The University of Chicago
Medical Scientist Training Program

50th Anniversary Celebration &
Annual Retreat

University of Chicago Campus &
Grand Geneva Resort, Lake Geneva, WI

June 23rd – 25th, 2017
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Friday, June 23rd, 2017

8:30 a.m. – 9:30 a.m.  Breakfast, The Quadrangle Club

10:00 a.m. – 11:30 a.m.  UChicago Campus Tour
Led by MSTP Students
Departs from Quadrangle Club Lobby

12:00 p.m. – 1:00 p.m.  Lunch, Gordon Center for Integrative Science Atrium

1:00 p.m. – 6:00 p.m.  Alumni Research Symposium, GCIS W301/303
History of UChicago MSTP and Opening Remarks by MSTP Director
Dr. Marcus Clark

1:30 - 2:00p.m.  Mark Krasnow, MD'85, PhD'83
2:00 - 2:30p.m.  Mark Anderson, MD'94, PhD'92
2:30 - 3:00p.m.  Justine Lee, MD'06, PhD'04
3:00 - 3:30p.m.  Feroz Papa, MD'98, PhD'95
Break
3:45 - 4:15p.m.  Anupam B. Jena, MD'09, PhD'06
4:15 - 4:45p.m.  Mary Dinauer, MD'81, PhD'79
4:45 - 5:15p.m.  Matthew Vander Heiden, MD'02, PhD'00
5:15 - 5:45p.m.  Christopher Walsh, MD'85, PhD'83

6:00 p.m. – 10:00 p.m.  Reception, The Smart Museum of Art
Drinks and Hors D’oeuvres
Saturday, June 24th, 2017

8:00 a.m. - 9:00 a.m. Breakfast, Hyde Park Hyatt
Harper Meeting Room

9:30 a.m. Charter bus departs for the Grand Geneva Resort
Meet in Hyatt Lobby before departure

12:00 p.m. - 1:00 p.m. Lunch, Chophouse Restaurant

1:00 p.m. – 4:00 p.m. Career Panels, Grand Ballroom Salon B/C
1:00 – 2:30 Panels
1. Using Your PhD in Clinical Practice
2. Using Your MD in Research
3. Developing Skills for Unique Career Trajectories
4. Women in Medicine
2:30 – 4:00 Rotating Roundtable Discussions on Panel Topics

4:15 p.m. – 6:15 p.m. Poster Session, Grand Ballroom Salon A

6:30 p.m. – 8:30 p.m. Drinks & Dinner, Fairview Lawn
Dinner served at 7:00 p.m.
In the event of rain, dinner will be held at the Chalet

9:00 p.m. Trivia, Linwood Room
Sunday, June 25th, 2017

8:00 a.m. - 9:00 a.m.  Breakfast, Evergreen Room
                      Luggage can be stored in Geneva Bay Boardroom

9:00 a.m. – 9:30 a.m.  “State of the Program” address, Evergreen Room
                      Dr. Marcus Clark

9:30 a.m. – 11:00 a.m. Roundtable Discussions, Evergreen Room
                      • F30 Workshop
                      • Early Career Planning (Residency, Funding, Etc.)
                      • General Mentoring

11:30 a.m. - 12:30 p.m. Lunch, Outdoor Pavilion

12:45 p.m.            Depart hotel for lake cruise

1:00 p.m. – 3:00 p.m.  Lake Geneva Cruise

3:45 p.m.            Charter bus departs the Grand Geneva
Mark Anderson, MD, PhD

Dr. Anderson earned his PhD from the Committee on Immunology in 1992 and his MD from Pritzker in 1994. He went on to do a Medicine residency at the University of Minnesota and completed an Endocrinology fellowship at Massachusetts General Hospital. He later completed postdoctoral studies at the Joslin Diabetes Center and is now a Professor of Medicine at the University of California, San Francisco and the Robert B. Friend and Michelle M. Friend Endowed Chair in Diabetes Research. His research focuses on autoimmune diseases and the control of immune tolerance. His laboratory has helped define the Autoimmune Regulator (Aire) gene as a critical factor in the maintenance of immune tolerance both in the thymus and in peripheral lymphoid organs. He is a practicing endocrinologist, the Program Director for the UCSF Medical Scientist Training Program, and an advocate for the training and development of future physician-scientists.

