

Pediatric Scientist Development Program

Research Opportunities in the Intramural Research
Program of the
Eunice Kennedy Shriver
National Institute of Child Health and Human Development
National Institutes of Health

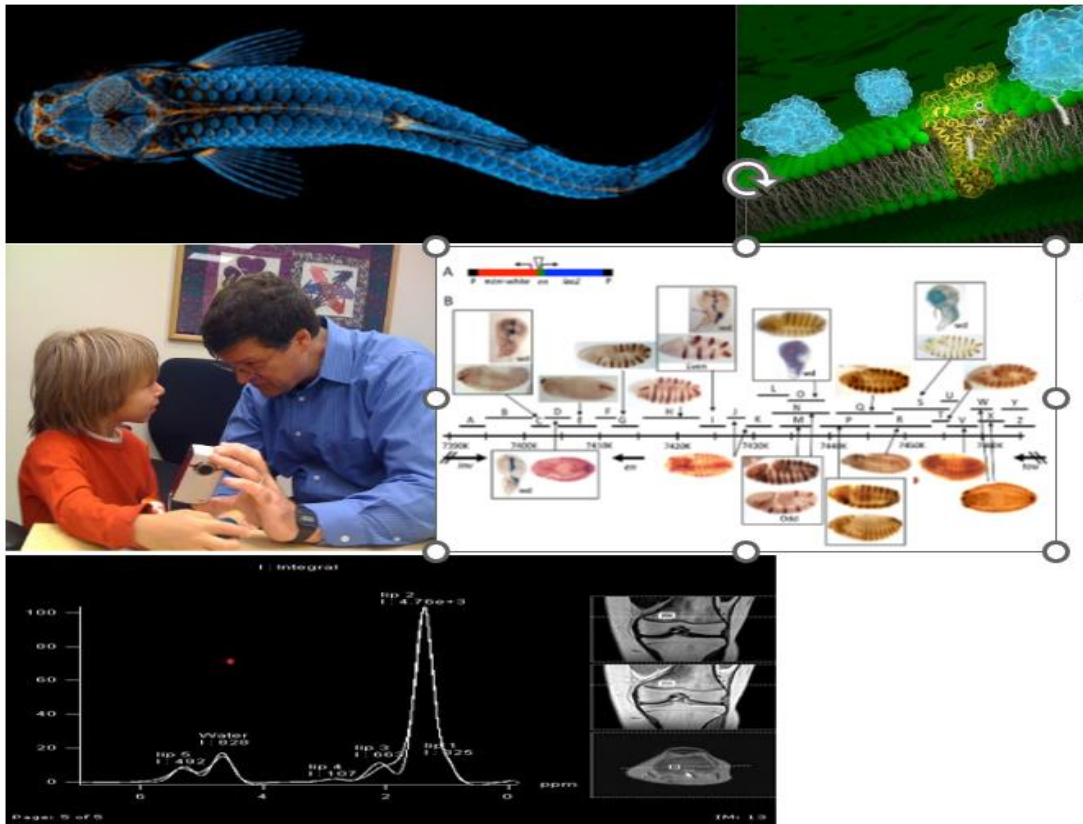


NICHD Intramural Research Program

Our mission is to plan and conduct the institute's laboratory and clinical research programs to seek fundamental knowledge about the nature and behavior of living systems through basic, clinical, and population-based research and determine how to apply such knowledge to illuminate developmental origins of health and disease and help ensure that women and men have good reproductive health, that children are born healthy, and that people develop to live healthy and productive lives.

Thirteen affinity groups comprised of over 60 units and sections, as well as the Division of Population Health Research, constitute the Division of Intramural Research (DIR).

DIR conducts laboratory, clinical, epidemiological, and statistical research programs to seek fundamental knowledge about the nature and behavior of living systems through basic, clinical, and population-based research. We use this knowledge to illuminate developmental origins of health and disease and to help ensure that women and men have good reproductive health, that children are born healthy, and that people develop to live productive lives. Research efforts are focused on the acquisition of information that will enhance our understanding of the biology of development and reproduction. Our research program emphasizes the importance of fundamental investigations into the physics, chemistry, and biology of cells, their component parts, and the processes that govern and regulate their function. As part of their investigative focus, the scientific researchers of DIR accord primary importance to the transmission of new information to future generations of scientists.



NICHD Mission

NICHD's mission is to lead research and training to understand human development, improve reproductive health, enhance the lives of children and adolescents, and optimize abilities for all.

For additional information:

NICHD and our 2020 Strategic Plan:

<https://www.nichd.nih.gov/>

<https://www.nichd.nih.gov/about/org/strategicplan>

NICHD Intramural Research Program:

<https://www.nichd.nih.gov/research/atNICHD>

<https://annualreport.nichd.nih.gov/>

For information or questions related to NICHD Intramural Research Program participation in the Pediatric Scientist Development Program please contact:

Dr. Catherine M. Gordon

Clinical Director and Senior Investigator

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For specific information related to individual NICHD intramural laboratories and research opportunities, please feel free to contact the Principal Investigators directly.

The cell biology of cellular lipid landscape
Tamas Balla, MD, PhD
Section on Molecular Signal Transduction (SMST)

Our group studies the mechanisms by which eukaryotic cells control the lipid composition of their various membrane compartments. Almost all biological processes are controlled by protein signaling complexes that assemble on the surface of cellular membranes. Consequently, most human diseases can be traced to molecular defects that change protein function as it relates to membrane interactions. Various cellular organelles have unique lipid compositions contributing to their identity and determining the signaling modalities that are associated with them. The biochemical basis and enzymology of lipid metabolism has been mostly worked out but the cellular compartmentalization of the lipid biosynthetic machinery and the transport processes that establish and maintain the lipid composition of organelle membranes are poorly understood. Moreover, the cellular decision making whether to use lipids as energy sources, membrane building blocks or to store them is critical for the metabolic fitness of cells and hence for the whole organism. The small amount of regulatory lipids, the phosphoinositides play central roles in cellular signaling, vesicular membrane trafficking and cellular lipid homeostasis. The major focus of our group is to develop molecular tools that allow visualization and acute manipulation of phosphoinositides in living cells to better understand the molecular basis of their pivotal roles in controlling lipid distribution and organelle dynamics. Our approach relies on the use of fluorescent proteins and protein engineering and hence a variety of fluorescence microscopy applications to induce or follow lipid dynamics in live cells. Trainees joining our group can learn molecular biology and structure-instructed molecule design as well as cell culture-based genome editing and fluorescence microscopy. They are exposed to lively discussions about the scientific literature experimental design and data analysis during our weekly lab-meetings and monthly journal clubs. Trainees also have a chance to present their work and improve their writing and presentation skills and these are in addition to the rich developmental programs offered by NICHD.

