

## **Management Services Section - HNT1264**

(1) Provides a variety of centralized administrative support services to Institute management and staff; (2) manages and monitors all assets and costs associated with NICHD facilities, leases, utilities, space and renovations/construction; (3) provides ongoing facilities support including Express Services (minor facility services) for NICHD facilities; (4) develops pre-planning concepts for design and construction projects of NICHD facilities; (5) coordinates relocation of Office of the Director and Extramural Staff offices; (6) manages institute wide property services including property accountability and control; (7) manages real property allocated to the Institute and acts as the Institute's contact point with NIH in the acquisition and renovation of real property; (8) manages central IC-wide administrative systems and communicates policy and system changes to all users; (9) represents NICHD on the NIH Critical Response Team; and implements decisions for all off-campus NICHD buildings regarding security, building access, and parking; (10) provides conference services support; (11) maintenance of employee directories for NICHD including the NIH Enterprise Directory (NED) System; and (12) mail and courier services.

***Eunice Kennedy Shriver National Institute of Child Health and Human Development - HNT***

(1) Provides leadership and formulates research goals and long-term plans to accomplish the Institute's mission of child health; maternal health; problems of human development, with special reference to intellectual and developmental disabilities; family structure and the dynamics of human population; the reproductive process; and medical rehabilitation; (2) conducts, fosters, and supports biomedical and behavioral research through research grants, research contracts, and research performed in its own laboratories; (3) supports training in fundamental sciences and clinical disciplines through individual and institutional research training awards; (4) promotes the application of research findings to clinical practice; (5) cooperates in government-wide efforts to improve health and provides consultation to Federal agencies and non-Federal groups in the development of programs to improve health; (6) coordinates and integrates research efforts with service-oriented health agencies; and (7) disseminates information related to research findings to practitioners and the general public for improving health.

## **Office of Acquisitions - HNT129**

(1) Manages and conducts comprehensive oversight of all research and development contracting, non-research and development contracting, station support contracting, commercial item acquisitions using simplified acquisition procedures, GSA Federal Supply Schedule acquisitions, and simplified acquisitions for customer ICs; (2) Provides advice and assistance regarding all phases of the acquisition cycle from planning to closeout.

## **NICHD Contracts Management Branch - HNT1292**

(1) Plans, manages, and carries out research and development contracting activities in support of the Institute's scientific mission, including the solicitation, negotiation, coordination, awarding, and monitoring of all actions; (2) provides advice and guidance to program staff to support their research activities in the most effective and efficient manner; (3) develops guidelines, procedures, and internal controls to ensure proper and continuing implementation of NIH and other applicable policies, laws and regulations; (4) coordinates with other branches within the Office of Acquisitions and elsewhere at NIH to develop new approaches and identify and implement best practices; and (5) provides liaison support and representation to the greater NIH acquisition community.

### **Acquisition Services Branch - HNT1293**

(1) Plans, manages and carries out non- research and development contracting activities in support of the Institute's scientific mission, including the solicitation, negotiation, coordination, awarding, and monitoring of all actions; (2) provides advice and guidance to program staff to support their research activities in the most effective and efficient manner; (3) develops guidelines, procedures, and internal controls to ensure proper and continuing implementation of NIH and other applicable policies, laws and regulations; (4) coordinates with other branches within the Office of Acquisitions and elsewhere at NIH to develop new approaches and identify and implement best practices; and (5) provides liaison support and representation to the greater NIH acquisition community.

## **Section A – HNT12932**

(1) Plans, manages and carries out non- research and development contracting activities in support of the NICHD, NIAAA, NIMHD & FIC’s scientific mission, including the solicitation, negotiation, coordination, awarding, and monitoring of all actions; (2) provides advice and guidance to program staff to support their research activities in the most effective and efficient manner; (3) develops guidelines, procedures, and internal controls to ensure proper and continuing implementation of NIH and other applicable policies, laws and regulations; (4) coordinates with other branches within the Office of Acquisitions and elsewhere at NIH to develop new approaches and identify and implement best practices; and (5) provides liaison support and representation to the greater NIH acquisition community.

## **Section B – HNT12933**

(1) Plans, manages and carries out non-research and development contracting activities in support of the NIDDK's scientific mission, including the solicitation, negotiation, coordination, awarding, and monitoring of all actions; (2) provides advice and guidance to program staff to support their research activities in the most effective and efficient manner; (3) develops guidelines, procedures, and internal controls to ensure proper and continuing implementation of NIH and other applicable policies, laws and regulations; (4) coordinates with other branches within the Office of Acquisitions and elsewhere at NIH to develop new approaches and identify and implement best practices; and (5) provides liaison support and representation to the greater NIH acquisition community.

## **NIAAA Contracts Management Branch - HNT1294**

(1) Plans, manages and carries out research and development contracting activities in support of the NIAAA scientific mission, including the solicitation, negotiation, coordination, awarding, and monitoring of all actions; (2) provides advice and guidance to program to support their research activities in the most effective and efficient manner; (3) develops guidelines, procedures, and internal controls to ensure proper and continuing implementation of NIH and other applicable policies, laws and regulations; (4) coordinates with other branches within the Office of Acquisitions and elsewhere at NIH to develop new approaches and identify and implement best practices; and (5) provides liaison support and representation to the greater NIH acquisition community.

## **Management Analysis and Workforce Branch – HNT12D**

(1) Advises and assists the Director, Deputy Director, EO and Division Directors on data driven decision making and workforce development and engagement; (2) Provides management advisory services, develops management and administrative policies and procedures and coordinates their implementation throughout the Institute; (3) provides data analyses on administrative functions (including workforce planning) to drive administrative efficiencies.

## **Management Analysis and Policy Section – HNT12D2**

(1) Provides management advisory services, develops management and administrative policies and procedures and coordinates their implementation throughout the institute; (2) Conducts studies and analyses of institute management functions, program and administrative operations, and policy compliance; (3) analyzes effects of changes in management and administrative policies and procedures and advises the Executive Officer of these effects; (4) Administers the A-76 Commercial Activities Program, emergency planning activities, and delegations of authority; (5) coordinates the Institutes Risk Management and controls program; (6) Coordinates, analyzes and provides advice on all organizational change proposals for the Institutes; (7) designs, develops, and performs management studies, analyses, surveys, reports, and related activities to improve management efficiencies, resource allocations, and policy compliance; and (8) plans, directs, and provides centralized administrative services and management support for the records management program.

### **Workforce Development and Planning Section – HNT12D3**

(1) Serves as staff resource for the Office of the Director, NICHD, and other key officials, providing administrative management services which includes personnel services, recruitment strategies, management analysis and other administrative functions; (2) Maintains and coordinates the Institute's performance appraisal systems and performance based awards programs; (3) coordinates and manages the Institute's special recognition programs including the NIH Director's Award and NICHD Director's Award's; (4) manages and acts as the point of contact for the NIH mandated training programs; (4) provides advice and oversight on the T42 appointments and pay adjustments for the IC; (5) manages training programs and provides advice to IC management on administrative and management training and executive development programs; (6) serves as liaison with OHR and with EDI; (7) provides advice, consultation and training to NICHD staff on ER and LR issues; (8) coordinates quality of work life and IC leave programs and develops policy; (9) handles oversight and analysis of FTE usage for NICHD; and (10) works with management to address and resolve administrative and operational issues which impact employees, performance, morale and the work environment.

## **Office of Global Health - HNT19**

(1) Plans, coordinates, and facilitates the Institute's international research activities; (2) provides guidance on international health concerns to the Director, Deputy Director, and senior scientific managers of the Institute; (3) plays a leadership role in fostering communication among NICHD managers and researchers and international scientific community; (4) works with program officers to set program priorities and identify new and unique opportunities for international cooperation; (5) develops an annual implementation plan for the Institute's international programs and establishes mechanisms for evaluating the effectiveness of the Institutes' international programs as a whole; (6) assures that the Office of the Director is aware of the latest information in national and international research having a bearing on the Institute's international programs; and (7) works with the Fogarty International Center, other Institutes, DHHS, the Department of State, embassies of foreign countries, ministries of health, research and technology experts in foreign countries, research organizations and universities in the United States and abroad, and international health organizations on issues related to international research policies, programs, and activities.

## **Office of Extramural Policy - HNTBH**

(1) Provides leadership in all aspects of extramural research and serves as an authoritative source of policy guidance, interpretation, and communication for NICHD and the scientific community; (2) serves as a focal point for coordination and communication of grant-related issues with other NIH staff; (3) conducts referral activities for NICHD, in accepting “large grant” and conference grant applications, and approving the transfer of grant applications to and from NICHD; (4) manages appeals of scientific peer review, human subjects, animal welfare, the inclusion of women, minorities and children in clinical research, and financial conflicts of interest (FCOI) for grantees; (5) coordinates council actions related to second-level review of grant applications and other council actions; (6) coordinates the development and publication of FOAs and Notices in the NIH Guide; (7) reviews administrative actions, special actions, funding pay lists; (8) collaborates with NICHD IT leadership in the design and development of electronic research administration (eRA) systems and provides technical support and user training on NICHD and NIH eRA systems as needed; (9) coordinates training, fellowship, and career development award programs for NICHD; (10) collaborates in the development of NIH-wide training policies; (11) reviews K99/R00 transition requests and conducts the second-level review for NICHD fellowship awards; (12) develops, implements, and manages the extramural staff training program for NICHD.

## **Administrative Management Branch - HNT4A**

(1) Serves as the coordinating point in handling all administrative and management problems; (2) advises the DIR Director and other key officials of administrative policies and practices; (3) provides overall administrative support in budget, management and program analysis, personnel, budget execution, facilities management, space, procurement and contract management, and animal management in the Division of Intramural Research; (4) provides day-to-day administrative support services and special projects for the laboratories and Office of the Scientific Director; (5) applies principles and practices of EEO and affirmative action in all phases of personnel management; (6) manages service contracts, such as securing management support, animal services, and logistics support services; (7) provides support for financial management; (8) advises Director, DIR, on clinical patient activities and patient care; and (9) advises and plans for the management analysis and automated system within the Division of Intramural Research.

## **Administrative Services Branch - HNT126**

(1) Provides management advisory services, develops management and administrative policies and procedures and coordinates their implementation throughout the Institute; (2) conducts studies and analyses of Institute management functions, program and administrative operations, and policy compliance; (3) serves as staff resource for the Office of the Director and other key officials, providing administrative management services which includes financial management, personnel services, travel, procurement, budget, management analysis, information technology, facilities management, property management and other administrative functions; (4) provides oversight of the Office of Administrative Management information technology (IT) program, and manages its portfolio of administrative and management applications and reporting technology tools; (5) oversees the strategic planning, development, integration and financial support for administration of technology applications; (6) partners with IRMB to ensure that the Office of Administrative Management's portfolio of IT applications and systems comply and operate within all infrastructure and security requirements created and supported by IRMB.

## **Bone and Extracellular Matrix Branch - HNT4W**

(1) Conducts research on the extracellular matrix of bone; and (2) studies clinical disorders caused by primary defects in matrix and resulting in abnormal bone structure and/or function to understand their etiology and mechanisms in order to use the novel information thus derived for improved clinical diagnosis and treatment and to obtain further insights into normal skeletal functioning.

## **Cell Biology and Metabolism Branch - HNT4J**

(1) Conducts research directed toward clarifying developmental aspects of intracellular structure and function; (2) develops methods for studying receptor biosynthesis, dynamics, regulation, and degradation, using the human transferrin receptor as a model; (3) conducts clinical research on the fundamental mechanisms and treatment of patients with genetic disorders of metal metabolism; (4) examines mechanisms by which intracellular architecture is maintained, providing the basis for the function and dynamics of cellular organelles, e.g., the Golgi apparatus and the microtubule system; and (5) conducts research on the biochemistry and ultra-structure of gametes, placing emphasis on cell biological aspects of fertilization, and the initiation of embryonic development.

## **Developmental Endocrinology Branch - HNT48**

(1) Conducts clinical and laboratory research on the role of the endocrine system in the biologic differentiation of humans, at the level of the cell, the organ, and the organism, so as to provide a more comprehensive understanding of the role of the endocrine system in fetal, pubertal, and senescent differentiation; (2) investigates hypothalamic/pituitary/gonadal interrelationships and hypothalamic/pituitary/adrenal interrelationships in growth and development and in health and disease; and (3) studies the pathophysiology of a number of related disorders, including precocious and delayed puberty, premature adrenarche, and congenital adrenal hyperplasia, anorexia nervosa, gynecomastia, abnormal sexual differentiation, the problems of male and female infertility, and certain endocrine neoplasms which include tumors of the pituitary, adrenal gland, and gonads.

#### **Division of Intramural Research - HNT4**

(1) Plans and conducts the Institute's laboratory and clinical research programs which encompass the biomedical and behavioral aspects of human development relating to reproductive biology, population, maternal health, and child health; (2) ensures maximum utilization of available resources in the attainment of the Institute's objectives; (3) evaluates research efforts and establishes program priorities; (4) allocates funds, space, and personnel ceilings and integrates ongoing and new research activities into the program structure; and (5) provides advice to the Institute Director and staff on matters of scientific interest.

## **Endocrinology and Reproduction Research Branch - HNT43**

Plans and conducts laboratory research in reproductive biology with emphasis on the broad fields of: (1) gonadal trophic hormones and their isolation, purification, measurement, and mechanism of action; (2) ovarian and testicular function, including steroid synthesis, receptors, oogenesis, and spermatogenesis; and (3) other structural and functional aspects of human gonadal, pituitary, and adrenal cell and molecular biology.

#### **Division of Intramural Research - HNT4**

(1) Plans and conducts the Institute's laboratory and clinical research programs which encompass the biomedical and behavioral aspects of human development relating to reproductive biology, population, maternal health, and child health; (2) ensures maximum utilization of available resources in the attainment of the Institute's objectives; (3) evaluates research efforts and establishes program priorities; (4) allocates funds, space, and personnel ceilings and integrates ongoing and new research activities into the program structure; and (5) provides advice to the Institute Director and staff on matters of scientific interest.

## **Office of the Scientific Director-HNT41**

(1) Leads the Division of Intramural Research (DIR) in planning and conducting the Institute's laboratory, clinical, and population-based research. OSD functions are to (a) ensures maximum utilization of available resources in the attainment of the Institute's objectives; (b) assists in the conducting of research by intramural laboratories by implementing all NIH and DHHS rules and regulations, and ensuring compliance to existing guidelines for laboratory safety, the responsible conduct of research, and related issues; (c) evaluates research efforts and establish program priorities with the help and advice of the Board of Scientific Counselors (BSC); (d) allocates existing funds, space, and personnel, while integrating ongoing and embarking on new research activities, with the advice of the BSC, oversight by the Office of the Director (OD) of the Institute, and reporting annually to the Institute's Advisory Council; and (e) provides advice to the Institute Director, OD staff and the Division of Extramural Research (DER) on scientific and organizational issues.

## **Office of the Clinical Director-HNT412**

(1) Facilitates translational and clinical research on etiology, diagnosis, prevention, and treatment of genetic and endocrinological diseases in children; (2) facilitates translational and clinical research to understand and treat infertility; (3) facilitates translational and clinical research on the cause, diagnosis, prevention, and treatment of endocrinological cancers; (4) facilitates the ethical and scientific review of clinical protocols; (5) provides administrative support for the NICHD Institutional Review Board and Data Safety Monitoring Committee; (6) provides management of the NICHD Biorepository; (7) serves as the interface between NICHD clinical investigators and both the NIH Clinical Center and the NIH Office of Human Subjects Research; and (8) represents NICHD on the NIH Clinical Center Medical Executive Board.

## **Office of Education-HNT413**

(1) Supports the needs of intramural scientists, fellows, and students at all levels as they relate to training, through: recruitment and development of academic support programs, including writing, grantsmanship, presentation skills, career development, management skills, meeting planning and delivery; counseling and problem solving for challenging personal and/or professional situations; creation of new training initiatives in response to external demands (e.g., responsible conduct of research, RCR); (2) oversees graduate and graduate medical education programs, to ensure compliance with regulations, program expectations, and maintenance of accreditation; (3) contributes to mentoring and evaluation of trainees; (4) support the needs of intramural tenure-track investigators; (5) serves as the grants office on behalf of applicants, both investigators and fellows; (6) advises the Scientific Director, Group of Senior Advisors, and institutional leadership of issues related to trainees; and (7) participates as team members in trans-intramural committees and programs on behalf of NIH trainees.

## **Administrative Management Branch-HNT41B**

(1) Serves as the coordinating point in handling all administrative and management issues for the Division of Intramural Research (DIR); (2) advises the Scientific Director and other key officials of administrative policies and practices; (3) provides overall administrative support in budget, management and program analysis, personnel, budget execution, facilities management, space, procurement and contract management, and animal management; (4) provides day-to-day administrative support services and special projects for the laboratories and Office of the Scientific Director; (5) applies principles and practices of EEO and affirmative action in all phases of personnel management; (6) manages service contracts, such as securing management support, animal services, and logistics support services; (7) provides support for financial management; (8) supports the Clinical and Scientific Directors with clinical patient activities and patient care; and (9) advises and plans for the management analysis and automated system within the DIR.

## **Research Animal Management Branch-HNT41C**

(1) Provides animal research support services to intramural investigators, including operational and management of three shared animal facilities as lead institute; (2) develops and implements procedures to ensure compliance with federal policy, regulations, and legislation governing the ethical use of animals in biomedical research and continuing accreditation by the American Association for Accreditation of Laboratory Animal Care (AAALAC); (3) provides a clinical veterinary medicine program, including clinical diagnosis and therapy; (4) provides animal disease control and a comprehensive preventive medicine program to prevent disease in laboratory animals and to prevent the spread of zoonotic diseases; (5) manages budgets for all animal holding costs; (6) provides administrative support to the NICHD Animal Care and Use Committee; (7) represents the interests of the NICHD on all aspects of animal research including participation on user committees for all NIH animal facilities that maintain NICHD animals; (8) formulates policies and standards for animal ordering and receipts; (9) evaluates animal facilities and holding areas for design, animal housing systems, environmental control, and general operation so as to minimize research complications due to environmental variation or animal disease; and (10) provides personnel with professional and technical consultation, training, and assistance in the field of laboratory animal science.