Mary Dinauer, MD, PhD

Mary Dinauer earned her PhD in 1979 and MD in 1981, followed by internship and residency training in Pediatrics at the University of California, San Francisco and a fellowship in Pediatric Hematology/Oncology at Boston Children’s Hospital and Dana-Farber Cancer Institute. Much of her career was spent at Indiana University School of Medicine, where she was also director of the Wells Center for Pediatric Research. Dr. Dinauer moved to Washington University in 2010, where she is currently a Professor of Pediatrics and Pathology & Immunology, the Fred M. Saigh Distinguished Chair in Pediatric Research, and the Scientific Director of the Children’s Discovery Institute, which funds early stage basic and translational child health research. She is a specialist in pediatric hematology, with a particular interest in the leukocyte NADPH oxidase and inherited defects in Chronic Granulomatous Disease, characterized by increased susceptibility to bacterial and fungal infections and as well as inflammatory conditions. Her research is focused on the leukocyte NADPH oxidase, which plays a critical role in microbial killing and is increasingly recognized to have important immunomodulatory functions.
Research Symposium Presenters

Anupam Jena, MD, PhD

Anupam Bapu Jena obtained his PhD in economics in 2006 and graduated from Pritzker in 2009. He completed his residency in Internal Medicine at Massachusetts General Hospital and is now the Ruth L. Newhouse Associate Professor of Health Care Policy at Harvard Medical School and a physician in the Department of Medicine at Massachusetts General Hospital. He is also a faculty research fellow at the National Bureau of Economic Research. As an economist and physician, Dr. Jena’s research involves several areas of health economics and policy including the economics of physician behavior and the physician workforce, medical malpractice, the economics of health care productivity, and the economics of medical innovation. In 2013, he received the NIH Director’s Early Independence Award to fund research on the physician determinants of health care spending, quality, and patient outcomes.

Mark Krasnow, MD, PhD

Mark Krasnow received his Ph.D. in Biochemistry and graduated from Pritzker in 1985. He went on to become a Helen Hay Whitney postdoctoral fellow with David Hogness at Stanford University, where he demonstrated that Drosophila homeotic proteins are transcription factors. He is currently a Professor and past Chair of Biochemistry at Stanford, a Howard Hughes Medical Institute Investigator, and the Executive Director of the Wall Center for Pulmonary Vascular Disease. He is using systematic genetic and genomic approaches to lung development, stem cells, and cancer, and the neural circuit of breathing and speech. He is a Fellow of the American Association for the Advancement of Science and of the American Academy of Arts and Sciences, and member of the National Academy of Medicine (IOM).
Justine Lee, MD, PhD

Justine Lee obtained her PhD in 2004 graduated from Pritzker in 2006. Her graduate work within the Committee on Immunology was focused on cytoskeletal degradation during apoptosis. She stayed at the University of Chicago for her Plastic and Reconstructive Surgery residency, then did her Craniofacial Surgery fellowship at the University of California, Los Angeles. She is now the Bernard G. Sarnat Endowed Chair for Craniofacial Biology in the Division of Plastic and Reconstructive Surgery at UCLA, and Associate Professor-in-Residence of Surgery effective July 1, 2017 (early advancement). In her laboratory, her primary research focus is on regenerative technologies for skeletal defects independent of exogenous growth factors or ex vivo progenitor cell amplification for rapid translation. In her clinical research, she is primarily interested in outcomes of pediatric craniofacial reconstruction.

Feroz Papa, MD, PhD

Feroz Papa earned his PhD in Biochemistry and Molecular Biology in 1995 and completed his MD in 1998. He then went to the University of California, San Francisco, for his Internal Medicine residency, an Endocrinology fellowship, and postdoctoral training in biochemistry. He is still at UCSF, where he is now a Professor of Medicine, with joint appointments in the Department of Pathology and the Department of Bioengineering and Therapeutic Sciences. His research interests currently include ER stress signaling in cell degenerative diseases and drug-based modulation of the unfolded protein response.
Matthew Vander Heiden, MD, PhD

Matthew Vander Heiden graduated with his PhD from the Committee on Immunology in 2000 and his MD from Pritzker in 2002. He went on to complete an Internal Medicine residency at Brigham and Women’s Hospital, his Medical Oncology fellowship at Dana-Farber Cancer Institute and Massachusetts General Hospital in Boston, and postdoctoral research at Harvard Medical School. He is currently Associate Professor at the Koch Institute for Integrative Cancer Research in the Department of Biology at Massachusetts Institute of Technology and Instructor in Medicine at Dana-Farber Cancer Institute. His lab studies how metabolism supports different aspects of cell physiology, with a focus on understanding the role of metabolism in proliferation and in cancer.

