A Letter From Our Chair

Genetics of Birth Defects

Both genetic and environmental factors contribute to human birth defects. We’ve learned a lot about the benefits of a healthy diet and avoiding alcohol and smoking in the past 50 years, yet much work needs to be done. To raise awareness of birth defects and promote healthy pregnancies, the U.S. Dept. of Health and Human Services designated January 2011 as National Birth Defects Prevention Month. Educating prospective mothers and improving access to prenatal care are critical steps towards reducing the risk of birth defects. Yet even if these challenges were met, many birth defects would still not be prevented.

Geneticists expect that identifying the molecular basis for disease will result in better prediction of risk, early detection and better treatment. The Michigan Newborn Screening Program detects potentially serious disorders in babies that appear healthy at birth. This program costs about $90 per baby and screens for 50 known disorders of metabolism, blood (such as sickle cell anemia), endocrine function, hearing, cystic fibrosis, and others. Phenylketonuria, the rare disease that launched newborn screening nearly 50 years ago, is an outstanding example of the value of early detection. Defects in the phenylalanine hydroxylase gene cause abnormal accumulation of phenylalanine and irreversible mental retardation, but if the genetic disorder is detected in the first week of life, implementation of a special diet and therapeutics permits normal brain development and function.

About 40% of the admissions to our children’s hospital have underlying genetic defects. (The new C. S. Mott Children’s and Von Voigtlander Women’s Hospitals will open on November 6, 2011). We know the genetic basis for about 3,000 human disorders, but there are almost 4,000 disorders that are Mendelian or suspected to be Mendelian for which the underlying genetics are unknown. What genes contribute to common birth defects in heart, neural tube and palate development? It’s tempting to speculate that the genetic basis for most of these diseases will be identified in the next five years, largely because of the existence of the human genome sequence and advances in gene sequencing technology. To what extent will this change the practice of medicine and impact people’s lives? Looking to the future, can we predict a tipping point when a whole genome analysis might make more sense than individual gene tests?

Researchers in the Department of Human Genetics are participating in the push to identify the genetic causes of birth defects, to understand how mutations in specific genes lead to clinical pathology, and to use this knowledge as a foundation for rational therapeutics. The following feature article presents vignettes of our research on fundamentals of chromosome segregation, skeletal development, hearing impairment, and state-of-the-art genetic testing. The Michigan Medical Genetics Laboratory offers 40 different tests that identify genetic disorders and monitor patients’ health. Among the most exciting developments is “molecular karyotyping” that detects variations in gene copy number (CNV) resulting from duplications and deletions in the genome. There is an astounding degree of genetic variation among healthy individuals: each of us carries more than 100 CNVs and more than 200 rare amino acid substitutions. Researchers are challenged to sort out the variations that contribute to disease from those that are tolerated. Another major challenge is that while we have sequence information for many human genomes, more than 10,000 human genes remain without known function. This is truly an exciting time to be a geneticist!

Sally A. Camper

Cover Image: Images of chromosomes (colored in magenta) in meiosis, a process that rearranges the maternal and paternal chromosomes to produce a recombined chromosome before it is inherited by the offspring. On the left, the maternal and paternal chromosomes are aligned along the entire length of the chromosome. On the right, after the rearrangement process (chiasma formation), the chromosomes are restructured to ensure that a single copy of each chromosome is received in the egg and sperm. The structural rearrangement of the chromosomes is best seen by visualizing a protein (colored in yellow) found within the axes of the maternal and paternal chromosomes. Photos courtesy of Ray Chan.
Ask any geneticist about reproduction and they will tell you that creating a baby is complex. Beyond the basic “facts of life” we learn in middle school, once you understand the intricate web of molecular processes that must happen to create and sustain new life, you can easily become amazed that it ever goes correctly. And yet it does go well, at least in the majority of pregnancies.

As any expectant parent fraught with the typical laundry list of health worries knows, our complex biological system of checks and balances does sometimes go wrong – genetic abnormalities, environmental exposures, or both, cause babies to be born with birth defects. In fact, according to the Centers for Disease Control, one in every 33 babies is born with a birth defect.

There are more than 4,000 different known birth defects, and while scientists have identified the underlying cause of many, the genetic origins of more than 60 percent of all birth defects remain a mystery. Geneticists at the University of Michigan, working with colleagues around the globe, are conducting research to better understand why birth defects occur and ultimately improve outcomes for patients. The influence of environmental toxins is an important area of current research.

“When a child is born with a birth defect, the first thing parents want to know is what caused the problem. Secondly, they want to know will it happen again if they have more children,” says Jeffrey Innis, MD, PhD, director of Pediatric Genetics at U-M. “Unfortunately, there is still so much we don’t know, and too often we have no good answers for parents. It’s a tough situation.”

Increasingly, there is hope for more rapid progress, as the field of genetics looks to new sequencing technology to identify the genetic underpinnings of birth defects. “It used to be that you would find an anomaly in an animal model, study it, and then figure out how it applies to humans,” adds Dr. Innis. “Now we can take unrelated populations of people with a common defect, run genetic sequencing and isolate the mutations or genetic variations they have in common. It puts you several steps ahead in the right direction.”

But it’s not as simple, and won’t happen as quickly as it sounds, cautions Dr. Innis. “It’s still largely a process of trial and error to identify the exact genetic cause of a birth defect. There can be substantial genetic variations among people with the same birth defect – differences not only in the affected genes but in the way the individual genes became mutated. And in rare defects where the populations of patients are very small, it can take years to verify a common genetic cause. That said, it’s still a very exciting time for our field.”