Lab website: <https://www.nichd.nih.gov/research/atNICHD/Investigators/balla>

Selected publications:

1. Pemberton JG, Kim YJ, Humpolickova J, Eisenreichova A, Sengupta N, Toth DJ, Boura E, Balla T. Defining the subcellular distribution and metabolic channeling of phosphatidylinositol. *J Cell Biol.* 2020 Mar 2;219(3). e201906130. doi: 10.1083/jcb.201906130.
2. Baba T, Toth DJ, Sengupta N, Kim YJ and Balla T. PI(4,5)P2 controls Rab7 and Plekhm1 membrane cycling during autophagosome-lysosome Fusion. *EMBO J.* 38: e100312, 2020
3. Sohn M, Korzeniowski M, Zewe JP, Wills RC, Hammond GRV, Humpolickova J, Vrzal L, Chalupska D, Veverka V, Fairn GD, Boura E, Balla T. PI(4,5)P2 controls plasma membrane PI4P and PS levels via ORP5/8 recruitment to ER-PM contact sites. *J Cell Biol.* 2018 May 7;217(5):1797-1813.
4. Sohn M, Ivanova P, Brown HA, Toth DJ, Varnai P, Kim YJ, Balla T. Lenz-Majewski mutations in PTDSS1 affect phosphatidylinositol 4-phosphate metabolism at ER-PM and ER-Golgi junctions. *Proc Natl Acad Sci U S A.* 2016 Apr 19;113(16):4314-9.
5. Kim YJ, Guzman-Hernandez ML, Wisniewski E, Balla T. Phosphatidylinositol-Phosphatidic Acid Exchange by Nir2 at ER-PM Contact Sites Maintains Phosphoinositide Signaling Competence. *Dev Cell.* 33:549-61, 2015.

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Jeffrey Baron, MD

Section on Growth and Development

Our research group investigates the cellular and molecular mechanisms governing childhood growth and development. One goal of this work is to gain insight into the many human genetic disorders that cause childhood growth failure and overgrowth. We also seek to develop new treatments for children with severe growth disorders.

Much of our work has focused on the growth plate which is controlled by multiple interacting regulatory systems, involving endocrine, paracrine, extracellular matrix-related, and intracellular pathways. Our group has studied growth plate regulation by FGFs, BMPs, C-type natriuretic peptide, retinoids, WNTs, PTHrP/IHH, IGFs, estrogens, glucocorticoids, and microRNAs. We have also investigated the mechanisms that cause bone growth to occur rapidly in early life but then to progressively slow with age and eventually cease.

For many children with disorders of growth and development, the etiology remains unknown. To discover new genetic causes of these disorders, we have used powerful genetic approaches including SNP arrays and exome sequencing. Using this approach, we have explored the roles of ACAN, QRICH1, BRF1, CYP26A1/C1, AND SPIN4 in disorders of human growth.

Currently, treatment approaches for linear growth disorders are limited. We have undertaken a project designed to improve treatment by targeting growth-promoting endocrine and paracrine factors specifically to the growth plate by linking these factors to cartilage-binding antibody fragments. When administered systemically, these hybrid molecules are preferentially taken up by growth plate cartilage, and thus can augment the therapeutic effect on the target organ while diminishing adverse effects due to action on other tissues.

Laboratory website link: <https://www.nichd.nih.gov/research/atNICHD/Investigators/baron>

Selected publications:

- Lui JC, Wagner J, Zhou E, Dong L, Barnes KM, Jee YH, Baron J. Loss of function variant in SPIN4 causes an X-linked overgrowth syndrome. *JCI Insight*, 8;8(9):e167074. doi: 10.1172/jci.insight.167074, 2023.
- Lui JC, Jee YH, Garrison P, Iben JR, Yue S, Ad M, Nguyen Q, Kikani B, Wakabayashi Y, Baron J. Differential Aging of Growth Plate Cartilage Underlies Differences in Bone Length and Thus Helps Determine Skeletal Proportions, *PLoS Biol*, 23;16(7):e2005263, 2018
- Lui JC, Colbert M, Cheung CS, Ad M, Lee A, Zhu Z, Barnes K, Dimitrov DS, Baron J. Cartilage-Targeted IGF-1 treatment to promote longitudinal bone growth, *Mol Ther*. 27:673-680, 2019.
- Lui JC, Nguyen Q, Ad M, Garrison P, Jee YH, Nilsson O, Barnes K, Baron J. EZH1 and EZH2 promote skeletal growth by repressing inhibitors of chondrocyte proliferation and hypertrophy, *Nat Commun*, 7:13685, 2016. PMID:PMC5477487
- Baron J, Säwendahl L, Phillip M, De Luca F, Dauber A, Wit JM, Nilsson O. Short and tall stature: a new paradigm emerges. *Nat Rev Endocrinol*, 11:735-46, 2015. PMID: PMC5002943

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Protein Trafficking in the Endosomal-Lysosomal System
Juan S. Bonifacino, PhD
Section on Intracellular Protein Trafficking

Our laboratory investigates the molecular mechanisms by which transmembrane proteins (referred to as “cargo”) are sorted to different compartments of the endomembrane system in eukaryotic cells. This system comprises an array of membrane-enclosed organelles including the endoplasmic reticulum (ER), the Golgi apparatus, the *trans*-Golgi network (TGN), endosomes, lysosomes, lysosome-related organelles (LROs) (e.g., melanosomes, cytotoxic granules), and different domains of the plasma membrane in polarized cells such as epithelial cells and neurons. Transport of cargo between these compartments is mediated by vesicular/tubular carriers that bud from a donor compartment, translocate through the cytoplasm, and fuse with an acceptor compartment. Work in our laboratory focuses on the molecular machineries that mediate these processes, including (1) sorting signals and adaptor proteins that select cargo for packaging into transport carriers, (2) microtubule motors and organelle adaptors that drive movement of transport carriers and other organelles through the cytoplasm, and (3) tethering factors that promote fusion of transport carriers to acceptor compartments. We study these machineries in the context of different intracellular transport pathways, including endocytosis, recycling from endosomes to the plasma membrane, retrograde transport from endosomes to the TGN, biogenesis of lysosomes and LROs, autophagy, and polarized sorting in epithelial cells and neurons. Knowledge gained from this basic research is applied to the elucidation of mechanisms of disease, including congenital disorders of protein traffic such as the pigmentation and bleeding disorder, Hermansky-Pudlak syndrome (HPS), hereditary spastic paraplegias (HSPs), and other neurodevelopmental disorders.