Christopher Walsh, MD, PhD

Christopher Walsh was the second PhD graduate of the brand new Committee on Neurobiology and received his MD in 1985. He did an internship in Medicine and a Neurology residency at Massachusetts General Hospital. He completed his postdoctoral training in the Harvard Medical School Department of Genetics and then started his own laboratory in the Department of Neurology at Beth Israel Deaconess Medical Center. He was promoted to Professor in 1999, and the Bullard Professor that same year. He became a Howard Hughes Medical Institute Investigator in 2002, and served as Director of the Harvard-MIT MD-PhD training program, from 2003-2007. He has mentored 12 MD/PhD students in his laboratory. In 2006, he moved to Boston Children’s Hospital as Chief of the Genetics and Genomics Division. His laboratory studies genetic disorders of human cortical development, which typically result in intellectual disability, seizures, autism spectrum disorders, or other conditions.
**Retreat Panelists & Mentors**

**David Adelman, MD, PhD**

David Adelman finished his PhD in the Department of Pathology in 2001 and his MD in 2003. He matched into a combined General Surgery and Plastic Surgery residency at New York University Medical Center, then completed a fellowship in Microsurgery at the University of Texas MD Anderson Cancer Center. He is currently Associate Professor in the Department of Plastic Surgery at UT MD Anderson, his clinical research interests focus on reconstructive outcomes in cancer patients. He studies reconstruction of the breast, abdominal wall, pelvis, and extremity. His basic science studies, in collaboration with a biotech company, focus on vascular development in engineered tissue. In addition to his busy clinical practice and research, he serves as an educator and mentor.

**Tammie Benzinger, MD, PhD**

Tammie Benzinger received her PhD in Pathology in 1998 and her MD in 2000. After graduating from Pritzker, she did her internship at Forest Park Hospital in St. Louis, followed by residency and postdoctoral research in Diagnostic Radiology and a Neuroradiology fellowship at the Mallinckrodt Institute of Radiology of Washington University School of Medicine. She is currently Associate Professor in the Division of Biology and Biological Sciences and the Departments of Radiology and Neurological Surgery at Washington University School of Medicine. She is also director of the Imaging Core of the Dominantly Inherited Alzheimer Network and its affiliated clinical trials, as well as director of the Knight Alzheimer Research Imaging Program. Her laboratory focuses on the integration of magnetic resonance (MR) and positron emission tomography (PET) for neuroimaging, which an emphasis on neurodegenerative diseases, specifically Alzheimer disease (AD) and clinical trials.
Diana Bolotin, MD, PhD

Diana Bolotin graduated with her PhD from the Committee on Molecular Genetics and Cell Biology in 2004 and earned her MD from Pritzker in 2006. She stayed at UChicago for her internship in Internal Medicine and residency in Dermatology, then went to Northwestern University for a fellowship in Mohs Micrographic Surgery and Cutaneous Oncology. She is currently Assistant Professor and Director of Dermatology Ambulatory Clinic and Dermatologic Surgery at UCM. She specializes in Mohs Micrographic surgery (advanced technique for the removal of certain types of skin cancer), procedural dermatology, and treatment of routine and complex cutaneous malignancies. Her research focuses on understanding how normal skin cells transform into cancer cells and performing collaborative population-based research studies on outcomes.