Sally Camper, PhD, chair of U-M’s Department of Human Genetics, couldn’t agree more. Nationally known for her work on the genetics of growth regulation and hearing, Dr. Camper’s lab identified one of the genes responsible for skeletal defects and is currently investigating therapeutic approaches to induce growth in spite of the mutation.

“We are also exploring the link between low levels of thyroid hormone and congenital hearing loss,” says Dr. Camper. “In our mouse models, about half of those with low thyroid function are born profoundly deaf, while the other half has only mild hearing impairment. Our work now is to understand, genetically, why and how that happens.”

Dr. Camper has identified a chromosomal region that appears to offer protection against hearing loss, and is working on narrowing down the region and finding the gene or genes that confer the protective effect.

“In deaf mice with low thyroid function, there are so many things that go wrong in the development of the inner ear that it is pretty amazing that there’s one location in the genome that can protect against poor development of all those things,” adds Dr. Camper. “That’s one of the reasons I’m excited about the hunt for the gene. There aren’t any genes in the region that are obvious candidates – nothing already known to have something to do with thyroid hormone.”
In addition to deafness, Dr. Camper is continuing her research on skeletal defects – an interest she shares with Dr. Innis, who is nationally known for his work on these conditions. “From a professional standpoint, I came to study skeletal defects by sheer happenstance. Low thyroid hormone or growth hormone causes dwarfism, so my colleagues across the country who knew I was interested in the genetics of growth insufficiency would send me their dwarf mice. As I studied these mice, I discovered that not all of them had thyroid deficiencies, and in many cases skeletal defects caused their small stature.”

Dr. Camper is also personally motivated to study these kinds of defects. “My son has a congenital skeletal condition that causes joint pain, so I’ve always kept up on the literature. I guess I’m like anyone who has a child with a birth defect – I want to understand why it happened and, more importantly, want to help develop new treatments for it. Unlike most parents, though, I’m in a unique position to do something.”

Catherine Keegan, MD, PhD, associate professor of Pediatrics and Human Genetics, is also studying skeletal defects as well as other malformations, in the lower half of the body. Her research centers on understanding the genetic basis for caudal regression syndrome, a rare disorder characterized by abnormal development of the lower end of a fetus, which includes the gastrointestinal and urinary systems and the lower spine.

“We really don’t know much about how the lower half of the body develops,” says Dr. Keegan. “Caudal defects are extremely complex. We suspect that they happen because of a spontaneous genetic error in either the sperm or the egg, rather than from a defect that is passed on from generation to generation. In most cases, no one else in the family has a caudal malformation.”

Dr. Keegan originally became interested in caudal defects because of her research on telomeres – the tail end of a chromosome that protects it from deterioration or from fusing together with neighboring chromosomes. “We knew that our mouse model had dysfunctional telomeres, but we were surprised to find that the mouse embryos had abnormal caudal development as well. We later showed that telomere dysfunction can trigger cell death in the developing embryo. The lower half of the body develops last, so we suspect that it is more susceptible to progressive cell death – if you don’t have the cells to support development, then the lower half of the body does not grow properly.”

“We also found that if we blocked one of the pathways that lead to cell death, we could rescue some of the embryo’s caudal defects. Although telomere defects are unlikely to be a common cause of caudal birth defects in humans, some of the underlying developmental mechanisms might be similar,” adds Dr. Keegan.

She is also interested in the role type I diabetes plays in the onset of caudal defects. “We know that caudal defects are 250 times more common in babies of mothers with type I diabetes, but we don’t know why. Despite being more common, caudal defects are not exclusive to babies of diabetic mothers, nor do all type I diabetics give birth to babies with birth defects, so there are clearly multiple factors at play in the onset of these conditions.”

Conditions like type I diabetes that have a known link with birth defects illustrate the complexity of pinpointing the underlying cause. “Clear hereditary conditions, when particular genetic variations or mutations (or defective genes) are passed on from one generation to the next and, have clear correlation with the disease, are easier to identify. Once we know the parents are carriers of those genes, then we can explain specifically how the defect occurred and predict risk of them happening again,” says Ray Chan, PhD, assistant professor of Human Genetics.

For example, Tay-Sachs disease, which attacks the central nervous system, causing seizures, blindness and dementia, is caused by a genetic defect that is passed on by the parents. If both parents carry the defective gene, there is a 25 percent chance their child will be born with the disease. “But what if a birth defect happened because of an error in the genetic material in one egg or one sperm? The error could have happened when the mother was a fetus herself, or from exposure to an environmental contaminant at some point during either parent’s lifetime. Those defects are harder to isolate and explain,” adds Dr. Chan.

Dr. Chan’s research centers on understanding how genetic mutations, hereditary or otherwise, occur in the first place. He is currently studying a class of proteins, called Structure Maintenance of Chromosomes (SMC) proteins, involved in chromosome reorganization during meiosis.

“Meiosis is a specialized way in which a germ cell divides to produce eggs (in girls) and sperm (in boys), which contributes to changes in our genome. In this process, nearly identical chromosomes from the mother and the father are recombined or rearranged so that each egg and each sperm receives a hybrid chromosome, if you will, that contains parts from both maternal and paternal chromosomes,” says Dr. Chan.
This rearrangement of chromosomes is important because it increases genetic diversity and ensures that each egg and each sperm receives only one copy of each chromosome. Errors in this process can ultimately produce a fetus with too many or too few chromosomes, which can cause miscarriage or result in birth defects, such as Down syndrome.

Errors in how chromosomes are rearranged can also lead to duplication and deletion of regions of a chromosome. “These are more subtle changes than the gain and loss of an entire chromosome, but they can have significant impact on the health of the individuals inheriting these genomic changes,” adds Dr. Chan.

