well as studies in breast, small cell lung, adrenocortical and pancreatic cancer; and 3) testing PARP inhibitor ABT-888 in breast, ovarian, and pancreatic cancer. Contact: Dr. Jeff Abrams, 301-496-2522, abramsj@mail.nih.gov **07-EY-101*** **Cost Effectiveness/Quality of Life: Tools to assess the impact of interventions on quality-of-life and cost effectiveness of ophthalmic treatments.** Fostering interdisciplinary collaboration with specialties such as health outcomes, economics, genetics, statistics, and clinical and bench science is needed to develop and improve instruments that measure the effect of ophthalmic treatments on the patient's quality-of-life and cost-effectiveness. Such teams could be used develop tools to evaluate and influence patient adherence with effective treatments in order to improve outcomes. Contact: Dr. Natalie Kurinij, 301-451-2020, kurinijn@mail.nih.gov **07-NS-101*** **Developing technology to increase efficiency and decrease cost of clinical trials.** Clinical trials are becoming increasingly expensive, and many US patients are unwilling to enroll, which has led to delays in trial completion and further cost increases. The challenge is to develop and test affordable, technologies to enable remote, centralized monitoring of physiologic, behavioral and neurologic indices as well as study medication compliance, and adverse effects in clinical trials. These technologies should provide opportunities to enhance efficiency in clinical trials, as well as to collect more "real life" data. Contact: Dr. Emmeline Edwards, 301-496-9248, ee48r@nih.gov; NIAAA Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **07-OD(OBSSR)-101*** **Improving and/or assessing external validity in randomized clinical trials (RCTs).** The practice of conducting RCTs with volunteer samples recruited from patients in clinical or community settings limits the generalizability of results, a critical problem for comparative effectiveness research. Research is needed to develop scientific tools for improving and/or assessing the external validity of RCT results to known populations, including methods for applying probability sampling in the identification and recruitment of RCT participants, measuring biases in RCT participant pools, and accounting for such biases in the analysis of RCT results. Contact: Dr. Ronald Abeles, 301-496-7859, abelesr@od.nih.gov; NIAAA Contact: Dr. Marcia Scott, 301-402-6328, mscott@mail.nih.gov; NHLBI Contact: Dr. Peter Kaufmann, 301-435-2467, kaufmannp@nhlbi.nih.gov; NIAMS Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **07-OD(ORDR)-101*** **Library of standardized patient registry questions.** Develop standardized questions and data elements that can be used when developing rare diseases patient registries. Having a standardized library of data elements will enable cross-indication analyses of patient populations, speed the development and deployment of patient registries, and allow registries to exchange and aggregate patient registry data. Contact: Dr. Rashmi Gopal-Srivastava, 301-402-4336, gopalr@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
	07-OD(ORDR)-102* **Rare disease genetic patient registry.** Support for an efficient infrastructure and expert staff in developing a registry capable of asking for rare-disease-specific information and capturing genetic results across any number of rare diseases, thereby ensuring patients are identified for trials as treatments become available. Contact: Dr. Rashmi Gopal-Srivastava, 301-402-4336, gopalr@mail.nih.gov; NIAMS Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
(08)Genomics	**08-AG-101* Genetic factors affecting rates of change in disease risk factors with age.** Human aging is associated with an increase in the levels of numerous chronic disease risk factors, but the rates at which these factors increase with age varies considerably among persons. There is evidence that genetic factors influence rates of age-related change, but there have been few studies to identify specific factors. The identification of genetic factors which protect against such adverse aging changes could contribute significantly to the development of interventions for healthier aging. The recent acquisition of genome-wide SNP data from several large long-term longitudinal studies provides the opportunity to identify genes affecting rates of change of important risk factors efficiently by analyzing phenotype data collected on individuals over decades, combined with information from the SNP scans. Such genes could also be identified by other approaches, such as linkage analyses and studies of rare variants in candidate genes. Proposals for analyses to identify relationships of specific genetic factors to rates of change with age in phenotypes measured in longitudinal studies of young, middle-aged, or older populations are encouraged. Contact: Ms. Winifred Rossi, 301-496-3836, rossiw@mail.nih.gov **08-CA-101* Augmenting Genome-Wide Association Studies.** Genome-wide association studies (GWAS) represent the starting point for a variety of experimental and epidemiological approaches designed to identify the functional gene variants and gene-environment interactions that increase or decrease the risk of cancer, and may thus provide new insights into risk prediction as well as preventive and therapeutic interventions. Linking genomic and molecular alterations within tumors (the Applied Molecular Pathology Lab and the Cancer Genome Atlas) with the germline variants uncovered by GWAS will further catalyze downstream biological research, and speed the translation of genomic discoveries into clinical practice. Furthermore, studies of the "dark matter" in the human genome that are not captured by the SNP-based GWAS (e.g., structural and rare gene variants, micro-RNAs, and epigenetics) are needed to fully understand the inherited component to cancer. Contact: Dr. Daniela Gerhard, 301-451-8027, Daniela.Gerhard@nih.hhs.gov **08-DE-101 * Planning Grants for Genome-wide Studies of Understudied Oral and Craniofacial Diseases and Disorders [Temporomandibular Joint Disorder, Oral Cancer, Sjögren's Syndrome, Periodontal Disease]**: Genome-wide studies have yielded significant insights into the genetic etiologies of many common complex diseases, but this approach has not been widely adopted for highly complex oral and craniofacial diseases such as TMJ disorder, oral cancer, Sjögren's syndrome, or periodontal disease. **Goal**: Assessment of the adequacy and consistency of clinical, risk factor, endophenotype, behavioral and demographic data of participants from different research groups; adequacy of tissue specimens for genome-wide technologies; and feasibility of the initial genome-wide study and follow-up studies. [High Priority Topic for NIDCR.] Contact**:** Dr. Emily Harris, 301-594-4846, harrisel@nidcr.nih.gov **08-EY-101* Genomics of complex eye diseases.