Creating the Healthiest Generation

Precision Health

Using data science to improve health

Treating the Untreatable

Advancing new therapies to enhance brain, neuromuscular and mental health

Moonshot Proposal

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UFHealth
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UF Health Moonshot Proposal: Creating the Healthiest Generation

Overview

It has been projected that for the first time in two centuries, today's generation of American children may have a shorter life expectancy than their parents. Recent studies suggest American life expectancy has grown worse in just one generation. Inspired by the need to help reverse these trends, the UF Health moonshot proposal identifies strategic opportunities where UF is uniquely positioned to improve the health and well-being of the next generation. The UF Health Deans and Directors Research Council and the UF College of the Arts are pleased to submit a joint proposal developed in collaboration with the academic health center's leading research teams, and for which all six UF Health colleges have agreed to participate. The proposal highlights opportunities to advance high-impact research with the potential for significant impact on human health/One Health, and to differentiate UF Health as a regional and national health care leader. The proposal is organized by two thematic areas of strength, each with five to six moonshot thrusts that bridge basic discovery science with clinical and translational research. Further, the proposal will develop observational and interventional cohorts across the lifespan in which Florida's diverse communities can participate as partners and stakeholders in our moonshot goal. Following this overview are brief descriptions that summarize each thrust's scientific premise, expertise, and goals and markers of success.

Theme 1: Pioneering Precision Health Approaches to Understand, Treat and Prevent Disease and Disparities

Rapid technological advances have led to faster and cheaper means by which to gather and interrogate medical, biological, lifestyle, environmental and community data, enabling correlation of factors that lead to good health and well-being versus sickness and suffering. Our expectation is that through large cohort analyses and precision health approaches, we can improve patient care, health outcomes, and quality of life while reducing healthcare expenditures through fewer adverse events and more efficient healthcare utilization, thus leading to a healthier generation.

Our moonshot proposal presents an opportunity for UF to springboard to national leadership in precision health by building on our international leadership in genomic research and medicine and by leveraging the statewide OneFlorida Data Trust, which includes electronic health record and claims data for 15 million people. Through the development of infrastructure, tools and methods for precision health, we can better harness "big data" science to improve health for individuals and populations. We have identified six key areas with demonstrated excellence where moonshot resources can spur UF's national and international leadership in the precision health arena:

1. **Reengineering the Clinical Environment for Precision Medicine**
2. **Developing Advanced Data Capabilities for Precision Health**
3. **Understanding Resistance, Resilience and Repair across the Lifespan**
4. **Employing Precision Health Modalities to Advance Understanding of Inflammation and Immune Response**
5. **Confronting the Threat of Emerging Pathogens and Eliminating Hospital-Acquired Drug Resistant Infections**
6. **Fostering Innovation at the Intersection of Arts and Public Health**

Theme 2: Treating the Untreatable to Enhance Brain, Neuromuscular and Mental Health for Future Generations

Brain disease, in its many forms, is increasingly common—as is chronic pain. Both can compromise cognitive function and the body's ability to move. They can occur at any stage of life, from early childhood to adulthood, yet treatments are often inadequate or nonexistent. UF Health is home to prominent research teams uniquely positioned to tackle unmet medical needs associated with brain and neuromuscular disorders, ranging from rare diseases affecting children to chronic pain management to the ravages of aging.

This moonshot proposal highlights opportunities spanning the therapeutic pipeline, including discovery of therapeutic targets, development of new therapies and vaccines, and implementation of new clinical trials and approved treatments – ranging from gene, cell and immune therapies to deep brain stimulation. We have identified five specific areas in which UF Health researchers are poised to "bend the curve" and create a healthier future for the next generation:

7. **Establishing the Legacy Program in Brain Cancer at UF Health – Brain Tumor Immunotherapy Initiative**
8. **Developing the Next Generation of Treatments for Parkinson's Disease**
9. **Targeting Neuromuscular Health to Preserve Function across the Lifespan**
10. **Alleviating Pain, Suffering and Addiction**
11. **Creating the Florida Center of Excellence for Neurodevelopmental Disorders**

Colleges and Collaborators

This moonshot proposal is led by faculty spanning seven colleges—Arts, Dentistry, Medicine, Nursing, Pharmacy, Public Health and Health Professions, and Veterinary Medicine—plus the UF Health system including its animal hospitals, UF Health Shands and UF Health Jacksonville. In addition, the 11 thrusts involve established and developing collaborations spanning seven additional UF colleges—Agricultural and Life Sciences/ IFAS, Education, Engineering, Journalism and Communications, Liberal Arts and Sciences, Law, Health and Human Performance—as well as the UF Health Libraries and 26 centers and institutes:

- Center for Arts in Medicine
- Center for Autism and Related Disorders
- Center for Autonomic Neuroengineering
- Center for Exercise Science
- Center for Immunology and Transplantation
- Center for Inflammation and Mucosal Immunology
- Center for Molecular Microbiology
- Center for Neurogenetics
- Center for Pharmacogenomics
- Center for Respiratory Research and Rehabilitation
- Center for Translational Research in Neurodegenerative Disease
- Clinical and Translational Science Institute
- Diabetes Institute
- Emerging Pathogens Institute
- Fixel Center for Neurological Disease
- Genetics Institute
- Informatics Institute
- Institute for Child Health Policy
- Institute for Therapeutic Innovation
- Institute on Aging
- Interdisciplinary Center for Biotechnology Research
- McKnight Brain Institute
- Myology Institute
- One Health Center of Excellence
- Pain Research and Intervention Center of Excellence
- UF Health Cancer Center

The proposal also will engage state partners and collaborators outside of UF, including the OneFlorida Clinical Research Consortium and Florida Department of Health.

Operational Leaders

Office of the SVP for Health Affairs and UF Health Deans and Directors Research Council (DDRC), which includes: Mark Atkinson, Director, Diabetes Institute; Patrick Concannon, Director, Genetics Institute; Isabelle Garcia, Dean, College of Dentistry; Todd Golde, Director, McKnight Brain Institute; Leon Haley, Dean, College of Medicine-Jacksonville; Julie Johnson, Dean, College of Pharmacy; Jonathan Licht, Director, Cancer Center; James Lloyd, Dean, College of Veterinary Medicine; Anna McDaniel, Dean, College of Nursing; Glenn Morris, Director, Emerging Pathogens Institute; Marco Pahor, Director, Institute on Aging; Michael Perri, Dean, College of Public Health and Health Professions; Betsy Shenkman, Director, Institute for Child Health Policy, and Co-Director, Clinical and Translational Science Institute; Stephen Sugrue (chair), Acting Associate Vice President for Research, UF Health; and Adrian Tyndall, Dean, College of Medicine.