### **Pediatric and Adolescent Gynecology Program – HNT41D**

(1) Trains gynecologists to function as consultants for other services in the gynecological care of children and adolescent from the prenatal period to age 21. This includes (a) management of pelvic masses, vulvar conditions, congenital anomalies, fertility preservation, gynecologic endocrine disorders including precocious and delayed puberty; (b) adolescent care including confidential services such as contraception and management of sexually transmitted diseases. (2) Trainees will master the gynecologic management of adults born with congenital conditions including anomalies, differences in sex development, complex medical conditions and bleeding disorders.

### **Bioinformatics and Scientific Programming Core – HNT41E**

(1) Provides comprehensive, custom bioinformatics and scientific programming support to intramural investigators; (2) acts as a central resource for bioinformatics for the institute by consulting, advising, and training researchers in bioinformatics, programming, and computational methodology; and (3) develops and maintains novel tools, software infrastructure, and web applications to support and improve intramural research programs.

## **Computer Support Services Core-HNT415**

(1) Provides clinical informatics, technology, and management support for the Clinical Trials Database (CTDB); (2) provides Information Technology (IT) support for clinical protocols with research data collection and analysis; (3) provides IT support and management of administrative web-based applications; and (4) provides supplemental IT services for the infrastructure of the Division of Intramural Research.

## **Microscopy and Imaging Core-HNT416**

(1) Provides training, support, and instrumentation for all investigators who require high-resolution microscopy in their research; (2) focuses on improving, automating, and providing enhanced access to all modes of advanced imaging technologies; (3) strives to educate its users, and provide full access to novel technologies in microscopy, image processing, sample preparation technologies; (4) provides image data archival training, support and image data curating.

## **Molecular Genetics Core-HNT417**

(1) Provides state-of-the-art DNA and RNA sequencing services to support research by intramural investigators; (2) provides bioinformatic services to support research by intramural investigators; and (3) serves as a resource for investigators with respect to clinical and diagnostic molecular biology techniques and data analysis.

## **Pediatric Endocrinology Fellowship Program -HNT418**

(1) Provides comprehensive training in clinical patient management and guidance in the development of research skills, ensuring the delivery of excellent pediatric endocrine care to patients at the Clinical Center and at affiliate sites; (2) sustains the mission of intramural research at the NIH clinical center, including training the next generation of physician researchers and mentoring trainees in the process of clinical research; (3) works towards fulfilling the mission of the NICHD, specifically with regard to helping children achieve their full potential for healthy and productive lives in the face of diseases related to impairment of the endocrine system; and (4) transforms fellows to become independent practitioners in pediatric endocrinology along the continuum of medical education by fostering the development of the skills, knowledge, and attitudes leading to proficiency in all the domains of clinical competence under the guidance and supervision of faculty members.

## **Inter-Institute Internal Medicine Endocrinology Fellowship Program-HNT419**

(1) Trains fellows to be competent to practice in endocrinology, diabetes, and metabolism in fulfillment of the requirements of the American College Graduate Medical Education such that trainees are competent to practice and eligible to sit for the American Board of Internal Medicine subspecialty board examination in endocrinology, diabetes, and metabolism; and (2) trains fellows in the conduct, interpretation, and consumption of clinical and translational research.

## **Reproductive Endocrinology and Infertility Fellowship Program-HNT41A**

(1) Trains fellows in a critical area of Women's' Health that includes: (a) endocrine disorders specific to women, (b) infertility (including IVF),(c) reproductive surgery; and (d) research relevant to the field.

## **Division of Developmental Biology-HNT4B**

(1) Conducts basic and translational research in the area of developmental biology, in support of the mission of the Division of Intramural Research (DIR); and (2) coordinates with the DIR to ensure the necessary resources and support is available to investigators and laboratory personnel.

## **Section on Eukaryotic DNA Replication-HNT4B2**

(1) Conducts research to understand how genome duplication is regulated during mammalian development; (2) determines how mammals restrict DNA replication to once per cell division; (3) determines how specialized cells undergo multiple rounds of genome duplication without cell division or apoptosis; and (4) aims to identify differences between cancer cells and normal cells that can be used to kill cancer selectively.

### **Section on Formation of RNA-HNT4B3**

(1) Pursues relationship of DNA stability affected by RNA/DNA hybrids and ribonucleoside monophosphates in DNA; (2) examines when and how these complexes are formed; (3) addresses how ribonucleases H (RNases H) resolve these complexes and the nature of potential substrates that avoid processing by RNases H; (4) examines how RNases H are related to HIV viral RNase H; (5) describes how RNase H is related to mitochondrial DNA replication and function; (6) examines defects in mice related to the human neurological disorder Aicardi Goutieres Syndrome and Systemic Lupus Erythematosus; (7) employs various model organisms to discover evolutionarily conserved means of damage by working with model organisms including prokaryotes, yeasts and mice; and (8) trains young scientists in molecular techniques, how to apply these mammalian systems, and how to be the best they can be.

## **Section on Hematopoiesis and Lymphocyte Biology-HNT4B5**

(1) Examines the role of T-cell antigen receptor (TCR)-mediated signaling in regulating T- cell maturation and formation of the mature T-cell repertoire; (2) identifies and characterizes proteins that transmit or modify TCR signaling; (3) investigates the mechanisms responsible for formation, maintenance, self-renewal and differentiation of Hematopoietic Stem Cells (HSCs); and (4) identifies genetic disorders of HSCs or hematopoietic progenitors that predispose to oncogenesis. Transgenic and gene targeting methods are used to create overexpression, dominant-negative, and loss-of-function mouse models for investigation and genome-wide screening is performed to analyze transcription, DNA binding of regulatory factors and epigenetic modifications that control gene expression.

## **Section on Molecular Regulation-HNT4B6**

(1) Seeks to understand how cells bacteria coordinate and adjust the expression of genomes to survive and to adapt to a variety of sources of physiological stress; (2) uses genetic, molecular and biochemical approaches to focus on understanding the regulatory properties of naturally occurring nucleotide analog regulators (pppGpp and ppGpp); (3) interests in how naturally occurring regulatory nucleotide analogs (e.g., pppGpp and ppGpp) have these effects on gene transcription; and (4) tries to understand how stress conditions are sensed to coordinate regulatory signaling to ensure appropriate global regulatory adjustments.

## **Section on Gene Expression-HNT4BA**

(1) Conducts experiments on the control of gene expression during development; (2) uses genetics, genomics, transgenesis, and biochemistry to investigate mechanisms of gene silencing and gene activation; (3) studies gene expression *in situ* in order to understand how DNA regulatory elements act together to control gene expression; and (4) studies how distant regulatory sequences regulate the correct target gene.

## **Section on Neural Developmental Dynamics-HNT4BB**

(1) Uses a combination of cellular, molecular and genetic approaches to investigate how interactions between cells coordinate morphogenesis, cell migration and cell fate specification in the nervous system; (2) studies the mechanisms that determine collective migration of the lateral line primordium; (3) studies mechanisms that determine morphogenesis of neuromasts within the migrating primordium; (4) studies mechanisms that determine sequential deposition of nascent neuromasts from the trailing end of the migrating primordium; and (5) develops integrative agent-based computational models to visualize how interactions between cells coordinate the self-organization of the posterior lateral line system.

## **Section on Vertebrate Organogenesis-HNT4BC**

(1) Studies the development of the vertebrate circulatory system using the zebrafish as an accessible genetic and experimental model system, as well as *in vitro* endothelial cell culture and mouse models; (2) studies how vascular and hematopoietic progenitors arise, how vessels acquire differentiated identities, and how vascular networks are assembled during development; and (3) studies mechanisms regulating vascular network assembly and hematopoietic differentiation in developing animals, in order to gain insights into how these processes might be altered or co-opted in human vascular and hematopoietic pathologies, and to uncover potential therapeutic approaches that might be useful in their treatment.

## **Section on Chromatin and Gene Expression-HNT4BD**

(1) Researches the role of chromatin structure in gene regulation, using budding yeast and mouse as model organisms; and (2) studies the functions and mechanisms of action of chromatin remodeling complexes to address their roles in transcription and cancer

## **Section on Epigenetics-HNT4BG**

(1) Conducts research on the role of epigenetics in regulating gene expression during normal development and in diseased states; (2) uses biochemical, molecular, and genetic analyses to identify mechanisms of genomic imprinting on a cluster of imprinted genes on the distal end of mouse chromosome 7 (syntenic to human 11p15.5); (3) generates mouse models for loss-of-imprinting and loss-of-function diseases in the 11p15.5 region; and (4) studies the interplay between disease progression and normal developmental pathways using cardiac diseases from this region as a model.

## **Section on Molecular and Cellular Biology-HNT4BH**

(1) Conducts basic biomedical research in genetics and biochemistry on the fundamental processes of RNA synthesis by RNA polymerase III and RNA metabolism, and their roles in growth, development, health and disease; (2) communicates research results to scientific journals; and (3) engages in the training of post-doctoral fellows

## **Section on Molecular Endocrinology-HNT4BJ**

(1) Investigates molecular basis of the control of gonadal function, with particular emphasis on the transcriptional regulation of the luteinizing hormone receptor directed to identify regulatory modalities and interactions essential for activation/silencing of its transcription; (2) investigates structural, transcriptional events and requisite signal transduction pathways, which participate in the function/regulation of the Prolactin Receptor relevant to physiological regulation, breast cancer progression and resistance to endocrine therapies; and (3) investigates the function and regulation of Gonadotropin Regulated Testicular RNA helicase (GRTH/DDX25), an essential post-transcriptional regulator of spermatogenesis, discovered in this laboratory, of relevance to male fertility and contraceptive development.

## **Section on Molecular Genetics of Immunity-HNT4BK**

(1) Conducts studies on epigenetic regulation of innate immunity, particularly during the development and in response to pathogen infection; (2) inquires how genes in the chromatin environment are transcribed in macrophages and related cells; (3) probes into the DNA binding transcription factor, IRF8, the histone binding and modifying factors, BRD4 and WHSC1; (4) explores the mode and mechanism of chromatin exchange involving the H3.3 histone; and (5) elucidates their effects on genome-wide functions by analyzing mutant mouse models.

## **Mouse Transgenic Core -HNT4BL**

(1) Uses site directed mutagenesis to generate novel mouse embryonic stem cell lines in vitro; (2) generates novel mouse strains by injection of mutant embryonic stem cells into wild type mouse blastocysts; (3) generates novel primary cell lines (embryonic stem cell, trophoblast stem cell, and embryonic fibroblast) from mutant and wild type mouse embryos; (4) cryopreserves embryos for long term storage of valuable mouse strains; (5) provides advice and training to NICHD researchers in regard to mouse genetics and husbandry; and (6) performs specialized surgeries to support NICHD research.

## **Zebrafish Core-HNT4BM**

(1) Facilitates access to zebrafish resources and protocols for laboratories without their own access; (2) maintains reagents, protocols and other resources of general utility for NICHD zebrafish-focused laboratories; (3) provides consultation, training and mentorship on zebrafish-related projects; and (4) performs scholarly activities in the field of Developmental Biology.

## **Section on Behavioral Neurogenetics – HNT4BN**

Identifies mechanisms underlying the functional development of neuronal circuits that mediate sensorimotor reflexes, using zebrafish as a model for understanding behavioral control in humans. The Section combines computational analysis of behavior with novel transgenic methods to locate the neuronal connections that select appropriate responses to stimuli. Classical genetic and cell-based manipulations are used to reproduce endophenotypes of neurodevelopmental disorders such as schizophrenia and reveal how perturbations disrupt sensory processing.

### **Section on Mammalian Development and Evolution – HNT4BP**

(1) Conducts basic research into the mechanisms governing the regulation of gene expression during development and its evolution in mammals; (2) Uses genetic, biochemical, and genomics approaches to explore the interplay between transcription factors, enzymes that regulate the chromatin packing of DNA, and cis-regulatory sequences; (3) Explores the functional impact of endogenous retroviruses (ERVs) and other transposable elements (TEs) on mammalian development by exploring the “arms race” between TEs and and Kruppel Associated Box zinc finger proteins (KRAB-ZFPs), which have adapted to bind and repress TE activity.

## **Division of Basic and Translational Biophysics-HNT4E**

(1) Conducts basic, clinical, and translational research in the areas of biophysics in support of the mission of the NICHD Division of Intramural Research (DIR); and (2) coordinates with the DIR to ensure the necessary resources and support is available to investigators and laboratory personnel.

## **Section on Molecular Transport-HNT4E4**

(1) Studies mitochondrial and bacterial membrane proteins that form “large” beta-barrel channels which are the gateways of metabolite exchange as well as the components of many toxins recognized as novel drug targets; (2) elucidates physical principles and molecular mechanisms which control metabolite flux under normal and pathological conditions by investigating channel interactions with cytosolic proteins, newly synthesized and clinically approved drugs, and membranes, as modified by the lipid composition and anesthetics; and (3) strives to determine how to design new agents and strategies to effectively correct the deviant molecular transport disorders that impede human wellbeing and healthy development.

## **Section on Integrative Biophysics-HNT4E5**

(1) Uses the expertise and the techniques they perfected over the years to address several biological and pathological problems that have in common the underlying regulation or disturbance of protein/lipid interactions by studying membranes, viruses, organelles, cells, tissues, and human subjects in order to understand (a) the molecular organization of cellular membranes; (b) the physico-chemical mechanisms of membrane remodeling, the molecular anatomy of tissues, and (c) the role physical forces play in the development of genetic, viral, parasitic, metabolic, developmental, and neoplastic diseases. Eukaryotic life must create the many shapes and sizes of the system of internal membranes and organelles that inhabit the variety of cells in nature. For cells to secrete signaling macromolecules, express surface transporters, import macromolecular cargo, store energy, and repair damaged plasmalemma, the membranes must remodel. Basic membrane mechanisms require highly regulated and highly organized hierarchies in space and time to allow the organism to thrive despite environmental challenges such as infections by other organisms, unpredictable food supply, and physical trauma.

## **Section on Membrane Biology-HNT4E6**

(1) Explores the molecular mechanisms by which proteins remodel membrane lipid bilayers during ubiquitous membrane fusion, essential in normal physiology, during development and in disease; and (2) combines in-depth analysis of the best-characterized fusion reactions such as cell entry by enveloped viruses with comparative analysis of less explored fusion reactions such as cell-cell fusion in development and maintenance of muscles and bones that can reveal new kinds of fusion proteins and yield new targets for drugs and novel drug-screening and drug-delivery approaches.

## **Section on Intercellular Interactions-HNT4E7**

(1) Studies normal and pathological cell functions in the context of tissues and tissue-like multicellular structures. Research in this section aims to identify key elements of cell-cell interactions in the context of complex multicellular systems and to understand critical mechanisms by which various microbes and other pathogenic factors modulate and disrupt these interactions causing diseases.

## **Division of Obstetrics and Maternal-Fetal Medicine-HNT4K**

(1) Conducts clinical and translational research to improve the understanding of the mechanisms of disease, diagnosis, prediction, treatment and prevention of complications of pregnancy responsible for maternal and perinatal morbidity and mortality

## **Perinatology Research Branch-HNT4K2**

(1) Conducts clinical and laboratory research to improve the understanding of normal pregnancy and the "great obstetrical syndromes", including preterm labor, preeclampsia, intrauterine infection, fetal growth disorders, congenital anomalies and fetal death; (2) uses a multi-disciplinary approach and brings expertise from clinical specialties (obstetrics, Maternal-Fetal Medicine, neonatology, placental pathology, diagnostic imaging), basic sciences (immunology, microbiology), and epidemiology to inform the prediction, diagnosis, prevention and treatment of complications of pregnancy; and (3) trains individuals in Maternal-Fetal Medicine, obstetrics, reproductive biology, reproductive immunology, and other disciplines whose goal is to improve pregnancy outcome.

## **Division of Translational Imaging and Genomic Integrity-HNT4P**

(1) Conducts basic, pre-clinical and clinical research in biophysics, neuroscience, and imaging sciences, and fundamental studies in DNA replication, repair and mutagenesis in support of the mission of the Division of Intramural Research (DIR); and (2) coordinates with the DIR to ensure that necessary resources and support are available to its Sections' investigators and laboratory personnel.

### **Section on Quantitative Imaging and Tissue Sciences-HNT4P3**

(1) Invents, develops, validates, and translates novel quantitative imaging methodologies and modalities, primarily MRI-based, with a goal to elucidate salient features and imaging biomarkers to help characterize normal and abnormal developmental trajectories, and to improve screening, diagnosis or prognosis of diseases, disorders, and disabilities primarily within the pediatric population; (2) advances basic and applied research in imaging physics and related areas of mathematical and imaging sciences; (3) performs basic and applied research in quantitative tissue sciences to improve understanding of structure/function relationships, primarily in extracellular matrix (ECM), in an integrative fashion, (i.e., over a hierarchy of salient length and time scales), using an array of biological, mathematical, physical, and computational methods, models, and model systems, including tissues, tissue components, and biomimetic tissue models; and (4) advances knowledge in tissue sciences through the application of principles of polymer physics and sciences, materials sciences and engineering, transport processes, physical biochemistry and related disciplines.

## **Section on Translational Biophotonics -HNT4P5**

Devises quantitative bio photonics imaging technologies and methodologies, translating benchtop studies to the bedside; (1) explores endogenous (scattering and absorption) and exogenous ( using fluorescence probes) optical contrast mechanisms for characterizing abnormal development and function in tissues such as placenta; (2) focuses on using near infrared spectroscopy and imaging to assess biomarkers for a wide range of brain development abnormalities and injuries, specifically, but not limited to, cognitive and behavioral disorders; and (3) is also involved in clinical and preclinical studies, aimed at characterization of growth and development of various abnormal tissues and monitoring the efficacy of their treatment using optical methods, such as fluorescence and multi spectral imaging.

## **Section on DNA Replication, Repair and Mutagenesis-HNT4P7**

(1) Studies molecular mechanisms of DNA replication, repair and mutagenesis; (2) investigates how cells cope with exposure to both endogenous and exogenous DNA-damaging agents and, in particular, how low-fidelity Y-Family DNA polymerases replicate through damaged DNA; (3) studies damage-inducible responses in bacteria, archaea and eukaryotic cells; and (4) utilizes a variety of molecular, biochemical, and structural biology techniques, including PCR, protein purification and characterization, enzymology, protein crystallization, and yeast/bacterial genetics.