** Opportunities exist to make scientific inroads into complex, but common eye diseases such as cataract, diabetic retinopathy, macular degeneration and primary open angle glaucoma. One approach would be to use comprehensive genomic profiling of ocular cell types in normal and disease states by using high throughput expression analysis methods (e.g., sequencing and exon arrays, methylation sequencing) Contact: Dr. Hemin Chin, 301-451-2020, chinh@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
	08-HG-101* Technology and resources for high-throughput functional analysis of functional elements in genomic sequences. Computational and experimental research programs are currently identifying thousands of putative functional elements (e.g., genes and regulatory sequences) based on their sequence properties; however, new, robust, high-throughput methods are needed to carry out functional assays to determine whether and how these elements operate to determine cell states, in development, and in health and disease. Such new methods should include both cellular and whole organism methods to allow systematic analysis of the effects of both genetic (normal variation and mutation) and environmental perturbations, and should include methods for both molecular (transcriptomic, proteomic) analysis and high-throughput phenotyping. Contact: Dr. Elise Feingold, 301-496-7531, elise_feingold@nih.gov **08-HL-101* Identify causal genetic variants associated with heart, lung, and blood diseases by application of targeted DNA capture and massively parallel sequencing technologies followed by selective genotyping of DNA samples from large well-phenotyped populations**. Genome-wide association studies (GWAS) have been successful in identifying high frequency genetic variants of modest effect that are associated with numerous common diseases, but identifying actual disease-causing genetic variants will require large-scale DNA sequencing of individuals from well-phenotyped populations. Two applications of this approach are needed: (a) targeted resequencing of entire chromosomal regions already known from GWAS findings to be strongly associated with disease, and (b) disease or other clinical trait-based exome-wide resequencing for the unbiased discovery of rare variants having large effects. Validation/replication of newly discovered genetic variants from both experimental designs would then have to be undertaken by selective genotyping of well-phenotyped populations, particularly from existing large consortia. This sequential strategy is needed to characterize the complete set of causal variants contributing to disease heritability and etiology. Contact: Dr. Alan Michelson, 301-594-5353, michelsonam@nhlbi.nih.gov **08-MH-101* Beyond GWAS: Deep sequencing of mental disorders.** Over the past 3 years, genotyping studies have identified several candidate risk genes for autism, schizophrenia, and bipolar disorder. Exploit new sequencing technologies that move beyond genotyping to identify rare variants and novel risk genes for these disorders in repository DNA samples. Contact: Dr. Thomas Lehner, 301-443-9869, tlehner@mail.nih.gov **08-MH-102* Schizophrenia interactome.** Explore candidate genes for schizophrenia and other major mental disorders and their relationship and expression patterns. Jumpstart the move from genomics to biology by identifying the patterns of gene expression in post-mortem brain from individuals with various candidate genes. Elucidate the complex functional interactions of their protein products. Contact: Dr. Douglas L. Meinecke, 301-443-1692, dmeineck@mail.nih **08-NR-101* Genetic and Epigenetic Predictors of Symptom Severity.** This initiative will support research on the genetic underpinnings of symptom severity. The findings from this research will identify individuals at greatest risk for symptoms from both acute and chronic conditions and design individualized interventions that will maximize symptom management. Contact: Dr. Joan Wasserman, 301-594-5971, wassermanje@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-

Broad Challenge Area	Specific Challenge Topic
	NIHChallengeGrants@mail.nih.gov; NIDA Contact: Dr. John Satterlee, 301-435-1010, satterleej@mail.nih.gov **08-NS-101* Cross-disease research to identify mechanisms common to Mendelian disorders of low incidence and genetically complex, high incidence disorders.** Progress in treating many common neurological and neurobehavioral disorders has been hindered by the complex genetics and heterogeneous etiologies of these disorders. However, analyzing related or clinically overlapping Mendelian disorders or studying rare genetic variants of large effect can yield unique biological insight into the mechanisms underlying common disease. This challenge encourages studies that dissect pathways common to simple and complex genetic disorders, with the goal of identifying potential therapeutic targets. Contact: Dr. Jane Fountain, 301-496-1431, fountai@ninds.nih.gov

