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

SCIENTIFIC VISION

THE NEXT DECADE

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

A MESSAGE FROM THE DIRECTOR

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), part of the National Institutes of Health (NIH), completed its scientific Visioning process as the Institute approached its 50th anniversary. Beyond celebrating the past, this anniversary inspired the NICHD to set compelling research directions for the future.

This was no easy task. Established in 1962, the NICHD has a broad mission that challenges us to ensure that every person is born healthy and wanted, that women suffer no harmful effects from reproductive processes, and that all children have the chance to achieve their full potential for healthy and productive lives, free from disease or disability, and to ensure the health, productivity, independence, and well-being of all people through optimal rehabilitation.

NICHD science spans the understanding of the basic mechanisms that transform cells into healthy and effectively functioning individuals, to clinical studies that can improve the lifelong health and well-being of women, children, and those with disabilities. With a focus on strengthening the stewardship of the research enterprise and the 50th anniversary approaching, the time was right for the NICHD to explore, with its community of stakeholders, what we might achieve together within the next decade.

The NICHD scientific Visioning process began with Institute staff and the National Advisory Child Health and Human Development Council identifying a set of broad themes to focus our science and discussions. These discussions were held in nine different workshops followed by a consensus-building meeting. In the process, the Institute convened more than 700 multidisciplinary experts, the vast majority from outside the NIH, to create this Vision and establish shared views of where and how to direct future research.

The resulting Vision statement includes key concepts derived from the workshops and the white papers they produced. The concepts are aggregated into seven distinct scientific areas, ranging from developmental biology to population dynamics. Each area encompasses both broad scientific goals and more specific research initiatives. These range from efforts involving the frontiers of molecular biology to investigations that can yield novel, evidence-based, public health interventions that can be adopted nationally and globally. In all cases, the concepts suggest future scientific directions, not just for NICHD, but for all of our research collaborators.

In the end, each of the workshops highlighted a similar theme—that the values and policies of the research enterprise must forge a positive future for the next generation of scientists and for society. This is addressed in the final section of this document, *Conduct of Science*.

Beyond creating a statement itself, the scientific Visioning process was designed to bring together diverse voices that could assemble and generate new perspectives for existing research problems and assist in identifying new opportunities. The Visioning process and the statement that follows acknowledge that we are entering a new and promising era in biomedical research. In the next decade, we must be ambitious and choose research questions not because they are the easiest to answer, but because they are the most important.

Alan E. Guttmacher, M.D.
NICHD Director

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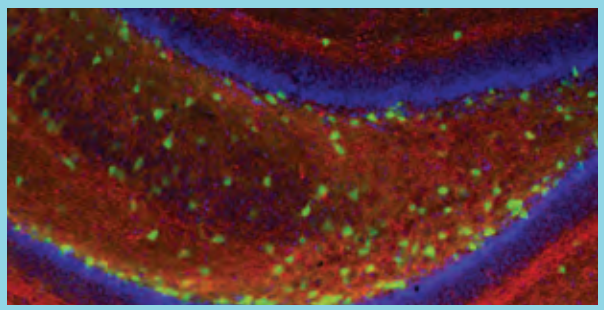
DEVELOPMENTAL BIOLOGY

Research in developmental biology expands our understanding of the earliest origins of many diseases and conditions. Starting at the molecular and cellular levels, this research provides the basis for understanding such key processes as embryogenesis, morphogenesis, organogenesis, and tissue growth and differentiation. Future developmental biology research should give scientists the knowledge and tools they need to predict and identify the pathways that allow them to prevent—or ameliorate the impact of—an array of human structural and functional variations.

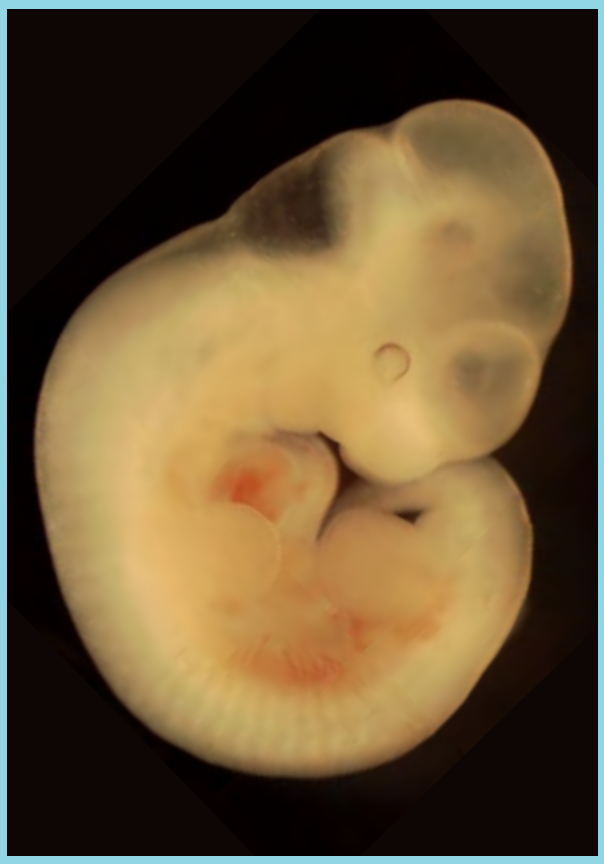
Animal Cells in Culture

Years of work in developmental biology now provide unique opportunities to benefit human health by offering new ways to apply genetic research and by supporting emerging fields such as regenerative medicine. Now it is essential to study cellular reprogramming as well as *in vitro* and *in vivo* approaches to organ development and cellular growth in three dimensions and over time. Advancing knowledge in genomic regulation and the integrative biology of development will allow researchers to understand various phenotypes in model organisms and in humans. These organisms could extend from prokaryotes to yeast, from sea urchins to zebrafish to mice, because no single animal model fully recapitulates the effects of a gene or a pathway on developmental processes. Researchers must also have open access to systematic cataloging of phenotypes in these organisms, made freely and widely available in databases that are expertly filled and continuously updated.

Basic research should include single-cell and single-molecule imaging and the development of bioinformatic tools to advance our understanding of systems biology. We must also seek to understand the effects—and the mechanisms of those effects—of the environment on early cellular developmental processes. Such information will be critical to guiding future research and health care, as regenerative and genomic ("personalized" or "individualized") medicine transforms the way scientists and clinicians investigate and apply new knowledge to address many developmental and other conditions.