The SMC proteins Chan studies facilitate the accurate rearrangement of chromosomes. He suspects that problems with SMC proteins may be the root cause of many errors in this critical process.

“Because errors in meiosis often lead to pregnancy loss or stillbirth in humans, I chose to study these genes in the roundworm, which can better tolerate abnormal chromosome rearrangements,” says Dr. Chan. “Using the roundworm as an experimental model, I am able to recover live offspring and study how their chromosomes are changed when SMC proteins are missing during meiosis. We can also use this worm model to ask what other genes are needed to minimize mistakes during chromosome rearrangement in meiosis. Since many genes in meiosis are conserved in humans, worms and other species, we can take what we learn about meiosis in the worm and extrapolate it to predict how a similar process works in humans.”

Understanding why and how these errors in chromosomal rearrangement occur has become more compelling than ever, as the list of human genomic disorders associated with recurrent genomic rearrangements is quickly expanding thanks to the types of technological advancement described by Dr. Innis.

Ultimately, this hunt for the genetic mutations responsible for each of the more than 4,000 known birth defects is meant to make a difference in patient care. “Identifying the genes involved is important for several reasons,” says Dr. Innis. “The first is diagnostic – it’s important to be definitive about what condition a patient has, so you can know for sure what you’re dealing with and families can rest assured that you’ve diagnosed the condition correctly.”

“The second reason is prognostic – knowing the genes responsible helps us assess the risk of it happening again and helps us prepare families for the likely outcomes. Knowing what to expect is incredibly important to families,” says Dr. Innis. “And finally, identifying the gene involved allows for the discovery of new therapies designed to treat the condition more effectively, or prevent it from happening in the first place.”

For example, the identification of the genes involved in Marfan syndrome – a condition that affects the development of connective tissue – led to the discovery that people with Marfan have increased TGF-beta signaling. This discovery has led to the development of drugs effective in downregulating TGF-beta signaling, which early studies show, reduces the incidence of aortic aneurysms (common among Marfan patients).

Increasing the speed at which scientists can make these discoveries and identifying the genes in play, is where the potential for new genetic sequencing technology really holds promise. Right now the technology is still too expensive for routine use, but that’s changing. Experts expect that genetic sequencing could cost as little as $1,000 per person and take days to complete.

“Beyond just speeding up the discovery process, this new technology gives us the chance to take the concept of personalized medicine to a whole new level,” adds Dr. Innis, visibly enthusiastic. “It gives us the chance to characterize diseases in the best possible way, and that means better care for the children who have these often debilitating conditions.”

For more information about U-M’s research on the genetics of birth defects, please visit http://www.hg.med.umich.edu To learn more about genetic screening currently available, please visit the Michigan Medical Genetics Laboratory website at http://sitemapmaker.umich.edu/michigan.medical.genetics.laboratories/home
PROMOTIONS, AWARDS, HONORS

Jeffrey Innis was installed as the Morton S. and Henrietta K. Sellner Professor in Human Genetics on July 15, 2011. Jeff is best known for his basic research on Hox genes and skeletal malformations in mouse and man. In clinic, he sees patients with a myriad of genetic disorders. Innis joined the University of Michigan Medical School in 1991, and has since become a leader in integrating basic science research into clinical care. He served as the Director of the Medical Genetics Residency Program (which he founded in 1996), the Director of the Division of Genetics in the Department of Pediatrics, and is the founder and Medical Director of the Michigan Medical Genetics Laboratories (MMGL). This laboratory offers dozens of biochemical and genetic tests that not only inform the treatment of known genetic diseases, but also serve as a research platform for discovery of new causes of disease.

Special guests at the July 15th event included Ascher Sellner, MD, whose parents, Morton S. and Henrietta K. Sellner, established the Sellner Professorship, and George Brewer, MD, former Human Genetics faculty member and first Sellner Professor. The Sellners were motivated to establish the Professorship to promote research on Wilson’s disease, a genetic disorder of copper metabolism. Dr. Brewer established the first FDA approved treatment for the disease.

Martin Arlt was promoted to Research Investigator, Department of Human Genetics.

David Burke received a 4 year Provost’s Award for a project entitled “Distributed Health Technologies” (with Mark Burns). Their goal is to design, build, and test new health-related technologies that can be widely dispersed and impact both local and global health care delivery. Dr. Burke also received the 2011 Teaching and Mentoring Award in Human Genetics for his contributions to our graduate course in molecular genetics and student mentoring guidance.

Sally Camper was named as Molecular Endocrinology Reviewer of the Year; Dr. Camper also received a University of Michigan Rackham Graduate School Mentoring Award.

Eric Fearon accepted the position of Division Chief of Molecular Medicine and Genetics as of November 2011. Eric continues holding joint appointments in the Departments of Human Genetics and Pathology, as well as being the Deputy Director of the UM Comprehensive Cancer Center.

David Ginsburg received a Distinguished Research Award in the Biomedical Sciences (November 2010), as one of 10 scientists in the country to receive national recognition for outstanding contributions to academic medicine and the global community. His research involves finding better ways to treat inherited bleeding and clotting diseases, with a focus on von Willebrand Disease; Ginsburg also received the Robert J. and Claire Pasarow Foundation 22nd annual Medical Research Award in Cardiovascular Disease (November 2010). The award celebrates achievement, creativity and distinction in research in cancer, cardiovascular disease and neuropsychiatry.

Sundeep Kalantry has been named as a New Innovator 2011 Award winner from the National Institutes of Health. With the award, Kalantry will receive $1.5 million to support his research over the next five years, studying X-chromosome inactivation to identify novel epigenetic factors. Sundeep’s research has the potential to provide novel targets for disease diagnosis and therapy. He also received an Ellison Medical Foundation 2011 New Scholar in Aging Award. The Foundation is a non-profit corporation that supports basic biological research relevant to understanding aging processes and age-related diseases.