Budget, Resources Pledged and Prospects for Sustained Funding

We are requesting $2M/year for 3 years from the Moonshot initiative, and UF Health will provide a 1:1 match. We are hopeful that the Office of Research will also provide a similar match to help support this high-impact research. To advance the 11 areas above, teams have requested resources for three general types of activities: pilot projects to test feasibility and generate preliminary data, capacity building to strengthen infrastructure (e.g., personnel, equipment, data), and collaboration building to foster cross-college initiatives and national visibility (e.g., symposia, summits). Based on preliminary project budgets and needs, we anticipate that roughly 50% of the moonshot resources will be used for pilots, 40% for capacity building, and 10% for collaboration building. The DDRC will develop a process and criteria for recommending allocation of moonshot resources across the 11 areas in a manner that will maximize efficiency, collaboration and cross-college impact; and facilitate development of high-quality pilot projects that are scientifically rigorous and have clear pathways to sustainability. The SVP UF Health will make final funding decisions.

Each area has identified compelling opportunities for sustainable funding, including federal and other grant opportunities. In addition, both thematic areas have significant potential for patents, licensing and spinoff companies.

Theme 1: Pioneering Precision Health Approaches to Understand, Treat and Prevent Disease and Disparities

1. Reengineering the Clinical Environment for Precision Medicine

Scientific Premise: The UF Personalized Medicine Program was established to place UF in a leading role in genomic medicine and to document the impact of genetically guided care on patient outcomes. We have since implemented this approach in multiple settings across UF Health, including in Jacksonville, and we have shown in the setting of antiplatelet therapy this approach reduces death, stroke and heart attack, and in the setting of chronic pain reduces use of opioids and improves pain control, among other interesting findings. We now seek to move this research initiative to a transformative clinical practice initiative, to launch us from national/international leadership in precision medicine research to also be leaders in precision health. This will improve the lives of patients we serve, and become a market differentiator for UF Health. Patient demand is also high for this. Presently 10 million Americans have had direct-to-consumer genetic testing, with that number projected to be 100 million by 2021, with 60 million having had whole genome sequencing by 2025. In addition, in May 2018, the NIH kicked off the All of Us research program, an historic precision medicine initiative to gather health and life data from 1 million people, including full genome sequencing, and for which UF is collaborating with the University of Miami, Emory and Morehouse to lead the All of Us Southeast Enrollment Center. The moonshot goal (not achievable with the current funds available) is to develop approaches and clinical tools for incorporating genomic and other biomarker data, personal lifestyle and community information into clinical decision-making. This is expected to improve patient care, clinical outcomes, and patient satisfaction and reduce healthcare expenditures through reduced adverse events and healthcare utilization, thus leading to a healthier generation. Herein we propose incremental steps to initiate this moonshot.

Team Expertise: Currently this team involves members from Colleges of Pharmacy, Medicine, PHHP, Dentistry, Journalism, UF Health Hospitals (GNV and JAX), Faculty Group Practice, Center for Pharmacogenomics and ICBR with extension to Nursing, and roles for IFAS, Arts and Engineering. We have assembled an effective trans-college, multidisciplinary team that has been highly engaged since the program was created in 2011 as part of the Clinical and Translational Science Institute. Recent additions to the team of Sonja Rasmussen (former CDC leader), Alex Parker (former leader of Mayo JAX Precision Medicine Program) and others will facilitate plans to catapult to the next level.

Goals and Markers of Success:

<u>Goals to be achieved in one year</u>

- To implement chip-based (or genome-wide) pharmacogenetic and selected disease risk testing in targeted populations as part of routine care (including cardiothoracic surgery, and primary care settings in patients with common complex diseases);
- To create an IT infrastructure that fully supports the program, including clinical decision support tools for clinicians;
- To develop a plan to broadly educate the health care community about the precision medicine tools available and provide pharmacogenetics/common disease genetics consult services.

<u>3-5 year goals</u>

- To have precision approaches to care be well understood and accepted across the health system;
- To document improved healthcare utilization and health outcomes through precision medicine approaches;
- To expand tools used for precision care beyond those used in year one (e.g. other genetic data, other biomarkers, other types of data);
- To impact coverage decisions by Florida Medicare, GatorCare, and other major third party payers for precision medicine approaches;
- To have precision health recognized as one of the reasons people seek care at UF Health.

2. Developing Advanced Data Capabilities for Precision Health

Scientific Premise: Inequities in health, in the face of ever-increasing health care expenditures, remain one of the greatest challenges that the United States faces. Health care expenditures were $3.7 trillion in 2017 and are projected to reach $5.7 trillion or almost 20% of the US economy by 2026. Transdisciplinary science that focuses on integrating genomic and epigenetic information with clinical, environmental, and social determinants of health data is needed for new discoveries and better targeted interventions. In this regard, we are taking the broad view of precision public health including genomics as one of many data points and methods that need to be considered to improve the health of populations.

Our overall goal in this project concept is creation of the data and methodology infrastructure required to identify and implement such interventions. We propose to build from the OneFlorida initiative and its Data Trust. We will begin by enhancing the integration of electronic health record, tumor registry, claims, radiographic images, prescribing, pharmacy, vital statistics, mother/baby, environmental, census tract, residential history, and insurance/health care delivery system data within the Data Trust. Further, we will focus on improving semantic and pragmatic data integration for these data elements (sometimes also referred to as *interoperability*), and to make the data maximally explicit. Currently the OneFlorida Data Trust contains selected clinical and geospatial information on 15 million Floridians spanning from 2012 to the present and is refreshed monthly. The individuals with information in the Data Trust are diverse in terms of age, race, ethnicity, social vulnerability, place of residence, and health status, providing incredible opportunity to understand health and disease in the third largest state in the US.

To accomplish the envisioned data integration, we will develop and apply methods and informatics toolsets to link and layer environmental, economic, education, and other community/social data with the existing clinical data. We will build re-usable informatics tools that will enable this integration and layering. For example, we will create semantically powered data catalogs, associated semantic data integration tools, tools to help build computable eligibility criteria and computable phenotypes, and tools to facilitate recruitment planning and generalizability assessments. Second, we will continue the integration with subsets of patients for whom "omics" and radiographic information is available. For example, among individuals with cancer, genomic information is available for some. We will work with UF Health and our OneFlorida partners to identify patient populations where genetic tests and other "omics" and imaging data are available, such as patients with cancer, and incorporate the information into the Data Trust. The proposed data integration and development of advanced data capabilities and methodologies will unlock transformative opportunities for research teams to address compelling population health issues.