Serotonin Receptor Activity in Mus Musculus
Courtesy Margaret I. Davis



Mus Musculus *Embryo, Day 11*

WITHIN THE NEXT 10 YEARS, SCIENTISTS SHOULD BE ABLE TO:

1. Begin to develop a comprehensive guide to developmental defects. This would include data from multiple organisms and descriptions of the molecular pathway(s) and the genomic and epigenetic regulation involved across developmental stages.
2. Construct a library of pluripotent cells that give rise to organs and/or tissues with potential clinical applications; eventually, for each pluripotent cell line, researchers should demonstrate organ and/or tissue development, with in vitro and in vivo testing in model organisms and, possibly, in humans.

DEVELOPMENTAL ORIGINS OF HEALTH AND DISEASE

We now know that the complex interactions between many different biological and external factors, starting before conception, can influence development across the life course and across generations. Unraveling this complex interplay demands a new level of interdisciplinary understanding and sophisticated delineation of systemic pathways. Key to this is understanding how specific genetic, biological, environmental, behavioral, and social factors interact over time to influence health and disease. This is particularly important to understand across a broad range of environmental exposures and interactions. Increasing our understanding of the developmental origins of health and disease promises a future in which clinicians can use novel methods to predict—and act to prevent, treat, or even reverse—many conditions or disabilities.

Human-Induced Pluripotent Stem Cells

Science, medicine, and society now face a wide range of chronic diseases as their next great challenge, having made substantial progress in the 20th century tackling the most common causes of early morbidity and mortality. Much of this success was related to tremendous improvements in such areas as prenatal and perinatal care, labor and delivery, vaccination, antibiotics, and surgical treatment of congenital and other defects. Partly due to these past advances, an increasing number of individuals—even those with chromosomal, single gene, or developmental disorders that were previously lethal early in life—now live long enough to develop chronic illness that may affect their well-being over many decades. This, and the delayed expression of heretofore unidentified individual genetic variants, has led to a population of patients with previously unseen issues that must be managed in later life.

In addition, environmental factors that are rapidly changing—due to technological advances and changes in the physical and built environment, human behavior, and societal and family patterns—increase the need to understand how disease, across the life course, has origins early in life. Fortunately, this need arises as new tools—such as the human genome map, increasingly more efficient means of genome analysis, and other "-omic" approaches—become more useful and easily accessible for biomedical research and wide-ranging health applications.

Understanding the developmental origins of health and disease will benefit from interdisciplinary and global studies, and from prioritizing research on today's most common chronic conditions and diseases, such as obesity, diabetes, heart disease, stroke, cognitive deterioration, and cancer. In addition, researchers must study specific at-risk cohorts and groups of unusually healthy subjects. This will help scientists identify genes, environments, molecular interactions, and epigenetic states that affect early or situational morbidity or extreme healthy longevity.

Some of the earliest origins of health and disease start during preconception, conception, pregnancy, labor, or delivery. These unique life stages warrant careful study for their individual and combined contributions to both risks and protections in later life. Researchers must also understand the effects of the environment on the maternal and paternal germlines, identify the early development of the zygote and cell lineages *in vitro* versus *in vivo*, and systematically investigate health outcomes of children born through assisted reproduction technologies. It is also essential for scientists to explore fully the role of the placenta, cataloging the effects of maternal and fetal exposures and understanding how different pathways, at various points of gestational age, may affect later health outcomes.

WITHIN THE NEXT 10 YEARS, SCIENTISTS SHOULD BE ABLE TO:

1. Make substantial progress on systematic tissue banking of placentas, which should be linked to genetic and epigenetic data, periodic and standardized phenotyping of the offspring, and the development of updated molecular tools to support sophisticated analyses of gene expression and genetic pathways.
2. Begin to develop an online, multi-institutional, and continuously updated study of multigenerational effects on health, growth, and development. This research would include data on individual genotypes with genomic structure and individual gene sequences; parenting, lifestyle, residence, and other environmental factors; phenotypes (e.g., cardiovascular fitness, bone health, measures of insulin resistance); and epigenetic changes in peripheral DNA and any diseased tissues.

PREGNANCY AND PREGNANCY OUTCOMES

Millions of mothers and infants in the United States and throughout the world are at increased risk for poor pregnancy outcomes. Understanding pregnancy processes and fetal development can pave the way for predicting and preventing these lifelong consequences. Basic research in this area starts by vastly expanding our current understanding of normative pregnancy mechanisms, beginning at the molecular and cellular levels. Scientists must fully understand implantation, placentation, and the full interplay of forces involved in two entities—living one within the other—that shape fetal development, birth outcomes, and the future health of the mother. Researchers would apply this knowledge to reduce the lifelong impact of pregnancy on women, improve the prospects of a healthy pregnancy for women with disabilities, and reduce disparities in outcomes for both mother and child.

Ultrasound of Human Pregnancy

The last century brought unequivocal advances in both the understanding and management of pregnancy. However, new technologies and the revolution in molecular tools are rapidly expanding opportunities to explain the basic processes underlying the physiology and pathophysiology of pregnancy, maternal-fetal interactions, and various pregnancy outcomes.

Better pregnancy outcomes will result from understanding the basic biology of pregnancy as an intricate process—one that modifies both maternal and fetal immunity and hormonal environments while interacting through the placenta and allowing the mother and fetus to react as both one and two units. Targets for new research should include delineating the gestome (the molecular network that harmonizes maternal-placental-fetal functions) and the exposome (the effect of the environment on the developing fetus).