Dawn Davis, MD, PhD

Dawn Davis earned her PhD in Pathology in 2001 and graduated from Pritzker in 2003. She completed her residency in Internal Medicine at the University of Washington in Seattle and her fellowship and postdoctoral research in Endocrinology, Diabetes, and Metabolism at the University of Wisconsin in Madison. She is now an Associate Professor at the University of Wisconsin in the Department of Medicine, Division of Endocrinology, Diabetes and Metabolism at and Section Chief of Endocrinology at the William S. Middleton Memorial Veterans Hospital. She runs a federally-funded lab focused on pancreatic beta cell biology. Her overall aim is to promote beta cell growth and survival to allow adequate insulin production to prevent or treat diabetes. Her lab studies transcriptional regulation of adaptive gene networks that signal cell proliferation and survival in times of cellular stress, as well as intra-islet production and function of incretin and incretin-like hormones that promote beta cell survival. Additionally, she participates in collaborative investigator-initiated clinical research on obesity and diabetes.
Andrew Hack, MD, PhD

Andrew Hack earned his PhD from the Department of Molecular Genetics and Cell Biology in 2000 and graduated from Pritzker in 2002. Since 2015, he has served as Chief Financial Officer of Editas Medicine, a NASDAQ-listed biotechnology company. Previously, from 2011 until 2015, he served as a portfolio manager at Millennium Management, where he ran a healthcare fund focused on biotechnology, pharmaceutical and medical device companies. Before Millennium, he was an analyst at HealthCor Management from 2008 to 2011. Prior to HealthCor Management, he served as an analyst at Carlyle-Blue Wave Partners and a principal of the MPM BioEquities Fund. He started his investment career at Banc of America Securities, covering the biotechnology sector. He was also a co-founder of Reify Corporation, a life science tools and drug discovery company. In addition, he is a member of the Board of Directors of Mersana Therapeutics, a privately-held biotechnology company.

William McDade, MD, PhD

William A. McDade, MD, PhD, a board-certified anesthesiologist, was elected to the American Medical Association Board of Trustees in June 2016. He serves as executive vice president and chief academic officer for the Ochsner Health System in New Orleans, which is Louisiana’s largest nonprofit, academic, multispecialty health care delivery system with more than 2,700 affiliated physicians and over 19,000 employees. He also heads the innovation mission of Ochsner with the goal of driving research in Ochsner’s Centers of Excellence and throughout the system.

A nationally recognized medical educator, Dr. McDade currently has served as a director for the Accreditation Council on Graduate Medical Education and is a member of the National Board of Medical Examiners. He also serves the U.S. Department of Education as a member of the National Committee on Foreign Medical Education and Accreditation. The founder of the Bowman Society, a mentoring organization that prepares minority scholars for academic medicine careers, Dr. McDade is a powerful advocate both for minorities in medical education and for the elimination of racial and ethnic health disparities. Most recently, Dr. McDade as appointed as a member of the Joint Commission. A member of Alpha Omega Alpha, Dr. McDade’s clinical care and research focuses primarily on clinical anesthesiology and the treatment of sickle cell disease.
Megan McNerney, MD, PhD

Megan McNerney earned her PhD from the Committee on Immunology in 2005 and graduated from Pritzker in 2007. She stayed at the University of Chicago to complete her residency in Clinical Pathology and her postdoctoral research in the Institute for Genomics and Systems Biology. She is now Assistant Professor, Department of Pathology and Department of Pediatrics, Section of Hematology-Oncology and an attending genomic pathologist. Her clinical focus is identifying cancer mutations by next-generation sequencing to guide diagnosis and treatment. Her research centers on genomics of myeloid malignancies and molecular diagnostics and she is developing a mouse model of high-risk myeloid leukemia for pre-clinical drug testing.

Warren Sandberg, MD, PhD

Warren Sandberg is Professor of Anesthesiology, Surgery, and Biomedical Informatics at Vanderbilt University Medical Center. He received his Ph.D. in biochemistry and molecular biology, and his M.D. from the University of Chicago, Pritzker School of Medicine. He was a resident/fellow in the Department of Anesthesia/Critical Care at Massachusetts General Hospital. Dr. Sandberg served on the Harvard faculty from 1998 until 2010, when he became Chair at Vanderbilt. At Vanderbilt, Dr. Sandberg's interests include: factors affecting physician-patient communication, patient care technology, perioperative systems design and OR workflow management, fiscal control, optimizing the value delivered in anesthesiology, and novel arenas where anesthesiologists can compete.
Judith Smith, MD, PhD

Judith Smith received her PhD in Immunology in 1997 and her MD in 1999. She went on to do her residency in Pediatrics and a Pediatric Rheumatology fellowship at Cincinnati Children’s Hospital. She is now an Associate Professor of Pediatrics at the University of Wisconsin School of Medicine and Public Health. Her research interests are diverse, but the main themes are the Unfolded Protein Response (UPR) and Host Pathogen Interaction. She has been investigating Brucella and Rhinovirus, as triggers of the UPR, and has another project looking into the pathogenesis of spondyloarthritis.