Laboratory website links:

<https://www.nichd.nih.gov/research/atNICHD/Investigators/bonifacino>;
<https://irp.nih.gov/pi/juan-bonifacino>

Selected publications:

- Gershlick DC, Ishida M, Jones JR, Bellomo A, Bonifacino JS, Everman DB (2019) A neurodevelopmental disorder caused by mutations in the VPS51 subunit of the GARP and EARP complexes. *Hum Mol Genet.* 28:1548-1560.
- Dell'Angelica EC, Bonifacino JS (2019) Coatopathies: genetic disorders of protein coats. *Annu Rev Cell Dev Biol.* 35:131-168.
- Ballabio A, Bonifacino JS (2020) Lysosomes as dynamic regulators of cell and organismal homeostasis. *Nat Rev Mol Cell Biol.* 21:101-118.
- Mattera R, De Pace R, Bonifacino JS (2020) The role of AP-4 in cargo export from the *trans*-Golgi network and hereditary spastic paraplegia. *Biochem Soc Trans.* 48:1877-1888.
- Saric A, Freeman SA, Williamson CD, Jarnik M, Guardia CM, Fernandopulle MS, Gershlick DC, Bonifacino JS (2021) SNX19 restricts endolysosome motility through contacts with the endoplasmic reticulum. *Nat Commun.* 12:4552.

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Social and Behavioral Sciences Branch

Stephen Gilman, ScD and Tonja Nansel, PhD

The Social and Behavioral Sciences Branch (SBSB) conducts innovative research on the social and behavioral determinants of maternal, child, and adolescent health, and designs and tests social and behavioral interventions to improve health. The disciplinary expertise represented in our Branch spans the fields of developmental, social, and community/clinical psychology; education; nutrition; and social and psychiatric epidemiology. Our research, which is situated within the Social and Behavioral Sciences and Health Disparities focus areas in NIH's Intramural Research Program, applies social and behavioral science theories and methods to population-based research in order to understand health, development, and behavior.

Dr. Stephen Gilman leads SBSB's research on the social determinants of child development and mental health, which aims to advance our understanding of the early life origins of socioeconomic and racial/ethnic disparities in children's physical and mental development with long-term ramifications for mental well-being.

Dr. Tonja Nansel directs SBSB's research on behavioral nutrition in children and families, which uses experimental and observational methods to investigate influences on health behaviors leading to optimal growth and development. This program of research includes both experimental and observational studies on the influences of reward-related eating on diet quality and relationships of diet and nutritional status with health outcomes in youth with type 1 diabetes.

Please see <https://www.nichd.nih.gov/about/org/dir/dph/officebranch/sbsb> for more information about SBSB's research,

Selected publications:

Gilman SE, Hornig M, Ghassabian A, Hahn J, Cherkerzian S, Albert PS, Buka SL, Goldstein JM. Socioeconomic disadvantage, gestational immune activity, and neurodevelopment in early childhood. *Proc Natl Acad Sci U S A*. 2017;114(26):6728-33. PubMed PMID: 28607066; PMCID: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5495226>

Nansel TR, Lipsky LM, Faith M, Liu A, Siega-Riz AM. The accelerator, the brake, and the terrain: associations of reward-related eating, self-regulation, and the home food environment with diet quality during pregnancy and postpartum in the pregnancy eating attributes study (PEAS) cohort. *Int J Behav Nutr Phys Act*. 2020;17(1):149. PubMed PMID: 33228724; PMCID: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7684737>

Lipsky LM, Burger KS, Faith MS, Siega-Riz AM, Liu A, Shearrer GE, Nansel TR. Pregnant Women Consume a Similar Proportion of Highly vs Minimally Processed Foods in the Absence of Hunger, Leading to Large Differences in Energy Intake. *J Acad Nutr Diet*. 2021;121(3):446-57. PubMed PMID: 33109504

Yu J, Ghassabian A, Chen Z, Goldstein RB, Hornig M, Buka SL, Goldstein JM, Gilman SE. Maternal Immune activity during pregnancy and socioeconomic disparities in children's self-regulation. *Brain Behav Immun*. 2020;90:346-52. PubMed PMID: 32919039; PMCID: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7544646>

Yu J, Patel RA, Gilman SE. Childhood disadvantage, neurocognitive development and neuropsychiatric disorders: Evidence of mechanisms. *Curr Opin Psychiatry*. 2021;34(3):306-23. PubMed PMID: 33587493

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Adolescent Bone and Body Composition Laboratory

Catherine M. Gordon, MD, MS

The major aim of my lab is to understand factors during adolescence that impact bone density and other health outcomes during the adult years. We are examining how modifiable factors such as nutrition and physical activity influence the development of peak bone mass, as well as variables such as skin pigmentation and an individual's genotype that are determined at birth. In both healthy youth and those with chronic disease, we are exploring the interrelationship between body composition, circulating hormones, and bone marrow adiposity on bone turnover and skeletal accrual.

Our laboratory is committed to identifying assessment tools that afford non-invasive measurements of bone density and skeletal strength in the pediatric and adolescent population. We are using dual-energy x-ray absorptiometry (DXA) to provide measurements of central bone density and body composition and high-resolution peripheral computed tomography (HRpQCT) to evaluate peripheral measurements of bone density and skeletal strength. We are using these tools to perform deep phenotyping of children and adolescents with chronic conditions.

A focus of our research is how physical and emotional health are compromised in adolescents and young women with premature ovarian insufficiency (POI). We are interested in both the presentation and causes of POI, including that seen in childhood cancer survivors, and ovarian dysfunction due to autoimmune, metabolic, genetic/syndromic, and idiopathic (unknown) causes. We are conducting a natural history study to characterize numerous health outcomes and are launching clinical trials to identify the optimal estrogen replacement regimen for adolescents and young women with this diagnosis. Other ongoing studies are exploring physical and behavioral health outcomes in adolescents with delayed puberty due to causes beyond POI, restrictive eating disorders, and inflammatory bowel disease.

Selected publications:

- Wasserman HM, Kalkwarf HJ, Altaye M, Yolton K, Kanj RV, Gordon CM. Characterizing the adolescent premature ovarian insufficiency phenotype: A case control study. *J Pediatr Adolesc Gynecol.* 2022; S1083-3188(22)00298-4. PMID: 36216307
- [Gordon RJ](#), Pappa HM, [Vajapeyam S](#), [Mulkern R](#), [Ecklund K](#), [Snapper SB](#), Gordon CM. Bone marrow adiposity in pediatric Crohn's disease. *Bone.* 2022 09; 162:116453. PMID: [35667602](#).
- DiVasta AD, Feldman HA, O'Donnell JM, Long J, Leonard MB, Gordon CM. Impact of adrenal hormone supplementation on bone geometry in growing teens with anorexia nervosa. *J Adolesc Health.* 2019 10; 65(4):462-468. PMID: [31227390](#).
- Vajapeyam S, Ecklund K, Mulkern RV, Feldman HA, O'Donnell JM, DiVasta AD, Rosen CJ, Gordon CM. Magnetic resonance imaging and spectroscopy evidence of efficacy for adrenal and gonadal hormone replacement therapy in anorexia nervosa. *Bone.* 2018 05; 110:335-342. PMID: [29496516](#).
- Kanj RV, Ofei-Tenkorang NA, Altaye M, Gordon CM. Evaluation and management of primary ovarian insufficiency in adolescents and young adults. *J Pediatr Adolesc Gynecol.* 2018 Feb; 31(1):13-18. PMID: [28782660](#).