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(09) Health Disparities	**09-AG-101* Geographic Disparities in Medicare Usage and Cost.** It is well documented that there are major geographic differences across the U.S. in quality of care and clinical outcomes for older adult populations. Moreover, these differences are not correlated with the extent and cost of Medicare usage. Research is needed to (1) foster evidence-based approaches to financing, staffing, public health programs, and clinical practice to reduce these disparities and (2) develop interventions to reduce disparities in one or multiple categories of health determinants − e.g., geography, socioeconomic status, race/ethnicity − using techniques that can be duplicated in a variety of community settings. Contact: Dr. Sidney Stahl, 301-402.4156, StahlS@mail.nih.gov **09-ES-101* Building trust between researchers and communities through capacity building in Environmental Public Health.** Building partnerships between researchers and community members is essential to conduct research which is responsive to the needs of communities for public health changes to protect human health. Two years of support will nurture newly evolving partnerships focusing on building trust and creating a common vocabulary with which to discuss community concerns arising from exposures to hazardous agents, needs to adapt to climate change, barriers to health care and services, and food insecurity. Building knowledge about health promotion behaviors will provide a new source of jobs to communities. Contact: Mr. Liam O'Fallon, 919-541-7733. Ofallon@niehs.nih.gov **09-MD-101* Creating Transformational Approaches to Address Rural Health Disparities.** Research will focus on approaches, partnerships, and technologies for improving rural health outcomes. In addition, NCMHD is interested in proposals that utilize innovative outreach strategies that involve collaboration among traditional and non-traditional groups including new categories of community health workers, non-traditional occupations and settings. Contact: Dr. Nathaniel Stinson, 301-402-1366, stinsonn@mail.nih.gov; NIDA Contact: Dr. Lula Beatty, 301-443-0441, lbeatty@nida.nih.gov **09-MD-102* Trans-disciplinary Research to Integrate the Biological and Non-biological Determinants of Health to Address Health Disparities.** Research interests include trans-disciplinary approaches to address health disparities through collaborative efforts and sustained partnerships with social scientists, policy researchers, health researchers, environmental scientists, and behavioral scientists, for example. Strategies that develop community infrastructure and networks, including non-traditional partnerships are also of interest. Contact: Dr. Kyu Rhee, 301-402-1366, rheekb@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **09-MD-103* Initiating Innovative Interventions to Prevent Family Violence.** NCMHD will focus on strategies to prevent family violence including domestic and intimate partner violence and enhance behavioral research efforts that build workforce infrastructure. The development of culturally and linguistically appropriate messages and tools, the use of non-traditional methods, along with marketing strategies are also of interest. Contact: Dr. Robert Nettey, 301-402-1366, nettyr@mail.nih.gov; NIAAA Contact: Dr. Ralph Hingson, 301-443-1274, hingson@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
(10) Information Technology for Processing Health Care Data	**10-CA-101* Cyber-Infrastructure for Health: Building Technologies to Support Data Coordination and Computational Thinking.** The National Science Foundation has identified research based on "*cyberinfrastructure*" as the single most important challenge confronting the nation's science laboratories (http://www.nsf.gov/news/special_reports/cyber/index.jsp). The challenge is based on a "grand convergence" of three trends: (a) maturation of the Internet as connective data technology; (b) ubiquity of microchips in computers, appliances, and sensors; and (c) an explosion of data from the research enterprise. The NIH, for example, has invested millions within its Genes, Environment, and Health Initiative (GEI) to develop new technologies for measuring environmental exposure to accompany the millions already spent on data from Genome Wide Association studies. The DHHS is spending millions to catalyze the deployment of interoperable electronic health records as a springboard for research (i.e., in the "learning health system"). Relatively little has been spent on accommodating the *petabytes* (i.e., 10^{15} bytes of data) of data expected from these investments. What is needed is a focused concentration of resources to stimulate the creation of new technologies to accommodate these data and accelerate knowledge discovery through computational means. Such a stimulus should help bootstrap a new sector of the knowledge economy, one that is dedicated to accelerating the pace by which data are turned into population health benefits. Contact: Dr. Bradford Hesse, 301-594-9904, hesseb@mail.nih.gov **10-EB-101* Engineering improved quality of health care at a reduced cost.** Target areas include: (1) developing informatics systems for electronic records that integrate image data with clinical data for more efficient health care decision support; or (2) developing a "universal interface" to effect transmission of image data across institutions/hospitals to reduce duplication. Dr. William Heetderks, 301 451-6771, heetderw@mail.nih.gov **10-HL-101* Develop data sharing and analytic approaches to obtain from large-scale observational data, especially those derived from electronic health records, reliable estimates of comparative treatment effects and outcomes of cardiovascular, lung, and blood diseases** . Advances in this area will address two important barriers to research on comparative treatment effects: ▪ inability to link data across disparate data platforms and health care settings ▪ inability to address confounding and on-treatment biases in observational studies based on data from clinical practice. The first could be addressed by creating an interoperable electronic health record (EHR)-based research platform that assures privacy and confidentiality while allowing questions to be addressed that could not be by using data from only one clinical practice, health plan, or health system; the second by developing new methods to address confounding when attempting to use observational data to compare treatment effects, e.g., instrumental variables, innovative quasi-experimental designs, facilitating ecologic analyses of clinical data using linkages of geographic and clinical data. Such approaches would increase the credibility and value of observational analyses of huge integrated EHR databases in identifying optimal treatment practices for cardiovascular, lung, and blood diseases with multiple available treatment options. Contact: Dr. Michael Lauer, 301-435-0422, ml580m@nih.gov