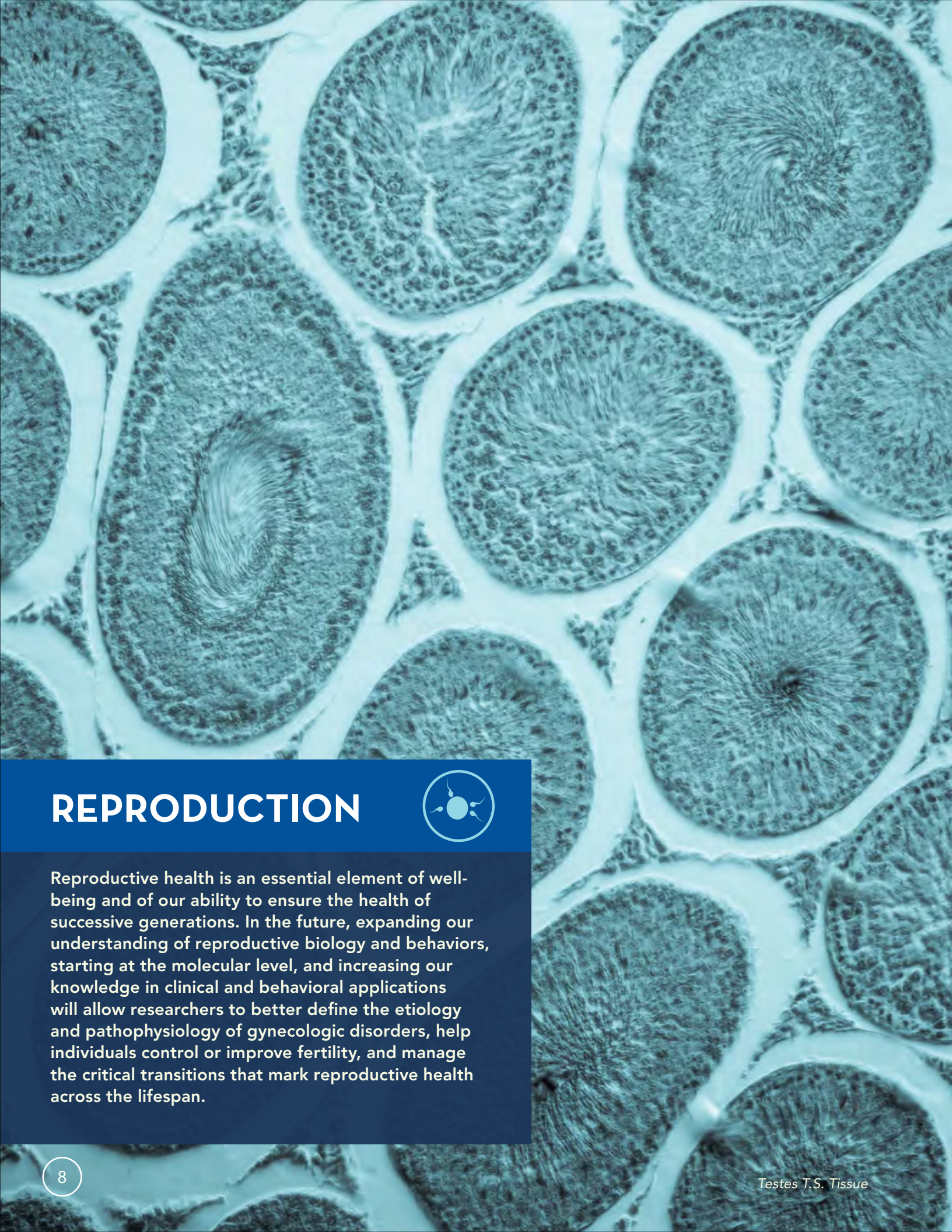
Fetal development and placental function, and their response to outside challenges (e.g., toxins, drugs, infections) are prime areas for clinical studies in pregnancy research. Identifying the multisystemic factors contributing to stillbirth and prematurity, including how genetic variation and the microbiome influence placental function and fetal development, would be an important achievement. It is also necessary to determine the full range of effects of timing and mode of delivery. New frontiers lie in improving hemodynamic measurement and imaging techniques for diagnosing placental disease, and in identifying the critical hormonal and other biomarkers of fetal maldevelopment, microbiomic effects, placental dysfunction, and prematurity. Biomarkers are also needed to enhance early recognition of fetal brain and other defects.

In their efforts to study and identify the complex causes of stillbirth and prematurity, researchers must develop and test evidence-based measures documenting prevention efficacy. Researchers must also work on improving neonatal care and outcomes for preterm infants. This will require conducting multi-institutional studies, understanding early environmental effects on infant development with linkage to pregnancy data, and applying individualized medicine and genetic/genomic data to maternal and newborn care.

To advance the health of women, researchers must study pregnancy as both a biomarker and as a cause of later disease in the mother. This involves examining events such as preeclampsia as a potential indicator of later stroke, or examining such conditions as metabolic syndrome of pregnancy as an indicator of later cardiovascular risk. Likewise, researchers should examine how pregnancy itself can contribute to later disease and develop interventions to lessen these effects. For the increasing number of pregnant women with chronic medical conditions or disabilities, researchers must delineate the effects of pregnancy on their infants' birth outcomes as well as on the mother's health during and after pregnancy.

WITHIN THE NEXT 10 YEARS, SCIENTISTS SHOULD BE ABLE TO:

1. Delineate the grid of the complex causes of stillbirth and prematurity and outline evidence-based measures (derived from a variety of sources, including multi-institutional studies) for their prevention.
2. Create a comprehensive four-dimensional atlas of in utero development. This would include data at the gene–cellular level, which delineate the effects of specific gene expression and epigenetic changes due to the physical environment and other influences (e.g., social environment, toxins, drugs), linked to information about resulting phenotypes.



REPRODUCTION

Reproductive health is an essential element of well-being and of our ability to ensure the health of successive generations. In the future, expanding our understanding of reproductive biology and behaviors, starting at the molecular level, and increasing our knowledge in clinical and behavioral applications will allow researchers to better define the etiology and pathophysiology of gynecologic disorders, help individuals control or improve fertility, and manage the critical transitions that mark reproductive health across the lifespan.

Testes T.S. Tissue

The ability for individuals to control their own fertility through a range of effective male and female contraception options and through improved assisted reproduction techniques is essential to health and well-being. Successful reproduction depends on the anatomy and function of both the female and male reproductive tracts and includes menstrual and hormonal function, gamete formation and development, fertilization, embryo development, implantation, placentation, and fetal development. Scientists must further research on all of these aspects of reproduction, while expanding our knowledge about reproductive behaviors and the economic, behavioral, and social factors in, and the effects of, family planning.

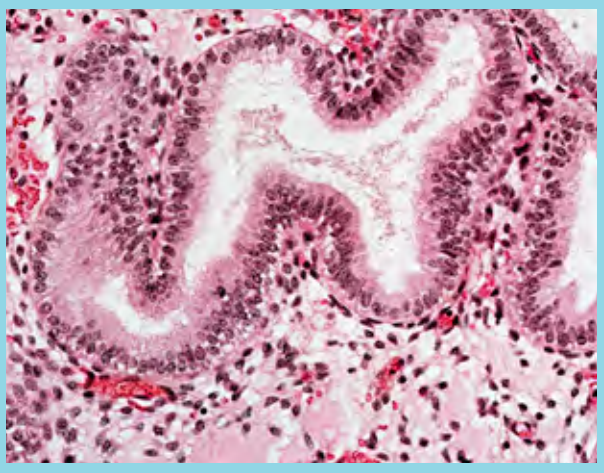
Today, researchers can take advantage of advanced technologies, bioinformatics, systems biology, and chemical genomics and related tools to develop biomarkers. These, in turn, can provide the foundation for identifying novel diagnostic and therapeutic targets for conditions affecting fertility and fecundity in males and females. It is also critical for additional studies to focus on stem cells, cellular differentiation, organogenesis, and tissue repair to strengthen the link between regenerative medicine and reproduction research.