Team Expertise: UF has top talent in biomedical informatics, data science, public health, medicine, pharmacy, and others who could contribute to this initiative, including the UF Informatics Institute, One Health Center of Excellence and the UF Health Libraries. Through the UF Rising initiative, UF has attracted top talent in data science, including in the areas of interpretable machine learning and deep learning. These methods are being used by UF researchers to build predictive models to prevent, identify, treat, and assess health outcomes for various conditions, in conjunction with robust inference and reproducibility analysis. Thanks to the interdisciplinary team, we are able to add the *interpretability* dimension to overcome well-known trust issues with 'black-box' machine learning.

Moreover, few other US institutions have the community-based programs that UF has at the policy, neighborhood, and health system levels to act on disparities and implement precision health approaches. For example, the UF Cooperative Extension Service from IFAS could precisely target its programs to the neediest groups within each county.

Integrating diverse data and applying novel methodologies and tools to those data will enable the development of an integrated precision medicine and precision public health program. We can immediately leverage the OneFlorida Data Trust infrastructure to expand the data linkages, build additional informatics toolsets for accomplishing meaningful data integration, and develop and test deep learning and other methodologies. The integrated data and tools will allow for the development of more precise prevention and treatment approaches as part of an overall integrated precision health initiative.

Goals and Markers of Success:

<u>Short-term goals (Years 1 and 2)</u>

- Integrate clinical (including imaging), environmental, census tract, and residential history for over 15 million Floridians whose electronic health record and other clinical data reside in the OneFlorida Data Trust;

- Enhance the semantic and pragmatic interoperability of the data, that is the extent to which data have a common format and encoding, are maximally explicit, and there is a shared understanding of how the data can be used; and
- Apply advanced data capabilities and tools, particularly in the area of machine learning, to build predictive models for prevention, treatment, and health outcomes for two use cases.

Long term Goals (Years 3 through 5)

- Maintain and continue to enhance the data integration, which requires ongoing receipt, processing, linkage, and transformation of data;
- Develop precision health strategies for prevention and/or treatment using predictive modeling and apply them in relevant settings at UF Health, OneFlorida and their surrounding communities.
- Expand the use cases and corresponding strategies to enhance the integrated precision health initiative.

3. Understanding Resistance, Resilience and Repair Across the Lifespan

Scientific Premise: The idea of successful aging is embedded in our culture and more recently in the scientific literature. Simply put, humans are captivated by the notions of escaping the functional declines and diseases associated with aging and maximizing our health-span. Scientific progress in this area remains slow and is largely correlative in nature, not mechanistic. We have limited insight into why some individuals remain resistant to the effects of aging or why those who are resilient can successfully bounce back from illness as they age. Indeed, we too often focus on disease processes and not what keeps us healthy.

The maintenance of physical independence of older Americans has emerged as a major clinical and public health priority. A critical factor in an older person's ability to function independently in the community is mobility, i.e. the ability to move without assistance. Efficient and reliable locomotion is a fundamental feature of human functioning, and indeed functioning across virtually all animal species. Older persons who lose mobility are less likely to remain in the community, to maintain a high quality of life and to perform many activities needed to be fully independent, such as shopping and engaging in community activities. Those who lose mobility also have higher rates of morbidity and mortality, have more hospitalizations and experience a poorer quality of life. Our goals are to identify effective health interventions spanning from behavioral, to nutritional, biological, hormonal, and pharmacological that will have an immediate impact on public health, clinical practice, and ultimately on elders' lives. The Anti-Aging Rejuvenation Research and Implementation Center will allow us to achieve these goals.

We will identify factors associated with successful aging by phenotyping and genotyping individuals, largely in the state of Florida, comprised of a uniquely diverse and multi-generational cohort, including people who are 90 years of age or older, and are still in good physical and mental health. The scale (thousands of participants) and the diversity of the participants that we propose to study are key factors that will distinguish this effort from prior efforts. We already know that we have access to medical information on, and ability to contact, at least 100,000 Floridians. By collecting and mining medical data and linked biospecimens, we can evaluate factors including genetics, epigenetics, metabolism, immune function, environment, and lifestyle in order to understand how they associate with successful cognitive and physical function during aging. Because of the racial and ethnic diversity of the elderly population in the State of Florida, we can conduct these studies not just in the Caucasian population but also in Hispanic/Latino, African American and other underrepresented populations.

These studies will provide new, potentially actionable hypotheses regarding factors associated with successful aging. In a second phase, we will leverage these data to move beyond associative analyses and conduct discovery science to understand the mechanisms by which factors associated with successful aging increase health-span. These studies will help answer the questions of what make someone resistant or resilient to the effects of aging. In a final phase, we will translate this enhanced mechanistic understanding into interventions that promote the health span. Indeed, our ultimate goal is to help identify interventions that will promote the health span in the elderly.

The screening and identification of novel interventions to promote health and independence of older adults will set the stage for opportunities to successfully compete for NIH center grants (e.g. Roybal Behavioral Center for Translational Research on Aging, Nathan Shock Center for Excellence in Biology of Aging), and large multicenter clinical trials. This study will have numerous impacts. Large-scale cohort studies with linked biospecimens that

include an over-90 population would position UF to be a world leader in this space. These studies are of interest to the commercial sector where biotech companies are being launched to combat the effects of aging (e.g., https://www.calicolabs.com/). This will be a highly visible translational research program that can position us to remain competitive for NIH and other extramural funding for decades. Indeed, healthy and highly successful aging, age-associated diseases such as Alzheimer's disease, and many forms of cancers remain areas of increasing investment by the NIH. Finally, there are significant public health implications with potential for huge impacts on health care and costs in a vulnerable and rapidly growing population.

Team Expertise: UF is uniquely positioned to carry out these studies. The infrastructure built by the Clinical and Translational Science Institute (CTSI) including the OneFlorida Data Trust put UF in an exceptional position to mine information from electronic health records of >100,000 Floridians age 90 and over, and importantly, contact them to participate in this research effort. In addition, the Data Trust has electronic health record data for even more individuals between 80 and 89 years old who can be followed to assess resilience and successful aging in this aging group. All individuals with electronic health record data in the Data Trust are geocoded to their census tract, providing information about environmental and community context where these individuals reside. The State of Florida has among the fastest growing and highest prevalence of older populations in the nation. UF has unique strengths in areas related to aging and multimodal interventions across multiple colleges, centers, and institutes, as well as a wealth of industry and NIH-funded center grants (P30, U01, U24, R01, R21 grants) and clinical trials, such as among many others, the Pepper Center, the CTSI, the Resource Centers for Minority Aging Research (RCMAR), The LIFE Study, the Molecular Transducers of Physical Activity, the Testosterone Trial, the Oxytocin trial, The ENRGISE trial, the Jacksonville Aging Studies Center (JAX-ASCENT), the Biophytis trial (botanicals), and the Longeveron trial (stem cells). UF has all the rich substrate needed to successfully establish the Anti-Aging Rejuvenation Research and Implementation Center.