Broad Challenge Area	Specific Challenge Topic
	10-LM-101* **Informatics for post-marketing surveillance**. Use computational data mining (artificial intelligence and natural language processing, among other techniques) of a large longitudinal medical records database to perform post-marketing surveillance (Phase 4 Clinical Trial). Large clinical data repositories exist that contain longitudinal health records for millions of people. Advanced computational techniques can be used to mine clinical notes, test data and abnormal images to undertake an *in silico* Phase 4 Clinical Trial, by searching for possible adverse drug events and side effects of drugs already in use. Contact: Dr. Milton Corn, 301-496-4621, cornm@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **10-LM-102*** **Advanced decision support for complex clinical decisions**. Use artificial intelligence techniques to provide practical support for complex decision making in health care and clinical research contexts. Most electronic data about patients and clinical research subjects exists at the level of raw data, individual test results and observations, and individual encounters. This mass of data obscures the view of the patient as a whole, hides key facts that deserve attention, and complicates the delivery of relevant electronic knowledge to improve decisions or identify candidate research subjects. Advanced computational techniques should be useful in generating a higher level picture of the patient that can support more effective clinical decision support. Contact: Dr. Valerie Florance, 301-594-4882, florancev@mail.nih.gov **10-OD-101*** **Adapt existing genetic and clinical databases to make them interoperable for pharmacogenomics studies.** In order for personalized approaches to drug therapy to be developed, genetic data and clinical data need to be superimposed. Analysis of the superimposed data will generate hypotheses concerning genetic control of drug efficacy. Contact: Dr. Joni Rutter (NIDA), 301-435-0298, jrutter@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **10-RR-101*** **Information Technology Demonstration Projects Facilitating Secondary Use of Healthcare Data for Research** Analysis of enormous amounts of aggregate, anonymous, healthcare data has potential to provide evidence for best practices and to identify promising areas for additional research. The increasing adoption of health information technology in the United States offers a source of large amounts of data. This initiative would fund development of policies and technology to ensure stringent protection of individual privacy for aggregate anonymous data used for research. Examples of responsive topics include, but are not limited to: multi-institutional data repository research querying projects; vocabulary and ontology standards in data repositories; policies, process, and governance of data repositories; Extract, Transform, Load (ETL) procedures for data for clinical data research repositories. Contact: Dr. Elaine Collier, 301-435-0794, colliere@mail.nih.gov **10-TW-101*** **Innovative information and communication technologies to enhance capabilities of U.S. institutions in global health research and research training.** Develop culturally adaptive, interoperable data management, long-distance communication, and distance learning applications that can enhance productivity and quality of active U.S.-international research and research training collaborations. Contact: Dr. Flora Katz, 301-496-1653, katzf@mail.nih.gov

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(11) Regenerative Medicine	**11-AR-101*** **Musculoskeletal And Skin Tissue Regeneration.** Define the molecular pathways that regulate the integration of muscle, tendon, and bone into functional units. Develop applicable animal models for regeneration of musculoskeletal or skin tissues. Define outcome measures, such as non-invasive analysis of disease, injury, and repair. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov; ORWH Contact: Dr. Indira Jevaji, 301-402-1770, jevajiip@od.nih.gov **11-DC-101*** **Hair Cell Regeneration and Maintenance.** One common cause of hearing impairment in humans is the progressive loss of the auditory transduction cells, or hair cells, in the inner ear. A similar loss of motion transduction cells in the vestibular organ is a probable cause of balance disorders. Once lost, these cells cannot be spontaneously regenerated in mammals. The Challenge is to develop and validate methods to regenerate and maintain hair cells in animal model systems with the eventual goal of successful translation to human treatments. Contact: Dr. Nancy Freeman, 301-402-3458, freemann@nidcd.nih.gov **11-EB-101*** **Vascular networks in engineered tissues.** Research on the design, optimization, and formation of a complete vascular network capable of delivering oxygen and nutrients and removing waste products in engineered tissues (i.e., vascularization of engineered tissue constructs). Dr. Rosemarie Hunziker, 301-451-1609, hunzikerr@mail.nih.gov **11-HL-101*** **Develop cell-based therapies for cardiovascular, lung, and blood diseases.** Cell-based therapies for cardiovascular, lung, and blood diseases offer a new paradigm for advancing and transforming patient care. Translational and early-phase clinical research has demonstrated that cell-based therapies may improve left ventricular function, reduce myocardial ischemia, and lead to improved lung function. Reconstitution of normal hematopoeisis using modified stem cell graft sources has great potential for treating specific genetic blood disorders. However, a number of significant challenges and barriers must be overcome to move the field forward toward broad clinical application. We encourage further research to determine the characteristics of the most promising target patient population, the best cell type and number of cells to use, the optimal methods and timing of delivery, and other preclinical parameters. Contact: Dr. Sonia Skarlatos, 301-435-0477, skarlats@nhlbi.nih.gov