To reduce the incidence of adult-onset male and female reproductive disorders, scientists must better understand a variety of developmental processes. This begins with creating a full understanding of both normative and etiological mechanisms, starting with early developmental processes *in utero* and continuing throughout infancy, childhood, puberty, and other reproductive transition stages. Researchers must gain a better understanding of the molecular physiology of puberty, the menstrual cycle in adolescents, and the impact of early environment and altered nutrition/disease on how reproductive functions develop or evolve over time. This research includes understanding the biology, special vulnerabilities, and life implications of reproductive transitions (e.g., puberty, andropause, menopause). These life phases must be destigmatized and their physiology well documented through normative anatomical, hormonal, and biochemical data.

Gynecologic disorders, including endometriosis, pelvic floor disorders, and fibroids, affect quality of life on multiple dimensions, especially when accompanied by comorbid conditions such as infertility, obesity, metabolic dysfunction, chronic pain, or mood disorders. Developing novel approaches to prevent, diagnose, and manage these often interrelated conditions, premised on a detailed understanding of normative and pathological mechanisms, could greatly improve quality of life for women across the lifespan. Because both reproductive health and sexual health significantly influence quality of life, any clinical study assessing overall quality of life should include these factors.

WITHIN THE NEXT 10 YEARS, SCIENTISTS SHOULD BE ABLE TO:

1. Develop means to characterize both female and male single germline cells at specific stages of development.
2. Develop novel male and nonhormonal contraceptive agents.
3. Understand how microbial flora change during periods of reproductive transition and the health effects of these changes.
4. Delineate the genetic, epigenetic, and environmental interactions underlying the etiology of at least three major gynecological disorders.



Human Endometrium

BEHAVIOR AND COGNITION

Behavioral factors can significantly promote positive health outcomes or increase the risk of adverse ones. Similarly, cognition—with its key relationships to neurodevelopment and learning—is part of a lifelong process that underlies overall human functioning. Basic and translational research that combines neuropsychological, behavioral, and social science perspectives, as well as new tools, will advance our understanding of the mechanisms underlying typical and atypical behavior and cognition. In the future, this enhanced understanding of behavior and cognition can ameliorate an array of developmental conditions or help individuals interact with the world in ways that can sustain or improve their health and well-being.

Positron Emission Tomography/ Computed Tomography Scan of Human Brain

Many research disciplines will need to work together to characterize the full range of typical and atypical behavioral and cognitive trajectories across the lifespan. First steps will involve identifying the mechanisms underlying behavioral and cognitive development at the molecular, cellular, and brain system levels; detailing how these mechanisms interact with complex environmental factors; and pinpointing sensitive periods for perception, learning, memory, language, reasoning, and executive function.

This will require researchers to use emerging technologies to characterize how the epigenome and gene expression not only influence, but also are influenced by, the interaction between behavior and the environment over time. It will also require researchers to exploit new technologies that allow them to visualize and identify the complex pathways through which targeted behavioral and pharmacologic interventions affect brain structure and function.

Together, this knowledge can help identify which periods during neurobiological and behavioral transitions are most susceptible to specific types of change or interventions. To hasten such advances, researchers must also develop innovative animal models of human behavior and robust behavioral markers or biomarkers of specific behaviors. These can also be used to predict or benchmark a wide spectrum of behaviors.

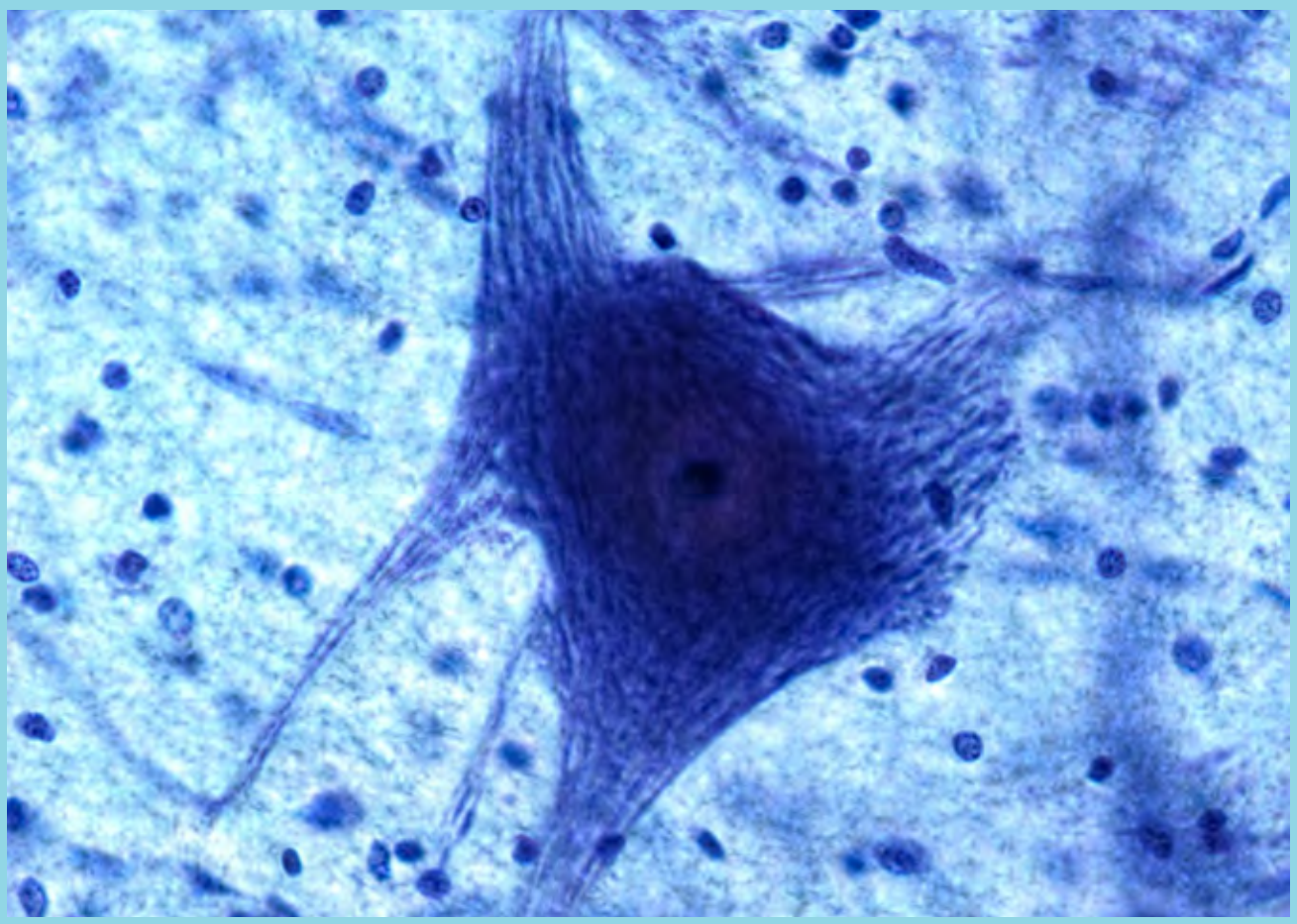
Identifying specific genetic variants that influence the development of behaviors or cognitive traits will also be important to unraveling the origins and mechanisms underlying normative behavioral and cognitive development. When combined with a better understanding of other individual, familial, and community-based factors, this critical genetic information will provide the foundation for developing more personalized interventions to improve health outcomes.

