

Translating Duke Health



Accelerating discovery and its translation



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Biomedical discovery is accelerating innovative and revolutionary advancements in our understanding of human biology, health and health care. The rapid proliferation of bioinformatics technologies and tools is opening doors to a depth of research potential unimaginable even a decade ago.

We meet this moment of unprecedented promise with the creation of Translating Duke Health, a multiyear, multidisciplinary program designed to capitalize on our collective strengths in research, clinical care and population health to address major health challenges. Translating Duke Health is one of the major endeavors animating *Advancing Health Together*, the 2016-2020 strategic planning framework, which

asserts that Duke Health is uniquely positioned to accelerate discovery and its translation, to deliver tomorrow's health care today, and to build healthy communities.

Translating Duke Health is a platform of resources – including people, services, technology, infrastructure and funding – focusing on areas where Duke Health can have the greatest impact on transformative treatments and prevention strategies. This, in turn, will accelerate and energize an enhanced environment of partnership and integration among the scientific, clinical, population health, big data science and computing communities across Duke.

Translating Duke Health is principally sponsored by the Duke University School of Medicine and the Duke University Health System, in collaboration with other Duke entities. This endeavor focuses initially on five opportunities selected by convening groups, which included representatives from across Duke.

- Preserving and restoring cardiovascular health
- Enhancing brain resilience and repair in brain disorders
- Ending disease where it begins
- Controlling the immune system
- Combatting solid tumor brain metastases

All five programs will seek to generate additional support and funding from a variety of sources to enable sustained discovery, translation and public benefit.

Duke Health's decades-long tradition of innovation, excellence and impact has positioned us to continue to lead in this time of transformational capabilities and potential. We believe Translating Duke Health will sustain Duke as a national and international leader in key groundbreaking areas of biomedical science and health care with broad impact on the health of people worldwide for many years to come.

Keeping the heart young

Cardiovascular diseases remain the most common cause of morbidity and mortality across the globe. While these diseases are distinct in their clinical manifestations, they have common biologic underpinnings and public health implications. To date, research and clinical care focused on active disease have led to a remarkable reduction in cardiovascular mortality over the last 30 years.

However, cardiovascular research has failed to embrace the extraordinary potential to improve individual and public health by preventing disease and preserving health. The need for this refocus is demonstrated by the persistent high prevalence of heart disease and associated significant morbidity despite reductions in mortality.

Our work will seek to understand the molecular machinery driving robustness, resilience and rejuvenation of heart tissue.

We will explore how to integrate and deploy this knowledge, develop action tools and strategies to apply it, and generate proof that doing so will improve cardiovascular health for individuals and advance population health.

Within Translating Duke Health, we will undertake a program of discovery to further elucidate the underlying biology, reveal actionable information such as biomarkers or imaging, and devise, implement and test effective tools and strategies to preserve and restore cardiovascular health for individuals and populations.

Globally, our work will inform future research and clinical trials in cardiovascular health by connecting individual phenotype/genotype information with prevention of disease across populations. Through dissemination of our research results and best practices, we anticipate changing cardiovascular care delivery and improving health for people worldwide.

Every 60 seconds
someone in the
United States dies
from a heart
disease-related event.



Cardiovascular Health

Problem: Cardiovascular disease is the most common cause of death worldwide.

Solution: Preserve cardiovascular health, enhance resistance to cardiovascular disease, and improve recovery and rejuvenation.

Impact: Improved health across populations, better quality of life for people and a new model for cardiovascular care applicable worldwide.



Brain resilience and repair

Brain disorders pose a daunting personal, societal and financial burden for people and their families around the globe.

Current research approaches have focused on identifying and studying pharmacological targets and therapies. Yet, critical opportunities exist for innovative exploration of the potential impact that could be achieved with a blend of behavioral, electrical, surgical and pharmacological strategies.

Our work with Translating Duke Health is based on the premise that effective interventions and eventually cures will emerge only from the critical knowledge gained as a result of a greater, deeper and disciplined scientific inquiry into the basic biology of the brain alongside studies of disease mechanisms in brain disorders.

Ultimately, we believe effective multimodal and therapeutic approaches to brain disorders must fundamentally enhance

neuroplasticity and brain resilience. We must detect and forestall underlying disease processes prior to the onset of symptoms in diseases such as Alzheimer's, Parkinson's and other neurodegenerative disorders and boost repair of disrupted brain circuits once symptoms appear.

Our clinical research will focus on the discovery of new early biomarkers for brain disease. Such biomarkers ultimately will enable us to intervene during the interval between the onset of disease and before the appearance of symptoms.

Our endeavor will explore multiple novel avenues to address a range of brain disorders and conditions to relieve families of the burden of brain disorders. It will complement and benefit from scientific tools developed through former President Obama's Brain Initiative.

Alzheimer's disease affects almost 6 million Americans and costs in excess of \$100 billion per year.



Brain Health

Problem: The need to forestall brain disease processes before symptoms appear and boost repair of disrupted circuits after onset of symptoms.

Solution: Understand the basic biology of the brain to identify early biomarkers, discover interventions that forestall underlying diseases prior to the onset of symptoms, and deploy new approaches to repair brain circuits once symptoms appear.

Impact: Breakthrough early diagnostic and therapeutic approaches to a range of conditions that relieve patients and their families of the burden of brain disorders, and a refined understanding of the brain for further research.