Carol Westbrook, MD, PhD

Carol Westbrook earned her PhD in Biochemistry in 1977 and graduated from Pritzker in 1978, then stayed at the University of Chicago for her residency. She did fellowships in Hematology/Oncology at the University of California, Los Angeles, and the University of Chicago. Dr. Westbrook held faculty positions in the Departments of Medicine and Genetics at the University of Chicago, the University of Illinois at Chicago, and Boston University Medical Center. During her years in academia, 1985-2006, her primary focus was on the genetics of cancer and the Human Genome. She was interested in finding the genes that occurred at the breakpoints of leukemia translocations, and developed in-situ hybridization for diagnosis of the Philadelphia chromosome, an invention for which she holds a patent and obtains royalties. She also helped identify the founder mutation for familial colon cancer in South Africa, now an important factor in public health in that community. She participated in the Human Genome Program, helping to map chromosomes and diseases. She retired from clinical practice in April 2016 and now consults in Medical Oncology and Hematology Forensics.
How did your training at UChicago impact your career/life?

Enormously. It established the foundation for how I approached science and medicine. I recognized the value of collaboration and spirit of collegiality that existed at the U. of C. I learned the value of mentorship. –MSTP Alum PhD’78 MD’79

It supplied me with very high standards for scientific rigor and excellence in patient care. This has impeded my "career" in terms of promotion and so on, as I am not inclined to do what is expected to advance a career in academia, but my real work in patient care and research is of higher quality as a result, so I am perfectly satisfied at how it has turned out. -Anne Buckley PhD’01 MD’03

I got married, met my best friends for life and started my career. Would be hard to say how it didn't impact my life. -Neal Sondheimer PhD’01 MD’02

The MSTP gave me research and clinical credibility to be competitive for a postdoctoral fellowship in clinical neuromuscular disease and a research postdoc, ultimately leading to a two-decade-long faculty career up to the full professor level at The Johns Hopkins School of Medicine. It gave me the breadth to seek higher positions later in other institutions as well. –Ralph W. Kuncl Ph'D’75 MD’77

Really made my career in academia and industry possible, great preparation. –MSTP Alum PhD’85 MD’87

It has opened doors far outside academia; taught me the value of properly controlled experiments whether in vitro or human trials. –MSTP Alum PhD’82 MD’83

Is there something you wish you knew at an earlier point in your career that you know now?

When you start an MD/PhD you don't need to exactly know where you will land up. Have faith in your training and change directions when necessary. –Robert Jenkins Ph'D’81 MD’83

No. I think everyone is pretty upfront about the length of the career path and the difficulties in pursuing it (including lack of funding, lack of academic positions available). Perhaps it's just hard to contemplate these realities as you are just starting your training. –William Zeiger Ph'D’11 MD’13

Take more risks, collaborate even more. –Mark Anderson Ph'D’92 MD’94

I wish I had known more about money issues. The biggest factor that turned me off from basic research was the ever present need to search for funding. Money issues are starting to impact the practice of medicine now as well with Medicare adjusting how they pay for care. –Andrew Philip Ph'D’05 MD’07
The most interesting career pathways are not linear, and one should be open to all sorts of possibilities. – Ralph W. Kunel PhD’75 MD’77

How hard it is to get research funding and the importance of finding a job with potential research mentors – Paul Kaplowitz PhD’75 MD’76

You don't necessarily have to do "R01 research" to have a fulfilling career in academic medicine. – MSTP Alum PhD’06 MD’08

…All hours are not the same. When you think that it's equivalent to show up at noon and work 'til 2 or 3am because you're still working 15 hours - you're wrong. Don't do it. Trivially, it reflects poorly on you. Substantively, it isolates you. This deprives you of critical interactions with other researchers that help to push your science forward, as well as the goodwill that comes from being a group (and results in people helping you out when you need it). Finally, it makes it much more difficult to interact with support staff; this delays your science in small ways that add up (e.g. if you place an order at 8pm, you'll get it a day later than if you place it at 8am). – MSTP Alum PhD’03 MD’05

What is your advice to your younger self, or advice that you got from someone else that’s worthy of being passed on?