Broad Challenge Area	Specific Challenge Topic
(12) Science, Technology, Engineering and Mathematics Education (STEM)	**12-OD-101* Efficacy of educational approaches toward promoting STEM competencies.** Research on efficacy testing of educational pedagogy, tools, and curricula (both classroom and non-classroom approaches) that are targeted at improving student understanding of science, technology, engineering, and math (STEM) concepts. Contact: Dr. Bruce Fuchs, 301-402-5225, fuchsb@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
(13) Smart Biomaterials - Theranostics	**13-DE-101* Novel Self-Healing Smart Dental and Bio-Restorative Materials**: Dental materials and other biomaterials have limited survival when placed in the human body. Goal: Development of a new generation of "self-healing" and "smart" dental and bio-restorative materials that can diagnose structural failure and repair themselves to minimize the loss of natural structures associated with materials failure. These new materials can also be designed with properties to survive in extreme and adverse conditions, such as in patients with xerostomia. Contact: Dr. James A. Drummond, 301-402-4243, drummondj@nidcr.nih.gov **13-EB-101* Theranostics: Combined delivery of diagnostic and therapeutic agents.** Development of novel approaches to deliver combined diagnostic and therapeutic agents to appropriate sites with high specificity and in adequate concentrations to realize the promise of combined diagnosis and treatment of diseases in a single sitting ("theranostics"). Dr. Lori Henderson, 301-451-4778, hendersonlori@mail.nih.gov ; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **13-ES-101* Methods to evaluate the health and safety of nanomaterials.** Evaluation of the health and safety risks of nanoscale products is critical as nanomaterials are being used in applications as diverse as medical devices, drug delivery, cosmetics, and textiles. The development of novel tools and approaches to determine the impact on biological systems and health outcomes of an array of engineered nanomaterials is necessary to protect human health. Biological, physical and chemical characterization of selected nanomaterials will be conducted to aid in setting standards for health and safety and developing computational models for the prediction of long term secondary effects. Contact: Dr. Sri Nadadur, 919-541-5327, Nadadurs@niehs.nih.gov

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(**14) Stem Cells**	**14-AG-101* Induced Pluripotent Stem (iPS) Cells for Aging and Neurodegeneration Research**. Studies have shown that human skin cells can be reprogrammed to become pluripotent stem cells and that such iPS cells act like embryonic stem cells in that they can develop into different cell types. Generating tissue-specific differentiated cells from iPS cells could allow studies on the molecular and cellular changes that characterize aging and neurodegenerative processes. Studies on iPS cells could determine whether they can be used as cell-based models of aging and disease, such as Alzheimer's disease. Two year challenge projects could stimulate the development of, and biological studies on, iPS cells derived from human tissue of different ages and disease states, and could lead to novel drug screening approaches and open up the possibility of individualized cell therapy. Understanding the differentiation of skin-derived iPS cells. Contact: Dr. Bradley Wise, 301-496-9350, wiseb@nia.nih.gov or Dr. Ronald Kohanski, 301-496-6402, Kohanskir@mail.nih.gov **14-AR-101* Delineate Factors That Control The Differentiation Of Pluripotent Stem Cells In The Skin And Musculoskeletal System Into Different Lineages**. Define the cells' phenotypes as they differentiate along these pathways. Develop a common vocabulary for stem cell differentiation. NIAMS Contact: Dr. Susana Serrate-Sztein 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **14-DE-101* Precise Reprogramming of Cells from Oral and Craniofacial Tissues**: Recent advances in reprogramming of somatic cells into induced pluripotent stem cells (iPS) cells constitute an important breakthrough, but the utility of iPS cells for future cell-based therapies is limited by the scarcity of efficient differentiation protocols to guide developmentally primitive iPS cells through a long progression of developmental stages toward fully-differentiated functional somatic cells. Goal: Development of novel approaches for partial reprogramming of somatic cells of the oral and craniofacial complex (e.g. periodontal ligament cells, pulp cells, oral mucosal cells, salivary acinar cells, fibrocartilaginous cells of the temporomandibular joint) for cell-based therapies to heal and restore these tissues following disease or trauma. Contact: Dr. Nadya Lumelsky, 301-594-7703, Nadya.Lumelsky@nih.gov **14-DK-101* Induced pluripotent stem cells--cellular and humanized mouse models of disease.** Somatic cells, such as fibroblasts, from patients with diseases can be used to create cell lines, tissues and, perhaps, organ systems, through induced Pluripotent Stem Cell (iPSC) technology. Such models could be used to elucidate underlying pathology of disease or screen for agents that could be used therapeutically. Combining this approach with mouse strains able to accept multiple human tissues without rejection could provide the microenvironmental milieu to support the tissue's physiological function within the context of the whole organism, enabling greater understanding of disease pathogenesis and providing a platform for preclinical testing of drug candidates. Contact**:** Dr. Dan Wright, 301-594-7717, wrightdan@mail.nih.gov; NIAAA Contact: Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov; NIAMS Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **14-EY-101* Development of stem cell treatment for degenerative diseases of the eye.** The restorative properties of stem cells hold the promise in the treatment of degenerative eye diseases such as macular degeneration, diabetic retinopathy, retinitis pigmentosa and glaucoma, and diseases of the ocular surfaces. There is a need for the identification of biomarkers that can define stem cells and the end-stage cells, as well as