Christopher Krebs was promoted to Assistant Research Scientist, Department of Human Genetics.

Jun Li received the 2011 IMHRO Johnson & Johnson Rising Star Translational Research Award, for “Genomic Analysis of Bipolar Disorder: Identification of Drug Targets via Exome Sequencing.” With his Rising Star grant, Li proposes a powerful new approach to finding high-impact candidate genes for bipolar disorder, and to revealing commonalities in how they malfunction. A better understanding of these genes may lead to new targeted therapies for this disease.

Catherine Keegan was promoted to Associate Professor of Pediatrics and Communicable Diseases; Associate Professor of Human Genetics.
Monica Marvin was awarded the “Leader Among Us” and profiled in a series in the National Society of Genetic Counselors Perspectives Newsletter (Spring 2011).

Donna Martin, was named as the Donita B. Sullivan, MD Research Professor of Pediatrics and Communicable Diseases, effective September 1, 2011.

Miriam Meisler was named as the Myron Levine Distinguished University Professor in Human Genetics (September 2011). This appointment is one of the highest honors the University can bestow upon an eminent member of the faculty, and Meisler chose to name the professorship after our emeritus faculty member, Myron Levine, who had a role in recruiting her to UM. Her inaugural lecture will take place on April 4, 2012. She also has a new secondary appointment, effective October 1, 2011 as Professor of Neurology.

JoAnn Sekiguchi was promoted to Associate Professor of Internal Medicine; Associate Professor of Human Genetics.

Wendy Uhlmann is the 2011 Recipient of the Natalie Weissberger Paul Lifetime Achievement Award. This award is the most distinguished honor within the National Society of Genetic Counselors. All who have worked or trained with Wendy have seen the passion and diligence that she extends to her work, profession, patients, and students.

The League of Research Excellence celebrates UM Medical School faculty who have well funded research. The inaugural group included those who have garnered $1 million or more in research awards or expenditures in the last year. The entire medical school community is inspired and proud of the accomplishments of this stellar group, and immensely appreciative of the quality and quantity of their work. Inductees into the League of Research Excellence at the University of Michigan included over 100 faculty scientists and physicians; Human Genetics faculty included Sally Camper, Stephen Gruber, Friedhelm Hildebrandt, and Miriam Meisler.

FACULTY COMINGS, GOINGS

Jeffrey Kidd joins the Human Genetics faculty as Assistant Professor in January 2012. Dr. Kidd received his BS in Biology in 2005 (summa cum laude) from Case Western University, where he also carried out undergraduate research with Dr. Mark Adams. He conducted his doctoral studies with Dr. Evan Eichler at the University of Washington. Jeff was instrumental at identifying copy number variation in the human genome. He published ~20 manuscripts as a student, including first author papers in *Cell* and *Nature*. Jeff currently is a postdoctoral fellow with Dr. Carlos Bustamante, studying how demographic history influences genetic diversity in human populations. In the future, Jeff wishes to employ modern genetics and genomics approaches to gain a complete understanding of how genomic variation contributes to human disease. Jeff is an outstanding scientist and has demonstrated himself as a leader in this burgeoning field.

Ryan Mills will join the Department of Human Genetics and CCMB (primary) in January, 2012. Currently, Ryan is a team leader for Bioinformatics and Medical Diagnostics at the Molecular Genetic Research Unit, Department of Pathology Brigham & Women’s Hospital, Harvard Medical School.

Elizabeth Petty accepted the position as Senior Associate Dean for academic affairs and Professor of Pediatrics at the University of Wisconsin School of Medicine and Public Health, effective June 1, 2011. With her guidance, our Genetics Counseling Program became widely recognized as one of the best in the country. Her wisdom, humor and dedication to excellence will be missed.

Noah Rosenberg joined the faculty of the Department of Biology at Stanford University as an Associate Professor in July 2011. His contributions to human genetics, ecology and evolutionary biology, biostatistics and bioinformatics will be missed. Noah received the Dean’s Award for Basic Science Research in 2011.

CONGRATULATIONS

To faculty members who marked significant milestones in their careers at University of Michigan:

5 Years
- Raymond Chan
- John Kim

10 Years
- Julie Douglas

20 Years
- Jeffrey Innis
Graduate Education

There are currently eleven postdoctoral research fellows in the labs of primary faculty appointees and twenty-eight doctoral students, five who are in the Medical Scientist Training Program (MSTP). Thirteen students are pursuing their master’s degrees in genetic counseling and one in human genetics. In addition, we have three CMB students and three Bioinformatics students in the labs of our primary faculty. Several of our students are supported by the Genetics Training Grant. In addition, two of our students have been awarded NSF funding.

Congratulations to the recent graduates of our PhD program:

**Michele Gornick (Gruber Lab)**
Defended her thesis (September, 2011) on “Quantitative Approaches to Understanding Cancer Genomics”. Michele begins a postdoctoral position in the Department of Environmental Health at the University of Michigan School of Public Health in the Fall of 2011 with Dr. Laura Rozek.

**Wanda Layman (Martin Lab)**
Wanda defended her thesis (June, 2011) on “Role of CHD7 in Neural Development and Maintenance”. Currently, Dr. Layman is pursuing postdoctoral research at St. Jude Children’s Hospital, in the laboratory of Dr. Jian Zuo.