This "moonshot" coalesces strengths of UF research across multiple colleges, institutes and departments. These studies have buy-in from all UF Health colleges and many affiliated institutes (CTSI, MBI, Aging, Genetics, Diabetes). The Institutes leverage strength in numerous preexisting areas of research across the UF campus (e.g., Muscle Aging, Brain Aging, Alzheimer's Disease, Immunology, Genetics, Metabolism, Cancer, Clinical Research, Informatics, Minority Population Recruitment), and would enable us to build on these strengths in novel synergistic fashions.

Goals and Markers of Success:

Goals Year 1-2

- Assemble a working group who will define objective screening criteria to identify a "successful aging" cohort
- Define the screening battery, the data collection protocol, case report forms, manual of operations and procedures
- Set a data coordination center and web-based data collection system
- Set a central IRB and IRB approval for data collection at the pilot sites
- Train the field centers to the study operations
- Conduct a pilot on a representative sample of the One Florida Data Trust to assess the expected prevalence, participation, and sample size of a uniquely diverse and multi-generational cohort, including those who have "successfully aged"
- Conduct feasibility studies regarding participation in the study and willingness to provide biospecimens (DNA, blood, etc.)
- Plan and estimate resources and budget for the full-scale study

Goals Year 3-5

- Identify genetic and epigenetic factors associated with successful aging by performing the largest study of the genetics and epigenetics of successful aging in a diverse multi-generational cohort, thereby enabling i) discovery science aimed at providing mechanistic insight into how these factors protect from disease and loss of functionality during aging, and ii) development of novel therapeutics designed to promote successful aging
- Identify the baseline cohort and conduct cross-sectional analyses
- Conduct longitudinal follow-up for the outcomes of interest

- Conduct pilot prevention studies (behavioral, nutritional, hormonal, pharmaceutical) in the "successful aging" cohort to maintain mobility and physical and cognitive independence
- Conduct pilot intervention studies (behavioral, nutritional, hormonal, pharmaceutical) in the cohort which did not qualify for "successful aging" to improve mobility and physical and cognitive independence

4. Employing Precision Health Modalities to Advance Understanding of Inflammation and Immune Response

Scientific Premise: A substantial number of major human chronic diseases, including autoimmune disorders, vascular disease, cancer, sepsis, chronic viral infections, obesity, Alzheimer's, infections of the craniofacial complex, and type 1 and 2 diabetes (T1D and T2D) are directly caused or exacerbated by chronic inflammation and immune dysregulation, either at a systemic (sepsis, SLE) or local (cancer, arthritis, type 1 diabetes) tissue level. The socioeconomic impact of these diseases is collectively well over $500 billion annually. Chronic inflammation and immune dysfunction arise from the interaction of susceptibility genes and environmental factors that include microbes, chemicals, and nutritional states. Importantly, recent studies suggest that factors promoting the resolution of inflammation have a dramatic impact on health. Examples include the prevention of autoimmunity in predisposed subjects, facilitated resolution of chronic viral infections, reduced atherosclerosis, improvements in T2D care, and the promotion of immune responses to tumors. Therefore, developing genetic screening for susceptibility, assessing biomarkers for disease activity and for factors that promote health, and implementing specific methods to reduce the potential for inflammation (e.g., pharmaceutical, nutritional and other interventions applied early, and perhaps throughout life) would potentially limit the development of or markedly impact these diseases. The goal of this concept proposal is to: 1) characterize the inflammatory process within the microenvironment (e.g. systematic discovery of biomarkers concordant between tissues, serum and other body fluids); and 2) develop personalized approaches to identifying individuals at risk for disease using a combination of genomic, immunophenotyping, metabolomics, metagenomics/ metatranscriptomics, modelling, and other technologies. We propose to initiate this program by studying the microenvironment of inflammatory responses in pancreatic cancers and in pancreata from individuals with autoimmune type 1 diabetes (T1D) using the techniques described above. The rationale for choosing these two diseases involves an attempt to better understand in the same target organ the genetic and molecular mechanisms of opposite immune responses, pro-inflammatory destruction of islets in T1D and anti-inflammatory mechanisms allowing tumor growth in pancreatic cancer. This model may be extended to thyroid cancer and Hashimoto's disease. In addition, areas of primary interest to the UF College of Dentistry with considerable ongoing basic and translational research include periodontal diseases, head and neck cancer, dental caries, and compromised wound-healing, along with conditions with manifestations/complications in the oral cavity, e.g. diabetes. Over time, the concept group will coordinate basic, clinical and epidemiological studies in other diseases and harmonize campus resources to create a collective inflammation/immune regulation science program. The ultimate goal will be to develop clinical trials using personalized medicine approaches derived from understanding genetic contributions, environmental factors and molecular mechanisms of these diseases. We will also seek to train the next generation of health scientists, be they undergraduate, graduate, professional (MD, DMD, DVM, DNP, PharmD) students, or residents in these disciplines.

Team Expertise: The University of Florida (UF) has a substantial number of recognized experts in inflammation and immune dysregulation in several colleges, institutes, centers and individual disciplines including aging, cancer, cancer immunotherapy, inflammatory bowel disease, metabolomics, neuroscience, oral biology, periodontology, autoimmunity and sepsis, just to name a few. We also have substantial expertise in immunogenetics, virology, epidemiology, the human microbiome and human nutrition to further develop inflammation science on campus, with the goal of using this knowledge to effectively control this process. This project will include faculty from the UFCC, College of Medicine, College of Dentistry, Genetics Institute, Diabetes Institute, CIMI, CIT, Departments of Surgery, Medicine, Pathology, and Pediatrics.

Goals and Markers of Success:

<u>Near-term goals (12 months)</u>

- To develop an effective interactive research team in the fields of inflammation/immune regulation that expands precision medicine capabilities integrated with the EMR that together will maximize UF's

opportunities to characterize disease mechanisms and provide new therapeutic approaches to prevent and treat pancreatic cancer and autoimmune type 1 diabetes.

Long-term goals (3-5 years)

- Create a nationally recognized program in inflammation/immune regulation to include collaborations focused on additional human and animal inflammatory diseases, to be selected from obesity/ type 2 diabetes, dementia, aging, cardiovascular diseases, oral infectious diseases, etc. The goals of this program will be to:
  - Use precision medicine approaches coupled with the EMR and develop validated biomarkers to identify individuals at risk for inflammatory diseases and immune dysfunction with an aim to prevent disease.
  - Develop a nutrigenomics program to investigate the effects of food production, nutritional factors, and weight loss on inflammation.
  - Interface with Precision Health moonshot projects 1 and 2 (Reengineering the Clinical Environment, Developing Advanced Data Capabilities) to expand the research infrastructure to support multi-layered precision medicine assessments and requisite biomedical informatics.
  - Work towards gaining support from UF Health and 3rd party insurance programs to integrate precision medicine best practices established in this program for the prevention and treatment of human diseases.