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The Biological Impact of Transposable Elements

Henry Levin, Ph.D.

Section of Eukaryotic Transposable Elements

Transposable elements were highly active throughout evolution resulting in genome landscapes dominated by sequence repeats. The regulatory sequences contained within transposable elements have been broadly dispersed to form gene regulatory networks important for many biological functions. Our current studies focus on the integration of transposable elements and how de novo insertion modifies host biology. Experimental systems include the LTR retrotransposon of fission yeast, and HIV-1 in human cells. Recent work relies on the vast databases of human genetics to understand the role of transposable elements in human disease. Our studies of integration include inserts throughout the fission yeast genome that revealed pol II transcribed promoters are the primary targets of Tf1 integration. We adapted high throughput sequencing and developed new technology to sequence 1 million insertion sites. These experiments show that Tf1 has a preference for stress response promoters and the targeting of integration involves the DNA binding protein Sap1. We have also applied new methods to sequence 1 million integration sites of HIV-1 in cultured cells. These data led to the important discovery that the integrase of HIV-1 directs integration to highly spliced genes and interacts with splicing factors. We continue to study the chromatin determinants of HIV-1 integration relying extensively on ChIP-seq experiments. We are also designing experiments to test expression activity of sequence variants of placenta resulting in low birth weight.

Laboratory website links:

<https://www.nichd.nih.gov/research/atNICHD/Investigators/levin>

<https://irp.nih.gov/pi/henry-levin>

Selected publications:

- Ahn HW, Worman ZF, Lechsinska A, Payer LM, Wang T, Malik N, Li W, Burns KH, Nath A, Levin HL. Retrotransposon insertions associated with risk of neurologic and psychiatric diseases (external link) *EMBO Rep.* 2023;24(1):e55197.
- Li F, Lee M, Esnault C, Wendover K, Guo Y, Atkins P, Zaratiegui M, Levin HL. Identification of an integrase-independent pathway of retrotransposition.(external link) *Sci Adv.* 2022;8(26):eabm9390.
- Lee SY, Hung S, Esnault C, Pathak R, Johnson KR, Bankole O, Yamashita A, Zhang H, Levin HL. Dense Transposon Integration Reveals Essential Cleavage and Polyadenylation Factors Promote Heterochromatin Formation.(external link) *Cell Rep.* 2020;30(8):2686-2698.e8.
- Esnault C, Lee M, Ham C, Levin HL. Transposable element insertions in fission yeast drive adaptation to environmental stress.(external link) *Genome Res.* 2019;29(1):85-95.
- Singh PK, Plumb MR, Ferris AL, Iben JR, Wu X, Fadel HJ, Luke BT, Esnault C, Poeschla EM, Hughes SH, Kvaratskhelia M, Levin HL. LEDGF/p75 interacts with mRNA splicing factors and targets HIV-1 integration to highly spliced genes.(external link) *Genes Dev.* 2015;29(21):2287-97.

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Defining the role of Metabolism in Oocyte Development
Mary Lilly, PhD
Section on Gamete Development

My laboratory uses the genetically tractable model organism *Drosophila melanogaster* to examine how meiotic progression is instructed by the developmental and metabolic program of the egg. Using a combination of molecular genetics, cell biology and biochemistry, we work to define the pathways that ensure the production and maintenance of high-quality oocytes. In mammals, studies on the early stages of oogenesis face serious technical challenges in that entry into the meiotic cycle, meiotic recombination, and the initiation of the highly conserved prophase I arrest all occur during embryogenesis. By contrast, in *Drosophila* these critical events of early oogenesis all take place continuously within the adult female. Easy access to the early stages of oogenesis, coupled with available genetic and molecular genetic tools, make *Drosophila* an excellent model for studies on the role of metabolism in oocyte development and maintenance. Chromosome mis-segregation during female meiosis is the leading cause of miscarriages and birth defects in humans. Recent evidence suggests that many meiotic errors occur downstream of defects in oocyte growth and the hormonal signaling pathways that drive oocyte differentiation. Thus, understanding how oocyte development and growth impact meiotic progression is essential to studies in both reproductive biology and medicine.

Laboratory website link

<https://www.nichd.nih.gov/research/atNICHD/Investigators/lilly>

Selected publications

- Yang S, Zhang Y, Ting CY, Bettedi L, Kim K, Ghaniem E, Lilly MA. (2020) The Rag GTPase regulates the dynamic behavior of TSC downstream of both amino acid and growth factor restriction. *Dev. Cell.* 2020 PMID: [32898476](#)
- Wei Y, Bettedi L, Ting CY, Kim K, Zhang Y, Cai J, Lilly MA. (2019). The GATOR complex regulates an essential response to meiotic double-stranded breaks in *Drosophila*. *eLife*. 8:e42149. PMID: [31650955](#)
- Cai, W., Wei, Y., Jarnik, M., and M.A. Lilly (2016) The GATOR2 Component Wdr24 Regulates TORC1 Activity and Lysosome Function. *PLoS Genetics*. <http://dx.doi.org/10.1371/journal.pgen.1006036>
- Wei, Y., Reveal, B., Reich, J., Laursen, W., Senger, S., Akar, T., Iida-Jones, I., Cai, W., Jarnik, M., and M. A. Lilly (2014) The TORC1 regulators Iml1/GATOR1 and GATOR2 control meiotic entry and oocyte development in *Drosophila*. *PNAS*. 111 (52) E5670-E5677.

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Hippocampal Interneurons and Their Role in the Control of Network Excitability

Dr. Christopher J. McBain, Ph.D.

Laboratory of Cellular and Synaptic Neurophysiology

Cortical and hippocampal GABAergic inhibitory interneurons (INs) are “tailor-made” to control cellular and network excitability by providing synaptic and extrasynaptic input to their downstream targets via GABA_A and GABA_B receptors. The axons of this diverse cell population make local, short-range projections (although some subpopulations project their axons over considerable distances) and release the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) onto a variety of targets. Distinct cohorts of INs regulate sub- and supra-threshold intrinsic conductances, regulate Na⁺- and Ca²⁺-dependent action-potential generation, modulate synaptic transmission and plasticity, and pace both local- and long-range large-scale synchronous oscillatory activity. An increasing appreciation of the roles played by INs in several neural-circuit disorders, such as epilepsy, stroke, Alzheimer’s disease, and schizophrenia, has seen this important cell type take center stage in cortical circuit research. With almost 30 years of interest in this cell type, the main objectives of the lab have been to understand: (1) the developmental trajectories taken by specific cohorts of INs as they populate the nascent hippocampus and cortex; (2) how ionic and synaptic mechanisms regulate the activity of both local circuit GABAergic INs and principal neurons (PN) at the level of small, well defined networks; and (3) how perturbations in their function alter hippocampal/neocortical networks in several neural circuit disorders. To this end, we use a variety of state-of-the-art electrophysiological, imaging, optogenetic, immunohistochemical, biochemical, molecular, genetic, and sequencing approaches in wild-type and transgenic mice using both *ex-vivo* (eg. brain slices, tissue homogenates) and *in-vivo* (awake behaving animals) experimental platforms. In addition, we have established robust pipelines to interrogate IN function and circuit participation in brain tissue from higher species such as human and non-human primate to evaluate evolutionary conservation or innovations of IN function.