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	reproducible protocols for the generation and purification of viable terminally differentiated cells. Contact: Dr. Grace Shen, 301-451-2020, sheng@mail.nih.gov **14-HL-101*** **Develop molecular signatures for heart, vascular, lung, and blood diseases by profiling reprogrammed induced pluripotent stem cells derived from affected individuals of defined genotype**. Large-scale profiling of RNA, proteins, and metabolites derived from normal and disease tissues has been instrumental in identifying the molecular etiologies of numerous disorders, but the applicability of this approach has been limited by the availability of relevant biological materials. Cell-based models of disease generated from stem cell technologies could be readily profiled with available high-throughput methods. Such studies could be undertaken on small numbers of control and affected individuals or on a larger population that would more broadly sample human genetic variation and thereby allow statistical associations to be established among genotypes, clinical traits, and molecular signatures that may elucidate causal mechanisms underlying complex diseases. Contact: Dr. Alan Michelson, 301-594-5353, michelsonam@nhlbi.nih.gov **14-MH-101*** **Developing iPS cells for mental disorders.** Create human induced pluripotent stem (iPS) cells from individuals with and without mental disorders and conduct exploratory studies. Goals might include maximizing derivation efficiency/reproducibility, modeling trajectories of cellular differentiation, or profiling differences in the molecular signature of cells. Contact: Dr. David M. Panchision, 301-443-5288, panchisiond@mail.nih.gov **14-NS-101*** **Reverse engineering human neurological disease.** It is now conceivable to reverse-engineer human neurological disease by generating and characterizing iPSCs from human control and patient populations. The relatively easy access of source tissue provides a means of elucidating patient-specific cell dysfunction or response to candidate therapeutics. Research topics can include maximizing derivation efficiency, maintenance, or reproducibility, studies of cellular differentiation, screening bioactive agents, or profiling the molecular signature as well as the functional properties of cells from controls vs. patients. There will be an emphasis on appropriate validation of iPS cells and their derivatives, evaluating the hetero/homogeneity of any cell populations to be screened and use of cellular assays relevant to normal development, organ function and disease. Contact: Dr. David Owens, 301-496-1447, do47h@nih.gov; NIAAA Contact: Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov

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(15) Translational Science	**15-AA-101* Determining If and How Adolescent Behaviors Affect Connections in the Developing Brain.** The brain develops throughout adolescence and into early adulthood, and there is accumulating evidence that behaviors exhibited during this period can influence lifetime health and well-being. Research is needed to address the critical question – do these behaviors actually rewire the developing brain thereby creating vulnerability for a number of persistent health problems including mental health disorders, eating disorders and addiction? Contact: Dr. Antonio Noronha, 301-443-7722, anoronha@mail.nih.gov; ORWH Contact: Dr. Indira Jevaji, 301-402-1770, jevajiip@od.nih.gov **15-AI-101* Explore the earliest events in HIV infection and use this information to develop new interventions for preventing and treating HIV infection:** Despite recent progress in HIV research, important questions remain: what molecular interactions regulate HIV expression and replication, why the host immune response cannot control the infection, and how reservoirs of infection persist in the body despite highly active antiretroviral treatment. Basic scientific information about how the virus attacks the body and how the body defends itself, especially in the earliest stages of infection, will identify new viral targets for the development of new prevention approaches and therapeutics. Contact: Dr. Sandra Bridges, 301-496-8198, sbridges@niaid.nih.gov **15-AI-102* Develop diagnostics and drugs for multiple or extensively drug-resistant tuberculosis (MDR/XDR TB):** To prevent the further emergence and spread of MDR/XDR TB, there is an urgent need to develop and test reliable technologies to rapidly diagnose TB and to identify drug resistance. There is a similarly urgent need to define the most effective use of existing TB therapies and other antibiotics for treating drug-resistant TB and to develop new drugs, particularly for MDR/XDR TB. Contact: Dr. Christine Sizemore, 301-435-2857, csizemore@mail.nih.gov **15-AI-103* Develop drugs for neglected tropical diseases, with a special emphasis on malaria:** The emergence of drug-resistant parasites has contributed to the spread of malaria in areas and populations where malaria had previously been controlled. A continuous pipeline of new and effective anti-malarial drugs is essential to achieve and sustain progress in disease control. Market forces have been inadequate to support development or deployment of interventions for malaria and other neglected tropical diseases. Therefore, there is an urgent need to support research leading to the development of novel and more effective interventions. Contact: Dr. John Rogers, 301-402-8304, jrogers@mail.nih.gov **15-CA-101* The Role of Cellular Architecture in Normal and Tumor Cell Biology.** The size and shape of a cell, as well as the placement of organelles and the arrangement of chromosomes within the nucleus are highly regulated and ordered. Changes in cell shape or rigidity of the microenvironment affect the patterns of gene expression and cell growth. These findings indicate that extracellular mechanical forces can alter a cell's behavior. Recent studies have demonstrated that genes are differentially positioned within the nucleus when they are silent or expressed. Furthermore, the genome is organized into chromosomal domains whose composition changes in different cell types and in cancer. These studies indicate that cellular architecture plays a critical role in regulating cell phenotype. Further studies are needed to define the relationship between cellular architecture and cell function, in both normal and tumor cells. Contact: Dr. Suresh Mohla,