5. Confronting the Threat of Emerging Pathogens and Eliminating Hospital-Acquired Drug Resistant Infections

Scientific Premise: Antibiotic resistance in healthcare settings is a significant threat to public health. Because almost all Americans will receive care in, or be a visitor at, a medical setting at some point, antimicrobial resistance threatens everyone. Antimicrobial resistance has become of major concern in the setting of modern, highly complex medical care, particularly for patients who are immunosuppressed or undergoing complex surgical procedures. Resistance to antimicrobial drugs occurs in viruses, bacteria, fungi, and parasites as a natural and unavoidable manifestation of their evolutionary capabilities. The ongoing decline in effectiveness of existing antimicrobial drugs is a consequence of complex interactions among natural selection, environment, and patterns of drug use and misuse/overuse. As a result, antimicrobial resistance has developed into a global public health issue, with emergence of microbes that defy treatment with commonly available therapeutic agents. We propose to develop a three-pronged strategy that will investigate the best ways to **prevent, treat, and implement interventions** to reduce the threat to the health and well-being of our patients from drug-resistant organisms.

We will strengthen research into the molecular basis for and molecular testing of emerging drug resistance to better characterize the ways in which resistant microorganisms emerge and are transmitted. We also will explore ways in which environmental factors impinge on emergence of resistance, in both the healthcare environment and the community. We will then intensify research and development of new therapeutics and vaccines, first-in-class drugs, and new combination therapies for treatment of infections resistant to “traditional” antimicrobials. Implementation will be achieved by investigating ideal interventions to reduce inappropriate antibiotic usage in inpatient settings and lower colonization and infection rates with resistant microorganisms of hospitalized patients.

Team Expertise: UF Emerging Pathogens Institute, UF Institute for Therapeutic Innovation, UF One Health Center of Excellence, Colleges of Medicine, Pharmacy, the College of Dentistry’s Department of Oral Biology, Public Health and Health Professions, Veterinary Medicine, and Nursing, Shands Hospital, Florida Department of Health. The Emerging Pathogens Institute, together with collaborating Centers and Institutes, is the focal point of many of the team members scattered throughout all of the colleges and partners mentioned above. The investigators involved have a long track record of success as individuals and teams of investigators in funding, publishing and bringing innovations to market. This initiative will focus that expertise on a specific problem on which many are working individually now.

Goals and Markers of Success:

Near-term Goals (12 months)

- To merge fundamental molecular pathogenesis research with molecular epidemiologic techniques (including whole genome sequencing) and incorporate into ongoing surveillance activities for antimicrobial-resistant microorganisms at UF Health, to optimize our ability to understand pathways by which resistant strains and resistance genes enter and are spread within medical facilities;

- To create and implement innovative strategies to further limit inappropriate use of antimicrobial drugs ("antimicrobial stewardship") in both inpatient and outpatient settings at UF Health, and put in place programs to monitor the outcomes of these strategies; and
- To systematically expand the programs for the identification of new drug compounds and/or drug combinations active against key resistance pathways, taking advantage of novel approaches being developed in the UF Institute for Therapeutic Innovation and the UF College of Pharmacy.

Long-term Goals (3-5 years)

- To identify primary routes of movement of resistant microorganisms into and within the healthcare system, and concomitantly reduce inappropriate antibiotic usage by 50% in outpatient settings and by 20% in inpatient settings;
- To achieve lower colonization and infection rates with resistant microorganisms at UF Health to levels consistently below national benchmarks for hospitalized patients, and develop strategies to share these approaches with other medical institutions at a national level;
- To develop new and innovative compounds and strategies for treatment of resistant microorganisms in both inpatient and outpatient settings.

We will submit NIH and/or CDC grants to provide continuing funding for studies and interventions in areas showing the greatest promise in control of antimicrobial resistance.

6. Fostering Innovation at the Intersection of Arts and Public Health

Scientific Premise: Over the past several decades, evidence has mounted to demonstrate that the arts and culture have measurable impacts on health and wellbeing. Today, innovation is taking root at the intersections of arts and public health throughout the nation. Creating Healthy Communities: Arts + Public Health in America has emerged as a national initiative designed to accelerate this innovation to build healthy communities in alignment with national public health goals through strategic cross-sector collaboration, research and translation. The initiative engages a comprehensive agenda – including research, collaboration, publication and mass communication – to drive significant advancements in precision health and public health through evidence-based use of the arts. Through it, precision health approaches utilizing individual differences to drive treatment will be unified with the ability to influence individual behaviors and lifestyle choices.

Inclusion of the Creating Healthy Communities: Arts + Public Health in America initiative in the Creating the Healthiest Generation proposal allows integration of the arts into several of the proposed moonshot projects. For example, the Center's ongoing randomized control trial of the impacts of live preferential music on opioid use in emergency and trauma care, in partnership with the Department of Emergency Medicine, has shown significant phase-two results and could contribute to the Alleviating Pain, Suffering and Addiction project. Likewise, arts participation has been shown to enhance symptom management, reduce primary care visits, and improve health and wellbeing among older adults, and could contribute to the understanding of resilience in the 90+ generation. The Creating Healthy Communities initiative includes research aimed at further documenting these impacts, thus contributing significantly to the moonshot goal.

Team Expertise: The Center for Arts in Medicine is recognized internationally as a pre-eminent force at the intersection of the arts and health. For over two decades, the Center has driven education, training, and professional standards for practice that have made the arts integral to care in over half of hospitals in the US. ArtPlace America recently awarded the Center $780,000 to lead a national initiative to accelerate the integration of the arts into public health. We have assembled a team of faculty, researchers, scholars and staff who are recognized leaders in the field, and have an Interdisciplinary Research Lab of 30 members (faculty, staff and students) dedicated to the project. Colleges and partners involved include the UF Center for Arts in Medicine, UF College of Public Health and Health Professions, ArtPlace America, Alliance for Arts in Research Universities, Georgetown University, Johns Hopkins University, and National Alliance for Arts in Health.

The College of Public Health and Health Professions is already a partner in the Creating Healthy Communities: Arts + Public Health in America initiative, and will be hosting a collision event in November to invite collaboration in the initiative among arts, public health and other faculty on campus. Inclusion of this highly visible national initiative

in the Creating the Healthiest Generation proposal engages health sciences faculty in the initiative's consortium, publications and national public health policy discussions, further establishing UF's leadership in engaging innovative interdisciplinary approaches for improving human health.