Lab website: <https://dir.ninds.nih.gov/Faculty/Profile/chris-mcbain.html>

Selected publications:

1. Pelkey KA, Chittajallu R, Craig MT, Tricoire L, Wester JC, McBain CJ. Hippocampal GABAergic inhibitory interneurons. *Physiol Rev* 2017;97:1619-1747.
2. Pelkey KA, Calvigioni D, Fang C, Vargish G, Ekins T, Auville K, Wester JC, Lai M, Mackenzie-Gray Scott C, Yuan X, Hunt S, Abebe D, Xu Q, Dimidschstein J, Fishell G, Chittajallu R, McBain CJ. Paradoxical network driven excitation by glutamate release from VGluT3+ GABAergic interneurons. *eLife* 2020;9:e51996.
3. Mahadevan V, Peltekian A, McBain CJ. Translatome analyses using ribosomal tagging in GABAergic interneurons and other sparse cell types. *Curr Protoc Neurosci* 2020;92:e93.
4. Chittajallu R, Auville K, Mahadevan V, Lai M, Hunt S, Pelkey KA, Zaghloul K, McBain CJ. Activity dependent tuning of intrinsic excitability in mouse and human neurogliaform cells. *eLife* 2020;9:e57571.
5. Wester JC, Mahadevan V, Rhodes CT, Calvigioni D, Venkatesh S, Maric D, Hunt S, Yuan X, Zhang Y, Petros TJ, McBain CJ. Neocortical Projection Neurons Instruct Inhibitory Interneuron Circuit Development in a Lineage-Dependent Manner. *Neuron* 102(5):960-975

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Section on Mammalian Development and Evolution Todd Macfarlan, PhD

At NICHD, our central mission is to ensure that every human is born healthy. Despite much progress in understanding the many ways the mother interacts with the fetus during development, we still know little about the genetic changes that promoted the emergence of placental mammals over 100 million years ago from our egg-laying relatives, nor those mechanisms that continue drive phenotypic differences amongst mammals. One attractive hypothesis is that retroviruses and their endogenization into the genomes of our ancestors played an important role in eutherian evolution, by providing protein coding genes like syncytins (derived from retroviral *env* genes that cause cell fusions in placental trophoblasts) and novel gene regulatory nodes that altered expression networks to allow for implantation and the emergence and continued evolution of the placenta. The primary interest of my lab is to explore the impact of these endogenous retroviruses (ERVs), that account for ~10% of our genomic DNA, on embryonic development and on the evolution of new traits in mammals. This has led us to examine the rapidly evolving Kruppel-associated box zinc finger protein (KZFP) family, the single largest family of transcription factors (TFs) in most, if not all mammalian genomes. Our hypothesis is that KZFP gene expansion and diversification has been driven primarily by the constant onslaught of ERVs and other transposable elements (TEs) to the genomes of our ancestors, as a means to transcriptionally repress them. This hypothesis is supported by recent evidence demonstrating the majority of KZFPs bind TEs and that TEs and nearby genes are activated in KZFP knockout mice. In the next several years we will continue to explore the impacts of the TE/KZFP “arms race” on the evolution of mammals. We will also begin a new phase exploring whether KZFPs play broader roles in genome regulation beyond gene silencing, and how these functions impact mammalian development.

Lab website: <https://www.nichd.nih.gov/research/atNICHD/Investigators/macfarlan>

Selected publications:

- Wolf G, de Iaco A, Sun MA, Bruno M, Tinkham M, Hoang D, Mitra A, Ralls S, Trono D, Macfarlan TS. KRAB-zinc finger protein gene expansion in response to active retrotransposons in the murine lineage. *Elife*. 2020 Jun 1;9:e56337. doi: 10.7554/eLife.56337.PMID: 32479262
- Mahgoub M, Paiano J, Bruno M, Wu W, Pathuri S, Zhang X, Ralls S, Cheng X, Nussenzweig A, Macfarlan TS. Dual histone methyl reader ZCWPW1 facilitates repair of meiotic double strand breaks in male mice. *Elife*. 2020 Apr 30;9:e53360. doi: 10.7554/eLife.53360.PMID: 32352380
- Patel A1, Yang P1, Tinkham M, Pradham M, Sun MA, Wang Y, Hoang D, Wolf G, Horton JR, Zhang X, Macfarlan T*, Cheng X*. DNA conformation induces adaptable binding by tandem zinc finger proteins. *Cell* 2018. Mar 22;173(1):221-233.e12 doi.org/10.1016/j.cell.2018.02.0581. PMID:29551271
- Wolf G, Rebollo R, Karimi MM, Ewing AD, Kamada R, Wu W, Wu B, Bachu M, Ozato K, Faulkner GJ, Mager DL, Lorincz MC, Macfarlan TS. On the role of H3.3 in retroviral silencing. *Nature* 2017 Aug 3; 548E1-E3. doi:10.1038/nature23277. PMID:28770848
- Yang P, Wang Y, Hoang D, Tinkham M, Patel A, Sun M-A, Wolf G, Baker M, Chien H-C, Lai N, Cheng X, Shen C-K J, and Macfarlan TS*. A placental growth factor is silenced in mouse embryos by the zinc finger protein ZFP568. *Science* 2017 May 19;356(6339):757-759. doi: 10.1126/science.aah6895. PMID:28522536

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Claire Le Pichon, PhD
Unit on the Development of Neurodegeneration
Molecular Medicine Affinity Group

Our work is dedicated to advancing our understanding of common molecular and cellular mechanisms of neurodegeneration with the ultimate goal of developing treatments for neurodegenerative diseases and even preventing them. One focus area is on mechanisms of axon damage signaling in neurons. Another lab theme is to understand fundamental differences between vulnerable and resilient populations of neurons in models of trauma and chronic disease.

The Le Pichon lab employs a multidisciplinary approach including mouse genetics, wide-scale imaging of whole cleared tissues, single cell transcriptomics, and cell biological studies in human iPSC-derived neurons to investigate the early events underlying the onset and progression of neurodegenerative disease. We have a particular interest in rare developmental neurodegenerative diseases that affect spinal motor neurons, such as SMA (spinal muscular atrophy) and juvenile ALS (amyotrophic lateral sclerosis), and in mechanisms of axon degeneration and regeneration.

Dr. Le Pichon is the recipient of a NIH Director's Ruth L. Kirschstein Award for Mentorship in 2021.