## **Section on Biomedical Optics – HNT4P8**

Develops models, methods, and devices for understanding and controlling light interactions with biological tissues. These methods are used to perform real-time quantitative measurements of clinically-relevant information, including: tissue blood flow, oxygen extraction, metabolic rate of oxygen consumption, and body/tissue composition including lean mass, hydration, and fat mass. Advanced capabilities include continuous dynamic monitoring of intrinsic physiological signals that can be used in feedback optimization for guiding therapies and clinical decision making. Our technology development effort includes portable, bedside, non-contact and wearable sensor platforms, as well as the design and integration of probes into instruments for minimally invasive surgical feedback and guidance.

## **Division of Translational Medicine-HNT4R**

(1) Conducts basic, translational, and clinical research on etiology, diagnosis, prevention, and treatment of genetic and endocrinologic diseases in children; (2) conducts basic, translational, and clinical research to understand and treat infertility; (3) conducts, basic, translational, and clinical research on the cause, diagnosis, prevention, and treatment of endocrinologic cancers; (4) utilizes biochemical, molecular, and cell biology techniques to elucidate the cause and study the pathogenicity of the above disorders; (5) utilizes cellular and animal models to study pathogenesis and develop therapies; (6) conducts clinical studies to determine natural history, define etiology and pathology, and to perform clinical trials to evaluate novel interventions; and (7) coordinates with the intramural programs to ensure resources and support necessary to the above are available to investigators and laboratory personnel.

## **Section on Growth and Development-HNT4R2**

(1) Investigates the cellular and molecular mechanisms governing childhood growth and development, focusing particularly on the mechanisms that regulate cell proliferation in growing tissues; (2) studies childhood growth disorders to discover the underlying etiology, focusing primarily on endocrine and genetic causes; and (3) conducts research designed to develop new therapeutic approaches to treat childhood growth disorders.

### **Section on Clinical Endocrinology-HNT4R3**

(1) Studies the physiology and pathophysiology of the hypothalamic-pituitary-adrenal (HPA); (2) focuses on clinical trials assessing the HPA axis and develops new diagnostic end therapeutic methods for human diseases of the HPA axis; and (3) assesses clinical applications of antiprogestins

## **Section on Medical Neuroendocrinology-HNT4R4**

(1) Conducts patient-oriented research about the etiology, pathophysiology, diagnosis, prognosis, and treatment of pheochromocytoma and paraganglioma; (2) uses new techniques developed at the NIH (e.g. plasma metanephrines and methoxytyramine, fluorodopamine positron emission tomography) for accurate biochemical diagnosis and localization of various pheochromocytomas and paragangliomas; and (3) conducts studies focusing on molecular, genetic, proteomic, and metabolomics to elucidate pathogenesis of pheochromocytoma and paraganglioma in order to search for new prognostic markers or therapeutic targets for metastatic disease.

## **Section on Physical Biochemistry-HNT4R6**

(1) Conducts translational studies of molecular mechanisms of extracellular matrix and connective tissue homeostasis and pathology in reproduction and child development; (2) develops new physical, chemical and biochemical experimental techniques and theoretical methods for imaging and analysis of molecular and cellular interactions involved in extracellular matrix and connective tissue homeostasis and pathology; (3) collaborates with intramural and extramural clinical researchers and molecular biologists on characterization of molecular pathophysiology in patients, animal models and in vitro systems; and (4) combines fundamental studies of common physical principles with practical application of the gained knowledge and novel technologies for diagnostics and therapy of connective tissue diseases as well as for connective tissue engineering and regeneration.

## **Section on Developmental Genetics-HNT4R9**

(1) Conducts basic laboratory studies to understand the molecular mechanisms of hereditary childhood neurodegenerative lysosomal storage disorders (LSDs); (2) analyzes the effects of potential therapeutic agents, identified during laboratory investigations, on animal models of neurodegenerative LSDs; and (3) applies pre-clinically tested promising small molecules in clinical trials.

## **Section on Molecular Dymorphology- HNT4RA**

(1) Conducts research on the biological processes underlying genetic syndromes that result in congenital malformations, cognitive impairment, and neurodegeneration; (2) focuses on a group of human syndromes caused by inborn errors of cholesterol homeostasis, primarily Smith-Lemli-Opitz syndrome and Niemann-Pick Disease type C; and (3) elucidates the molecular, biochemical, cellular, and developmental processes that underlie the pathological processes found in these disorders and to apply this knowledge to develop and test therapeutic interventions. Study of these relatively rare genetic syndromes may give insight into normal biological processes and into other more common disorders.

## **Section on Cellular Signaling-HNT4RB**

(1) Investigates experimentally and theoretically the cell signaling process in neuroendocrine and endocrine tissues of developing, adult, and aging mammals. The main focus of investigation is on the excitable hypothalamic and pituitary secretory cells and the cell-type-specific signalosome required to control their particular functions. This includes three lines of studies: (a) structural and functional characterization of receptors and channels natively expressed in these cells, their activation by orthosteric ligands and voltage, modulation of their activity by allosteric ligands, and their desensitization, inactivation and deactivation; (b) transmission of signals from receptors and channels to a variety of transducers and amplifiers to produce intracellular signaling; and (c) spatial and temporal aspects of cell signaling pathways, roles of intracellular messengers in modulating excitability, gene expression, and hormone secretion by constitutive and regulated exocytosis, and the influence of steroid hormone milieu and their intracellular receptors on the plasma membrane signaling cascade and effector responsible for modulating cellular responses.

## **Section on Endocrinology and Genetics-HNT4RC**

(1) Conducts clinical and laboratory research on genetic syndromes with an endocrine phenotype studying unique populations of patients from around the world, applying genomic approaches and other novel genetic tools and methods to identify genes or molecular pathways that are responsible for these diseases. Animal models (mice, fish and flies) are an essential part of the work of the Section. Patients are admitted to the Clinical Center on investigational protocols.

## **Section on Growth and Obesity-HNT4RD**

(1) Conducts research on the physiological and psychological processes underlying conditions that cause obesity focusing on elucidating the genetic underpinnings of the metabolic and behavioral endophenotypes that contribute to the development of obesity in children; (2) studies patients with monogenic and polygenic obesity, to advance our understanding of energy balance regulation during childhood; (3) examines genetic and phenotypic factors predictive of progression to adult obesity in children who are in the “pre-obese” state, allowing characterization of phenotypes unconfounded by the impact of obesity itself using a unique longitudinal cohort of children at-risk for adult obesity who have undergone intensive metabolic and behavioral phenotyping; (4) intensively studies genetic variants that are linked to obesity which impair gene function; and (5) carries out proof-of-concept clinical studies examining approaches to prevent and treat obesity and its co-morbid conditions in children and adults. These approaches are expected to improve our ability to predict which children are at greatest risk for obesity and its comorbid conditions and to lead to more targeted, etiology-based prevention and treatment strategies for pediatric obesity.

## **Section on Cellular Differentiation-HNT4RE**

(1) Conducts research directed toward applying biochemistry and molecular genetics to studies that will translate into clinical benefits for patients. Major emphasis is to move from molecular genetics and immunology of heritable human disorders to establish proof of mechanisms that form the basis of moving into clinical studies. Techniques utilized include transgenic animals, biochemical, immunological, and molecular biological methodologies.

## **Division of Neurosciences and Cellular and Structural Biology-HNT4T**

(1) Conducts basic and translational research in the area of the neurosciences, in support of the mission of the Division of Intramural Research (DIR); and (2) coordinates with the DIR to ensure the necessary resources and support is available to investigators and laboratory personnel.

## **Developmental Branch-HNT4T2**

(1) Studies mechanisms controlling neuronal excitability and development, utilizing various patch clamp, molecular, imaging and immunohistochemical techniques from mammalian CNS neurons maintained in a variety of in vitro preparations; (2) characterizes inhibitory and excitatory synaptic transmission, developmental processes governing neural development, and the role of ion channel activity with current emphasis on excitatory amino acid receptors using both physiological and pharmacological approaches and experimental approaches ranging from patch clamp recordings from single neurons using infra-red video microscopy, analysis of synaptic activity between pairs of neurons, imaging of intracellular signals, to transgenic approaches; and (3) investigates mechanisms of short- and long-term plasticity of synaptic transmission, differential targeting of synaptic receptors, pathophysiological processes in clinically relevant neuronal migration disorders, ion channel regulation of development and excitability and drug action at L-glutamate receptor subtypes.

## **Section on Cellular and Synaptic Physiology-HNT4T22**

(1) Focuses on three main aspects of cortical and hippocampal function: (a) the properties and roles of glutamatergic and GABAergic receptors and synapses made onto inhibitory interneurons and their downstream targets within the hippocampal formation; (b) the control of well-defined inhibitory interneuron subtypes and the circuits in which they are embedded by both intrinsic and extrinsic neuromodulatory circuits; and (c) genetic approaches to examine the embryogenesis, migration and development of specific cohorts of medial- and caudal-ganglionic eminence derived inhibitory interneurons. The overall goal of these studies is to elucidate the developmental trajectory taken by specific cells of the cortex and hippocampus, to understand their role in the emerging cortical physiology and how these systems are perturbed during pathophysiological processes.

## **Section on Molecular Signal Transduction-HNT4T23**

(1) Investigates the molecular basis of signal propagation that links stimulation of cell surface receptors to specific cellular responses in eukaryotic cells; (2) studies biological processes that determine the unique identity of cellular membranes to serve as platforms for the assembly of protein signaling complexes; (3) studies include the cloning and characterization of enzymes that regulate inositol lipid second messengers to determine their impact in defining the identity of cellular membranes; (4) devotes significant efforts to generate new molecular tools for the visualization and artificial modification of signal transduction events using fluorescence techniques in single living cells; (5) utilizes these approaches to understand how cells organize their signaling compartments to ensure spatial and temporal integration during intracellular signal propagation; and (6) aims to uncover molecular defects that underlie developmental defects and other human disease conditions.

## **Section on Molecular Neurophysiology and Biophysics-HNT4T24**

(1) Studies the roles of voltage-gated and neurotransmitter-activated channels in regulating neuronal development and synaptic plasticity in the mammalian hippocampus using electrophysiological, molecular, and biochemical techniques; (2) studies the molecular mechanisms of voltage-gated channel trafficking and expression; and (3) works to identify the functional role of voltage- and neurotransmitter-gated channels expressed in hippocampal dendrites during development, memory formation and in pathophysiological processes thought to have a synaptic basis, including Autism, Fragile X Syndrome and Alzheimer's disease.

## **Section on Sensory Coding and Neural Ensembles-HNT4T25**

(1) Studies fundamental mechanisms by which sensory information is collected, transformed, stabilized, and compared as it makes its way through the nervous system; (2) studies roles and neural mechanisms of oscillatory synchronization of neurons; studies information-encoding and decoding strategies of sensory neurons and interneurons; (3) studies formats of neural codes; (4) studies innate sensory preferences and development of acquired preferences; studies spatio-temporal population codes used by the brain to represent environmental stimuli; (5) studies mechanisms of learning and memory; and (6) uses electrophysiological, anatomical, histological, genetic, and computational strategies.

## **Molecular Medicine Branch-HNT4TA**

(1) Works to understand the pathophysiology of inherited diseases using biochemistry, molecular biology, imaging, and neurobehavioral studies in animal models (mouse, zebrafish) that recapitulate the disease phenotypes, as well as cells from affected patients; (2) translates insights about disease pathogenesis into treatments that can improve patients' lives, including viral-mediated gene addition, antisense RNA, and small molecules; and (3) conducts clinical protocols and preclinical studies in mouse models to lay the groundwork for other first-in-human clinical trials.

## **Section on Human Iron Metabolism-HNT4TA2**

(1) Conducts research on the molecular and cellular mechanisms that maintain human iron homeostasis. Understanding the regulation of genes encoding proteins of iron metabolism has provided unique insights into the mechanisms by which cells regulate the fate of mRNAs. The expression levels of ferritin H and L chains, transferrin receptor 1, hypoxia inducible factor 2 alpha and numerous other proteins are post-transcriptionally mediated by the RNA binding proteins, iron regulatory proteins 1 and 2; (2) studies how iron sulfur clusters are synthesized and inserted into proteins, including cytosolic aconitase; (3) conducts experiments aimed at elucidation of molecular mechanisms underlying regulation of genes of iron metabolism, including those involved in intestinal iron uptake, sequestration, trafficking, release into the circulation, and processing of iron by macrophages; (4) studies the physiology of iron metabolism in murine and human settings, and addresses pathophysiology of human diseases such as microcytic anemia, erythropoietic protoporphyria, pulmonary hypertension, adult onset motor neuron disease, vasculitis and renal failure due to heme oxygenase 1 deficiency, and ISCU myopathy, a disease caused by malfunction of the iron sulfur cluster assembly machinery; and (5) studies of iron sulfur cluster biogenesis are relevant to numerous rare genetic diseases with different clinical presentations, ranging from Friedreich's ataxia to sideroblastic anemia.

## **Cell Biology and Neurobiology Branch-HNT4TB**

(1) Conducts research directed toward elucidating developmental aspects of cell structure and function; (2) studies the mechanisms of intracellular protein trafficking and the diseases that result from their dysfunction; (3) uses emerging visualization technologies to study the biogenesis and maintenance of intracellular organelles; (4) investigates the structure and mechanisms of integral membrane proteins; (5) studies the regulation of the cell cycle during early oogenesis; (6) studies the mechanisms of cellular communication during patterning and synapse development; (7) conducts research toward understanding how experience regulates synaptic plasticity, neuronal network function, behaviors and cognitive processes during neurodevelopment; and (8) investigates the assembly and function of visual circuits.

## **Section on Intracellular Protein Trafficking-HNT4TB2**

(1) Investigates the molecular mechanisms by which membrane proteins such as receptors, transporters and adhesion molecules are sorted to different compartments within the cell. Key to these mechanisms is the interaction of sorting signals with adaptor proteins that are components of vesicle coats; (2) analyzes the roles of these proteins in normal cell physiology and in pathological states. Of particular interest are genetic diseases caused by mutations in adaptor proteins such as certain types of the Hermansky-Pudlak syndrome, MEDNIK syndrome and hereditary spastic paraplegia; and (3) studies how some pathogens such as HIV-1 exploit the host's protein sorting machinery for replication.

### **Section on Molecular Neurobiology-HNT4TB3**

(1) Studies how experience (i.e. activity) regulates synaptic plasticity, neuronal network function, behaviors and cognitive processes during neurodevelopment, and how genetic variants that regulate these neural processes may constitute liabilities for developing psychiatric disorders in adolescence; (2) focuses on the neurotrophic factor Neuregulin and its tyrosine kinase receptor ErbB4, an activity-dependent signaling pathway genetically associated with psychiatric disorders that functions to regulate synaptic plasticity and excitatory\inhibitory (E\I) balance - key features thought to underlie the etiology of numerous developmental psychiatric disorders and neurological diseases, such as: schizophrenia, autism, ADHD and epilepsy; (3) investigates the functional role of Neuregulin-ErbB4 signaling during neurodevelopment, we use a combination of multi-disciplinary techniques that include: regional- and developmental-specific gene targeting in mice using transgenic crosses or stereotaxic viral injections, electrophysiological recordings in acute brain slices from genetically targeted mice, multi-electrode field recordings and reversemicrodialysis neurochemistry from brains of freely moving rodents, confocal fluorescence microscopy in fixed and live tissue, proteomics, and behavioral testing. The ultimate goal of this multi-disciplinary approach is to generate holistic models to investigate the developmental impact of genes that modulate E\I balance and neuronal network activity, which consequently affect behaviors and cognitive functions altered in psychiatric disorders.

## **Section on Gamete Development-HNT4TB4**

(1) Conducts research on the regulation of meiotic progression and gamete development during oogenesis; (2) studies how metabolism impacts oocyte development and genome stability; (3) identifies new regulators of metabolism using forward genetic and biochemical strategies; and (4) defines the mechanisms by which metabolic signals interphase with the cell cycle machinery to influence meiotic progression.

### **Section on Cellular Communication – HNT4TB8**

Conducts research on the molecular mechanisms that regulate formation and function of synapses during development and homeostasis using the *Drosophila* model system. Studies key processes in synaptogenesis, including (1) trafficking of components to the proper site, (2) organizing those components to build synaptic structures, and (3) maturation and plasticity of the synapse to optimize its activity. Characterizes the agonist/antagonist selectivity and gating properties of ionotropic glutamate receptors. Studies the role of auxiliary subunits on the distribution and function of glutamate receptors. Analyzes how intercellular communication, in particular signaling by TGF- $\beta$  factors, functions to sense synapse activity and to coordinate synapse structure and function. Searches for novel synaptogenic activities and evolutionarily conserved mechanisms utilized to assemble functional synapses and to fine-tune them during plasticity and homeostasis; these functions may be disrupted in pathologic conditions, such as neurological disorders.

## **Division of Molecular and Cellular Biology-HNT4U**

(1) Conducts basic and translational research in the area of molecular and cellular biology, in support of the mission of the NICHD Division of Intramural Research (DIR); and (2) coordinates with the DIR to ensure the necessary resources and support is available to investigators and laboratory personnel.

## **Division of Intramural Population Health Research – HNT4X**

(1) Designs, implements and manages an original program of epidemiological, social and behavioral, and biostatistical, modern computational statistics and bioinformatics research on topics relevant to the health of populations and consistent with the mission of the Institute; (2) uses intramural resources and contracting mechanisms to initiate research in epidemiology, social and behavioral sciences, biostatistics and bioinformatics, and collaborative trans-disciplinary research with the goals of identifying risk and protective factors, including associated health disparities, and evaluating interventions to improve health during sensitive windows of human reproduction and development spanning from pre-conception through pregnancy, infancy, childhood, adolescence, and early adulthood; (3) provides expertise and service to the Institute, NIH, DHHS and other governmental agencies or research organizations; (4) advises the Institute Director on topics relevant to the population sciences; (5) develops and participates in trans-NIH and trans-DHHS initiatives in areas relating to Division responsibilities; (6) disseminates research findings to the scientific community and the general public; (7) train and build a diverse team of epidemiologists, social and behavioral scientists, biostatisticians, modern computational statisticians, and bioinformaticians; (8) and engages in the sharing of data and biospecimens originating from Division studies.