Goals and Markers of Success:

Short Term Goals

- Add two PHHP faculty investigators to our core research and publication team
- Host a national Creating Precision Health: Harnessing the Arts for Community Engagement and Behavior Change conference at UF to present research findings, best practice models, and an evidence-based framework for using the arts to address social determinants of health and behavior change in Precision Health.

Long Term Goals

- Development of a national Arts + Public Health Consortium Network with 500+ members
- Inclusion of the arts or arts-based program models in national precision health and public health practice recommendations
- Inclusion of the arts in national precision health and public health policy documents
- The development of funding opportunities supporting use of the arts in precision health and public health by major funding bodies, including the National Endowment for the Arts, the NIH, and major foundations
- Inclusion of arts-related tracks or topic areas in major precision health and public health conferences

Theme 2: Treating the Untreatable to Enhance Brain, Neuromuscular and Mental Health for Future Generations

7. Establishing the Legacy Program in Brain Cancer at UF Health – Brain Tumor Immunotherapy Initiative

Scientific Premise: The focus of the Legacy Program in Brain Cancer is to catalyze the development of safe and effective treatments for children and adults with brain tumors by enlisting the power and specificity of the immune system. This objective will be achieved through a sustained collaborative research initiative that leverages recent advances in cancer genetics, machine-based learning, nanotechnology, and cancer immunology to rapidly translate new discoveries into first-in-human clinical trials. Importantly, we also have the objective of advancing already promising early-stage brain tumor immunotherapies, developed by UF investigators, into larger and more definitive phase 2 clinical trials. As such, we seek to build upon a remarkable foundation of successful clinical investigation in brain tumor patients in order to maximize the potential for impactful and durable treatment outcomes. Towards that end, the Legacy Program in Brain Cancer has two overriding specific aims: to advance promising early-stage immunotherapy treatments for refractory brain tumors through completion of more definitive phase 2 clinical trials; and to identify mechanisms of failure during immunotherapy treatment of malignant brain tumors and develop novel strategies to overcome treatment resistance.

Team Expertise: Our program leverages the strengths of leading investigators within many UF colleges and departments to bring to bear unique expertise and capabilities against our translational research objectives. Neurosurgery leads include Duane Mitchell, Catherine Flores, Elias Sayour, Jianping Huang, David Tran, Maryam Rahman. Current and actively engaged collaborators include Greg Sawyer (Engineering), Jon Dobson (Engineering), John Wingard (BMT), Biljana Horn (BMT), Carlos Rinaldi (Chem Engineering), Chenglong Li (Chemistry), Chris Xing (Chemistry), Rowan Milner (Vet Med), Hendrick Leusch (Chemistry), Jeffrey Harrison (Pharmacology), Todd Golde (Neuroscience). Additionally, we are leading multi-institutional collaborations with leading brain tumor centers throughout the United States (i.e. Duke University, Children's National Medical Center, Children's Hospital Los Angeles, MD Anderson Cancer Center, Dana Farber Cancer Research Institute).

Goals and Markers of Success:

The Legacy Program consists of four main UF investigator-led translational research projects organized within the framework of a NIH Specialized Program of Research Excellence (SPORE) in Brain Cancer. We believe these projects have the greatest potential for near-term significant and lasting impact in the clinical arena:

- **Project 1:** Adoptive cellular therapy targeting cancer neoantigens
- **Project 2:** Stem cell immunomodulatory therapy for refractory brain tumors
- **Project 3:** Targeting myeloid suppressor cells within malignant gliomas
- **Project 4:** RNA-nanoparticle vaccines for pediatric brain tumors

In addition to these four main projects, we currently have a number of developing immunotherapy initiatives with strong potential to grow into fully translational research programs culminating in investigator-initiated clinical trials. These include: Engineering and molecular imaging of CD70-specific CAR T cells, Machine-based learning to identify master regulators of cancer, Next generation dendritic cell vaccines for glioblastoma, Adoptive cellular therapy targeting metastatic brain tumors and AAV-delivery of immune modulatory agents to brain tumors.

8. Developing the Next Generation of Treatments for Parkinson's Disease

Scientific Premise: The single greatest treatment advance in Parkinson's disease since the introduction of dopamine pills has been deep brain stimulation. UF has been emerging as one of the top centers in the world for next generation deep brain stimulation. Clinicians and researchers from the Fixel Center for Neurological Diseases have pioneered new deep brain stimulation approaches and devices including a technology called adaptive deep brain stimulation. This approach identifies electrical biomarkers in the brain. These biomarkers are automatically matched to clinically disabling disease symptoms (e.g. tremor, rigidity, slowness, walking issues). The device(s) can be trained to deliver pulses to the brain to treat the symptoms of the disease in real time before the symptoms emerge as disabling for a patient. This moonshot proposal will add the exciting possibility of stimulating specific cell types to maximize benefits and limit side effects through the use of a technique called optogenetics.

Similar to deep brain stimulation, gene therapies and immunotherapies are a promising next generation approach for the treatment of Parkinson's disease. In simple terms, delivery of a gene to the brain, editing the human genome or harnessing the power of the immune system to target pathological protein deposition in the brain has great potential to treat disabling symptoms or to slow disease progression in Parkinson's and neurodegenerative diseases.

This moonshot proposal will build programs in next generation Parkinson's therapies. We will assemble the current multi-departmental and college talent, but also recruit key scientists to lift us to the next level. The moonshot will aim to provide a surge in the areas of adaptive deep brain stimulation, optogenetics, gene therapy, gene editing and in vaccine development. This surge will include recruitment of one or two key scientists.

Team Expertise: Our group is a few investigators short of transforming into the top neuromodulation clinical and research group in the world. Drs. Okun, Ramirez-Zamora, Almedia, Shukla, Hess and Deeb together make the largest single group of clinical and clinical research neurologists in the country focused on Parkinson's disease and neuromodulation. Dr. Foote is one of the world's top DBS neurosurgeons and is now one of the busiest and most sought-after DBS surgeons in the nation. The group also has a concentration of neuromodulation related researchers in biomedical engineering (Otto, Oweiss, Gunduz, Principe, Judy), neuropsychology (Price, Bowers, Bauer), psychiatry (Ward, Carr), speech and swallowing (Hegland, Plowman, Humbert), gait, occupational therapy and balance (Hass, Ferris, Seidler). The Fixel Center also has a large dedicated group of rehabilitation specialists covering all clinical areas (physical, occupational, speech therapy, nutrition, social work). UF has also been developing a footprint (drawn from the departments of neuroscience, pediatrics and medicine) in optogenetics (Setlow, Bizon), gene therapy/editing (Golde, Byrne, Rodriguez-Lebron, Licht), and immunotherapies (Mitchell, Flores, Vedam-Mai).