The MSTP program is not the end point; it is only the beginning. Word hard and get it done, then move on. – MSTP Alum PhD’87 MD’89

Pursue whatever your secret dream is, not just what it seems like you are supposed to do. – Andrew Hack PhD’00 MD’02

It is possible to be a surgeon and a scientist. Choose the clinical field that you actually enjoy doing, not what other people think you should do. And prepare for your career to be very different from what you thought it would be. – MSTP Alum PhD’99 MD’01

Don't judge your research potential based on your PhD experience alone. – MSTP Alum PhD’97 MD’99
Learn as much as you can because you can never know enough. – Cynthia Go PhD’91 MD’94

Find something you are passionate about that fills an unmet clinical need - find or develop a network of "trust" to work on the problem together and absolutely do not fear the unknown - embrace it - it is an opportunity. – David Rye PhD’86 MD’88

You can switch paths even late in career and be successful and happy. Don't let anyone tell you if you fail one item, you've lost out. - MSTP Alum PhD’82 MD’83

Most of the time you will fail. Tenacity is key. – MSTP Alum PhD’81 MD’83
Pay attention to clinical medicine; research funding is fickle, but medicine will always be there. Try hard, do well, and choose a specialty you love. – MSTP Alum PhD’12 MD’14
What’s different about practicing medicine or conducting research since your training?

Almost everything except for the intellectual process. It's more collaborative (of necessity), faster-paced, and larger-scale. It's also more cross-disciplinary. Paradoxically, this means that people often become more focused in their expertise. You don't need to be a clinical or scientific generalist if you're working in a team of people all of whom are content experts. However, you need to make sure that there are good bridges so that everyone understands how the pieces fit together. That bridging is something that MD-PhDs are uniquely suited to provide. –MSTP Alum PhD’03 MD’05

It's much more difficult to "master" the literature than it used to be, even though it's much easier to access it. There's much more evidence-based practice, but it also leads to much more knee-jerk practice. –Doug Gelb PhD’82 MD’84

Clinical work is less profitable in general, so there is not as much "free money" floating around and you have to justify your existence clinically. On the basic science side, NIH funding is much worse than when I was training. –Sudarshan Rajagopal PhD’01 MD’02

Very different training environment for medical education. Much less autonomy in early stages. –Louis Muglia PhD’86 MD’88

The increased difficulty of obtaining funding and of getting published. There is less room for academic pursuits with the increased workload in medical practice. –Anne Buckley PhD’01 MD’03

A lot more pressure to produce clinically, many more regulations, and a lot less federal funding for research. It can be a really brutal career - satisfying but very very hard. Easy to burn out. –MSTP Alum PhD’99 MD’01
The best advice you received from a mentor or favorite scientific quote:

“Through our scientific genius, we made of the world a neighborhood, but we failed through moral commitment to make of it a brotherhood, and so, we've ended up with guided missiles and misguided men.” - Rev. Dr. Martin Luther King, Jr.

(William McDade, PhD’88 MD’90)

"We think scientific literacy flows out of how many science facts can you recite rather than how was your brain wired for thinking. And it's the brain wiring that I'm more interested in rather than the facts that come out of the curriculum or the lesson plan that's been proposed." -Neil deGrasse Tyson

I particularly like this quote, because at Pritzker, we are taught HOW to think critically about science and medicine, rather than to merely memorize the facts and treatments of the day. I believe this has always distinguished our educational environment from many if not most other institutions.

(David Adelman, PhD’01 MD’03)

"Skate to where the puck is going... " --Wayne Gretzky

(Mark Krasnow, PhD’83 MD’85)

“Title is not important. What counts is how much money and space you control directly. As an MD scientist you have a valuable asset that non-MD's don't have: the ability to control the clinical material for research. Make it your focus. “

(Carol Westbrook, PhD’77 MD’78)

"Nothing in the world can take the place of Persistence. Talent will not; nothing is more common than unsuccessful men with talent. Genius will not; unrewarded genius is almost a proverb. Education will not; the world is full of educated derelicts. Persistence and determination alone are omnipotent. The slogan 'Press On' has solved and always will solve the problems of the human race.” -attributed to Calvin Coolidge