Wanda Layman’s PhD research showed that a defect in neural stem cell proliferation is the mechanism for reduced ability to smell (hyposmia) in a genetically engineered mouse with CHARGE syndrome. CHARGE syndrome is a leading cause of congenital deafness and blindness, and most individuals with the syndrome have mutations in the CHD7 gene (Chromodomain-helicase-DNA-binding protein 7). CHARGE stands for Coloboma of the eye, heart defects, Atresia of the nasal choanae, retardation of growth and/or development, genital and or urinary abnormalities and ear abnormalities and deafness. This multiple congenital anomaly syndrome can manifest with hyposmia. This shows the expression of CHD7 in the olfactory epithelium of a mouse (red) and an olfactory marker protein (green).

**Cris Van Hout (Douglas Lab)**
Cris defended his thesis (April, 2011) on “The Genomic Landscape of the Old Order Amish”. Cris recently moved to Ithaca, New York to conduct postdoctoral research in population genetics with Andrew Clark at Cornell University.

**Matthew Vasieých (Ginsburg Lab)**
Matt defended his thesis (June, 2011) on “The Function of Mammalian COPII Components Sec23a and Sec23b”. Matt is now at the UM Medical School completing the MD portion of his degree through the MSTP Program; his family welcomed a son, born in March, 2011.

We are very proud of the recent graduates of the Master’s Program in Human Genetics: Diana Dlugash, Elizabeth Haak, Min-Lee Yang.

Genetic Counseling Program 2011 Graduates

The graduates and their new jobs include:

**Gina Cowing**, Genetic Counselor, The Queen’s Medical Center, Honolulu, Hawaii

**Rebecca Frysinger**, Genetic Counselor, Department of Ophthalmology, Oregon Health and Science University, Portland , Oregon

**Barbara Hamlington**, Genetic Counselor, Rocky Mountain Cancer Center, in Colorado

**Darcy Huismann**, Genetic Counselor, University of Michigan Cardiovascular Genetics, Ann Arbor, MI

**Jessica Ordonez**, Genetic Counselor, University of Miami, Miami, FL

Class of 2011: Jessica Ordonez, Barbara Hamlington, Rebecca Frysinger, Gina Cowing, Darcy Huismann.
Graduate Student and Fellowship Awards

Heather McLaughlin (Antonellis Lab)
Heather was this year’s recipient of the Rackham predoctoral award. The focus of Heather’s research is Charcot-Marie-Tooth (CMT) disease—a heterogeneous group of inherited peripheral neuropathies characterized by progressive distal muscle weakness and wasting and sensory loss. Mutations in several genes encoding aminoacyl-tRNA synthetases (ARSs) have been implicated in CMT. ARSs are ubiquitously expressed, essential enzymes responsible for charging tRNA molecules with cognate amino acids, thus completing the first step of protein translation. Heather’s dissertation research is aimed at addressing three critical issues relevant to ARS-related peripheral neuropathy: finding other genes that cause CMT disease, understanding why ARS mutations cause CMT, and developing a method to distinguish normal variation in ARS from disease causing mutations.

The 2011 James V. Neel Fellowship Award winners included two Ph.D. students:

Matthew Avenarius, (Kohrman lab)
Matthew’s thesis work has provided important insight into molecular mechanisms of sensory cell development and function and the genetic etiology of human hearing loss. Matt is also the recipient of the new Basic Science EDGE award (Endowment for Development of Graduate Education).

Mutations in Grxcr1 cause deafness and vestibular dysfunction in mouse and man. The exact function of the gene is not understood. Matt has been investigating the role of the related gene Grxcr2 in inner ear development and function. He has generated a targeted mutation of Grxcr2 in mouse and demonstrated that the mutant strain has severe hearing loss although no overt vestibular dysfunction. Hearing loss is associated with early defects in sensory cell maturation that indicate a role for Grxcr2 in controlling the organization and polarity of stereocilia, the actin filament-rich structures critical for mechanotransduction. He has also studied mutant versions of the GRXCR2 protein and a related protein GRXCR1 to understand structure-function relationships that are important for the biological roles of these proteins in the inner ear.

Lev Prasov (Glaser Lab)
Lev has been studying the molecular pathway leading to embryonic development of the retinal ganglion cells in the mammalian eye, controlled by the ATOH7 transcription factor. His studies involve transgenic and mutant mouse models, and human families with hereditary malformations of the optic nerves and retinal vasculature. Among his recent accomplishments is the discovery of a causative mutation for autosomal recessive persistent hyperplastic primary vitreous (arPHPV). In addition to the Neel award, Lev received the Excellence-in-Teaching-and-Service prize from PIBS (2011) and won tennis championships in the Ann Arbor City (2009, 4.0 division) and VTA (2011, 4.5 division) tournaments.

Cheryl Jacobs (Sekiguchi Lab) received an NIH-NSRA Fellowship.

Temina Masud (Sekiguchi Lab) received the Anna Olcott Smith Fellowship from Rackham.

Emily Maclary (Kalantry Lab) Received the Anita and Howard Cramer Family Fellowship for academic excellence.

Genetic Counseling

Brittany Batte received a research grant from the Jane Engelberg Memorial Fellowship program, with the National Society of Genetic Counselors (NSGC). Since 1993, the Jane Engelberg Memorial Fellowship (JEMF) has been available to members of the NSGC as a mechanism to obtain funds to pursue professional development and scholarly investigation related to the genetic counseling profession. For the first time in JEMF history, in 2011 research proposals were solicited from genetic counseling students with the intent of fostering research and grant writing skills at an early stage in students’ genetic counseling training. Brittany Batte is an inaugural recipient of this award.