Laboratory website links:

<https://irp.nih.gov/pi/claire-le-pichon>

<https://www.nichd.nih.gov/research/atNICHD/Investigators/lepichon>

Selected Publications:

- Wlaschin JJ*, Donahue C*, Gluski J*, Ramos L, Osborne J, Silberberg H, **Le Pichon CE**. [Promoting regeneration while blocking cell death preserves motor neuron function in a model of ALS Brain](#). (2023)
- Alkaslasi MA, Piccus ZE, Hareendran S, Silberberg H, Chen L, Zhang Y, Petros TJ, **Le Pichon CE**. [Single nucleus RNA-sequencing defines unexpected diversity of cholinergic neuron types in the adult mouse spinal cord](#). *Nature Communications*. 2021 12, Article number: 2471.
- Nguyen MQ, **Le Pichon CE**, Ryba N. [Stereotyped transcriptomic transformation of somatosensory neurons in response to injury](#). *Elife*. 2019 Oct 8;8. doi: 10.7554/eLife.49679. PubMed PMID: 31592768.
- Wlaschin JJ, Gluski JM, Nguyen E, Silberberg H, Thompson JH, Chesler AT, **Le Pichon CE**. [Dual leucine zipper kinase is required for mechanical allodynia and microgliosis after nerve injury](#). *Elife*. 2018 Jul 3;7. doi: 10.7554/eLife.33910. PubMed PMID: 29968565; PubMed Central PMCID: PMC6029846.
- **Le Pichon CE***, Meilandt WJ*, Dominguez S, Solanoy H, Lin H, Ngu H, Gogineni A, Ghosh AS, Jiang Z, Lee S, Maloney J, Gandham VD, Pozniak C, Wang B, Lee S, Siu M, Patel S, Modrusan Z, Liu X, Rudhard Y, Baca M, Gustafson A, Kaminker J, Carano RAD, Huang E, Foreman O, Weimer R, Searce-Levie K, Lewcock J. Loss of dual leucine zipper kinase signaling is protective in animal models of neurodegenerative disease. *ScienceTranslMed*. 2017 Aug 16;9(403).

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Clinical and Basic Investigations of Rare Genetic Disorder

Forbes D. Porter, M.D., Ph.D

Section on Molecular Dysmorphology

My research team combines both clinical and basic research to study the molecular, biochemical, and cellular processes that underlie genetic disorders resulting from impaired cholesterol homeostasis and lysosomal dysfunction. Our ultimate goal is to identify and test potential therapeutic interventions. The disorders that we study include Smith-Lemli-Opitz syndrome (SLOS) and Niemann-Pick disease, type C (NPC). SLOS is an inborn error of cholesterol biosynthesis that results in multiple congenital malformations as well as cognitive and behavioral issue. NPC is a lethal, progressive, neurodegenerative disorders due to lysosomal dysfunction. My basic research group utilizes multiple model systems including induced pluripotent stem cells mouse models. These preclinical models are used to both investigate pathological mechanisms and to test potential therapeutic approaches. Mechanistic studies include single cell/nuclear and special transcriptomics. We are performing high throughput chemical/drug and genomic screens to identify potential therapeutic compounds that can be evaluated in our mouse models. We are also exploring gene therapy for NPC. Our basic research is complemented by ongoing natural history trials for both disorders. As part of our natural history trials, we have established large cross-sectional and longitudinal collections of cell lines, urine, serum/plasma and cerebral spinal fluid from well-phenotyped patients. These biomaterials are being used to identify diagnostic, prognostic and therapeutic responsive biomarkers. We have also engaged in multiple phase 1/2a and phase 2b/3 therapeutic trials.

Laboratory website: <https://annualreport.nichd.nih.gov/porter.html>

Selected publications:

Francis KR et al. Modeling Smith-Lemli-Opitz syndrome with induced pluripotent stem cells reveals a causal role for Wnt/beta-catenin defects in neuronal cholesterol synthesis phenotypes. *Nat Med* 2016;22:388-396.

Ory DS et al. Intrathecal 2-hydroxypropyl- β -cyclodextrin decreases neurological disease progression in Niemann-Pick disease, type C1: an ad-hoc analysis of a non-randomized, open-label, phase 1/2 trial. *Lancet* 2017;390(10104):1758-1768.

Cougnoux A et al. Single cell transcriptome analysis of Niemann-Pick disease, type C1 cerebella. *Int J Mol Sci* 2020;21(15):5368.

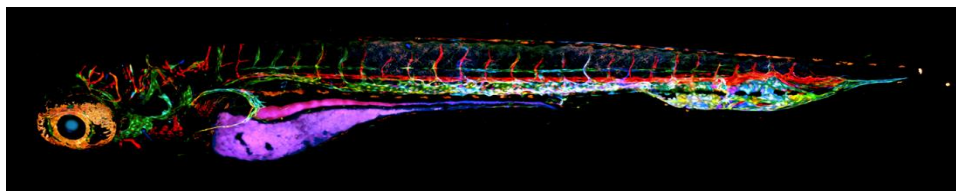
Solomon B et al. Association of miglustat with swallowing outcomes in Niemann-Pick disease, type C1. *JAMA Neurol* 2020;77(12):1-6.

Agrawal, N et al Neurofilament light chain in cerebrospinal fluid as a novel biomarker in evaluating both clinical severity and therapeutic response in Niemann-Pick disease type C1, *Genet. Med.* 2023; 25(3): 100349

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Genetic causes lead to novel therapies for complex lymphatic anomalies

Sarah Sheppard MD PhD MS



Laboratory Description and Research Opportunity

The primary goal of Dr. Sheppard's translational research group is to develop more efficacious therapies for individuals affected by complex lymphatic malformations. Specifically, her research has focused on a subtype of complex lymphatic anomaly, called central conducting lymphatic anomaly (also known as channel type lymphatic malformation), with severe morbidity and mortality. Previously, we determined distinct central lymphatic patterns that correlate with genotype. We identified *KRAS* as a cause for central conducting lymphatic anomaly, leading to increased lymphangiogenesis and dilation of the lymphatics, and that MEK inhibition was efficacious *in vitro*, *in vivo*, and in single human cases. We applied multiple genomic techniques including liquid biopsy to improve genetic diagnosis and treatment in individuals affected by vascular anomalies. In the clinic, we study the natural history of these disorders (NCT05731141) to define features and evolution of the disease over time. In the laboratory, we investigate the cellular and molecular mechanisms for RAS-pathway related lymphatic disorders using *in vitro* and *in vivo* methods such as organoids and the zebrafish to create models for the genetic causes of lymphatics. Using our genetic models, we are screening new therapies with the goal to translate these into clinical trials.

Laboratory website link: <https://www.nichd.nih.gov/research/atNICHD/Investigators/sheppard>

Selected publications:

- Li D*, Sheppard SE*, et al. Genomic profiling informs diagnoses and treatment in vascular anomalies. *Nat Med*. 2023 Jun 1. doi: 10.1038/s41591-023-02364-x. Epub ahead of print. PMID: 37264205.