Similarly, understanding the neurobiological bases, developing the full developmental spectrum and trajectories, identifying key biologic markers for behavioral or cognitive disorders, and characterizing endophenotypes for specific disorders should allow researchers to identify the most promising therapeutic targets. This knowledge will also allow researchers and clinicians to determine the most sensitive time periods and the most effective behavioral interventions to prevent these disorders, ameliorate their symptoms, and maximize function.

For specific conditions such as autism spectrum disorders, Down syndrome, and Fragile X syndrome, for which a stream of multidisciplinary advances is emerging, researchers should be able to identify the key mechanisms and primary causal factors leading to these conditions. This, in turn, should provide the cornerstone for developing a broad range of more timely and effective interventions.

Of growing interest are the effects that emerging technologies and media have on cognitive trajectories through their influence on the developing central nervous system, learning, problem solving, social interaction, and communication. It is important to understand how new technologies affect cognition, particularly during sensitive developmental periods, in different populations and settings. It is also important to identify how these technologies can be used to prevent, remediate, or treat a range of learning and developmental conditions.

Another research frontier lies in fully uncovering and understanding how specific physical (whether natural or engineered) and social environmental exposures



Human Neuron

shape behaviors or alter developmental trajectories and influence health outcomes. These exposures may be as direct as the use of neonatal incubators or as complex as growing up in poverty, surviving early traumatic events or injuries, being exposed to violence, or coping with incarceration as a youth. Projecting the impact of these exposures and identifying which individual, family, or community factors are most likely to promote positive outcomes, such as resiliency, are essential for developing protective interventions.

Researchers must take an interdisciplinary approach to identify how differing cognitive abilities and behaviors influence individual, family, and community health and well-being. Intervention research and studies to optimize the lives of individuals with a range of typical and atypical cognitive abilities and behaviors must also assess the costs and benefits to family members and society. Incorporating these perspectives can significantly alter how scientists interpret and implement cognitive and behavioral research advances.

WITHIN THE NEXT 10 YEARS, SCIENTISTS SHOULD BE ABLE TO:

1. Identify 5,000 genetic variants that influence specific behaviors or cognitive traits.
2. Fully understand the neurobiological bases, delineate the full developmental spectrum and trajectories, and identify the key biologic markers for five behavioral or cognitive disorders.
3. Identify the causes of autism spectrum disorder, and begin to employ that knowledge to develop effective and targeted interventions.

PLASTICITY AND REHABILITATION

Understanding plasticity—the mechanisms underlying adaptive or maladaptive change at the cellular, tissue, organ, or system level—in its broadest sense is core to understanding both human development and rehabilitation. Given emerging scientific insights, researchers have left behind the era when plasticity was thought to exist only early in life and now have substantial evidence about how it occurs across the human lifespan. Our current challenge is to build upon these insights and learn how to harness plasticity more effectively to improve functioning across organ systems and to remodel, maintain, or enhance functioning in response to a range of biological challenges such as injury, other forms of trauma, and disease.

Human Spinal Cord Neurosphere
Courtesy Micheal Weible, Department of Anatomy and Histology, University of Sydney Sydney, Australia

Plasticity is often viewed in terms of neural plasticity, as it affects physical, behavioral, and cognitive functioning; however, changes to other organ systems can also influence the ability to develop, maintain, or regain function or to heal. The challenge for scientists is to generate fundamental knowledge about plasticity, understand how it responds to both endogenous and exogenous factors, and translate this knowledge into interventions that can maximize developmental and rehabilitative outcomes.

As a first step, researchers must develop novel model organisms. These must be capable of acting in a variety of environmental situations and represent a spectrum of plastic behaviors influenced by a broad range of perturbations. Such models can rapidly advance the scientific understanding of plasticity at the cellular and molecular levels. In addition, researchers must contrast normative plasticity in developing systems to plasticity in more mature systems that may have suffered injury, developmental maladaptation, or disease. This will help researchers understand whether and how the ability to habilitate under specific developmental conditions relates to expected variations in, or abnormal regulation of, normative plastic forces. Researchers must also understand tissue- and organ-specific regenerative, repair, adaptive, and restorative processes across the lifespan, starting in the neonatal period, if not during pregnancy. The ultimate goal is to identify the normative and optimal range of plasticity for different populations.