Leslie Kiedrowski and Diane Schlegel received The Rackham Merit Fellowship; the (RMF) program helps sustain the academic excellence and inclusiveness of the Michigan graduate community by promoting the values of diversity and inclusion, and encouraging the admission of students who represent a broad array of life experiences and perspectives. The RMF is competitive and recognizes entering students who have outstanding academic qualifications, show exceptional potential for scholarly success in their graduate program, and demonstrate promise for contributing to wider academic, professional, or civic communities.
Introducing HG Postdoctoral Fellows

Megan Brewer Ph.D. (Antonellis Lab)
Megan was born in Korea and raised in Sydney, Australia. She graduated in 2006 from the University of New South Wales with a BSc(Hons) in molecular biology and media communications. Her honours project focused on identifying the gene mutation causing an X-linked form of the inherited peripheral neuropathy, Charcot-Marie-Tooth (CMT) disease. Megan was awarded a PhD from the University of Sydney earlier in 2011, and will officially graduate in December. Since February, she has been working in the Antonellis lab where she continues to study CMT disease, and is currently analysing DNA sequences that regulate expression of mutations in SOX10 that cause Waardenberg Syndrome and Hirschsprung’s disease.

Guy Lenk, Ph.D. (Meisler Lab)
Guy is a Michigan native who earned his BS in biochemistry at the University of Michigan, Dearborn, and PhD in Molecular Biology and Genetics from Wayne State University in 2007. Guy is a member of the Meisler lab; his research project is focused on neurodegeneration.

Huira Chong-Kopera, Ph.D. (Moran Lab)
Huira completed her undergraduate studies at Northwestern University, where she first did undergraduate research in the lab of Rick Morimoto, working on heat shock proteins. She worked several years as a research technician in the reproductive endocrinology lab of Teresa Woodruff at NU prior to starting graduate school at the University of Michigan. She began her thesis work in Kun-Liang Guan’s lab in the Department of Biological Chemistry studying the RAS/MAPK intracellular signaling pathway. In 2005, she joined the Moran lab where she now studies the mechanism of integration of LINE-1 retrotransposons. These elements can cause mutations when they integrate. She and her husband, Steve, had their first child, Jason, in 2010.

Aurelien Doucet, Ph.D. (Moran Lab)
Aurelien went to University of Paris XI, earning a BS in biochemistry in 2002, followed by a MS in genetics from the same university in 2004. He moved to the Centre Nationale Recherche Scientifique (CNRS) - Institute of Human Genetics in Montpellier, in the laboratory of Dr Alain Bucheton, where he earned a PhD degree in 2008. He worked under the direction of Dr Nicolas Gilbert, a former DHG postdoctoral fellow, on two aspects of the mechanism of human L1 retrotransposition. Aurelien is currently a postdoctoral fellow in the laboratory of John Moran, studying the translation of the L1 second ORF, ORF2, epigenetic silencing that occurs after L1 insertions in embryonic carcinoma cells.

Qing Fang M.D., Ph.D. (Camper Lab)
Qing is originally from China, where she earned her medical degree at Tongji Medical College, Wuhan, China. In April, 2011, she received her PhD in Human Genetics at the University of Michigan. Her research in the Camper lab includes molecular genetics of hereditary deafness. Qing lives in Ann Arbor with her husband and two daughters, ages seven and two, and recently returned from a family visit to China after eight years in the United States.

Srimonta Gayen, Ph.D. (Kalantry Lab)
Srimonta is a postdoctoral fellow in the lab of Sundeep Kalantry. In 2003, he earned a BSc in Chemistry (Hons) in physics, mathematics at the University of Calcutta, India, followed by a MSc in biotechnology in 2005. Srimonta received his PhD in biotechnology in 2011. He and his wife live in Ann Arbor.

Peter Gergics, M.D., Ph.D. (Camper Lab)
Peter earned his medical degree at the Semmelweis University, Budapest, Hungary in 2004. During his PhD studies, he worked in the field of clinical research of endocrine tumors, and participated in various projects in connection with hormone sensitivity. He completed the residency program at his home university in internal medicine in 2010. Peter was honored to participate in the International Endocrine Scholars Program of The Endocrine Society and received a postdoctoral fellow position in the lab of Sally Camper. Here he focuses on basic research aspects of pituitary development and tumorgenesis. Peter lives in Ann Arbor with his wife and two children.

Elizabeth LaPensee, Ph.D. (Robins Lab)
Elizabeth is originally from Virginia, where she received her BS from the College of William & Mary. She received her PhD from the University of Cincinnati; her thesis work focused on the role of hormones in chemoresistance in breast cancer. Beth is in Diane Robins’ lab, where she studies androgen receptor mutations in prostate cancer. Beth and her husband, Chris, who is also a postdoc at UM, live in Ann Arbor.

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Megan Brewer Ph.D. (Antonellis Lab)
Megan was born in Korea and raised in Sydney, Australia. She graduated in 2006 from the University of New South Wales with a BSc(Hons) in molecular biology and media communications. Her honours project focused on identifying the gene mutation causing an X-linked form of the inherited peripheral neuropathy, Charcot-Marie-Tooth (CMT) disease. Megan was awarded a PhD from the University of Sydney earlier in 2011, and will officially graduate in December. Since February, she has been working in the Antonellis lab where she continues to study CMT disease, and is currently analysing DNA sequences that regulate expression of mutations in SOX10 that cause Waardenberg Syndrome and Hirschsprung’s disease.

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Qing Fang M.D., Ph.D. (Camper Lab)
Qing is originally from China, where she earned her medical degree at Tongji Medical College, Wuhan, China. In April, 2011, she received her PhD in Human Genetics at the University of Michigan. Her research in the Camper lab includes molecular genetics of hereditary deafness. Qing lives in Ann Arbor with her husband and two daughters, ages seven and two, and recently returned from a family visit to China after eight years in the United States.