The Fixel Center is a multi-departmental (10 departments), multi-college (6 colleges) and multi-institute (Brain, Genetics, Cancer) entity that provides an ideal environment for development of next generation therapies in Parkinson's disease. The Departments of Neuroscience and Neurology rank 3rd among public universities in NIH funding. The Fixel Investigators garnered $36 million in recent NIH and foundation funding.

Goals and Markers of Success:

<u>Near Term Goal (12 months)</u>

- We will design the pilot studies necessary to move to first-in-human trials for next generation Parkinson's disease therapies.

<u>Long Term Goal (3-5 years)</u>

- We will make strategic recruitments and execute the first-in-human trials necessary for next generation Parkinson's disease therapies within the next 36-60 months, and we will apply and become a NIH Udall Parkinson Center.

9. Targeting Neuromuscular Health to Preserve Function Across the Lifespan

Scientific Premise: We often take our ability to both move and think for granted. Only when we, or someone close to us, suffers an injury or is affected by a disease that affects our cognitive abilities or our ability to move do we realize how much impairment in either of these interconnected functions dramatically reduce quality of life. Whether it is a loss of brain function due to head injury, stroke, Alzheimer's disease, Parkinson's disease or less common neurodegenerative disorders, or an impediment in movement due to spinal cord injury, inherited neuromuscular disorder, or age-associated loss of muscle function, there is often little the medical community can offer. Indeed, despite huge advances in understanding the root cause of many of these disorders, development of effective treatment strategies that benefit patients has lagged. Further, even with the promise of regenerative medicine, for acute injuries our current paradigms are to try to save what is there, prevent any ongoing damage, and then hope that extensive rehabilitation will lead to some functional improvement.

There is hope. We are now enabled by a better understanding of the underlying disease processes, more predictive disease and injury models, and better biomarkers to track the disease or injury process. Further, we are on the cusp of a whole new generation of biologic, cellular and gene-based therapies.

We propose to develop a more predictive translational road map to ensure that efforts from basic science to clinical trial design are capable of meeting the challenge of developing therapies for currently untreatable brain and neuromuscular disorders. This road map will address both knowledge and technology gaps necessary to make these advances. With its leadership in neurodegenerative and neuromuscular diseases, acute brain and spinal cord injury, muscle biology, exercise/rehabilitation, imaging and aging, UF can lead the field in finding solutions to preserve brain function, neuromuscular health, and mobility throughout the lifespan. Indeed, UF is exceptionally well positioned to identify unique targets and develop innovative therapeutic strategies to restore and maintain brain health, tackle neuromuscular diseases, and improve mobility, with highly productive interdisciplinary collaborations across UF Health, Engineering and HHP.

Our goal is to change lexicon regarding select brain and neuromuscular disorders from untreatable, incurable, and inevitable to a new reality in which these disorders are treatable, curable and preventable. This UF-wide initiative will be devoted to finding the cures needed to restore health in those with devastating childhood and adult disorders that attack the brain, spinal cord and muscle, and the toll of age that compromises brain and muscle function in the elderly. This proposal will include basic scientists, engineers and clinical researchers with established NIH funding records, substantial existing infrastructure, and international visibility and leadership. We are specifically requesting "moonshot" funding to create novel new partnerships that have the potential to have a transformative impact in the field of neuromuscular health, lead to additional funding from both NIH and industry, and enhance the visibility of UF.

Team Expertise: UF has tremendous strength in brain, spinal cord and muscle research across the campus. The faculty in these areas are already highly collaborative, and work in a programmatic and interdisciplinary fashion. Especially in the area of disease models, gene therapies, physical rehabilitation and magnetic resonance imaging biomarkers, we are world-class.

These efforts would include faculty and staff from Colleges of Medicine, Public Health and Health Professions, Veterinary Medicine, Engineering, and Health and Human Performance. Key research centers at the heart of this initiative include the McKnight Brain Institute, the Myology Institute, the Center for Translational Research in Neurodegenerative Disease, the Center for Respiratory Research and Rehabilitation, the Center for Exercise Science, the Movement Disorders Center, the Powell Gene Therapy Center, and the fledgling Center for Autonomic Neuroengineering. To state it simply, there are few, if any, institutions in the world that can match the collective strength of the University of Florida in this area.

Goals and Markers of Success:

<u>1 year goal</u>

- Establish at least 5 new and highly innovative research projects to identify or advance novel interventions addressing some of the most challenging brain and neuromuscular disorders.

3 year goal

- Obtain NIH funding supporting 3-4 new research consortiums targeting novel interventions addressing some of the most challenging brain and neuromuscular disorders.

5 year goal

- 5 or more novel interventions identified, extramurally funded and advancing towards clinical trials.

10. Alleviating Pain, Suffering, and Addiction

Scientific Premise: Approximately 100 million Americans suffer from chronic pain, which is the number one cause of adult disability in the US, and an additional 50 million have surgery each year, which leads to acute pain that often transitions to chronic pain and/or opioid misuse. Each year, 200 million prescriptions are written for opioids, a rate that has tripled in 20 years. Deaths from prescription opioids, heroin and illicit synthetic opioids have surpassed traffic accident death rates, and opioid overdose deaths have been identified as an important factor in the recent declines in life expectancy. By Executive Order, the White House declared the opioid crisis a national emergency. To promote further action, NIH Director Dr. Francis Collins and NIDA Director Dr. Nora Volkow jointly published a special report in The New England Journal of Medicine entitled, "The Role of Science in Addressing the Opioid Crisis," and NIH is adding $500 million in funding annually to address pain and addiction. Not to be forgotten is the unmitigated cost of the abuse of other pharmacological classes including nicotine, cannabis, alcohol, stimulants, and benzodiazepines. To promote the "Healthiest Generation," our UF faculty team is taking bold, interdisciplinary and cross-college action to catalyze discoveries that will lead to more effective pain and addiction management strategies. If left unchecked, the opioid crisis will overburden the health of future generations. We have branded our effort the UF Center for Research to Investigate Substance Use and Pain (UF-CRISP), and we are currently submitting an NIH National Institute on Drug Abuse (NIDA) Center of Excellence grant. We will create new and innovative directions of research focused around the complex interactions of chronic pain and substance use, employing a community-to-bench and then back-to-community approach, enhancing our existing and robust "Substance Abuse Research Bench to Community" effort. We seek moonshot funding to address this critical issue for the health and well-being of the population and to jump-start the UF-CRISP center, broaden its focus to engage more stakeholders, and help ensure that successful NIH funding follows, with the goal of improving national health, pain management and addiction treatment.