Ending disease where it begins

Prenatal and childhood development influences health and disease risk for the entirety of an individual's lifespan. The molecular underpinnings of diseases such as asthma, metabolic syndrome, heart disease and neuropsychiatric diseases originate in pre- and early postnatal life. These biological processes can be exacerbated by extrinsic factors such as environmental exposures, socioeconomic status and stress that, over time, result in adult diseases that represent substantial health care and economic burdens.

An impressive body of highly regarded research has demonstrated that early childhood development directly influences long-term health, economic and social outcomes for individuals and society. Early exposure to adverse influences – social, economic, health or environmental – can create health deficits that last a lifetime. By identifying early risk factors and mitigating prevention and treatment strategies, we can improve the health of society as a whole.

This ambitious children's discovery endeavor will bring together experts from across Duke Health and Duke University to study four interrelated drivers of early life influences on long-term health:

- Genes and biology
- Physical environment
- Health and behavior needs
- Social and economic factors

Research across these areas will elucidate the early life factors having the greatest impact on lifelong health and wellbeing. Our research will inform early prevention, risk screening and treatment, as well as provide training opportunities for the next generation of clinician-scientists to learn from Duke's cadre of experts.

Taking a holistic approach to identifying early life factors that influence health and wellbeing, we will develop innovative strategies to improve the health of children . . . and the adults they become.

Inequalities in health
and socio-emotional
functioning
emerge by age three.



Early Life Origins of Health and Disease

Problem: The origins of childhood and adult diseases often begin in prenatal and early postnatal life.

Solution: Identify early risk factors in genes/biology, physical environment, behavioral needs and socio-economic status to address disease before it manifests.

Impact: Develop preventive strategies, diagnostics and early therapies to promote health in child and adult populations.



Controlling the immune system

The immune system is responsible for protecting the human body from attack by foreign organisms by recognizing potentially harmful agents, isolating and eliminating them, and then remembering them so that future invasions can be dealt with more swiftly.

Our work will focus on controlling the immune system and will engage the considerable immune expertise within Duke Health to define the population norms for immunity and correlate that profile with the systemic manifestations of disease. In addition, we will develop a generalizable approach toward understanding immune function that will allow us to anticipate and prevent the development of tumors, infections and autoimmune diseases such as multiple sclerosis and type 1 diabetes.

We will apply our investigative abilities across the spectrum of immune biology to seek out the critical secrets of how immune

function naturally controls the vast majority of cancer, infections and autoimmune uprisings, and then to translate those discoveries into actionable therapeutic strategies with the goal of developing pharmacological control of all aspects of immunity. We will progressively acquire the ability to finely tune an immune response against a specific organism or tumor, and to forestall a damaging immune response to a specific organ in the case of transplantation or autoimmunity.

This advanced understanding of immunity will lead to careful control of tolerance, which would save lives by making it possible for all transplantation to be successful. Additionally, expanding our understanding of tolerance will allow us to train each person's immune system to recognize cancer as foreign and redirect all cancer therapies towards immune-modulation, and to prevent infectious diseases such as HIV by vaccination of populations.

According to NIH,
annual direct health care
costs for autoimmune
diseases approach
\$100 billion.



Immunology and Transplant

Problem: Diseases occur when the immune system mistakenly identifies cells of the body as foreign, or fails to distinguish foreign organisms from healthy cells or transplanted organs.

Solution: Control the immune system as a therapeutic strategy.

Impact: Immunotherapy treatments for cancer, reversal of autoimmune diseases like diabetes and multiple sclerosis, prevention of infectious diseases such as HIV by vaccination of populations, and improved ability to transplant cells, tissues and organs.

Solid tumor brain metastasis

Brain metastases arising from solid tumors (e.g. lung, breast, melanoma and renal cancers) are a devastating consequence of late stage cancer and are associated with poor prognoses and limited treatment options. In the past decade, the incidence of brain metastasis has significantly increased as many patients are surviving longer due to effective cancer therapies that do not prevent or treat brain metastases. In contrast to non-brain metastasis settings, there has been only modest improvement over the past 20 years in the survival of patients with brain metastasis.

On a more promising note, the advent of next-generation sequencing, RNA transcriptional analysis and immune profiling has begun to shed new light on the complex biology of brain metastasis. These advances lay the foundation for a dedicated effort to evaluate the efficacy of targeted agents and other novel therapeutic approaches to address brain metastasis.

Our teams will deliver multidisciplinary cancer care to patients with different tumor types that have metastasized to the brain and apply novel imaging, surgical and radiation techniques,

along with research-driven therapeutic development, with the goal of making transformative changes in their survival and quality of life.

In addition to streamlining the multidisciplinary care of this complex patient population, this initiative will include the following three strategic research priorities:

- Investigating immune modulation and its effects on the development, propagation and treatment of brain metastasis.
- Improving and monitoring drug and other therapeutic delivery throughout the intracranial compartment.
- Accelerating novel therapy development through templated and streamlined clinical trials across tumor types.

Our goal is to transform the way brain metastases are prevented, diagnosed and treated. Ultimately, we seek to improve outcomes and quality of life for patients at Duke and around the world.

Brain metastasis is a devastating and increasingly common situation faced by cancer patients. Novel preventive, diagnostic and therapeutic options are desperately needed.



Combatting Cancer

Problem: Brain metastasis is universally associated with devastating symptoms and poor outcomes.

Solution: Novel approaches to prevention, early diagnosis and treatment gained through patient-centric, multidisciplinary research and care for patients.

Impact: Better quality of life for patients with solid tumor brain metastasis through more effective treatments and improved diagnosis.

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Health
Together

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