Srimonta Gayen, Ph.D. (Kalantry Lab)
Srimonta is a postdoctoral fellow in the lab of Sundeep Kalantry. In 2003, he earned a BSc in Chemistry (Hons) in physics, mathematics at the University of Calcutta, India, followed by a MSc in biotechnology in 2005. Srimonta received his PhD in biotechnology in 2011. He and his wife live in Ann Arbor.

Peter Gergics, M.D., Ph.D. (Camper Lab)
Peter earned his medical degree at the Semmelweis University, Budapest, Hungary in 2004. During his PhD studies, he worked in the field of clinical research of endocrine tumors, and participated in various projects in connection with hormone sensitivity. He completed the residency program at his home university in internal medicine in 2010. Peter was honored to participate in the International Endocrine Scholars Program of The Endocrine Society and received a postdoctoral fellow position in the lab of Sally Camper. Here he focuses on basic research aspects of pituitary development and tumorgenesis. Peter lives in Ann Arbor with his wife and two children.

Elizabeth LaPensee, Ph.D. (Robins Lab)
Elizabeth is originally from Virginia, where she received her BS from the College of William & Mary. She received her PhD from the University of Cincinnati; her thesis work focused on the role of hormones in chemoresistance in breast cancer. Beth is in Diane Robins’ lab, where she studies androgen receptor mutations in prostate cancer. Beth and her husband, Chris, who is also a postdoc at UM, live in Ann Arbor.

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The eleventh annual James V. Neel Lectureship was held on May 19, 2011, and featured award-winning geneticist, David C. Page, MD, Investigator of the Howard Hughes Medical Institute, Professor of Biology at MIT, and currently, Director of the Whitehead Institute. Dr. Page earned his BA from Swarthmore College in 1978 and an MD from Harvard Medical School and the Harvard-MIT Health Sciences and Technology Program in 1984. He was elected to the National Academy of Sciences in 2005 and the Institute of Medicine in 2008. Dr. Page studies the genetic and developmental foundations of human reproduction, including genetic differences between males and females. His laboratory conducts DNA sequence-based explorations of human and other vertebrate sex chromosomes, with particular attention to the male-specific Y chromosome and its roles in sperm production and male infertility. The Page laboratory is also elucidating the fetal and postnatal development of sex cells—the precursors of eggs and sperm.

Following meetings with Human Genetics faculty and students, Dr. Page presented his lecture, “Rethinking the Y Chromosome” at the BSRB Auditorium, followed by a poster session and reception. A dinner honoring Dr. Page and the Neel student fellowship award winners was held at Barton Hills Country Club later that evening.

The lectureship honors James Van Gundia Neel, MD (1915-2000), a pioneer in developing human genetics research, who established the first Department of Human Genetics in 1956, at the University of Michigan. Funds for the J.V. Neel Lectureship and Graduate Student Fellowship come from generous donations from the Neel family, current and former Human Genetics faculty, alumni, postdoctoral fellows, staff, and friends of the Department.
Human Genetics Summer Picnic

This year’s picnic was held June 15 at Washtenaw County’s Delhi Park. Department members and their families and friends enjoyed good food, fun and games at this annual event. “The Accelerator” was a hit with adults and children alike. Catered barbeque and an ice cream cart provided delicious offerings for all, including those competing in the annual Tug of War competition, won by the Glaser Lab. Kudos to Dave Burke, Karen Grahl, and the picnic committee, for an outstanding job planning and organizing such an enjoyable afternoon.

The Department of Human Genetics 23rd Annual Retreat

The Annual Retreat was held in mid-September at the Kellogg Biological Station on Gull Lake. Tony Antonellis, Linda Peasley and the student and event representatives (Jake Higgins, Peter Larson, Emily Maclary, Serina Mazzoni and Yu-Yu Ren) organized a terrific weekend of science presentations, posters and a mentoring workshop. Our keynote speaker was Dr. Gregory Crawford, Assistant Professor in the Institute for Genome Sciences and Policy at Duke University Medical Center, whose talk was entitled “A Comprehensive Atlas of Open Chromatin to Identify Gene Regulatory Elements that shape Cell-Type Identity”. Joining Greg Crawford on the mentoring panel were Dr. Barbara Sears, Professor of Plant Biology from Michigan State University, Dr. Peter Hitchcock, Professor of Ophthalmology and Visual Sciences and Director, Medical School Office of Postdoctoral Studies at the University of Michigan, Dr. Martin Arlt, Research Investigator in the Department of Human Genetics at the University of Michigan, and Shawna Feely, M.S., Assistant Professor in the Department of Neurology at Wayne State University. Great entertainment was provided on Friday evening by musicians and singers of the HG Retreat Band, Tony Antonellis, Sally Camper, Aurelian Doucet, Bob Lyons, Russ Peasley, Bev Yashar and Kim and Courtney White.
Diane Baker Alumni Award

The Genetic Counseling Program hosted the inaugural Diane Baker Alumni Awardee, Barbara Biesecker, MS, PhD, in January 2010. Barbara visited our campus and spent the day sharing her expertise with students and faculty of the Genetic Counseling Graduate Training Program and the Department of Human Genetics. These visits provide a unique opportunity for our trainees to learn from University of Michigan alumni who are national leaders in genetic counseling.