## **Biostatistics and Bioinformatics Branch – HNT4X2**

(1) Develops original biostatistical, modern computational statistics and bioinformatics research relevant for the research mission of the Division and the Institute; (2) engages in collaborative research with the Division, Institute, NIH, DHHS, and extramural investigators working in research areas relevant for the Division and Institute; (3) provides service to the Division, Institute, NIH, DHHS, and other government agencies via consultation, collaboration, and assistance to advance the scientific disciplines of the branch and the mission of the Institute; and (4) recruits and mentors highly qualified students and trainees at various stages of their careers to position them for professional careers in biostatistical, modern computational statistics, and bioinformatics research.

### **Epidemiology Branch – HNT4X3**

(1) Designs and conducts investigator-initiated and collaborative epidemiologic research focusing on reproductive, perinatal, and pediatric health endpoints to identify etiologic mechanisms, at risk subgroups, and interventions aimed at maximizing health and preventing, diagnosing and/or treating disease; (2) provides service to the Division, Institute, NIH, DHHS, and the profession via consultation, collaboration, and assistance to advance the scientific discipline of epidemiology and the goals of the Institute; and (3) recruits highly qualified students and trainees at various stages of their careers to position them for professional careers in reproductive, perinatal and pediatric epidemiologic research.

#### **Social and Behavioral Sciences Branch – HNT4X4**

(1) Conduct research to understand the social and behavioral determinants of health and health-related behaviors; (2) Develop and test educational, behavioral, and environmental strategies for improving health and health-related behaviors; (3) Conduct research on the problem of disparities in health, the developmental mechanisms underlying health disparities over the life course, and modifiable intervention targets to reduce disparities; (4) Position highly qualified students and trainees for professional careers in the social and behavioral sciences; and (5) Provide service to the Division, Institute, NIH, DHHS, and the profession via consultation, collaboration, and assistance to advance the goals of the Institute.

## **Section on Nutrient Control of Gene Expression-HNT4U2**

(1) Conducts fundamental research on basic molecular mechanisms of eukaryotic cell biology to enhance understanding of how dysregulation of these processes contributes to human disability and disease; and (2) enlists a powerful combination of yeast genetics, molecular biology and biochemistry to achieve a better understanding at the molecular and cellular levels of (a) the initiation, elongation, termination, and recycling stages of protein synthesis, and mechanisms for their regulation; (b) the mechanism and regulation of transcriptional activation; and (c) signal transduction pathways that couple gene expression to nutrient availability.

## **Section on Eukaryotic Transposable Elements-HNT4U3**

(1) Studies particle assembly, reverse transcription and integration using LTR-containing retrotransposons such as Tfl of the fission yeast *Schizosaccharomyces pombe* as a model; (2) conducts intensive genetic analysis of Tfl proteins and host cell factors required for transposition in an organism with powerful genetics, including a fully sequenced genome and a comprehensive collection of gene deletions; (3) develops innovative methods of genome analysis that rely on transposable elements to identify gene function; and (4) studies the cellular machinery that promotes the integration of HIV-1.

## **Section on Cell Cycle Regulation-HNT4U4**

(1) Studies cellular pathways that assure the integrity of genomic transmission during each cell division in human and other vertebrate cells; (2) investigates the controls that govern the transitions of cells into and out of mitosis, the loss of which during development leads to chromosome mis-segregation and birth defects, or the disruption of which later in life results in the genetic aberrations that are characteristic of many cancers; and (3) investigates mechanisms of mitotic chromosome segregation, and how important structural molecules perform distinct functions in different parts of the cell cycle.

## **Section on Protein Biosynthesis-HNT4U5**

(1) Studies the basic mechanism and regulation of eukaryotic cellular protein synthesis using molecular genetic studies in yeast and biochemical approaches to characterize the structure-function properties of the factors that promote translation; (2) examines how translation is controlled by the GTP-binding proteins eIF2 and eIF5B, and how dysfunction of these and other translation factors leads to disability or disease; (3) studies phosphorylation of eIF2 by stress-responsive protein kinases to identify determinants of substrate recognition, the regulation of eIF2 kinases by viral inhibitors, and eIF2 dephosphorylation by protein phosphatase PP1; and (4) analyzes the function of the factor eIF5A and its unique hypusine modification in promoting translation elongation especially for poor substrates like proline.

## **Section on Molecular Morphogenesis-HNT4U6**

(1) Studies the molecular mechanisms governing postembryonic development in vertebrates by using thyroid hormone (TH)-dependent amphibian metamorphosis as a model; (2) investigates the developmental roles of TH receptors (TRs) and their cofactors by using transgenesis and gene knockout/knockdown approaches to alter the levels and/or function of TRs and their cofactors during development; and (3) identifies and functionally characterizes candidate genes which are regulated by TH and critical for postembryonic organ development, particularly adult stem cell formation, in vertebrates.

## **Section on Nervous System Development and Plasticity-HNT4U7**

(1) Conducts experimental research directed toward understanding how neural impulse activity regulates development of the brain in fetal life through adulthood; (2) investigates intracellular signaling pathways that control gene transcription and other adaptive responses of neurons and glia to impulse activity to identify genes that are regulated by neural activity and determine the functional consequences on nervous system development and function; (3) investigates the mechanisms of short-term and long-term plasticity of synaptic transmission in cell culture and brain slice preparations; and (4) studies neuron-glia interactions in the CNS and PNS to investigate the mechanism and functional significance of this activity-dependent communication, with particular emphasis on myelination.

## **Section on Cellular Neurobiology-HNT4U8**

(1) Plans and conducts research on the processing, trafficking, secretion and function of protein intercellular messengers in endocrine cells and neurons; (2) investigates molecular maturation mechanisms that are correlated with their intracellular (organelle) locations, and the molecular signals and mechanisms which determine the intracellular routing and expression of these proteins; (3) identifies novel intra and intercellular signaling molecules (e.g., neurotrophic factors, transcription regulators) expressed in endocrine cells and neurons and study their role in the nervous system (e.g. in neuroprotection, neurodevelopment) and in cancer; and (4) employs cell and molecular biological techniques and whole animal and human studies to understand the functions of these signaling molecules in health and disease, such as neurodegenerative diseases, depression and cancer metastasis.

## **Section on the Mechanism and Regulation of Protein Synthesis-HNT4U9**

(1) Studies the molecular mechanisms underlying protein synthesis in eukaryotes; and (2) identifies and dissects regulatory pathways controlling gene expression at the level of protein synthesis.

## **Section on Environmental Gene Regulation-HNT4UA**

(1) Conducts research on the roles of regulatory small RNAs in cell physiology and regulatory networks; (2) develops methods for the identification of proteins of less than 50 amino acids; (3) conducts research on the functions of the small proteins of less than 50 amino acids with the ultimate goal of exploiting these regulators; (4) mentors students and postdoctoral fellows; and (5) contributes to the scientific community by serving on committees and review boards of NIH as well as American and International organizations.

### **Section on Microbial Pathogenesis – HNT4UB**

Conducts research on the bacterium *Legionella pneumophila* to discover strategies used by pathogens to infect and exploit humans; (1) Develops methods to study host-pathogen interactions at a molecular, cellular, and structural level; (2) Identifies novel therapeutic approaches to combat diseases caused by *L. pneumophila* and related pathogens; (3) Trains and mentors students and postdoctoral fellows; and (4) Contributes to the scientific community by serving on committees and review panels within the NIH as well as other domestic and international scientific institutions.

## **Section on Heritable Disorders of Bone and Extracellular Matrix – HNT4UC**

(1) Studies genetic defects in bone extracellular matrix, primarily osteogenesis imperfecta, and the causative defects in collagen and collagen-related proteins. Patient samples and genetically modified mice are utilized for studies to understand etiology and mechanism of these disorders and their clinical relevance. Each genetic defect has illuminated normal bone formation as well as a rare bone disorder; and (2) clinical studies conducted by the section focus on the natural history of OI and on controlled drug trials.

## **Extramural Administrative Services Section - HNT1262**

(1) Advises the NICHD Extramural Divisions/Center staff on optimal administrative and business management practices; (2) provides administrative and business management services to customers that include personnel management, acquisitions, travel, and other extramural administrative functions; (3) provides financial management of the research management and support (RMS) and service center budgets; and (4) develops policies, guidelines, and procedures on matters relating to administrative management and disseminates to relevant staff.

**Financial Management Branch - HNT122**

Plans and coordinates the Institute's financial management, including budget, accounting, and the cost advisory aspects of the administration of grants and contracts.

## **Heritable Disorders Branch - HNT46**

(1) Conducts clinical and basic research on the etiology, diagnosis, prevention and correction of heritable disorders in children; (2) develops new methods of prenatal and neonatal diagnosis of human genetics diseases; (3) studies the biochemical and molecular basis of these diseases; (4) conducts studies, including the establishment of animal models, on the pathophysiology of genetic disorders of intermediary metabolism; and (5) conducts studies on the control, both positive and negative, of expression of disease producing genes.

## **Information Resources Management Branch - HNT127**

(1) Advises the Director and senior managers on information systems, technology, and resources management and policy; (2) plans, coordinates, and reports on the Institute's information systems, technology, and resources activities; (3) manages the Institute's computer security program; (4) evaluates, provides, and supports information systems and technology within the Institute; (5) coordinates implementation of Institute information technology with external organizations to assure the availability of reliable information technology services in support of the Institute mission; (6) advises and assists NICHD staff on management policy issues, organization, procedures, and related management matters; (7) conducts management studies and prepares management reports; (8) establishes and coordinates an NICHD issuance system for institute policies and procedures; (9) provides direction in forms and records management; and (10) advises the Director and senior staff on the applicability of the Privacy Act to the Institute's operations and programs.

## **Laboratory of Cellular and Molecular Biophysics - HNT4E**

Studies the elements of biological phenomena to elucidate their physical basis, to provide a foundation for understanding physiological and pathophysiological mechanisms. Develops and uses novel, non-invasive technologies to probe physical parameters of living systems and their components. Studies systems of well defined molecular composition and structure which exhibit an essential biological functions. This approach provides an environment that supports investigation of the physico-chemical basis of molecular, physiological, and pathological processes. Research in the Laboratory includes the biophysics of gas phase organic ions and peptides, polymer organic chemistry for separation of biological macromolecules and particles, membrane biophysics and electrophysiology of ion channels and membrane merger, cellular biophysics of parasite entry and viral infection, and the cellular and tissue basis of human lymphoid tissue function and HIV pathogenesis therein.

## **Laboratory of Cellular and Molecular Neurophysiology - HNT4G**

(1) Studies mechanisms controlling neuronal excitability, utilizing voltage-clamp and single channel recording from mammalian CNS neurons grown in cell culture; and (2) characterizes ion channel activity, with current emphasis on excitatory amino acid receptors, using both physiological and pharmacological approaches ranging from fluctuation analysis and rapid perfusion techniques, to analysis of synaptic activity between pairs of neurons.

## **Laboratory of Cellular and Synaptic Neurophysiology - HNT4T**

(1) Studies mechanisms controlling neuronal excitability and development, utilizing various patch clamp, molecular, imaging and immunohistochemical techniques from mammalian CNS neurons maintained in a variety of in vitro preparations; (2) characterizes inhibitory and excitatory synaptic transmission, developmental processes governing neural development, and the role of ion channel activity with current emphasis on excitatory amino acid receptors using both physiological and pharmacological approaches and experimental approaches ranging from patch clamp recordings from single neurons using infra-red video microscopy, analysis of synaptic activity between pairs of neurons, imaging of intracellular signals, to transgenic approaches; and (3) investigates mechanisms of short- and long-term plasticity of synaptic transmission, differential targeting of synaptic receptors, pathophysiological processes in clinically relevant neuronal migration disorders, ion channel regulation of development and excitability and drug action at L-glutamate receptor subtypes.

## **Laboratory of Clinical Genomics - HNT4S**

The manifestations of disease in man are caused by dysfunction in gene-gene, gene-environment and cell-cell interactions. (1) Studies the sequence of events from gene expression leading to normal or altered cellular function; (2) studies the regulation of gene expression, protein function and signal transduction in cultured cells obtained from patients with heritable diseases; and (3) the purpose of the studies is to enhance our understanding of genotype/phenotype variation and the pathophysiology that controls them.

## **Laboratory of Comparative Ethology - HNT4H**

(1) Plans and conducts laboratory and clinical research in humans, primates, and other animal models on the biological basis of behavior; (2) undertakes studies on cognitive development, social development, personality development, learning, and communication/language development aimed at a comparative understanding of the development of behavior; and (3) explores the interactions of genetic and environmental factors in the evolution of biobehavioral phenomena.

## **Laboratory of Developmental and Molecular Immunity - HNT4C**

(1) Conducts research into the age-related development of immunity, using the methods of immunology, biochemistry, genetics, and molecular biology; (2) develops an understanding of the pathogenic mechanisms by which capsular polysaccharides confer virulence to invasive bacteria, and of the sequential development of immune mechanisms responsive to these virulence factors; (3) develops vaccines composed of bacterial capsular polysaccharides and other substances designed to confer T-independence and greater immunogenicity upon these vaccines; (4) studies the ontogeny, structure, and function of major histocompatibility (MHC) antigens known to control immune reactions to macro-molecular substances, and investigates the structure of the genomic DNAs encoding these antigens; (5) explores the mechanism of MHC gene activation during mammalian development; (6) conducts studies using hybridoma cultures, regulatory molecules involved in H2 antigen differentiation and function; and (7) uses cloned regulatory and effector T-cells to map immune cell circuitry and interactions within the immune network.

## **Laboratory of Gene Regulation and Development - HNT4U**

(1) Conducts research on the regulation of gene expression in response to environmental or developmental signals, chromosome structure, cell cycle control, and the propagation of transposable elements, employing several model eukaryotic systems including budding yeast, fission yeast, and the frog *Xenopus*; (2) investigates the nutrient control of gene expression in budding yeast to elucidate how eukaryotic cells sense nutrient limitation or environmental stress, and transduce these signals into altered patterns of gene expression to explore the structures and functions of regulatory proteins and their interactions with general factors involved in the initiation of transcription or translation, which are conserved between yeast and humans; (3) analyzes LTR-containing retrotransposons in fission yeast to define the processes of particle assembly, reverse transcription and integration of viral DNA into the host genome, aspects of which are shared between these transposons and mammalian retroviruses; and (4) studies regulation of the cell cycle in vertebrate animals, with a focus on factors controlling the onset and completion of mitosis.

## **Laboratory of Genomic Integrity - HNT4V**

(1) Studies the molecular events that influence the fidelity of the genome, facilitating both evolution and species stability, at both the DNA and RNA level; (2) employs all tools available to molecular biologists to answer questions regarding how genes are up- or down-regulated in response to DNA damage; how cells repair DNA/RNA lesions generated after exposure to endogenous DNA damaging agents, such as those produced during normal metabolism, or by exogenous DNA damage, such as prolonged sunlight exposure; and how any unrepaired lesions may be processed via mutagenic pathways that lead to the onset of cancer in humans; and (3) studies the cellular response to DNA-damaging agents in a wide variety of organisms ranging from the simple bacterium, *Escherichia coli*, to those including cultured human cells, including detailed in vitro biochemical studies as well as Cell biology-based in vivo studies.

## **Laboratory of Integrative and Medical Biophysics - HNT4P**

Carries out cross-disciplinary research in molecular, cell and tissue biology, incorporating specialized techniques commonly associated with physical or engineering science research. Conducts both theoretical (e.g., mathematical and computational) and experimental studies directed towards elucidating physical and chemical mechanisms underlying cell and tissue behaviors. Develops novel research methodologies to probe dynamic processes and structural changes over a wide range of time and length scales, and devises techniques to investigate complex phenomena which require an integrative approach to their study. Develops new modalities for medical diagnosis and therapy involving, but not limited to optical, magnetic resonance, laser microdissection, and other physical techniques.

## **Laboratory of Mammalian Genes and Development - HNT45**

(1) Studies the molecular aspects of gene control in mammalian cell and in the transgenic mammalian organism. Currently: (a) focuses on genes that control cell growth, tissue differentiation, and embryonic development; (b) investigates genes that affect the organization of specific organ systems; and (c) develops animal models for the study of malignant growth AIDS and of specific human genetic diseases.

## **Laboratory of Molecular Genetics - HNT4B**

(1) Conducts research directed towards understanding the molecular mechanism of genetic information transfer from parent to progeny and from the gene to its functional product; (2) studies the developmental regulation of gene expression that leads to regional and temporal differentiation of functions in the developing animal; (3) develops, using genetic, biochemical, biophysical, immunologic, and ultrastructural techniques, methods to assess the basic process of genetic replication and recombination, gene transcription and translation, and their respective regulatory mechanisms; (4) adapts model systems involving the use of unicellular as well as highly differentiated organisms and their viruses in order to examine these processes; (5) emphasizes mechanisms of gene regulation in response to environmental factors in bacteria and in yeast; (6) studies retrovirus replication by structural and functional analysis of the viral polymerase; (7) places particular emphasis on the study of molecular genetic mechanisms of early development in different animals, including *Drosophila*, *Xenopus*, and the mouse; and (8) employs gene transfer techniques to study gene function in the intact animal and to generate animal models for disease states.

## **Laboratory of Molecular Growth and Regulation - HNT49**

Conducts research on the interrelated aspects of mammalian cell growth control. The primary goal is to increase understanding of normal control mechanisms and of disorders in growth control that are manifested as cellular immortalization, transformation, and senescence. Within this framework, emphasis is placed on the following areas: (1) characterization of negative growth regulatory pathways, including anti-oncogenes and genetic mechanisms responsible for cellular senescence; (2) identification of genes that operate at the interface between signal transmission networks and the DNA replication apparatus; and (3) investigation of novel growth regulatory mechanisms (the methodologies which are emphasized in this laboratory include molecular cloning, site-specific mutagenesis, and gene transfer).