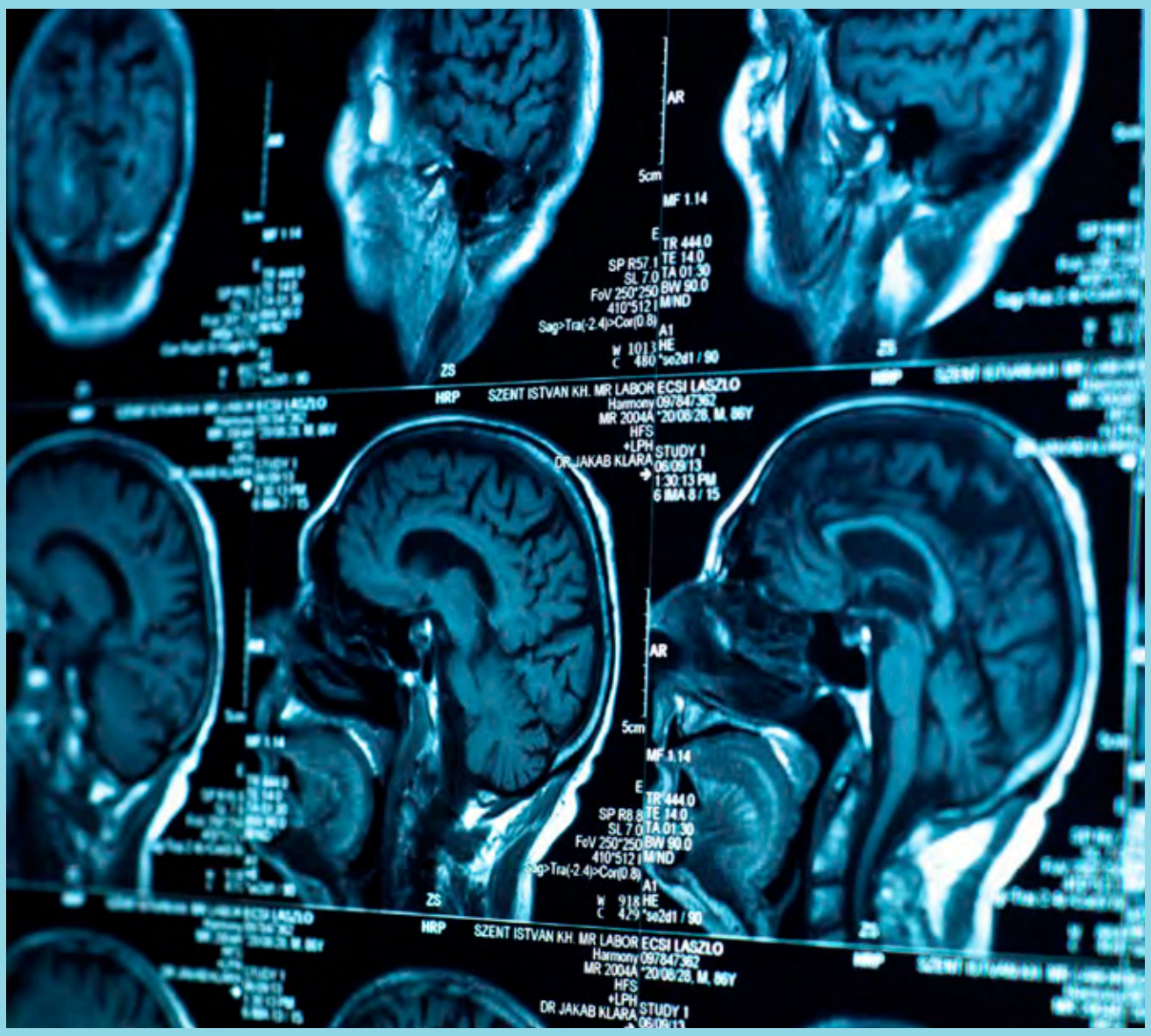
Additional studies must unravel the influence of various factors, such as those associated with gender and the tropic function of hormones, and how genetic or epigenetic mechanisms influence plasticity. In doing so, it is important to distinguish harmful changes from those that maintain homeostasis. Together, such studies will provide the basis for identifying and defining the most sensitive periods—and the most appropriate mechanisms and strategies—for modulating plasticity. To translate this advanced understanding of mechanisms underlying plasticity into interventions that induce repair or enhance rehabilitation, researchers must also identify the primary environmental or extrinsic factors that influence plasticity and their substrates.

Such extrinsic factors can range from diet and exercise to stress, family, and other social influences. Knowledge of such factors will provide additional targets for developing new cellular and molecular (e.g., stem cell and gene therapies), pharmacologic, and clinical (e.g., electrical stimulation or therapeutic exercise) interventions. Such foundational knowledge is also important for creating new generations of assistive devices.

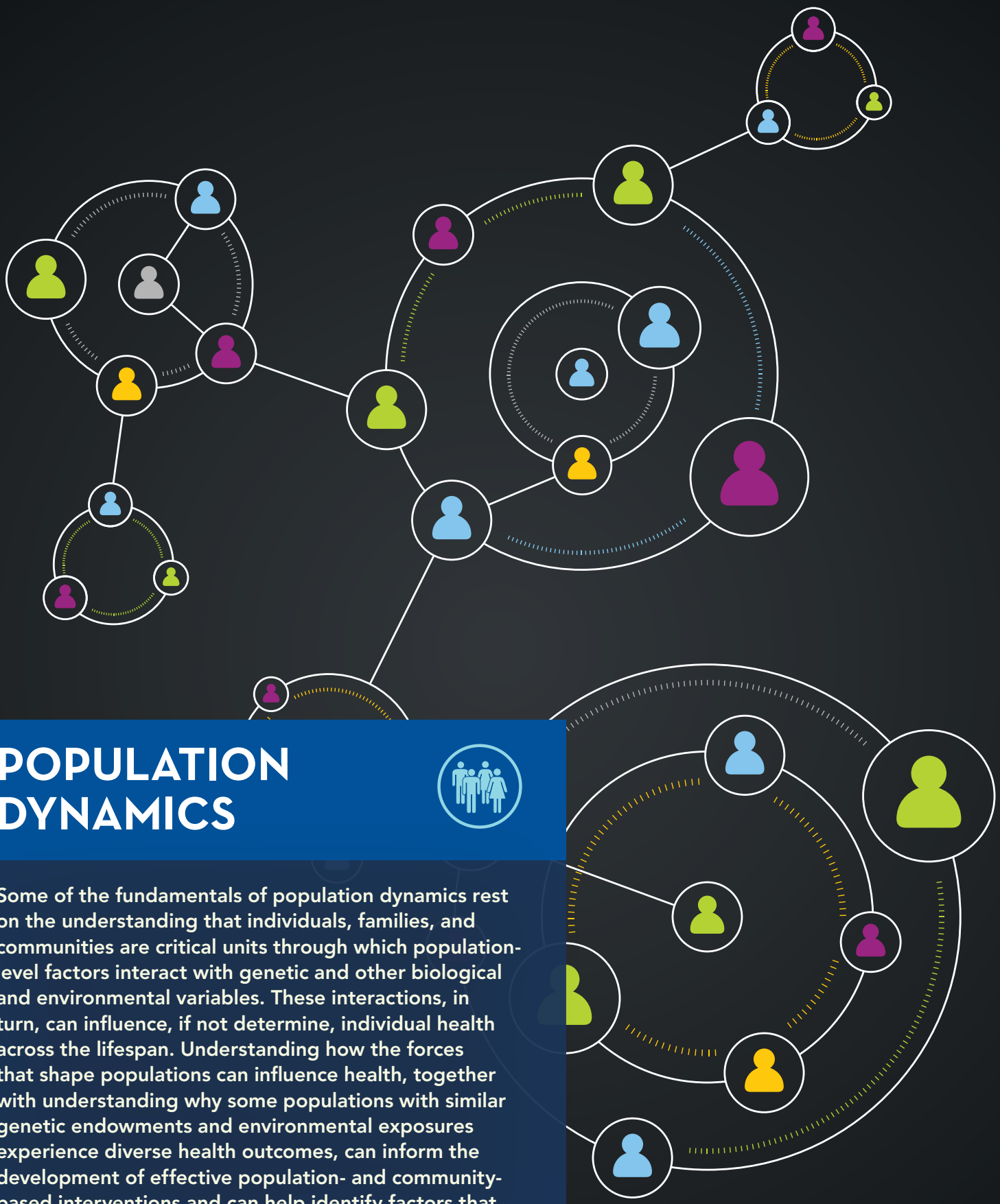
Creating new, or enhancing existing, interventions or therapies will not be enough. To optimize the impact, researchers must bring together sophisticated combinations of biomarkers and technology to predict which interventions or therapies, and combinations thereof, are most likely to succeed. In addition to being clinically and functionally significant, surrogate measures must be able to track intervention success, discern responders from nonresponders, and indicate the ability of different groups of patients to sustain progress under a variety of circumstances.