Team Expertise: Key personnel for this project arise from multiple UF colleges. A non-inclusive list of leaders in these areas is: Pharmacy (McCurdy, McMahon, Avery, Turgeon, Stephan Schmidt, Winterstein, Peris, Cavallari), Dentistry (Fillingim), Medicine (Setlow, Nixon, Tighe, de Kloet, Parvatenini, Siegfried Schmidt), Public Health and Health Professions (Cottler, Cook, Robinson, Boissoneault, Bishop), Nursing (Wilke, Lyon, Horgas), CLAS (Daniels, Ebner, Grenning, Knackstedt, Moradi, Roitberg, Schwendt, Yost), Engineering (Judy). A substantial portion of this group has met twice monthly for over one year to create a P30 grant proposal to be submitted September 26, 2018, under PAR-18-225, NIDA Core "Center of Excellence" Grant Program. That team identified a need for additional clinical scientists with expertise in pain and addiction research and treatment. The proposed moonshot funding will jump-start the center and allow quick engagement of a larger portion of the UF pain and addiction community into the center. The goal will be to solidify the participation of existing UF drug abuse researchers in the UF-CRISP mission, and attract other UF researchers not primarily focused on pain and drug abuse research who can expand and complement the goals of UF-CRISP.

Goals and Markers of Success:

Short-term Goals

- NIH P30 funded July 2019, or if not funded then resubmission in September 2019 and funding July 2020.
- Steering committee meeting/retreat of existing UF center faculty, interested UF faculty and stakeholders, and 3 external advisers of the nation's best addiction/pain scientists.
- Southeastern US regional pain/addiction summit/conference to engage other state universities in Florida and beyond.

- Monthly UF-wide pain/addiction seminar series to attract international experts.
- New cross-college, multi-PI NIH R01 *submissions* resulting from pilot projects and/or new collaborations that arose from center.

Long-term Goals

- Newly *funded* cross-college, multi-PI NIH R01 projects and P01 projects.
- New drugs discovered, including non-opioid approaches, for pain and addiction management.
- Improved clinical management of pain and addiction to alleviate pain, suffering and addiction.
- All of these advances will be the basis for successful P30 center renewal.

11. Creating the Florida Center of Excellence for Neurodevelopmental Disorders

Scientific Premise: Neurodevelopmental disorders represent one of our greatest challenges in the arena of childhood wellbeing in the 21st century. This group of disorders include any impairment that arises due to a disruption in the growth and development of the central nervous system, or brain. Likely, the neurodevelopmental disorder most recognized by the public at present is autism spectrum disorder, which itself represents a range and variety of disorders from ones that mildly influence a child's development to severe disorders that prohibit a child from ever functioning independently in society. However, other impairments that can be categorized as neurodevelopmental disorders include dyslexia, language impairments, fragile X syndrome, sensory disorders, attention deficit disorder, and fetal alcohol spectrum disorder.

Whether the incidence of these disorders is genuinely on the rise or our ability to recognize and diagnose them has simply been honed can be debated, but is largely irrelevant to addressing the problem. Now that we are so keenly aware of these disorders of the central nervous system, we are compelled to address them in a comprehensive manner in order to design more effective intervention strategies.

The causes of neurodevelopmental disorders are myriad. The development of the central nervous system is controlled by tightly regulated and timed gene expression that is influenced by input from the environment. Causes of neurodevelopmental disorders include: genetic anomalies; prenatal and perinatal viral agents that can infiltrate the genetic code held in a cell's nucleus; prenatal bacterial infections, such as congenital syphilis; prenatal and perinatal toxins, including alcohol and lead; experiential deprivation, as frequently accompanies childhood poverty; and disruptions in appropriately timed sensory inputs, as happens in sensorineural or conductive hearing loss, including ear infections.

Team Expertise: Given the broad array of causal agents, it is imperative that an interdisciplinary team addresses the problem. The University of Florida is uniquely positioned to house a center on neurodevelopmental disorders. One reason is simply the large and diverse population of the state. Building on models of state-wide extension programs that have been pioneered by IFAS, we would establish programs across the state to collect data from large cohorts in a consistent manner, provide in-service training to clinicians and teachers who work with these children, and establish model programs of education and teaching.

Another reason the University of Florida is uniquely positioned to explore the causes of neurodevelopmental disorders and design more effective interventions involves the faculty who are present. These faculty come from: the Department of *Environmental and Global Health*, where there is ongoing work on viruses such as Zika; *Pediatrics*, where clinical faculty are already designing a state-of-the-art intervention program for children on the autism spectrum; the *Center for Autism and Related Disorders*, which also already provides services to children on the autism spectrum; the *Psychology* department, where faculty study Applied Behavior Analysis as a treatment for children on the autism spectrum; the *College of Education* where faculty are part of the Anita Zucker Center in Early Childhood Studies, so can contribute to the development of interventions; *Speech, Language, and Hearing Sciences* where faculty are exploring the influences of sensory (hearing) disorders on development of the central nervous system; the *College of Nursing*, where faculty have had PCORI funding to study autism; and finally, the *Levin College of Law* of the University of Florida where faculty are engaged in efforts to influence policy decisions regarding interventions for children and their families.

Thus, this moonshot proposal is that we develop an integrated Center of Excellence to explore the causes of neurodevelopmental disorders, design more effective intervention strategies, and implement policies and model

facilities to ensure that affected children and their families have access to the services they require. Support could be expected from NIH agencies, such as the National Institute on Child Health and Human Development, as well as private donors with an interest in childhood wellbeing.

Goals and Markers of Success:

One-year Goals

- Convene a meeting of faculty at the University of Florida who have agreed to be involved in this center to discuss specific aims, division of labor, and future directions.
- Develop an advisory board consisting of faculty members and stakeholders from the statewide community, such as individuals with neurodevelopmental disorders (ND), professionals elsewhere serving individuals with ND, and parents of children with ND.
- Establish an administrative infrastructure, consisting of a team leader, clinical and research coordinators, and administrative staff.
- Advertise and begin hiring new researchers and clinicians.
- Purchase the equipment and materials needed to achieve our goals.
- With the help of IFAS staff, develop the statewide network of collaborators needed to recruit clients and research participants.

Three- to Five-Year Goals

- Develop a self-sustaining clinical facility that provides comprehensive, interdisciplinary evaluations, as well as intervention services to children with ND and their families.
- Develop a system of evaluating treatment strategies.
- Establish a statewide network for disseminating outcomes of treatment studies, and providing in-service training.
- Obtain funding from the National Institutes of Health and other agencies, as appropriate, to support research efforts.
- Develop a training program for University of Florida students in research and clinical professions.
- Build a distance-learning program to disseminate treatment strategies to professionals unable to attend in-service training sessions at satellite locations.