- Sheppard SE, et al. Lymphatic disorders caused by mosaic, activating *KRAS* variants respond to MEK inhibition. *JCI Insight*. 2023 May 8;8(9):e155888. doi: 10.1172/jci.insight.155888. PMID: 37154160.

- Liu M, ..., Sheppard SE. Genetics etiologies and genotype phenotype correlations in a cohort of individuals with central conducting lymphatic anomaly. *Eur J Hum Genet*. 2022 May 24;. doi: 10.1038/s41431-022-01123-9. [Epub ahead of print] PubMed PMID: 35606495.

- Foster JB, et al. Kaposiform lymphangiomatosis effectively treated with MEK inhibition. *EMBO Mol Med*. 2020 Oct 7;12(10):e12324. doi: 10.15252/emmm.202012324. Epub 2020 Sep 7. PubMed PMID: 32894644; PubMed Central PMCID: PMC7539180.

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Development of Sensory Processing
Mark Stopfer PhD
Section on Sensory Coding and Neural Ensembles

All animals need to know what is going on in the world around them. Brain mechanisms have thus evolved to gather and organize sensory information to build transient and sometimes enduring internal representations of the environment.

Using relatively simple animals and focusing primarily on olfaction and gustation, we combine electrophysiological, anatomical, behavioral, computational, optogenetic, and other techniques to examine the ways in which intact neural circuits, driven by sensory stimuli, process information. Our work reveals basic mechanisms by which sensory information is transformed, stabilized, and compared, as it makes its way through the nervous system.

We use three species of insects, each with specific and interlocking experimental advantages, as our experimental preparations: locusts, moths, and fruit flies. Compared to the vertebrate, the insect nervous system contains relatively few neurons, most of which are readily accessible for electrophysiological study. Essentially intact insect preparations perform robustly following surgical manipulations, and insects can be trained to provide behavioral answers to questions about their perceptions and memories. Ongoing advances in genetics permit targeting specific neurons for optogenetic or electrophysiological recording or manipulations of activity. And further, the relatively small neural networks of insects are ideal for tightly constrained computational models that test and explicate fundamental circuit properties.

How do the sensory capacities of animals develop? Animals often demonstrate, through their innate sensory preferences, the existence of inborn information. How is this information encoded, and how does it differ from information acquired through direct experience? This research opportunity will focus on understanding these fundamental questions.

Laboratory website: <http://stopfer.nichd.nih.gov>

Selected publications:

- Ray, S., Aldworth, Z., Stopfer, M. (2020) Feedback inhibition and its control in an insect olfactory circuit. *eLife*, 2020;9:e53281 DOI: 10.7554/eLife.53281.
- Gupta, N., Singh, S.S., and Stopfer, M. (2016) Oscillatory integration windows in neurons. *Nature Communications*, 7, 13808 doi: 10.1038/ncomms13808.
- Huston, S.J.*, Stopfer, M.*, Cassenaer, S., Aldworth, Z.N., and Laurent, G. (2015) Neural encoding of odors during active sampling and in turbulent plumes. *Neuron*, 88(2), 403–418.
- Reiter, S., Campillo Rodriguez C., Sun, K., and Stopfer, M. (2015) Spatiotemporal coding of individual chemicals by the gustatory system. *Journal of Neuroscience*, 35(35), 12309 –12321.
- Aldworth, Z., and Stopfer, M. (2015) Tradeoff between information format and capacity in the olfactory system. *Journal of Neuroscience*, 35(4), 1521-1529.

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Genomics of Pituitary Neuroendocrine Tumors

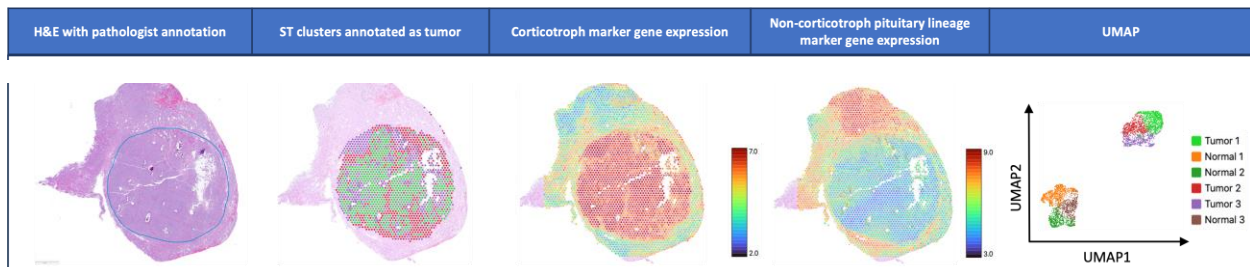
Christina Tatsi, MD, MHSc, PhD

Laboratory Description and Research Opportunity

Pituitary Neuroendocrine tumors (PitNETs) are associated with high morbidity because of hormone dysregulation, mass effects and post-surgical complications. Understanding the pathophysiology and genetic drivers of pituitary tumorigenesis will provide therapeutic targets and improved outcomes. To achieve this, our lab is following two approaches:

1. Whole genome sequencing of germline and tumor DNA to detect driver mutations/genomic alterations, and
2. Transcriptomic analysis of PitNETs to detect dominant pathways involved in tumor formation.

Specifically, our lab presented the first analysis of spatial transcriptomics of PitNETs (Figure below depicting consistency of histopathology annotation of the tumor with transcriptomic clustering, striking differences in expression for select gene markers and uniform manifold approximation and projection analysis of the identified clusters).



The visiting trainee will focus on analyzing primary data from spatial transcriptomic analysis of PitNETs from different subtypes of tumors and characterizing variable cell populations composing intratumor heterogeneity.

Laboratory website links

<https://www.nichd.nih.gov/research/atNICHD/Investigators/tatsi>

Selected publications

- Piña JO, Faucz FR, Padilla C, Floudas CS, Chittiboina P, Quezado M, Tatsi C. Spatial Transcriptomic Analysis of Pituitary Corticotroph Tumors Unveils Intratumor Heterogeneity. medRxiv. 2023 Aug. Preprint. PMID: 37662403 (Under Review in peer review journal)
- Tatsi C et al. Large Genomic Aberrations in Corticotropinomas Are Associated With Greater Aggressiveness. J Clin Endocrinol Metab. 2019 May 1;104(5):1792-1801.

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Vascular Zebrafish
Brant M. Weinstein, Ph. D.
Section on Vertebrate Organogenesis

The Weinstein laboratory studies blood and lymphatic vascular development, meningeal development, and developmental epigenetics using a variety of molecular, cellular, genetic, transgenic, microscopic imaging, and next-generation sequencing approaches. The zebrafish is our primary research model, but we also use mice, cell culture, and Mexican cavefish (*Astyanax mexicanus*) models in our research work.