WITHIN THE NEXT 10 YEARS, SCIENTISTS SHOULD BE ABLE TO:

1. Identify distinct biological mechanisms that translate explicit factors in the exposome to specific neuroplastic responses, and identify novel markers of these processes.
2. Develop a range of robotics that will enable individuals with developmental or acquired disabilities to obtain or maximize daily function in their home settings.



3. Develop practical, effective, and inexpensive rehabilitative interventions, such as upper and lower extremity prostheses, that can be developed as prototypes and manufactured, maintained, and used in a variety of global and resource-poor settings.
4. Determine the magnitude of risk and long-term impact of concussive injuries to understand how the brain responds to a range of such injuries. This would include targeting injuries that may not be easily discernable and are most common for a range of developmental stages, from infancy through adulthood. This work would also include designing developmentally appropriate and effective measures for prevention, protection, and treatment.
5. Understand and begin to compare, at the genetic and epigenetic levels, the key factors controlling the plasticity of neonates, infants, children, and adolescents to those controlling plasticity of adults.



POPULATION DYNAMICS

Some of the fundamentals of population dynamics rest on the understanding that individuals, families, and communities are critical units through which population-level factors interact with genetic and other biological and environmental variables. These interactions, in turn, can influence, if not determine, individual health across the lifespan. Understanding how the forces that shape populations can influence health, together with understanding why some populations with similar genetic endowments and environmental exposures experience diverse health outcomes, can inform the development of effective population- and community-based interventions and can help identify factors that can eliminate health disparities.

A key challenge in population dynamics starts with understanding the rapid and profound changes shaping families in the United States and around the world. This includes understanding how biological, social, and other environmental factors, in concert with population dynamics, influence the health and well-being of mothers, fathers, children, families, communities, and societies. Such research would include identifying how extremes in maternal and paternal age and their impacts on fecundity, pregnancy outcomes, gender roles, and family formation affect the modern family. Researchers must also examine how family structures and the intergenerational transmission of such factors as knowledge and economic security affect child health and developmental outcomes. Innovative, multidisciplinary approaches are needed to unravel how complex patterns of migration and urbanization influence health over generations by altering social, economic, and educational dynamics, including the ethnic and cultural characteristics of neighborhoods, communities and societies. Other vital research area will involve characterizing how technology is altering social interactions and access to information, thereby influencing family choices, behaviors, and well-being.

To understand how population dynamics and other factors interact to transform health, scientists must create and employ a new

generation of cutting-edge data collection approaches, sophisticated analytic methods, and novel, rigorous statistical measures. These strategies must be able to assess biological, physical, and social processes in a range of diverse families, communities, and populations. To identify the most salient biological and social factors and processes amenable to intervention at the individual, family, and community levels, scientists can study distinct populations with shared genetic characteristics, environmental exposures, or social experiences, using new approaches based on observational research, naturally occurring experiments, and clinical trials. Other ambitious methods include mapping the exposome and conducting exposome-wide association studies (EWAS) of susceptible populations over time.

An important population dynamic is emerging as individuals with intellectual, developmental, and physical differences are now living longer, with varying degrees of health and functioning, due to medical and other advances. To maximize the quality of life and productivity for these populations, researchers must better document the scope, range, and impact of these trends and better understand how they influence the health and well-being of families, neighborhoods, and communities. Based on this understanding, researchers must also conduct an array of multidisciplinary studies to inform policies, design programs, and enable leaders to implement activities that meet basic needs (e.g., housing, learning, employment, other social opportunities). This research must provide the comprehensive evidence for what works and how to scale programs at the population level, accounting for unique biomedical factors, individual behaviors and needs, family and community characteristics, and social forces. This might include conducting EWAS for these distinct groups of individuals, and identifying the key points and types of interventions most likely to maximize health and quality of life.

WITHIN THE NEXT 10 YEARS, SCIENTISTS SHOULD BE ABLE TO:

1. Catalog and identify interrelated environmental and genetic factors that are key to mediating the health of individuals, families, and communities, focusing particularly on populations with distinct genetic characteristics or environmental exposures.
2. Understand the changing population dynamics associated with increasing the health and longevity of persons with a range of physical, intellectual, and developmental disabilities and, based on this knowledge, develop better community- and population-based health care and living options for individuals with intellectual, developmental, and physical differences.

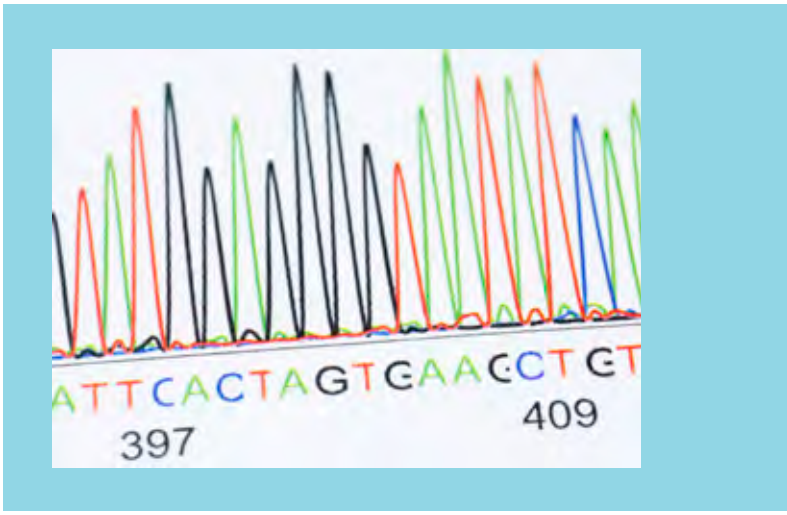
CONDUCT OF SCIENCE

The NICHD's scientific Visioning process identified not only many promising opportunities across the scope of our mission, but also more universal ideas about how we must conduct science to enhance future progress in virtually all areas of biomedical research. Although many of these issues are not unique to the Institute's mission, many are particularly pronounced and critical to achieving our future goals. One avenue to success will involve finding multiple ways to advance transdisciplinary science. Another will involve creating novel approaches to address the vast amount of scientific information to be accumulated from complex longitudinal studies and repositories housing lifetimes of biological specimens. And yet another path will be to continue to develop and sustain a diverse cadre of scientists and biomedical researchers. Ultimately, however, our future success will be measured not by research investments or publications alone, but by our ability to translate and implement our scientific advances into actions that improve the health of all women, children, persons with disabilities, and communities around the world.