We are excited to announce that Jill Stopfer is the recipient of the 2011 Diane Baker Alumni Award. Jill received her graduate degree from the Michigan Genetic Counseling Program in 1988. While Jill’s clinical work has encompassed a wide variety of clinical settings including prenatal diagnosis, pediatrics and adult genetics, she is best known for her work in the field of cancer genetics, where her pioneering efforts helped meld the fields of oncology and genetic counseling. Ms. Stopfer has shown an unwavering commitment to the development of the field of cancer genetic counseling. As described in her nomination, “Her collegiality and professionalism truly exemplifies what Diane Baker has imparted upon her students, which makes Jill an outstanding counselor who is held in the highest regard.” Jill truly embodies the values, ambition and ideals of the University of Michigan’s Genetic Counseling Program and is an exemplary role model for all practicing and training genetic counselors. She will be visiting the Michigan campus this year as the second recipient of Diane Baker Alumni Lecture Award.

Thomas D. Gelehrter, M.D., Medical Genetics Lectureship

The second annual Thomas D. Gelehrter Medical Genetics Lectureship was held in October 2010, featuring Francis S. Collins, MD, PhD, Executive Director of the National Institutes of Health. Collins was a faculty member at University of Michigan for 9 years prior to his move to NIH to lead the Human Genome Project. Collins is a superb speaker, and the lecture hall was packed with a standing room only crowd. The title of his presentation was “Exceptional Opportunities in Biomedical Research.” He spoke about changes brought about by the completion of the genome project and gave specific examples of how knowledge of the genetic basis for disease had laid the foundation for treatments that showed promise in clinical trials. He also took time out of his busy day in Ann Arbor to give an impromptu and very inspiring speech to a group of prospective students who were visiting the University of Michigan’s Graduate Program in Biomedical Sciences to learn about career opportunities in biomedical research. The day’s events continued with a celebration at Barton Hills Country Club, hosted by Dick Tashian. Faculty took turns telling stories about their interactions with Collins during his time at University of Michigan.

We look forward to the next Thomas D. Gelehrter Medical Genetics Lectureship on May 2, 2012, which will be given by Professor Kay Davies, FRS, Head of the Department of Physiology Anatomy and Genetics, University of Oxford, whose research is focused on the understanding of muscle disease, movement and behavioural disorders.

Our goal is to fully endow this lectureship, and we are very grateful for the generous donations that we have already received from over 40 alumni, faculty, staff and friends of the Department. We are very fortunate and especially pleased to announce that an anonymous lead donor has pledged $40,000 in matching funds for donations collected this year. If we are successful in raising funds to meet this challenge, then we will be very close to a fully endowed lectureship.
Department of Human Genetics 2011 Donor Honor Roll

We would like to recognize the following individuals who have given generously during the past year to support the Department of Human Genetics:

**Thomas D. Gelehrter, M.D., Medical Genetics Lectureship Fund**
Funds an annual lecture focused on research advances in genetics that are changing the practice of clinical medicine. This work honors Dr. Gelehrter’s legacy of excellence in teaching, basic research, clinical care and service to the Department and University of Michigan. An anonymous donor has pledged to match donations received during the coming year up to $40,000. Please consider making a donation this year.
**Goal: $100,000, Current status: $21,000**

- Jack Billi
- Carolyn Bruzdzinski
- Peter Byers
- Raymond Chan
- Toby Citrin
- Thomas M. Glaser
- Thomas W. Glover
- Jun Z. Li
- John V. Moran
- Bishr Omary
- Michael E. Ray
- Diane M. Robins
- Lana Spillman
- Richard E. Tashian
- Wendy Uhlmann

**James V. Neel Lectureship Fund**
Annual lecture by inspiring researcher in human genetics.

- Thomas W. Glover

**James V. Neel Fellowship Fund**
Awarded to a Ph.D. and an M.S. student each year for outstanding research.
**Goal: $800,000, Current status: $300,000**

- Steven J. Ferrucci
- David Ginsburg
- Thomas W. Glover
- John V. Moran
- Priscilla Neel
- Frank Probst
- Myron Levine
- Charles Pelzer
- Michael E. Ray
- Diane M. Robins
- Donald Rucknagel
- Jennifer Schneider
- Peter E. Smouse
- Richard E. Tashian
- Samuel Young

**Diane Baker Alumni Award**
Honors an alumna each year and subsidizes a trip and lecture for education and career development of current students.
**Goal: $100,000**

- Sally A. Camper
- Thomas W. Glover
- Diane M. Robins
- Karol Rubin
- Wendy Uhlmann

**Anita and Howard Cramer Family Fellowship Fund**
Awarded to a Ph.D. student each year for outstanding academic achievement.

- Harvey S. Cramer
Carole McTague Genetic Counseling Student Enrichment
Used to offset travel expenses of our genetic counseling students to national meetings.

Tom Rebbeck and Jill Stopfer
Patricia Arscott
Wendy Uhlmann

Graduate Education
This is an expendable fund used to support PhD student education and activities.

Arlene Braker
Raymond Chan
Steven J. Ferrucci
David Ginsburg
Thomas W. Glover
Fred J. Grundbacher
Jeffrey W. Innis
Miriam Meisler
Elizabeth M. Petty
Margaret Wade

Please alert us to any errors or omissions.

2011 Human Genetics Faculty
1st row: Jane Schuette, Beverly Yashar, Myron Levine, Richard Tashian, Diane Robins, Sally Camper, Catherine Keegan, Wendy Uhlmann, Donna Martin, Monica Marvin, JoAnn Sekiguchi, Miriam Meisler
2nd row: Charlie Sing, Benjamin Koester, Gilbert Omenn, David Ginsburg, Martin Arlt, Raymond Chan, John Kim
3rd row: Ernest Chu, Tom Glover, Sundeep Kalantry, Jeff Innis, Julie Douglas, David Burke, Friedhelm Hildebrandt, Jun Li, Tony Antonellis, Christopher Krebs