## **Laboratory of Physical and Structural Biology - HNT4Q**

Creates a practical science of the forces that organize biomolecules, a new logic for thinking about molecular recognition and conformation. Measures interactions between proteins, nucleic acids, lipids, polysaccharides particularly by the application of osmotic stress to build a data base for general and practical use such as in drug design. Studies the action of intermolecular forces on the organization of supramolecular assemblies. Examines solvation as a controlling factor in macromolecular function. Improves physical probes to delineate molecular assembly, e.g., by x-ray diffraction.

## **National Center for Medical Rehabilitation Research - HNT8**

(1) Conducts, fosters, and supports research and research training, including research on the development of orthotic and prosthetic devices, the dissemination of health information, and other programs with respect to the rehabilitation of individuals with physical disabilities resulting from diseases or disorders of the neurological, musculoskeletal, cardiovascular, pulmonary, or any other physiological system; (2) establishes program priorities and allocates program resources in support of multi-disciplinary medical rehabilitation research including clinical trials; (3) plans and directs extramural (grant and contract) programs and cooperative agreements in support of medical rehabilitation related research; and (4) coordinates the activities of the Center with other Institutes and components of the Federal Government and with similar activities of other public and private entities.

## **Office of Administrative Management - HNT12**

(1) Advises the Director and senior staff on administrative matters and the implications and impact of plans and programs from other Departmental levels and Federal agencies that affect the administration and management operations of the institute; (2) conducts studies and analyses of Institute management functions, program and administrative operations, and policy compliance; (3) plans and directs financial, personnel, equal employment, contracts, information technology, and administrative management functions of the Institute; and (4) develops and implements Institute-wide policies and procedures on administrative matters.

## **Office of Legislation, Public Policy and Ethics - HNT16**

1) Provides leadership for the legislative activities of the Institute which includes analyzing and tracking legislation relevant to the mission of the Institute and makes recommendations for legislative proposals; and Conducts and coordinates policy analysis related to human development throughout the life process (2) Supports NICHD Federal Advisory Committee Act (FACA) committees and (3) implements and administers the Institute's Ethics Program.

## **Legislative and Public Policy Branch – HNT162**

(1) Develops, coordinates, and implements broad programs of liaison between the public and the Institute's programs in the fields of population research; research on the health of mothers, children, and families; and medical rehabilitation research; (2) advises the NICHD Director and staff on matters relating to public policy emanating from Congress, the Executive Branch (including the GAO), and public and professional advocacy groups; (3) monitors, analyzes, and reports on public policy activities relevant to the NICHD and the NIH; (4) develops and issues reports, briefing materials, and other compilations of the Institute's activities, programs, and policies for use in preparation for governmental and non-governmental hearings, briefings, and meetings; (5) oversees, facilitates, promotes, and coordinates the Institute's appropriate input from its broad array of constituencies, including the NIH, HHS, other Executive Branch agencies, and the public; (6) assists the Director and Deputy Director in communicating to administrative and scientific program staff of the Institute the public, congressional, and Executive Branch interest in their programs, and in assuring that directives affecting these programs are implemented; (7) in coordination with the Office of the Director, manages and conducts the Institute's official correspondence assigned by the Executive Secretariat of the NIH, seeking input from program staff and approvals from the NICHD Director and Deputy Director as necessary and appropriate; (8) provides assistance and input on the Institute's public-private partnerships as needed, and (9) implements special projects on an as-needed basis, as directed by the Director or Deputy Director

### **Ethics Branch – HNT163**

In consultation with NICHD Deputy Ethics Counselor (DEC): (1) implements and administers the Institute's Ethics Program, including serving as primary liaison and point of contact between the Institute and the NIH Ethics Office; (2) administers the annual public and confidential financial disclosure process; (3) manages the outside and official duty activity review and approval process in accordance with NIH, HHS, and Federal regulations; (4) reviews and makes recommendations on requests for activities with outside organizations for conformance with regulations and policies; (5) reviews, analyzes, and makes recommendations on other ethics clearance matters such as waivers, Widely Attended Gathering awards, and recusals; (6) provides ethics advice and analysis to managers, supervisors, and individual employees; and (7) arranges for employee awareness, training, and compliance relative to ethics matters and manages and maintains all records and databases associated with NICHD's Ethics oversight.

## **Committee Management Branch – HNT164**

(1) Serves as a competitive service center and responsible for oversight, management, and reporting of the activities and costs of Federal advisory committees for the NICHD and participating Service Center clients; (2) ensures compliance with the Federal Advisory Committee Act (FACA) in the management of Federally funded chartered committees; (3) prepares charter packages for the establishment, amendment, and termination of committees; (4) develops committee nomination packages; (5) prepares and reviews all Special Government Employee financial disclosure documentation (OGE-450), waivers and waiver addendums and foreign activities documentation; (5) monitors and ensures that all committee activities follow necessary laws and regulations and that each meeting is properly advertised in the Federal Register; (6) develops and prepares FACA required annual report, ethics report, financial operating plan report, annual comprehensive review report on federal advisory committees , and female/minority report; and (7) provides oversight and administration for the NICHD Scientific and Evaluation Activities program.

## **Office of the Director - HNT1**

(1) Develops, directs, coordinates, and evaluates the Institute's programs, plans, and policies; (2) provides and/or oversees management and administrative services; (3) coordinates communications and outreach efforts; (4) provides leadership in the areas of prevention and clinical research; (5) plans research concerned with special populations, including women, minorities and rural area residents; and (6) conducts and coordinates interagency, intergovernmental, and international activities.

## **Perinatology Research Branch - HNT4K**

Conducts clinical and laboratory research on factors responsible for perinatal morbidity and mortality. Emphasis is placed on a strong multi-disciplinary approach utilizing expertise from clinical specialties (obstetrics, neonatology, perinatal pathology and diagnostic imaging), basic sciences and epidemiology to improve the etiologic understanding, diagnosis, treatment, and prevention of causes of low birth weight and perinatal morbidity and mortality.

## **Referral and Program Analysis Branch - HNT142**

(1) Responsible for developing and updating scientific content and related systems, such as the Child Health Information Retrieval System, used to track and monitor NICHD's research portfolio (grants, contracts, and intramural projects) over time; (2) uses such systems to perform critical portfolio and program analyses that support planning and evaluation for the NICHD and that support authoritative responses to wide-ranging inquiries from Congress, DHHS, NIH, other Federal agencies, the media, and outside organizations; (3) leads, implements, and coordinates activities to ensure that NICHD scientific and related data contained in NIH research and other analytic databases, such as the Research, Condition, and Disease Categorization system, are accurate and complete; and (4) has primary referral responsibility within the Institute, assigning all research grant applications to appropriate program areas, using criteria developed in collaboration with program staff based on historical trends and changing program emphases.

## **Reproductive Biology and Medicine Branch - HNT4R**

Conducts basic and clinical research in reproductive biology with a clinical emphasis on reproductive endocrinology and basic research in processes required for reproductive success. Research encompasses implantation biology, ovarian and endometrial physiology and endocrinology as well as stem cell biology.

## **Research Animal Management Branch - HNT4L**

Provides animal research support services to NICHD investigators and represents the interests of the NICHD on all aspects of animal research. Directs NICHD animal disease control programs. Provides a clinical veterinary medicine program, including clinical diagnosis and therapy. Provides a comprehensive preventive medicine program to prevent disease in laboratory animals and to prevent the spread of zoonotic diseases. Manages budgets for all NICHD animal holding costs. Formulates policies and standards for animal ordering and receipts. Provides administrative support to the NICHD Animal Care and Use Committee. Operates the Building 6B Shared Animal Facility, the Building 10/6C127 Animal Facility, and the NICHD/NIMH Shared Animal Facility. Represents the NICHD on user committees for all NIH animal facilities that maintain NICHD animals. Evaluates animal facilities and holding areas for design, animal housing systems, environmental control, and general operation so as to minimize research complications due to environmental variation or animal disease. Develops and implements procedures to assure compliance with federal policy, regulations, and legislation governing the ethical use of animals in biomedical research and to facilitate continued accreditation by the American Association for Accreditation of Laboratory Animal Care (AAALAC). Provides personnel with professional and technical consultation, training, and assistance in the field of laboratory animal science.

## **Section on Endocrine Physiology - HNT487**

Conducts studies on the mechanisms of regulation of mineralocorticoid secretions and circulatory homestatis, and neuroendocrine mechanisms of adaptation to stress. Research includes *in vivo* and *in vitro* studies on the activation mechanisms and interactions of hormonal regulators in the control of adrenal and vascular sensitivity to angiotensin II; (2) Investigates the releasing factor, and other stress-related hormones in the central nervous system and pituitary gland during normal hormone regulation and stress.

## **Section on Bacterial Disease, Pathogenesis and Immunology - HNT4C2**

Devises methods to increase the immunogenicity of the capsular polysaccharides of bacteria associated with invasive human diseases. Semisynthetic conjugates of these polysaccharides are prepared which increase their immunogenicity and convert their immunogenic properties to those of T-cell independence. These conjugates are also used to characterize the ontogeny and genetic control of the serum antibody responses in humans. Physical-chemical characteristics of the bacterial toxins (i.e. the subunit structure), and their relation to such molecules' toxic and protective activities, are also being studied. Monoclonal antibodies to the subunits of various toxins are used as probes for the cloning of the genes which encode these toxins.

## **Section on Biomedical Stochastic Physics - HNT4P5**

Investigates new approaches for noninvasive, quantitative optical spectroscopic and tomographic imaging of deep tissue structures for clinical screening and monitoring of physiological parameters. Multifaceted research program includes theoretical, computational, experimental, and clinical work on such subjects as time-resolved transillumination of thick tissue (e.g., for quantitative spectroscopy of breast tumors), use of specific fluorescent markers for identifying the molecular biology of disease processes (applied, e.g., to noninvasive biopsy of Sjögren's syndrome), fluorescent lifetime imaging (e.g., to assess tumor vascularization), oblique angle reflectometry (e.g., for noninvasive monitoring of inflammation in the oral cavity), and static fluorescent imaging (e.g., for sentinel node detection). Collaborative investigations involve using rodents as test cases for quantitative imaging concepts; also participates as part of larger teams in clinical studies, including the use of optical methods to evaluate drug response (e.g., in the antiangiogenesis drug treatment of Kaposi's sarcoma). Related biomedical applications of stochastic physics also are undertaken (e.g., modeling tumor-induced angiogenesis).

## **Section on Cell Biology and Signal Transduction - HNT4T9**

Studies the molecular mechanisms of cellular signaling and signal transduction in cells of the nervous system employing include high-resolution fluorescence microscopy of living cells combined with cell biological techniques of immunocytochemistry with high resolution confocal microscopy to measure calcium transients and other ions in neurons and glial cells; analyzes problems concerning molecular mechanisms of calcium based long distance signaling in glial cells, mechanisms of regulation in pineal cell excitability in circadian control of melatonin secretion and neuronal-glial cell interactions.

## **Section on Cell Biophysics - HNT4P2**

Conducts research aimed at understanding biophysical aspects of critical cell activities, such as intracellular macromolecular trafficking, cell locomotion, and cell division, that involve expanded supramolecular structures. Utilizes a combination of techniques, including mathematical and physical theory, to investigate how cellular components such as lipids, proteins, and glycolipids interact to form organelles and cytoskeletal structures. Develops new analytical methods, involving optical, x-ray, neutron, and other physical techniques, to assess details of molecular and cell function. Devises mathematical theories to understand integrative aspects of cell physiology, and to support the development of new methodologies for biomedical diagnosis.

## **Section on Cell Cycle Regulation - HNT4U4**

(1) Studies the cell cycle regulatory checkpoints that govern the onset and completion of mitosis through biochemical investigation of two closely linked biochemical pathways, both of which have been genetically implicated in mitotic regulation; (2) investigates the controls that govern the transitions of cells into and out of mitosis, the loss of which during development leads to chromosome mis-segregation and birth defects, or the disruption of which later in life results in the genetic aberrations that are characteristic of many cancers; and (3) gains an improved understanding of conjugation pathways which have been implicated in the process of nuclear trafficking in an effort to address the molecular defects that cause human disease and offer ways to prevent or treat such conditions.

## **Section on Cellular and Developmental Biology - HNT453**

The goal of this section is to understand the cellular and genetic events that regulate thymocyte development and selection. Current studies are focused primarily on the role of T-cell- receptor-mediated signals in the formation of the mature T-cell repertoire. To analyze the function of specific signal transducing proteins, transgenic and gene targeting methods are used to create overexpression, dominant-negative, and loss-of-function mutants in mice. In addition, molecular genetics techniques are being employed to identify and characterize novel genes that are expressed in early thymocytes.

## **Section on Cellular and Synaptic Physiology - HNT4T2**

Studies the roles of voltage-gated and neurotransmitter-activated channels in regulating neuronal excitability in the mammalian hippocampus; studies glutamatergic and GABAergic synaptic transmission using electrophysiological, molecular, and immunohistochemical techniques; studies mechanisms of short- and long-term plasticity of synaptic transmission in identified hippocampal inhibitory neuron and principal cell populations with regard to both pre- and postsynaptic mechanisms; works to identify the functional role of voltage-gated potassium channel subunits, expressed in morphologically distinct hippocampal GABA-ergic inhibitory interneurons, during development, oscillatory behavior and pathophysiological processes.

## **Section on Cellular Differentiation - HNT468**

Conducts research on the mechanisms of gene function and regulation during mammalian development. Major emphasis is on the investigation of biochemical and molecular changes associated with normal and abnormal differentiation processes. Techniques utilized include tissue and organ culture, and recombinant DNA methodology.

## **Section on Cellular Neurobiology - HNT4T7**

Plans and conducts research involving post-translational modifications of proteins and peptides (e.g., limited proteolysis, acetylation, and amidation) in endocrine cells and neurons. Investigates molecular maturation mechanisms that are correlated with their intracellular (organelle) locations, and the molecular signals and mechanisms which determine the intracellular routing of specific proteins and peptides. Studies the effects of intercellular messengers (e.g., neurotransmitters) on the regulation of specific protein and peptide expression. Employs recombinant DNA techniques to characterize the genes responsible for specific post-translational processing enzymes. Studies the temporal/spatial expression of neuropeptide genes during embryogenesis, determines the pattern of processing and role of these peptides in neural development.

## **Section on Cellular Signaling - HNT4TC**

Studies cellular signaling cascade in endocrine and neuroendocrine cells operated by G protein coupled receptors and the interactions between plasma membrane electrical events and receptor-mediated signaling. The research includes electrophysiological characterization of spontaneous and agonist-induced plasma membrane and endoplasmic reticulum membrane excitabilities, the patterns and mechanisms of calcium oscillations, the interactions between plasma membrane and endoplasmic reticulum in control of cellular calcium homeostasis, the spatial and temporal patterns of calcium signaling, and the control of hormone secretion and the expressions of early response genes. Cellular and molecular techniques are applied to cultured and immortalized pituitary and hypothalamic cells, including patch-clamp electrophysiological techniques, photometric and imaging calcium recordings, confocal microscopy, simultaneous calcium-current/membrane potential and calcium/current-single cell secretion recordings, RT-PCR and nucleotide sequence analyses, expression, mutation, and transfection methods, secretion in perfused cells, radioimmunoassays for several hormones, specific assays for phospholipase C and phospholipase D-derived intracellular messengers, etc.

### **Section on Child and Family Research - HNT4H3**

Investigates early influences on human development, and the interaction of genetic and environmental factors in determining cognitive and personality development during the early years of life. Develops methods for studying conceptually derived dimensions of the early environment. Current investigations include the study of mother-infant interactions in various social and cultural groups; factors influencing the development of focused attachments in infancy and early childhood; and the influence of the child's personality characteristics on parental behavior. Investigates the family as an interactive unit, with particular emphasis on the cognitive development, personality structure, and socialization of the child; studies the range of variation in family structure and parental behavior among different cultural groups and its effect on the developing child.

### **Section on Clinical Genomics - HNT4S3**

Studies the pathophysiology and etiology of heritable disorders and malformations in children and adults. Attempts to apply genomic and proteomic technologies to achieve these ends. The research has focused on disorders of sexual differentiation, biochemical genetic disorders and multifactorial diseases. Some of the research efforts have led to the development of array technology to study the thrombophilias and disorders associated with intracranial hypertension. Present protocols explore factors that enhance risk for the development of multifactorial diseases such as breast cancer. An existing focus of research investigates the role of epigenetic factors during development, and maturation into adulthood, as well as its relevance to the relationship of antenatal events and the pathogenesis of adult-onset diseases. A major focus for this section is the training of clinician scientists in these technologies

## **Section on Comparative Behavioral Genetics - HNT4H4**

Investigates the interactions of genetic and environmental influence on biobehavioral development through comparative ontogenic study of nonhuman primates and other animals. Determines the neuroanatomical, electrophysiological and biochemical concomitants of developmental changes in behavioral repertoires and cognitive capabilities from birth to maturity and into senescence. Documents species-normative patterns, and studies the origins, defining characteristics, and developmental outcomes of deviant cases. Investigates the physiological mechanisms and related neural substrates underlying auditory communication during development. Particular emphasis is placed on nonhuman primate models of the infant cry and other affective vocalizations.

## **Section on Developmental Biology - HNT4B8**

The molecular basis of embryogenesis in *Xenopus* is a major focus of interest in this lab. Early tissue differentiation depends on cell interactions (termed embryonic induction), which are mediated by several classes of growth factors, notably members of the FGF and TGF-beta families. The biological consequences of growth factor action in the embryo are being studied by analysis of rapidly induced genes. One of these genes, named *Xlin-1*, has been shown to be expressed in the so-called Spemann organizer region. Transcriptional regulation of this and several other genes expressed in specific regions of the early embryo is being studied. This work is complemented by an analysis of the corresponding genes in the embryo of the zebrafish.

## **Section on Developmental Genetics - HNT469**

Emphasis biochemical, cellular, and immunological studies on early mammalian development and differentiation. Conducts basic and clinical studies in order to understand the basis of ethanol intolerance in man and the etiology of the fetal alcohol syndrome. Techniques utilized include tissue culture and physiological studies on fetal non-human primates.