We have an active research program on vascular development, angiogenesis, and lymphangiogenesis. Our laboratory pioneered many of the key tools and resources used for vascular biology research in the fish, including numerous vascular-specific transgenic fish lines and methods for high resolution *in vivo* time-lapse imaging of zebrafish vessels. We have made a variety of seminal discoveries in the areas of vascular specification, differentiation, and patterning, including a novel pathway regulating arterial identity, a role for neuronal guidance factors in vascular patterning, a mechanism for vascular lumen formation *in vivo*, and identification and characterization of a lymphatic vascular system in the zebrafish.

We also study the meninges and meninges-associated cell types, and the brain neurovascular interface. The meninges are complex, multilayered, highly vascularized tissues surrounding the brain that play a critical role in brain homeostasis and protection and are involved in a variety of brain pathologies. Our laboratory recently discovered that the zebrafish has a meningeal architecture very similar to that of mammals, and we are exploiting the advantages of the fish as a powerful new model for genetic and experimental dissection of this critical tissue. We are also interested in using the zebrafish to better understand the neurovascular interface throughout the brain, using the sophisticated genetic and imaging capabilities of the zebrafish.

Our laboratory has also recently developed an interest in studying the "genetics of epigenetics." Epigenetic mechanisms such as DNA methylation and histone modifications are critical for establishing and maintaining differentiated cell and tissue identities, but the mechanisms directing this in vertebrate animals are largely unknown. We have discovered novel epigenetic mechanisms regulating hematopoietic development and eye development, and we are currently carrying out the first large-scale forward-genetic screen in a vertebrate for tissue-specific epigenetic regulators using a novel transgenic reporter. This highly successful ongoing screen has resulted in the identification of a large number of new vertebrate epigenetic regulators, which we are now in the process of further characterizing and studying.

Lab website:

<https://www.nichd.nih.gov/research/atNICHD/Investigators/weinstein>

For a listing of **Weinstein Lab publications**, see:

<https://www.ncbi.nlm.nih.gov/sites/myncbi/brant.weinstein.1/bibliography/48861132/public/?sort=date&direction=descending>

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Basic, Clinical, and Translational Pediatric Obesity Research

Jack A. Yanovski, MD, PhD

Section on Growth and Obesity

Laboratory Description and Research Opportunity:

The primary goal of the Section on Growth and Obesity is to elucidate the genetic underpinnings of the metabolic and behavioral endophenotypes that contribute to the development of obesity in children. Using an integrated program of basic and clinical translational research, our ongoing studies of patients with monogenic and polygenic obesity and volunteer children of all weight strata aim to advance our understanding of energy balance regulation during childhood. Using our unique longitudinal cohorts of children who have undergone intensive metabolic and behavioral phenotyping, we examine genetic and phenotypic factors predictive of progression to adult obesity in children who are in the “pre-obesity” state, allowing characterization of phenotypes unconfounded by the impact of obesity itself. Once identified as linked to obesity, genetic variants that impair gene function are studied intensively. 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.

Trainees may conduct hypothesis-driven clinical-translational research involving energy balance (including pharmacotherapeutic investigations) or acquire molecular and cellular biology skills in the basic science laboratory, where current projects seek to understand 1) how transglutaminases participate in obesity-linked inflammation and 2) the role of the melanocortin 3 receptor in body weight regulation. Novel investigations may also be proposed by trainees.

Laboratory website link: <https://www.nichd.nih.gov/research/atNICHD/Investigators/yanovski>

Selected publications:

- Han JC, Liu QR, Jones M, Levinn RL, Menzie CM, Jefferson-George KS, Adler-Wailes DC, Sanford EL, Lachawan FL, Uhl GR, Rennert OM, Yanovski JA. Brain-derived neurotrophic factor and obesity in the WAGR syndrome. *N Engl J Med*. 2008;359(9):918-27.
- Lee B, Koo J, Yun Jun J, Gavrilova O, Lee Y, Seo AY, ... Chen F, Gardner R, Koutzoumis D, Sherafat Kazemzadeh R, Roberson RB, Yanovski JA. A mouse model for a partially inactive obesity-associated human MC3R variant. *Nat Commun*. 2016;7:10522.
- Haws R, Brady S, Davis E, Fletty K, Yuan G, Gordon G, Stewart M, Yanovski J. Effect of setmelanotide, a melanocortin-4 receptor agonist, on obesity in Bardet-Biedl syndrome. *Diabetes Obes Metab*. 2020;22(11):2133-2140.
- Loch LK, Tanofsky-Kraff M, Parker MN, ... Brady SM, Bowling AI, Chen KY, Yanovski JA. Associations of Food Reinforcement and Food- Related Inhibitory Control with Adiposity and Weight Gain in Children and Adolescents. *Physiol Behav* 266: 114198, 2023.

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Pediatric Epidemiology

Edwina Yeung, PhD

Epidemiology Branch, Division of Population Health Research, Division of
Intramural Research

Laboratory Description and Research Opportunity:

Dr. Yeung's team leads large epidemiologic studies to understand how early exposures lead to long-term health outcomes among children and adults. In particular, the Upstate KIDS study, a large exposure matched cohort from New York State, was formed to determine whether children conceived by infertility treatment differ from their peers in growth and development from birth to age 3 to 9 years. As a birth cohort, the study has served as a rich resource for understanding important aspects of child health ranging from early development to dietary patterns (see selected publications below). We are also exploring the possible mechanisms underlying associations with prenatal exposures, including DNA methylation.

Laboratory website link: [Upstate KIDS Study](#)

Selected publications:

- Yeung EH, Sundaram R, Bell EM, Druschel C, Kus C, Ghassabian A, Bello S, Xie Y, Buck Louis GM. Examining Infertility Treatment and Early Childhood Development in the Upstate KIDS Study. *JAMA Pediatrics*. 2016; 170(3):251-258. PMID: 26746435. PMCID: PMC5000851
- Trinh M, Sundaram R, Robinson S, Lin TC, Bell EM, Ghassabian A, Yeung E. Association of Trajectory and Covariates of Children's Screen Media Time. *JAMA Pediatrics* 2019 Nov 25;174(1):71-78. PMID: 31764966 PMCID: PMC6902189
- Robinson SL, Sundaram R, Putnick DL, Gleason JL, Ghassabian A, Lin TC, Bell EM, Yeung EH. Predictors of age at juice introduction and associations with subsequent beverage intake in early and middle childhood. *Journal of Nutrition* 2021;151(11):3516-3523. PMID: 34486676 PMCID: PMC8564695
- Putnick DL, Trinh M-H, Sundaram R, Bell EM, Ghassabian A, Robinson SL, Yeung E. Displacement of peer play by screen time: Associations with toddler development. *Pediatric Research* 2022 Aug 19;1-7. PMID: 35986149 PMCID: PMC9390097
- Polinski KJ, Robinson SL, Putnick DL, Guan W, Gleason J, Mumford SL, Sundaram R, Mendola P, London S, Yeung EH. Epigenetic gestational age and the relationship with developmental milestones in early childhood. *Hum Mol Genet* 2023 Jan 6:ddac302. doi: 10.1093/hmg/ddac302. PMID: 36617164 PMCID: PMC10448630

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