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	301-435-1878, mohlas@mail.nih.gov **15-CA-102* Understanding mechanisms of hormone refractory cancers for therapeutic targeting.** Steroid receptors continue to play a major role in controlling the growth of hormone-refractory cancers and appear to accomplish this by: the activation of steroid receptors by alternate ligands; local production of steroid hormone; stabilization of steroid receptors and mutations that render steroid receptors hypersensitive to very low levels of the ligands. In addition, recent findings demonstrate that in patients treated with herceptin, ER levels and ER-mediated signaling is enhanced, while in patients treated with antiestrogens, Her 2-mediated signaling is enhanced. Furthermore, at least 25% of the genes modulated in these cancers are via non-genomic signaling. A comprehensive understanding of the molecular underpinnings of steroid receptor dependence of hormone-refractory tumors as well elucidating the subtleties of these regulatory pathways and their crosstalk will support personalized, predictive and preemptive medicine in human breast and prostate cancer. Contacts: Dr. Judy Mietz, 301-496-9326, mietzj@mail.nih.gov; Dr. Dinah Singer, 301-496-8636, singerd@mail.nih.gov **15-DA-101* Novel Approaches to Improve Immunogenicity of Vaccines Against Small Molecules** Innovative approaches to enhance the immunogenicity of small molecules (e.g., toxins, carcinogens, influenza epitopes, drugs of abuse) could lead to revolutionary advances in our ability to preempt, minimize the impact, or help reverse the course of preventable diseases. These approaches may leverage a variety of research strategies, including nanoparticle technology, hapten-tagging of virus-like particles, synthetic adjuvant systems, and novel immunomodulators and delivery systems. Contact: Dr. Nora Chang, 301-443-5280 or 301-443-8099, nchiang@nih.gov **15-DE-101* Molecular Profiling and Developing Mouse Models for Salivary Gland Tumor Research**: The biggest challenge in salivary gland tumor research is the lack of molecular phenotypic characterization of a heterogeneous class of tumors, and the lack of appropriate mouse models for charting the molecular pathogenesis of and testing therapeutic agents for the tumors. **Goal**: Initiation of systematic and comprehensive profiling of the genomics, proteomics, epigenomics, metabolomics and glycomics of salivary gland tumors. Informed by this information, develop xenograft models, MMTV-associated transgene models, and transgenic and knock-out gene-disruption models for preclinical testing in mice. Contact: Dr. Yasaman Shirazi, 301-594-4812, Yasaman.Shirazi@nih.gov **15-DE-102* New Models and Measures in Pre-clinical Chronic Pain Research**: Existing animal models of temporomandibular or orofacial pain conditions inadequately reflect the pathology or the phenotypes of the human state. **Goal**: Development of new animal models to study the transition from acute to chronic pain in temporomandibular joint disorders or other orofacial pain disorders. Coupled with the development of new functional and behavioral assays of acute and chronic pain, these animals models would be a powerful means to enhance our understanding of the biological mechanisms underlying the development of these chronic pain conditions and the responses of patients to therapeutic interventions. Contact: Dr. John Kusiak, 301-594-7984, John.Kusiak@nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov; ORWH Contact: Dr. Lisa Begg, 301-402-1770, BeggL@od.nih.gov **15-DK-101* Identification of bioactive macronutrients in the diet that impact metabolic state.** Recent studies suggest that specific types of macronutrients in the diet,

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	such as resistant starch or branched chain amino acids, may have selective effects on nutrient absorption, insulin sensitivity, and lipid metabolism. Elucidation of the metabolic impact of specific dietary components may well result in improved efficacy of lifestyle approaches to reduce obesity and metabolic diseases. Pilot studies are encouraged to identify specific bioactive components in the diet and study their mechanisms of action**.** Contact: Dr. Sue Yanovski, 301-594-8882, yanovskis@mail.nih.gov. **15-ES-101*** **Effects of environmental exposures on phenotypic outcomes using non-human models.** The complex etiology of many chronic diseases is difficult to explain. If most diseases arise from an interaction between genetic factors and environmental exposures, experiments that challenge animal models, such as rodents and alternate species, which mimic human disease phenotypes with stressors from the physical and social environment, can provide new information to help elucidate etiology. Non-human models now exist for many diseases and critical phenotypes and can be strategically exploited to understand the basic mechanisms of action in key organ systems. The results from these experiments can lead to enhanced mechanistic understanding of the underlying biology and opportunities for prevention and/or intervention. Contact: Dr. Cindy Lawler, 919-316-4671, lawler@niehs.nih.gov **15-EY-101*** **Protein misfolding in degenerative diseases of the eye.