## **Section on Developmental Genetics - HNT4S2**

(1) Studies the role of genetic regulation of mammalian sexual development; (2) using two syndromes, (familial male-limited precocious puberty (FMPP) and Leydig cell hypoplasia/LH resistance (LCH) which are caused by mutations of the LH receptor which cause either constitutive activation or inactivation of the receptor) as models, studies the chain of genetic events triggered by binding of the LH to its receptor and the subsequent events influencing sexual development and identify the genetic lesions using knowledge of the signal transduction pathway and its genes; and (3) defines the pathophysiologic events and delineates the genetic mechanisms of LH signaling in spermatogenesis and oogenesis using microarray, SAGE analysis and post receptor events in transfected cells.

## **Section on DNA Replication, Repair and Mutagenesis - HNT4V2**

(1) Studies molecular mechanisms of DNA replication, repair and mutagenesis; (2) investigates how cells cope with exposure to both endogenous and exogenous DNA-damaging agents and, in particular, how low-fidelity Y-Family DNA polymerases replicate through damaged DNA; (3) studies damage-inducible responses in bacteria, archaea and eukaryotic cells; and (4) utilizes a variety of molecular, biochemical, and structural biology techniques, including PCR, protein purification and characterization, enzymology, protein crystallization, and yeast/bacterial genetics.

## **Section on Drosophila Gene Regulation - HNT4B9**

The goal of this section is to understand the molecular mechanisms that integrate information from multiple cisregulatory elements in a single gene in order to regulate the levels of gene expression. Regulation of the homeotic genes of the Antennapedia and bithorax complexes in *Drosophila* requires multiple cis-acting DNA sequences for both positive and negative regulation. Many of the mutations that fail to properly regulate the homeotic genes, of the Antennapedia and bithorax complexes in *Drosophila* requires multiple cis-acting DNA sequences for both positive and negative regulation. Many of the cis-acting elements are redundant and located up to 100kb from the promoter. By screening for mutations that fail to properly regulate the homeotic genes, the lab has identified many new trans-acting factors required for the function of these cis-acting regulatory elements. One of the new trans-acting factors, the BRAHMA protein, is conserved from yeast to man. BRAHMA is a DNA-stimulated ATPase that is part of a large protein complex that facilitates transcription by altering chromatin structure. Factors that interact with BRAHMA have been identified by genetic interactions and are currently under study. We believe that another trans-acting factor, MOIRA, is also a DNA-stimulated ATPase related to BRAHMA. Cis-acting elements and several new trans-acting factors required for negative regulation have also been identified.

## **Section on Endocrinology and Genetics - HNT489**

Conducts clinical and laboratory research on endocrine tumors using unique populations from a worldwide collection of patients and applying positional cloning and other novel genetic approaches, respectively. Using animal models and tools provided by the Human Genome Project, identifies genetic defects (mutations in genes, chromosomal re-arrangements and other genetic processes) responsible for a number of human diseases associated with maldevelopment and/or neoplasms of endocrine and other tissues.

## **Section on Environmental Gene Regulation - HNT4J6**

Conducts research on the cellular defenses against oxidative stress. Transcriptional regulators whose activities are directly sensitive to oxidative stress are identified using bacterial and yeast model systems. Defines the mechanisms by which these transcription factors are activated by oxidation using biochemical and genetic approaches. Develops methods for the identification and characterization of additional sensors and regulators of the oxidative stress response. Studies the antioxidant roles of genes whose expression is induced by oxidative stress.

## **Section on Eukaryotic DNA Replication - HNT494**

Conducts research to understand how DNA replication is controlled in Eukaryotic cells, with emphasis on DNA replication in mammalian chromosomes. Identifies specific DNA sites in mammalian cell chromosomes that function as origins of bidirectional DNA replication in vivo and demonstrates that site-specific initiation of mammalian DNA replication can be achieved in a cell free system. Elucidates the role of nuclear structure in establishing replication origins, identifying the DNA sequences responsible for site specificity, and identifying the initiation factors provided by *Xenopus* eggs.

### **Section on Eukaryotic Transposable Elements - HNT4U3**

(1) Studies particle assembly, reverse transcription and integration using LTR-containing retrotransposons such as Tfl of the fission yeast *Schizosaccharomyces pombe* as a model; and (2) conducts intensive genetic analysis of Tfl proteins and host cell factors required for transposition in an organism with powerful genetics, including a fully sequenced genome, leading to detection of defects in the integration of Tfl cDNA into the genome and identification of proteins required for import of Tfl into the nucleus.

## **Section on Gene Expression - HNT4BA**

This laboratory studies the control of gene expression during *Drosophila* development. As an animal develops, genes are expressed and inactivated (silenced) in specific patterns. Mis-expression of some genes can lead to developmental defects, thus keeping genes silenced is very important. In this lab, the molecular mechanisms which lead to stable gene silencing are studied using the techniques of molecular biology, biochemistry and genetics. DNA sequences necessary for stable gene silencing are identified and the proteins which interact with them isolated and characterized. The goal is to understand how these proteins act together to silence transcription.

## **Section on Genetic Disorders of Drug Metabolism - HNT462**

Investigates "Phase II" drug metabolism studies conjugation reactions in which enzymes (UDP glucuronosyltransferases) use as substrates bilirubin, endogenous steroids or oxygenated drugs, carcinogens and other environmental pollutants; explores mechanisms of gene expression and enzyme induction via immunochemical and recombinant DNA techniques, inbred mouse strains, and normal and mutant cells in culture; seeks to understand the basis for human genetic diseases involving variants of the Phase II enzymes.

## **Section on Genome Imprinting - HNT454**

(1) Conducts research on the role of epigenetics in regulating gene expression during normal development and in diseased states; (2) uses biochemical, molecular, and genetic analyses to identify mechanisms of gene regulation for a cluster of imprinted genes on the distal end of mouse chromosome 7; and (3) the syntenic region in humans on 15p15 is highly conserved in genomic organization and gene regulation and is associated with Beckwith Wiedemann Syndrome, Wilms' Tumor, and long QT syndrome. Using the novel information from this system, better understand the role of chromatin organization in gene expression to generate and characterize mouse models of the human diseases.

## **Section on Growth and Development - HNT48A**

Investigates the cellular and molecular mechanisms governing bone growth and development. Research focuses on the regulation of endochondral bone formation in the growth plate which is the fundamental process responsible for longitudinal bone growth. Primary goal of this work is to improve medical treatment of growth disorders and childhood metabolic bone diseases. Research seeks to uncover general principles of developmental biology since the cellular processes underlying bone growth, such as cell proliferation, terminal differentiation, angiogenesis, and cell migration, are also essential for development in other tissues. Thus the growing skeleton may serve as a model to explore fundamental issues related to morph

## **Section on Growth and Metabolism - HNT488**

Studies the roles of insulin-like growth factors (IGFs) in normal growth differentiation, and in the maintenance of peak function of musculoskeletal, nervous and reproductive systems in the adult and aging individual. Both clinical and basic studies are employed to investigate IGF functions as circulating hormones, and as tissue-specific autocrine or paracrine factors in normal physiology and in a variety of pathological conditions. Mechanisms governing IGF gene expression and mediating IGF signal transduction are studied using *in vivo*, *in vitro*, and transgenic systems.

## **Section on Heritable Bone Disorders - HNT4W2**

(1) Conducts an integrated program of laboratory and clinical research on genetic bone disorders, focusing especially on Osteogenesis Imperfecta as a model disorder of extracellular matrix resulting in severe osteoporosis; (2) using murine models and patient bone and skin samples, seeks to determine the mutations that cause the disease and to elucidate the complex mechanisms involved in phenotypic expression; and (3) conducts research aimed at gene therapy for primary collagen disorders, drug treatments to improve bone structure and function, and improved understanding of the neurological and pulmonary features of the disorder.

## **Section on Hormonal Regulation - HNT434**

Pursues studies on the regulatory aspects of peptide hormone action at the target cell level. In particular, the factors concerned in hormone-receptor interaction and stimulus-response coupling are investigated. These studies concentrate upon the control of gonadal steroidogenesis by pituitary gonadotropins and the regulation of aldosterone secretion by angiotensin II and other factors.

## **Section on Human Cell Genetics - HNT492**

Conducts research on RNA polymerase III-transcribed interspersed repetitive DNA sequences, which are ubiquitous in the genomes of higher eukaryotic cells. Alu elements, the most abundant family of interspersed repetitive DNA sequences in the human genome, have been selected for detailed study. Lines of investigation into Alu function include: (1) identification and cloning of single-copy gene-encoded regulatory factors that bind these elements at the DNA or RNA levels, and (2) determinations as to whether Alu elements can effect cell growth as cis-acting DNA structures, trans-acting RNA structures or both.

### **Section on Human Iron Metabolism - HNT4J3**

Conducts research on the molecular and cellular basis of human iron metabolism. Understanding the regulation of genes encoding proteins of iron metabolism has provided unique insights into the mechanisms by which cells regulate the fate of mRNAs. The expression levels of ferritin and the transferrin receptor are posttranscriptionally mediated by the RNA binding proteins, iron regulatory proteins 1 and 2. Conducts experiments aimed at complete elucidation of molecular mechanism of regulation, and identification of new genes of iron metabolism, including those involved in intestinal iron uptake, sequestration, release into the circulation, and processing of iron by macrophages. Studies the physiology of iron metabolism in murine and human settings, and addresses pathophysiology of human iron overload in diseases such as hereditary hemochromatosis.

## **Section on Implantation and Oocyte Physiology - HNT4R5**

Conducts patient-oriented research regarding failures in regard to normal reproduction; this will include infertility, recurrent pregnancy wastage, and failed treatment modalities. The focus will relate to implantation and oocyte physiology.

## **Section on Intercellular Interactions - HNT4E7**

Section of Intercellular Interactions studies normal and pathological cell functions in the context of tissues and tissue-like multicellular structures. Research in this section aims to identify key elements of cell-cell interactions in the complex multicellular systems and to understand critical mechanisms by which various microbes and other pathogenic factors modulate and disrupt these interactions causing diseases.

## **Section on Intracellular Protein Trafficking - HNT4J5**

Conducts research on the molecular mechanisms by which integral membrane proteins are sorted to different cellular compartments. Studies the signals that determine targeting of integral membrane proteins to endosomes, lysosomes and elements for the signals. Characterizes the interactions between signals and adaptors using recombinant DNA, biochemical and morphologic procedures. Searches for novel adaptor complexes that may be involved in sorting to other cellular compartments. Analyzes the role of signal-adaptor interactions in normal cell physiology and in disease states caused by inborn genetic defects or by viral infections.

### **Section on Macromolecular Analysis - HNT4E3**

Pursues the improvement of analytic and preparative electrophoresis. By investigating the electrophoretic behavior of macromolecules in gels and polymers, they aim to provide a systematic approach to separation science, which is presently dominated by trial and error. This section has a long history of potent contributions to separation science. Currently, the section is using an automated apparatus with on-line determinations of macromolecular concentration profiles to probe the dependence of electrophoretic mobility on gel and polymer concentrations. The section also develops theoretical and computational tools to specify the optimally resolving gel concentration and migration time. They are objectively evaluating the resolving power of separation methods and of the "molecular sieving" capacity of polymers. The theory of "molecular sieving" was further developed to account for the triphasic relation between retardation and particle or polymer size. The section also is attempting to isolate microsomal components by modification of design and procedure of free-flow electrophoresis, and by application of automated gel electrophoresis apparatus using gels and polymer solutions.

## **Section on Macromolecular Recognition and Assembly - HNT4Q4**

Investigates the coupling of forces, structure, and dynamics of biologically important macromolecules. Measures directly forces between biological macromolecules in macroscopic condensed arrays using osmotic stress and x-ray scattering. Studies changes in hydration accompanying specific recognition reactions of biologically important macromolecules in dilute solution. The primary focus is on the role of water and water structuring forces on the interaction of molecules at close approach. The ability to take advantage of the increasing number of protein and nucleic acid structures determined by x-ray crystallography and solution NMR will depend critically on understanding the physics of interactions between molecules in aqueous solution; both to understand the strength and specificity of interactions among biologically important macromolecules that control cellular function and to design rationally agents that can effectively compete with those specific interactions associated with disease.

## **Section on Mammalian Molecular Genetics - HNT452**

The regulation of development and mouse models of human genetic diseases are two major topics of current research. Uses standard procedures of molecular genetics, including *in situ* analysis of *in vivo* gene activity, as well as advanced transgenic and gene knockout technologies. Embryonic development is the topic of a study that examines the role of LIM-homeobox genes in the differentiation of specific components of the central nervous, hematopoietic, excretory, and neuroendocrine systems. The second topic concerns mouse models for human disorders. Mutant mice that carry specific gene defects provide useful animal models for neoplasia, lipid storage disease, dyskinesia, and diabetes mellitus.

## **Section on Mass Spectrometry and Metabolism - HNT4E4**

Applies knowledge of the physical chemistry of ions in their gas phase to basic biomedical research. In their project on the dynamics of the growth and development of bone, they have made fundamental contributions to the dynamics by which calcium is accreted to and removed from bone during human growth and development. Basically, stable isotopes of calcium are used as tracers for the entrance and distribution of calcium in the body, allowing calculation of rates of absorption and excretion, from which rates of calcium accretion to and resorption from bone can be estimated. An overall understanding of the developmental aspects of calcium absorption, excretion and distribution to bone as a function of development in humans is emerging as a nutritional science, the section has turned to more fundamental physical chemical research to provide missing, critical information needed for the biophysical characterization of macromolecular and membrane interactions -- a characterization of the energy required for noncovalent bonds to exist between molecules or ions in solution. Much of the current activity in theoretical studies of molecular configuration is utterly dependent upon the values assigned to solute/solvent or peptide/metal bonds, yet reliable quantities often do not exist. By adapting mass spectrometric concepts on cluster formation in systems of small ions and molecules, they are investigating the energetics of formation involved in interactions of solutes, including lipids, amino acids and small model peptides, with water.

## **Section on Medical Biophysics - HNT4P4**

Carries out cross-disciplinary biophysics research to help understand mechanisms of disease progression. Performs research on the interaction of light with complex biological systems and with biomimetic analogs. Develops quantitative methodologies for biomedical research applications utilizing an understanding of informatics and optical sciences. Develops and evaluates new diagnostic and therapeutic technologies through a variety of clinical collaborations.

## **Section on Medical Neuroendocrinology - HNT4R4**

Conducts patient-oriented research about the etiology, pathophysiology, diagnosis, prognosis, and treatment of pheochromocytoma. Uses new techniques developed at the NIH (e.g. plasma metanephrines, fluorodopamine positron emission tomography) for accurate biochemical diagnosis and localization of various pheochromocytomas. Conducts studies focusing on molecular and genetic mechanisms and proteomics to elucidate pathogenesis of pheochromocytoma and to search for new prognostic markers or therapeutic targets for malignant disease.

## Section on Membrane and Cellular Biophysics - HNT4E5

Studies membrane remodeling, the basis of cell membrane assembly, mitosis, Golgi trafficking, secretion, enveloped viral infection, insulin release, histamine release, and fertilization. The group's chief aim is to elucidate structural intermediates in biological membrane fusion and determine their energetic requirements. They detected an intermediate providing ionic continuity between the two aqueous spaces separated before membrane fusion -- fusion pore. They also characterized a pore in the invasion of an intracellular parasite, *Toxoplasma gondii*, and showed that the vacuole surrounding parasites is derived mostly from the plasma membrane of the host cell. For the mechanisms of intracellular membrane fusion, they plan to assign functional roles to proteins involved in membrane docking and fusion by studying their localization and binding partners, and by reconstituting their function in docking and fusion, linking function to kinetic models, and providing a tangible biochemical and physical basis for understanding the mechanism of intracellular membrane fusion. In studies on the role of lipids in membrane fusion, they are continuing to probe fusion along the lines of their hypothesis -- that the fusion pore is a lipidic structure, sensitive to lipid curvature, in the midst of a hemifusion diaphragm having the opposite sensitivity.

## **Section on Membrane Biology - HNT4E6**

The aim of this Section is to uncover the mechanisms by which specific proteins first break and then reseal lipid bilayers during membrane remodeling processes such as enveloped virus entry into cells by membrane fusion and exit from cells by membrane fission. We have uncoupled membrane rearrangements from preceding stages of membrane-docking and fusing-triggering altering the membrane lipid composition to that non-permissive for fusion. To fuse, membranes must bend. We hypothesize that all biological fusion processes involve transient formation of bent lipid-involving intermediates. The energy of these intermediates depends on the elastic properties of membrane monolayers. Fusion proteins may control the energy of fusion intermediates and, thus, the fusion rates by altering the particular geometry of fusion sites. To test this hypothesis, we systematically study the effects of the different membrane properties, the relationship between the structure and function of the proteins involved, and the physics of protein - lipid bilayer and membrane - membrane interactions.

## **Section on Metabolic Regulation - HNT4TB**

Conducts research on the regulation of metabolic processes pertinent to peptide hormone action in normal and disordered target tissues. Emphasis is on the hormonal regulation of glycogen metabolism mediated through the covalent modification of the rate-limiting enzymes. Investigates the normal and pathological developments which affect glycogen metabolism. Purifies the enzymes regulating this metabolic process, develops antibodies against target enzymes, identifies hormonal effects on the enzyme activities, and defines the pathological defects in the target enzymes.

## **Section on Microbial Genetics - HNT4B5**

This lab studies the mechanisms of genetic recombination and transcription termination in *E. coli* and its bacteriophages. One project comprises investigation of a recombinase that acts specifically at special sites in DNA; the aim is to determine which domain of the protein interacts with recognition sequences in DNA and to learn how mutation changes the specificity of a protein-DNA interaction. A second project involves investigation of gene expression in a virus whose chromosome contains signals that normally terminate the elongation of transcripts. The virus suppresses transcription termination by converting the host RNA polymerase to a terminator-resistant form. Suppression requires cis-acting viral sequences that are recognized by cellular proteins. The aim is to identify by mutational analysis the sites and proteins that are required for suppression of termination, and to demonstrate their activity in a cell-free system.