Transdisciplinary science needs to become more common. This requires both novel ways to remove current systemic structural obstacles to such research and enhanced rewards for its pursuit. Our commitment must go beyond promoting traditional collaborations to changing and enhancing the way in which multiple disciplines interact. This may include the support of multidisciplinary group sabbaticals, "transdisciplinary incubators," and other innovative programs that set aside dedicated time and space for scientists from different disciplines to learn from each other and to frame and solve problems jointly.

Opportunities must increase for researchers from different disciplines and institutions to obtain joint funding and publish together. Criteria for academic advancement must take into account and actively promote the involvement of researchers in transdisciplinary and team research. The scientific community needs to acknowledge that today's researcher can contribute significantly by being a "middle author" of a 20-author publication. Increasingly, academia will need to award credit for grants with co- or even multiple-principal investigators who are often not in the same department, or school, or even institution.

Training the biomedical researchers of the future requires awareness that, although solitary scientists and single discipline groups will continue to make important contributions, transdisciplinary research is a growing part of science that requires a different skill set, experiential background, and way of working. Even though it may be neither efficient nor effective to train large numbers of researchers with deep expertise in more than one discipline, such scientists clearly will have important roles to play. Perhaps more common will be scientists with deep expertise in a single discipline, but whose training has equipped them with "fluency" in others. The ability to read and analyze publications in other disciplines, to understand and utilize the tools and approaches of other disciplines, and to communicate effectively with those in other fields will be



DNA Sequence Results

major assets. Teaching such abilities usually will require a transdisciplinary approach, including training experiences and mentorship in multiple disciplinary frameworks.

Sustaining transdisciplinary research will profit from novel ways to work with private industry and nonprofit organizations, new media tools, and expanded efforts to facilitate communication and public outreach. Hosting registries and blogs, developing interactive curricula, supporting programs that match young researchers to multiple mentors, and creating incentives to attract and retain researchers from different disciplines all along their career trajectories will further transdisciplinary research.

A transdisciplinary view must be applied to how we study, frame, and measure health outcomes. New perspectives are particularly needed for assessing quality of life for women, infants, children, families, and individuals with disabilities. Data collected through longitudinal studies of healthy and at-risk cohorts will help researchers better understand correlations among specific exposures and individuals' health, across the lifespan and across generations. Scientists must create novel ways to acquire these data, exploiting technologies created in other fields (e.g., geographic information systems) and developing toolkits and multidisciplinary rapid-response teams that allow for the collection of exposure and outcome data in the event of "natural experiments."

Biorepositories with diverse sample types will also be invaluable for future research. These should be linked to a wide variety of environmental exposures and multidimensional phenotypes, starting before pregnancy and including the perinatal period and healthy individuals. Gathering these data will require researchers to develop a new generation of tools in molecular imaging, microscopy, biosensors, biomanipulators, and the expansion of "-omic" and other libraries that go across the lifespan.

Future, rapid, and transdisciplinary research advances will depend on our ability to harness bioinformatics and the resulting data that come from computational biology. The challenge will be finding creative and more efficient ways to analyze, store, disseminate, and share data—both new and from older studies—widely and effectively. This will require transdisciplinary and other researchers to create standardized ontologies and nomenclatures, harmonize data systems, and increase access to shared databases that also provide innovative analytic tools. To support these efforts, the scientific establishment will need to find appropriate ways to recognize and reward the intellectual contributions of those who gather the data and create the tools.

Finally, expanded and more widely linked and accessible data will demand finding new ways to protect the confidentiality and privacy of research participants. This must be a shared responsibility, as researchers move to a default ethos in which data, especially those derived with government funding, belongs not to the principal investigator,

but to society. Enhancing confidentiality and privacy must also be done in a way that maximizes the efficiency and effectiveness of research, with any redesign of appropriate rules or regulations completed in a way that protects participants while furthering science.

Clinical research is essential for translating basic scientific advances into improved health outcomes. To maximize what can be learned from often labor-intensive and costly clinical trials and to help ensure participant safety, researchers can fully analyze existing clinical and preclinical research before embarking on such trials. Creating centralized, accessible, and intuitively organized electronic warehouses of clinical research would help immensely. Clinical researchers must also identify the most effective clinical research strategies for diverse contexts, including low-resource settings. As this is done, it is critical to integrate economic impact analysis of interventions into the full array of clinical research. Together, these actions will help all fields identify why some interventions fail to produce expected results, and develop the best strategies to translate advances into evidence-based health care practice.

Public involvement will remain essential to ensuring that research is implemented in ways that sustain progress and improve health. All who support biomedical research must disseminate information to scientists, health care practitioners, and the public in ways that improve transparency, create new insights, and inform practice. All involved in the support and conduct of research must also build strong ties with communities, continuously engaging their members so that they can actively participate in framing the research that is most likely to identify the factors that influence their health. This engagement will enable scientists to respond immediately to emerging situations and enhance the possibility of developing more timely and effective interventions. All fields must take advantage of new ways to communicate advances, ensuring that their scientific meaning and health implications are transmitted clearly to a wide array of audiences.

None of the changes in the ways that we conduct science will be possible without continuously renewing and re-energizing our scientific workforce. We must capture the attention of students much earlier in the learning pipeline and expose them to, and excite them with, the full range of science inherent in the NICHD mission. This means enhancing interest in everything ranging from basic physiology and pathophysiology to the behavioral sciences. It also requires developing new ways to enhance interdisciplinary fluency and equip students with the biocomputational skills they need to analyze and interpret the surge of linked, longitudinal, and complex research information.

Given the globalization of research and the health problems that the NICHD seeks to address, tomorrow's scientists must overcome a wide array of complex challenges inherent in working in international environments and addressing the health problems of diverse populations. This will be difficult to achieve without a more diverse body of scientists. We need to create more effective ways of attracting and retaining researchers from underrepresented population groups, such as viewing young research participants as a pool of diverse individuals from which to recruit future scientists.

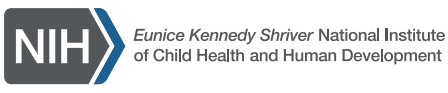
WITHIN THE NEXT 10 YEARS, SCIENTISTS SHOULD BE ABLE TO:

1. Develop biorepositories that capture the diversity of the U.S. population.
2. Involve the public in better reporting, identification, and definition of normal life processes, including pregnancy, child development, and adolescence.
3. Change the predominant model for data use to one of open access.

IN APPRECIATION

The NICHD's scientific Vision process and resulting statement would not have been possible without the dedicated efforts of more than 700 multidisciplinary experts and numerous Institute and other staff.

We thank you all for your invaluable contributions.



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