** A number of ocular genetic diseases occur due to misfolding/aggregation of proteins, for example the visual pigment protein, rhodopsin in retinitis pigmentosa, crystallins in age-related cataracts, and myocillin in glaucoma. Identifying therapeutic pharmacological agents/drugs that prevent the misfolding/aggregation of proteins could provide new tools for treating these diseases. Contact: Dr. Neeraj Agarwal, 301-451-2020, agarwalnee@mail.nih.gov **15-HD-101*** **Developing New Antimicrobials from Oligosaccharides**. Oligosaccharides are the third most prevalent component of human breast milk and have been shown to have antimicrobial properties against organisms including Campylobacter jejuni and caliciviruses. Research is needed to determine how oligosaccharides prevent infections and to stimulate the development of synthetic oligosaccharides that can be used to treat such conditions as necrotizing enterocolitis, newborn sepsis, or other infections in children or adults that may have become resistant to existing antibiotics. Contact: Dr. Gilman Grave, 301-496-5593, gg37v@nih.gov **15-HD-102*** **Pelvic Pain**. New animal models and epidemiologic studies are urgently needed to increase understanding of the mechanisms underlying the development of chronic pelvic pain conditions in women, including but not limited to uterine fibroids, vulvodynia, and endometriosis. Research is needed specifically to identify and measure the biological, clinical, and behavioral factors involved in determining the responses of patients to therapeutic interventions for chronic pelvic pain conditions. Contact: Dr. Estella Parrott, 301-435-6971, parrotte@mail.nih.gov; ORWH Contact: Dr. Lisa Begg, 301-402-1770, BeggL@od.nih.gov **15-LM-101*** **Presenting genome information in electronic health records**. Develop approaches for presenting relevant genomic information in an understandable way, in the context of a patient's electronic health record**.** As genomic data becomes available for more individuals, these data must be integrated into electronic health records in ways that: help clinicians and patients to understand the significance of the data; provide an avenue for alerting clinicians and patients when new knowledge from GWAS, etc. rises to the level of potential clinical impact; and enable linking to effective decision support. Contact: Dr.

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	Jane Ye, 301-594-4882, yej@mail.nih.gov **15-NR-101* NIH Partners in Research Program: Pathways for Translational Research.** This two year initiative will develop strategies for dissemination of interventions with demonstrated effectiveness for translation into clinical practice by teams of academic and community research partners. This initiative will provide the knowledge to more rapidly move scientific findings into communities to improve health. Contact: Dr. David Banks, 301-496-9558, Banksdh@mail.nih.gov **15-NS-101* Manipulating the blood-brain-barrier to deliver CNS therapies for Mental/Nervous System Disorders.** Neuroscience discoveries have led to promising therapeutic strategies for treatment of severe neurological disorders. However, the blood brain barrier presents a major hurdle to delivering potentially exciting agents such as RNA therapies, genes, critical enzymes, antibodies, other molecular entities, or cell therapies. The challenge is to develop potentially useful means of CNS drug targeting and delivery systems. Contact: Dr. Tom Jacobs, 301-496-1431, tj12g@nih.gov; NIAAA Contact: Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov **15-OD(ORDR)-101* Pilot projects for prevention, early detection and treatment of rare diseases.** Design research projects to provide preliminary results to demonstrate feasibility of novel approaches to rare diseases. Potential approaches to research in rare diseases could include but will not be limited to: identification of molecular targets for rare diseases; development of models (vertebrate, invertebrate, computational); development of micro arrays and tissue micro arrays which are applicable to screening or detection of rare diseases; development of tools for drug discovery (e.g. development of assays for screening compounds); and clinical trials. Contact: Dr. Rashmi Gopal-Srivastava, 301-402-4336, gopalr@mail.nih.gov **15-OD(ORDR)-102* Collaborative translational research platform for rare diseases.** Create a collaborative platform by disease area to allow researchers to create virtual project teams, update status reports, collaboratively score targets and nominate molecules for screening. Having these data in a centralized, common system should reduce redundancy and potentially identify non-obvious associations of research across the rare disease spectrum. Contact: Dr. Rashmi Gopal-Srivastava, 301-402-4336, gopalr@mail.nih.gov **15-RR-101* Applied translational technology development.** This program will support two-year applied translational projects to move advanced technologies from the prototype stage into the clinic. Novel, cost-effective tools for clinical care or clinical research will be modified, hardened, and tested. Interdisciplinary teams of technology developers, basic researchers and clinicians will address scientific and engineering problems associated with clinical applications of new technologies. Contact: Dr. Douglas Sheeley, 301-594-9762, sheeleyd@mail.nih.gov; NIDA Contact: Dr. Kris Bough, 301-443-9800, boughk@mail.nih.gov **15-TW-101* Models to predict health effects of climate change**. Quantitative and predictive models of effects of climate change on disease burden and health outcomes are needed. Approaches may include statistical, spatial or other modeling methods to quantify the current impacts of climate on a diversity of communicable or non-communicable diseases, or project impacts of different climate and socio-economic scenarios on health.

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	For example, new and innovative approaches to develop projections of changes in disease burden in specific regions or populations will facilitate public health planning. Existing databases on population and environmental variables, such as air quality and climatologic episodes should be used to test the utility of these models where possible. Contact: Dr. Joshua Rosenthal, 301-496-1653, joshua_rosenthal@nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov; NHLBI Contact: Dr. Lawrence Fine, 301-435-0305, finel@nhlbi.nih.gov; NLM Contact: Dr. Valerie Florance, 301-594-4882, florancev@mail.nih.gov