## **Section on Molecular and Cellular Biology - HNT496**

Conducts research on the molecular mechanisms that control gene expression. Toward this goal, this section investigates the structure-function relationships of genes and the proteins that drive their expression, focusing on eukaryotic RNA polymerase III as a model system. Human polymerase III is responsible for synthesizing essential tRNAs, 5S ribosomal RNA and small nuclear RNAs, as well as Alu retroposon RNAs. Several viruses also rely on pol III for the expression of their small RNA genes. A growing list of pathogenic viruses encode proteins that work in part through protein subunits of the pol III transcription machinery.

## **Section on Molecular and Signal Transduction - HNT4TA**

Investigates the molecular basis of signal transduction pathways that link hormonal stimulation to specific cellular responses in endocrine and other cells. Studies include the characterization and cloning of enzymes that regulate inositol lipid second messengers and their hydrolytic products. Novel molecular tools are also being developed to visualize signal transduction events with fluorescence techniques in single living cells. These approaches are utilized to understand how peptide-hormone receptors traffic between cellular compartments and to uncover the molecular determinants of important signaling proteins that contribute to the spatial and temporal constraints during their activation. These studies address the spatial regulation of intracellular signaling molecules defects of which are most often the underlying causes of human diseases.

## **Section on Molecular Biophysics - HNT4Q2**

Measures changes in molecular conformation (such as of hemoglobin) and combination (such as specific vs. Non-specific DNA/protein interaction) as a function of the controlled activity of water, the bathing medium. Uses x-ray scattering and related probes as well as the theoretical physics of forces to see how forces operate between and within proteins, lipids, nucleic acids. Derives new theories of molecular interaction to be applied to molecular assembly and to be incorporated into computation algorithms to know the forces that animate the structures of biological molecules. Seeks to relate the behavior of molecules in solution to behavior within the confines of virus or cell. Another aspect of this Section connects the forces measured between macromolecules to the energetics of the conformational transitions seen in the opening and closing of ionic channels. Seeks principles of information transduction in systems of voltage dependent of external noise sources. Converts the physical "noise" of ionic currents to observe the association/dissociation, and of the motions of the channels as they are created in lipid membranes. Develops a unified view of protein conformation and its relations to molecular solvation. Still another portion of this Section measures forces between helical macromolecules with primary focus on understanding the interactions responsible for self-assembly of protein and solvent accompanying protein interaction and assembly. Combines measurements with development of theory of intermolecular forces and of complex systems. Elucidates forces responsible for the normal function and pathology of tissues formed by fibrous proteins.

## **Section on Molecular Dysmorphology - HNT46A**

(1) Conducts research on the biological processes underlying genetic syndromes that cause malformations and mental retardation. (2) Research focuses on a group of human malformation/mental retardation syndromes caused by inborn errors of cholesterol synthesis and homeostasis, the most common of which is Smith-Lernli-Opitz syndrome (SLOS). (3) Aims to elucidate the molecular, biochemical, cellular, and developmental processes that underlie the pathophysiological processes that cause the birth defects and learning problems found in these disorders and to apply this knowledge to the treatment of SLOS. Study of these relatively rare genetic syndromes may give insight into normal biological processes and into other more common disorders.

## **Section on Molecular Endocrinology - HNT436**

Investigates the molecular basis of peptide hormone action, with particular emphasis on the control of gonadal and adrenal function; analyzes the nature of gonadotropin receptors and activation of steroid biosynthesis in testis and ovary; and investigates the properties and biological activity of circulating gonadotropins in physiological regulation, as well as in disorders of pituitary and gonadal function.

### **Section on Molecular Genetics of Immunity - HNT493**

Conducts studies on the molecular mechanisms of the development of the immune system. Employs molecular techniques to investigate the expression of histocompatibility Class I genes, and cellular oncogenes relevant to the development of immune functions. Studies the developmental expression of these genes to elucidate the mechanisms of transcriptional regulation using cells of early and mid-gestational mouse embryos.

## **Section on Molecular Morphogenesis - HNT4U6**

(1) Studies the molecular mechanisms governing postembryonic development in vertebrates by using thyroid hormone (TH)-dependent amphibian metamorphosis as a model; (2) investigates the developmental function of TH receptors (TRs) and the underlying mechanisms *in vivo* by using transgenesis to investigate effects and molecular basis of altering the levels and/or function of TRs and their cofactors during metamorphosis; and (3) identifies and functionally characterizes genes which are critical for postembryonic organ development in vertebrates by studying TH-induced genes encoding matrix metalloproteinases (MMPs) as key players that affect cell fate and behavior through specific experiments including *in vivo* functional analysis through transgenesis and identification and characterization of MMP substrates.

## Section on Molecular Neurobiology - HNT4T8

This Section studies the molecular pathways that couple synaptic activity to specific changes in gene expression in the nucleus, known as activity-transcription coupling. The circuits formed between motoneurons and skeletal muscle, and interneuronal connections in the brain, are used as model systems because neural activity regulates the properties of these circuits in response to experience during development. The Section takes a multi-disciplinary approach using cellular and molecular biology to study activity-transcription coupling. Transgenic mice, *in situ* hybridization and immunohistochemistry are used to analyze the promoters and expression of genes regulated by neural activity. The DNA regulatory elements of these genes are identified by analyzing the activity of reporter constructs in transfected mammalian cells and in transgenic mice. These DNA regulatory sequences are subsequently used to isolate and characterize the novel transcription factors mediating the activity-dependent responses, by utilizing expression cloning, yeast-1-hybrid screens and gel shift assays. Gene knock-out mice and mis-expression studies in transgenic mice are employed to confirm the function of these transcription factors *in vivo*.

## **Section on Molecular Regulation - HNT4B6**

This section is interested in how cells coordinate the Expression of their genomic repertoire in the course of adaptation to nutrient availability, with the focus on amino acid and energy source exhaustion. The molecular mechanisms governing the ensuing alterations of gene expression are studied by genetic, biochemical, and molecular approaches. The lab is specifically interested in how regulatory nucleotides (e.g., ppGpp) simultaneously can exert both positive and negative effects on global transcription specificity, how stress conditions result in regulatory signaling, and how pleiotropic regulatory effects are integrated in the organism.

### **Section on Molecular Transport - HNT4Q3**

(1) Investigates the physical principles and structure-function relationships of metabolite and macromolecular transport occurring through large (mesoscopic) ion channels, such as mitochondrial and bacterial porins, gap junctions, and pore-forming toxins to understand the molecular mechanisms of apoptosis, toxicity of bacterial infection, and antibiotic action; and (2) studies the role of noise in information transfer on the molecular level of intra- and inter-cell communication to elucidate its significance in cellular processes as well as in sensory biology.

## **Section on Nervous System Development and Plasticity - HNT4-9**

Conducts research directed toward understanding how neural impulse activity regulates development of neurons and glia. Investigates intracellular signaling pathways that control gene transcription and other adaptive responses of neurons and glia to impulse activity to identify genes that are regulated by neural activity and determine the functional consequences on nervous system development and function. Investigates the mechanisms of short-term and long-term plasticity of synaptic transmission in cell culture and brain slice preparations. Studies neuron-glial interactions in the CNS and PNS to investigate the mechanism and functional significance of this activity-dependent communication.

## **Section on Neural Development and Plasticity - HNT4T5**

Studies the roles of neurotrophic factors in brain development and plasticity. Two fundamental issues are investigated: 1) the mechanisms underlying the acute and long-term regulation of synapses by neurotrophic factors; and 2) how diffusible neurotrophic factors achieve activitydependent and synapse-specific modulation.

## **Section on Neural Developmental Dynamics - HNT4BB**

Conducts research on how the nervous system is divided into discrete compartments and how neurons are made in the correct number and location within these compartments, using the zebrafish as a model organism. The broader goal of the section is to understand how neurogenesis is regulated in the vertebrate embryo, a process that is essential for the growth and development of a healthy nervous system.

## **Section on Neuroendocrinology - HNT46B**

Determines the molecular mechanisms involved in neuroregulatory processes, with special emphasis given to the role of the pineal gland in regulating reproduction. Employs the pineal system as a model for pharmacological and molecular biologic studies of regulation of gene expression by the nervous system.

## **Section on Neurophysiology and Biophysics - HNT4G2**

(1) Studies the mechanisms controlling neuronal excitability and synaptic transmission, utilizing patch clamp recording from neurons in dissociated culture and in acutely dissociated preparations, and from cell lines and oocytes expressing cloned receptors and ion channels; and (2) employs kinetic analysis, simulation techniques, and concentration jump experiments, with emphasis on using pharmacological probes to explore at the molecular level the function of ligand binding sites, ion permeation mechanisms of channel block, and allosteric regulation of receptor function.

## **Section on Nutrient Control of Gene Expression - HNT4U2**

(1) Studies how yeast cells regulate gene expression in response to nutrient availability, with emphasis on transcriptional regulation of genes involved in amino acid biosynthesis by probing signal transduction pathways at the molecular level; and (2) analyzes with powerful combinations of yeast genetics and biochemistry the molecular architecture and biochemical activities of multisubunit complexes containing general factors involved in transcription or translation to provide insight into the nutrient control of gene expressions in humans.

## **Section on Organelle Biology - HNT4J7**

Studies the mechanisms underlying the maintenance and biogenesis of eukaryotic organelles. Characterizes the membrane transport pathways through which organelles communicate and divide into daughter cells. Develops optical imaging techniques to characterize protein transport and mobility, and protein-protein interactions in living cells. Utilizes pharmacological perturbants and dominant negative gene products to elucidate the molecular mechanisms underlying organelle transformations in response to cell signaling and during mitosis. Defines the roles of cytoskeletal elements in the subcellular localization and movement of organelles and transport intermediates. Examines how organelles subcompartmentalize, including lipid and protein partitioning into membrane microdomains and recruitment of cytosolic protein complexes to form coated membrane surfaces.

## **Section on Pediatric Endocrinology - HNT4R2**

The SPE studies the physiology and pathophysiology of the hypothalamic-pituitary-adrenal (HPA) and -gonadal (HPG) axes and the autonomic nervous system, as they relate to each other and as they influence growth, development, metabolic and immune functions. Both the developmental and static functions of these neurohormonal systems are studied at the integrated level in health and disease. Also, the cellular/subcellular and genomic actions of the key effector molecules of these systems are studied as they relate to normal physiology and disease-related pathophysiology.

#### **Section on Physical Biochemistry - HNT4-4**

Studies recognition reactions between DNA, collagen and other biological macromolecules with a particular emphasis on pathology of collagen fiber formation in Osteogenesis Imperfecta (OI) and other bone and connective tissue disorders. Develops new physical, chemical and biochemical experimental techniques and theoretical methods for investigation of folding DNA self-assembly, and of thermal stability, posttranslational modification, extracellular processing, fibrillogenesis and intermolecular interactions of normal and mutant collagens. Collaborates with intramural and extramural clinical researchers and molecular biologists on characterization of mutant collagens from animal models, patients and cell cultures. Combines fundamental studies of common physical principles with practical application of the gained knowledge and newly developed techniques for diagnostics, characterization and treatment of OI and other collagen related diseases.

## **Section on Protein Biosynthesis - HNT4U5**

(1) Studies the mechanism and regulation of eukaryotic protein synthesis and, in particular, the structure/function properties of the universally conserved translation initiation factor eIF5B and its interaction with the ribosome; (2) analyzes how the function of the factor eIF2 is down-regulated by phosphorylation; and (3) studies the determinants of substrate recognition by the eIF2 protein kinases and the structure and regulation of these enzymes to identify mutations which increase or decrease inhibition of pseudosubstrate inhibitors.

### **Section on Reproductive Endocrinology - HNT4R3**

The SRE studies the physiology and pathophysiology of the hypothalamic-pituitary-gonadal (HPG) axis at the *in vivo* integrated and cellular, subcellular and genomic levels. The physiologic studies include evaluation of the normal human menstrual cycle at the hypothalamic, pituitary, ovarian and target tissue levels, and study of endocrine and immune functions during normal human pregnancy and the postpartum. The pathophysiologic studies include a detailed clinical and hormonal evaluation of patients with endometriosis and introduction of novel therapies for this condition as well as the influence of gonadal steroids or diseases with increased prevalence in women.

### **Section on the Formation of RNA - HNT4B3**

Interactions between RNase H and RNA-DNA-hybrids are being examined in human cells, in retroviruses (e.g., HIV), in yeast and in bacteria using a wide range of molecular approaches. RNA-DNA hybrids, used as sites of initiation of DNA replication, are influenced by RNase H. Reverse transcription, involved in the replication of retroviruses, also produces an RNA-DNA hybrid; here too, RNase H plays an important role. Similarities between HIV RNase H and E. coli RNase H allow the lab to use the bacterially derived enzyme as a model for the reverse transcriptase RNase H. The 3-D structures of both E. coli (determined in this lab) and HIV RNase H permit this lab to examine the differences in the properties of these two related proteins.

## **Section on Social and Emotional Development - HNT4H5**

Conducts research on the factors affecting psychosocial and emotional adaptation in infancy, childhood, and adolescence in a variety of cultural and social contexts; designs research projects to explore the effects of out-of-home care experiences on the development of children and youth; studies the nature and effects of child care practices, arrangements and beliefs on children raised in diverse environments; examines antecedents and consequences of adolescent pregnancy and parenthood.

## **Section on Steroid Regulation - HNT438**

Research is performed on the hormonal and molecular events responsible for adrenal steroid biosynthesis and secretion in mammals, using a comparative approach. Studies include: (1) identification and purification of specific steroid-binding proteins in the adrenal cortex, (2) the role of cytoskeleton in steroidogenesis, (3) detection and characterization of soluble factors in the adrenal (particularly proteins) that will directly influence the rate-limiting mitochondrial step in steroid synthesis, (4) differential structure and function of zones of adrenal cortex, and (5) growth and functional characteristics of adrenocortical cells in tissue culture.

### **Section on Tissue Biophysics and Biomimetics - HNT4P3**

Carries out research primarily in tissue biology, directed toward understanding the physical and chemical principles underlying various physiological phenomena (e.g., electrical excitability), and toward explaining the physical and chemical properties of tissues (e.g., the load bearing and transport characteristics or extracellular matrix) in terms of ultrastructure, composition, and organization. Conducts experiments with complex biological systems that often require the development of new physical theories, mathematical and computational models, and biomimetic tissue analog systems to aid in the design and interpretation of these experiments. Combines an understanding of fundamental physiological mechanisms with a knowledge of physical and engineering methodologies to develop new modalities for biomedical research and medicine (e.g., diffusion tensor: MRI and osmotic stress titration methods).

## **Section on Vertebrate Development - HNT4B7**

The general goal is to understand how tissue differentiation is controlled in vertebrate embryos. The lab is concentrating on the formation of epidermis in embryonic frogs and mice, and on neural crest differentiation in frogs and zebrafish. The epidermis project focuses on the regulation and function of XD112; Xenopus homolog of the Drosophila homeobox gene Distal-less expressed primarily in skin. Neural crest development is being addressed by analyzing receptor tyrosine kinase genes that are expressed in embryonic neural tissues, and also by studies in zebrafish of cadherins, cell adhesion molecules important in cell migration and differentiation.

## **Section on Vertebrate Organogenesis - HNT4BC**

Research in the Section on Vertebrate Organogenesis is devoted to studying the development of the vertebrate circulatory system, using the zebrafish as an accessible model system. Specific research topics include studying how vascular progenitors arise, how vessels acquire arterial-venous and other differentiated identities, and how vascular networks are assembled during development.

## **Section on Viral Gene Regulation - HNT4B2**

This research is directed towards understanding the replication of mammalian retroviruses, such as HIV and murine leukemia virus (MuLV). Currently, the lab is using genetic and biochemical approaches to investigate the functional relationship between the polymerase and RNase H domains of reverse transcriptase. Mutants having defects in one domain which alter polymerase and RNase H activities are being characterized. Studies on the requirements for plus-strand DNA synthesis and specificity of RNase H cleavage have been initiated. The group also uses mutational analysis to study regulated expression of the MuLV pol gene, which occurs by translational suppression of the UAG condon at the gag-pol junction.

### **Section on Women's Health Research - HNT483**

(1) Studies the physiology and pathophysiology of female growth and development, reproduction and aging. (2) Examines the biological roles and mechanisms of action of estrogen and progesterone. (3) Conducts both clinical and basic research on causes and treatment of obesity, menstrual cycle disorders, endometriosis, premature ovarian failure, polycystic ovarian disease, infertility, breast and uterine tumors and osteoporosis.

## **Division of Extramural Research - HNTB**

Advises the Director on research contract, grant, and training program policies; (2) represents the Institute on overall NIH extramural and collaborative program policy committees and coordinates such policies within the Institute; (3) coordinates the Institute's research grant and training programs within NICHD; (4) provides the Institute's program branches with grants management; (5) provides coordination and management of the Institute's public advisory committees; (6) provides initial scientific merit review of research grants and contracts for the Institute; (7) develops, implements, and coordinates cross-cutting, multi-disciplinary activities in the mission areas of NICHD; and (8) develops and provides extramural staff training and enhances communication across the Institute regarding standardized approaches, policies, methods, and procedures.

## **Child Development and Behavior Branch - HNTB2**

(1) Develops and supports research and research training programs in the various areas of developmental science which explore cognitive, affective, and social development, developmental psychobiology, cognitive and behavioral neuroscience, trajectories of typical development, behavioral pediatrics, and the genetic and environmental influences on all of these areas; (2) promotes studies of the development of language, learning, attention, reasoning, planning, problem solving, and concept formation in children; (3) delineates the effects of environment and context (social, cultural, societal, familial, neurobiological) on child and adolescent development and behavior and on family functioning; (4) investigates temperament, motivation, self-concept, attitudes, and values, and examines the developmental sequelae of peer relationships, group formation and social networks; (5) examines the effects of parental and non-parental child care and preschool attendance on social, emotional, cognitive, behavioral, and academic outcomes; (6) elucidates the neurobiological and genetic basis of behavioral development and learning, employing animal models and human subjects; (7) studies the basic mechanisms of learning, sensation, perception, memory, and psychomotor performance; (8) investigates basic biobehavioral mechanisms involved in risk-taking behaviors, their prevention and resilience to risk, especially in adolescence; (9) promotes studies to define, classify, prevent, remediate, and map the developmental course of learning disabilities affecting reading, writing, mathematics and disorders of attention and self-regulation; and (10) elucidates the etiological role of environmental, cognitive, linguistic, perceptual, educational, genetic, and neurobiological mechanisms in learning and learning disabilities and typical learning development, including executive function, self-regulation and attention.

## **Population Dynamics Branch - HNTB4**

(1) Develops and supports research and research training programs in demography and population dynamics; (2) supports research in the causes and consequences of population structure and change-including fertility, family demography, urbanization, migration; (3) promotes and supports research on the influence of behavioral and social science on reproductive health-including sexually transmitted diseases, HIV/AIDS, family planning, and infertility; and (4) supports research on data collection and human health, productivity, behavior, and development at the population level using such methods as inferential statistics, natural experiments, policy experiments, statistical modeling, and gene/environment interaction studies.

## **Developmental Biology and Structural Variation Branch - HNTB5**

(1) Develops and supports a comprehensive national research and training program to increase our understanding of the biological processes controlling both normal and abnormal development. Using a variety of vertebrate and invertebrate model systems to provide insights in to normal and abnormal human development, supported research; (2) elucidates the effects of genetic and epigenetic factors, biochemical and biophysical influences on fundamental developmental and regenerative processes; (3) studies cellular differentiation including the mechanisms controlling the flow of genetic information, cell migration, differentiation, proliferation, cell death, cellular interactions, and pattern formation during normal and abnormal development, as well as processes directing the differentiation of embryonic stem cells and iPSCs from pluripotent cells to specific cell types; (4) investigates the mechanisms underlying the normal development of organ primordia [organogenesis] against which aberrations of normal developmental processes can be better understood; (5) promotes studies in developmental neurobiology, including central and peripheral nervous system formation, early pattern formation, neurogenesis, control of neuronal cell fate, neural crest formation and differentiation, growth cone pathfinding and target recognition, neurulation, and neural tube defects; (6) examines the genetic basis of development in model systems and humans with emphasis on gene organization, regulation of gene action, gene regulatory networks associated with the orderly control of development, differentiation, growth and the genetic basis of variation and birth defects; and (7) elucidates the role of environmental and pharmacologic agents acting at the molecular, cellular, and organ levels using epidemiologic, clinical, and basic biological research.

## **Pediatric Growth and Nutrition Branch - HNTB6**

(1) Serves as the focal point for nutrition science and pediatric endocrine research and training; (2) supports research aimed at understanding the mechanisms of growth and development at the gene-molecular level and at higher levels of cell and organ function; (3) determines the role of nutrition throughout the life cycle, with an emphasis on the needs of women of reproductive age, preterm and term infants, children and adolescents, to promote health, optimal growth and development, and to prevent disease; (4) explores the role of nutrients in reproduction, immune function, cognition and behavioral development; (5) elucidates the interactive roles played by nutrients and hormones in growth and development of the central nervous system and its interactions with the gastrointestinal tract; (6) determines the roles played by lactation and breastfeeding in infant nutrition, including studies of the non-nutrient components of breast milk and their roles in the development of the intestinal microbiome, and the role of breast milk in protecting against infections and enteric diseases; (7) improves our understanding of the antecedents and sequelae of childhood obesity as well as the nutritional and developmental origins of health and disease; (8) highlights the cultural and behavioral aspects of food selection and eating behavior; (9) elucidates the neuroendocrine basis of linear growth and the onset of puberty; and (10) ascertains the antecedents of bone health and the early origins of osteoporosis with an aim to developing preventive strategies.

## **Intellectual and Developmental Disabilities Branch - HNTB7**

(1) Develops and supports research and research training programs in intellectual and developmental disabilities (IDD), including common and rare neuromuscular and neurodevelopmental disorders, such as Down, fragile X, and Rett syndromes, inborn errors of metabolism, autism spectrum disorders, and others; (2) promotes studies designed to understand the etiology and pathophysiology of abnormal nervous system development; (3) promotes studies to delineate genetic, genomic, and epigenetic bases of IDD; (4) promotes studies designed to examine the screening, diagnosis, treatment, and management of IDD and other conditions identified by newborn screening or other screening methods; (5) administers a program of support for centers for research in IDD; (6) promotes multidisciplinary and translational research in IDD through programs that integrate basic and applied research, training, and service activities; and (7) partners with other federal agencies, organizations, and advocacy groups to advance efforts toward the prevention and diagnosis of IDD as well as early intervention and treatment for these conditions.

## **Obstetric and Pediatric Pharmacology and Therapeutics Branch - HNTB8**

(1) Develops and supports research and research training programs to improve safe and effective use of drugs in obstetrics and pediatrics; (2) promotes and supports translational and clinical pharmacological and pharmacogenomics research in obstetrics and pediatrics through contracts, cooperative agreements and other grants; (3) conducts safe and well designed clinical trials in pediatrics and obstetrics; (4) works with the FDA to improve labeling of drugs for use in obstetrics and pediatrics; (5) contracts for the performance of clinical trials; (6) educates pediatric and obstetric practitioners; (7) provides training in pharmacology research; and (8) develops a nationwide infrastructure to support clinical trials in obstetric and pediatric pharmacology.

## **Maternal and Pediatric Infectious Disease Branch - HNTB9**

(1) Develops and supports both domestic and international research and research training programs for the study of the epidemiology, diagnosis, clinical manifestations, pathogenesis, transmission, and prevention of HIV infection and associated infectious (such as tuberculosis, malaria, and hepatitis) and non-infectious complications as well as other infectious diseases in pregnant and non-pregnant women, infants, children, adolescents, and the family unit as a whole; (2) develops and supports domestic and international clinical trials of specific and adjunctive treatment and preventive therapies for HIV and other infectious diseases in these populations (including safety and pharmacokinetics of antimicrobial agents), either independently or in collaboration with other Institutes and Agencies; (3) investigates the effect of HIV and other infectious agents and their therapies on the pregnant woman, pregnancy outcome, the fetus, and infant, and the impact of pregnancy on the course of HIV disease and other infectious diseases; (4) elucidates the impact of therapies used during pregnancy or breastfeeding for treatment or prevention of infectious diseases on the long-term outcome of exposed infants, children and adolescents; (5) investigates the gender-specific manifestations of HIV and other infectious diseases, and therapies to treat such manifestations; (6) evaluates vaccines and other biomedical modalities for prevention of HIV infection, HIV-related infections, and other high-priority infectious diseases in the populations of interest; and (7) develops and supports interventional research to support the full scope of prevention activities for HIV infection and other infectious diseases among adolescents.

## **Pregnancy and Perinatology Branch - HNTBA**

(1) Develops, stimulates and supports basic, translational and clinical research and research training programs related to pregnancy, preconception care, maternal and neonatal health, fetal development and growth, and fetal and infant well-being including; (2) studies to understand the pathophysiology of preterm birth and to identify effective interventions, strategies, and biomarkers to optimize outcome for the preterm neonate and infant; (3) normal physiology of pregnancy, parturition and transition for the fetus/neonate; (4) high-risk pregnancies and high-risk newborn outcomes, including preeclampsia, stillbirth, Sudden Infant Death Syndrome, and infant mortality; (5) maternal physiology, complications of pregnancy, initiation of labor, behavioral and psychosocial dynamics of pregnancy, the impact of medications, drug use and addiction, tobacco use, obesity, and infections on the outcome of pregnancy and well-being of newborns; (6) normal and abnormal physiologic factors influencing pregnancy including the impact of diet, physical activity, and racial/ethnic disparities on the mother and intrauterine conditions; (7) biological and behavioral antecedents of abnormal fetal growth including both growth restriction and excess growth; (8) cooperative research networks in clinical research on high-risk pregnancies and newborns, such as the Maternal-Fetal Medicine Units Network and Neonatal Research Network, among others; (9) research related to neonatal intensive care, including infant feeding, breastfeeding and neonatal conditions and disorders, and (10) antecedents of health and disease for both mother and child.

## **Fertility and Infertility Branch - HNTBB**

(1) Develops and supports basic, clinical and translational research and research training programs focusing on male and female fertility and infertility; (2) examines specific processes underlying fertility regulation such as gonadal development and function including gamete formation and sex steroid production, neuroendocrine control mechanisms, ovulation, fertilization, uterine receptivity and implantation, and pre-implantation development including the biology of embryonic stem cells; (3) promotes research that identifies targets for fertility regulation; (4) investigates the underlying mechanisms and hereditary transmission of diseases and disorders that affect fertility; (5) supports efforts to preserve and restore fertility; and (6) provides support for study of assisted reproduction including approaches to and outcomes from.

## **Gynecologic Health and Disease Branch - HNTBC**

(1) Develops and supports basic science and clinical research programs related to gynecologic health in women and adolescent girls; (2) promotes research in gynecological health through grants, cooperative agreements and contracts; (3) emphasizes studies of the menstrual cycle, uterine fibroids, endometriosis, pelvic floor disorders, and perimenopause/menopause transition; (4) studies the mechanisms underlying chronic pelvic pain, vulvodynia and dysmenorrhea; and (5) supports research training and career development programs of investigators interested in women's reproductive health.

## **Pediatric Trauma and Critical Illness Branch - HNTBD**

(1) Develops and supports research and research training in pediatric trauma and critical illness; (2) investigates the continuum of psychosocial, behavioral and physiological influences that impact child health outcomes in trauma, injury and acute care; (3) investigates the short and long term impacts of acute traumatic experiences such as natural and man-made disasters, all forms of child maltreatment, violence and violence exposure; (4) develops research linking pediatric emergency and critical care medicine and science to the epidemiology, prevention, and treatment of childhood physical disabilities; and (5) supports research on prevention, treatment, management, and outcomes of physical and psychological trauma and the surgical, medical, psychosocial and systems interventions needed to improve outcomes for critically ill and injured children across the developmental trajectory.

## **Grants Management Branch - HNTBE**

(1) Performs administrative/business management and internal control/acquisition functions for all NICHD grant programs, including the management review and approval of grant applications prior to award and the obligation of NICHD grant funds; (2) develops and maintains an operating relationship with the scientific program staff to provide advice and consultation necessary to carry out the objectives of the research grants program and assure proper stewardship of public funds (3) negotiates awards with the grantees; (4) provides liaison with components of the DHHS, NIH, NICHD, and grantee institutions; (5) participates in the development of policies and procedures and interprets NIH and higher level policies related to the grant program; (7) responds to inquiries from grantees orally and in writing; (8) makes staff field and project site visits; (9) attends meetings of the Council and committees; and (10) maintains project files and records.

## **Scientific Review Branch - HNTBF**

(1) Responsible for direction and oversight of all phases of scientific and technical merit review activities within NICHD; (2) develops, distributes, and coordinates policies and procedures for various aspects relevant to review requirements; (3) directs and carries out scientific and technical merit reviews of research and training grant applications and research contract proposals; (4) organizes and coordinates scientific and technical merit reviews on all research grant applications and contract proposals that receive initial review within NICHD; (5) collects and distributes background data, such as grants management data of research support, providing these to review groups to assist in the comprehensive review of research proposals; (6) prepares summary statements reflecting committee deliberations and recommendations for second-level review; (7) reviews program announcements and RFAs for adherence to NIH and NICHD policy and procedural guidelines; and (8) reviews requests for contracts (RFC) for appropriate technical evaluation criteria and relevance to the NICHD mission and for adherence to NIH and NICHD policy and procedural guidelines.

## **Office of Science Policy, Reporting, and Program Analysis - HNT14**

(1) Conducts or assimilates studies on emerging science or policy issues within the fields of NICHD scientific interest; (2) develops and issues reports, briefing materials, and other compilations of the Institute's activities programs, and policies for use in science policy development, communications, and in program planning and implementation at all levels of the Federal government; (3) supports trans-Institute policy and program analyses and evaluations through the collection, classification, summarization, analysis, and interpretation of research and training data, scientific literature, scientific coding, and technical reports; (4) tracks and monitors NICHD's research portfolio over time and performs critical portfolio and program analyses; (5) coordinates activities to select program objectives and scientific priorities for the Institute; (6) develops and implements processes to translate these priorities into scientific research agendas, and into long-term strategic plans for the Institute; (7) develops and implements processes to ensure annual operational plans are developed by staff to help implement scientific priorities and policies of the NICHD; (8) serves as the Institute grants referral office; (9) assists the Institute's research divisions with research and reporting coordination across the NICHD, the NIH, and DHHS; and (10) develops mechanisms to coordinate all Office functions with other relevant organizations across the NICHD, NIH, DHHS, and other federal agencies as appropriate.

## **Science Policy, Planning and Evaluation Branch - HNT145**

(1) Coordinates activities to support Institute leadership and staff in determining and implementing NICHD's policy, programmatic and scientific objectives and priorities; (2) facilitates decision making processes with regard to Funding Opportunity Announcements, conferences, and other activities; (3) conducts rigorous program evaluation research to analyze, assess, and report on the results of the Institute's efforts; (4) coordinates strategic planning activities at the Institute, research, and program levels; (5) prepares reports and responses to queries from multiple sources, including the NTH Office of the Director, outside organizations, and Congress, for information on NICHD-supported research and related activities and achievements; (6) develops, populates, and maintains detailed databases and repositories of information to describe the Institute's scientific portfolio and research results, for use by NICHD program, public liaison, and communications staff, as well as other NIH colleagues; and (7) collaborates with the NICHD Office of the Director, other NIH Institutes, Centers and Offices, and trans-NIH and HHS committees in carrying out these functions.

## **Office of Communications—HNT1B**

(1) Develops and conducts a comprehensive communications program to interpret and disseminate to the public, the media, the biomedical community, and specialized groups via online, print, and other means the findings of research supported and conducted by NICHD; (2) responds to inquiries from lay and professional audiences, the media, and specialized groups and develops materials appropriate to such inquiries; (3) collaborates with PHS, HHS, and other federal agencies, academic and research institutions, volunteer and advocacy groups, and scientific and professional organizations to disseminate research knowledge; (4) designs and implements broad promotional/outreach efforts including media products, nationwide awareness campaigns and programs, and health education materials aimed at health professionals and other target audiences; (5) manages the content and design of NICHD public websites as well as the Institute's new media channels; (6) provides strategic communications counsel to NICHD staff and maintains liaison with the NIH Office of Communications and Public Liaison and other relevant NIH offices; (7) maintains integrity of the NICHD identity to ensure a clear and consistent look and feel across all Institute communications and to ensure appropriate use of that identity outside of the Institute; and (8) advises staff on the application of the Freedom of Information Act to NICHD's operations and programs.

## **Office of Data Science and Sharing – HNT1C**

Office of Data Science and Sharing (1) Serves as the principal advisor to the NICHD Director and senior leadership on bioinformatics and data science, data management, and emerging technologies; (2) Serves as the primary liaison with the NIH Office of the Director's Office of Data Science and Strategy, ensures engagement in large NIH data science and emerging technology programs, and ensures alignment of NICHD programs with NIH programs and policies; (3) Promotes strong governance and stewardship of data science and emerging technology programs and coordinates closely with the Chief Information Officer of NICHD and NIH as needed; (4) Develops effective and innovative strategies that advance basic and applied research to promote health and provide understanding, prevention and treatment for the populations of import to NICHD by providing leadership, strategic guidance, planning and vision to the coordination, planning and execution of bioinformatics and related omics and technology programs, initiatives, and activities across NICHD; (5) Coordinates bioinformatics and related biospecimen and technology programs, initiatives, and activities across NICHD that encourage innovation, exploits emerging technologies, provides a big data readiness environment and promotes a framework to maximize collaborative efforts within intramural and extramural communities; (6) Coordinates and supports big data ready environment across NICHD for data management and supports data sharing by developing, implementing, and coordinating data platforms for housing and indexing data generated by NICHD extramural programs and intramural laboratories; (7) Builds novel public-partnerships to develop innovative programs in bioinformatics and technology development; (8) Provides leadership in domestic and international data sharing efforts, initiatives, programs, and policies related to open access and FAIR principles with consideration of data security and privacy issues; (9) Provides leadership for programs developing innovative state of the art technologies and computational platforms, tools, and predictive models to identify predictive signatures for health, disease, and treatment or intervention; (10) Oversees compliance of NICHD genomics and technology projects, programs and initiatives with US government directives, policies, regulations and guidelines; (11) Coordinates dissemination of data, open source software and computational tools, data standards from NICHD funded intramural and extramural programs including dissemination of clinical research data, and participate in publication of standards with NIH repositories and international coordinating bodies; (12) Coordinates training efforts in bioinformatics and computational tools across NICHD staff and the broad extramural community.

## **Office of Health Equity – HNT1A**

(1) Coordinates, facilitates, and supports programs within NICHD to develop and strengthen the Institute's commitment to ensuring the health and well-being of children, adults, families, and communities by addressing and lessening health disparities through the participation of diverse populations in biomedical and behavioral research within the United States and abroad; (2) works with the Division of Extramural Research and the extramural community to enhance research capacity development of research institutions both domestically and abroad; and (3) informs and educates the public about issues related to health equity.

### **Contraception Research Branch - HNTB3**

Develops and supports research and research training programs in the field of contraception, including developing and evaluating new contraceptive methods and conducting behavioral research to understand factors influencing uptake and continuation rates of contraceptive methods among diverse domestic and global populations.

Accomplishes this by: (1) conducting basic research to discover new contraceptive targets and determining the mechanism of action and medical effects of contraceptive and reproductive hormones, drugs, devices, and procedures;

(2) developing and conducting experimental studies in animals and clinical trials in humans to determine optimal formulations and dosages of contraceptive agents; (3)

conducting behavioral and acceptability assessments to inform development of novel contraceptive methods and delivery systems; (4) investigating the interplay between users' characteristics (e.g., age, socio-economic status, lifestyle, stress/depression, violence victimization, cognitive capacity) and social and physical contexts (e.g., fertility norms, community infrastructure/access issues, culture, gender roles), and the effects on family planning, contraceptive use, and behavior (5) developing

behaviorally-based interventions to promote effective family planning and contraception use; (6) conducting epidemiologic, statistical, and clinical studies for post-market surveillance of reproductive products, devices, and procedures; and (7) collecting and analyzing data from national health surveys, metabolic studies, clinical trials, and epidemiologic assessments of the health and fertility effects of contraceptive practices, drugs, devices, and procedures.