(Warren Sandburg, PhD’91 MD’94)
**Jeffrey Bunker (G5, Immunology)**

*Specificity of IgA Responses*

Jeffrey Bunker, Steven Erickson, Theodore Flynn, Jason Koval, Carole Henry Dunand, Dustin Shaw, Marlies Meisel, Benjamin McDonald, Isabel Ishizuka, Alexander Dent, Bana Jabri, Patrick Wilson, Dionysios Antonopoulos, and Albert Bendelac

Immunoglobulin A (IgA) is prominently secreted at mucosal surfaces and coats a fraction of the intestinal microbiota. However, the commensal bacteria bound by IgA are poorly characterized and the type of humoral immunity they elicit remains elusive. We used bacterial flow cytometry coupled with 16S rRNA gene sequencing (IgA-Seq) in murine models of immunodeficiency to identify IgA-bound bacteria and elucidate mechanisms of commensal IgA targeting. We found that residence in the small intestine, rather than bacterial identity, dictated induction of specific IgA. Most commensals elicited strong T-independent (TI) responses that originated from the orphan B1b lineage and from B2 cells, although atypical commensals including segmented filamentous bacteria and *Mucispirillum* evaded TI responses but elicited T-dependent IgA.

We further probed the clonal reactivities of the IgA repertoire by cloning and characterizing hundreds of monoclonal antibodies from murine IgA plasma cells, precursors, and naive B cell subsets. Surprisingly, IgAs were not specific to individual bacterial taxa but rather polyreactive, with broad reactivity to a diverse but defined subset of microbiota. These antibodies arose at low frequencies among naïve B cells, and were selected into the IgA repertoire upon recirculation in Peyer’s patches. Remarkably, this selection process occurred naturally, independent of microbiota or dietary antigens. Furthermore, while some IgAs acquired somatic mutations, these did not substantially influence their reactivity. These findings reveal a primitive endogenous mechanism driving homeostatic production of polyreactive IgAs with innate specificity to microbiota.

**Dan Camacho (G4, Immunology)**

*IRF4(+) dendritic cells promote allergic Th2 responses in the lungs*

Daniel F. Camacho, Chanie L. Howard, Eli P. Darnell, Cara L. Hrusch, and Anne I. Sperling

A role for dendritic cells (DCs) in promoting adaptive immune responses is well-appreciated, but the specific mechanisms by which DCs initiate type 2 allergic responses are not completely understood. We previously found that mice lacking the transcription factor IRF4 in DCs do not develop type 2 lung inflammation in response to the common allergen house dust mite (HDM). Further, T cells restimulated with HDM by IRF4-deficient DCs were deficient in Th2 polarization in ex vivo cultures. We hypothesized that IRF4 is necessary for DCs to perform one or more of the many functions required to successfully initiate T cell responses in vivo.

Here we demonstrate that IRF4 in DCs is not required for DC uptake of allergen in the lungs, nor for the presence of HDM-bearing DCs in the lung-draining lymph nodes (LLNs) during HDM sensitization. Similarly, IRF4-deficient DCs are capable of antigen processing. However, IRF4-deficient CD24(+) CD11b(+) cDCs express lower levels of the Th2-associated costimulatory molecule OX40L during in vivo HDM sensitization. CD4(+) effector/memory T cell recruitment to the lungs and CD69 expression by CD4(+) T cells in the lung parenchyma after HDM sensitization is impaired in mice with IRF4-deficient DCs. These findings suggest that DC expression of IRF4 regulates DC-T cell interactions that lead to Th2 differentiation in response to allergens in vivo.
Sofija Canavan (G4, Computational Neuroscience)

A parrot species has complex sleep structure in common with mammals and songbirds

Sofija V Canavan and Daniel Margoliash

Mammals exhibit specialized forms of sleep, namely slow wave sleep (SWS), stage 2 sleep, and rapid eye movement sleep (REM), which are central to hypotheses of mammalian sleep function. It remains unclear, however, how and why complex sleep evolved. Early work suggested that while avian sleep has surface resemblance to its mammalian counterpart, it may have evolved independently. Birds were thought to have sparse amounts of “rudimentary” REM, no stage 2 sleep, and different patterns of time-dependent SWS and REM regulation. However, this was challenged by recent work in songbirds.

Here we examine sleep architecture in budgerigars (*Melopsittacus undulatus*), a parrot species. Parrots are the sister group to songbirds and one of three orders of birds that possess vocal learning abilities. Our main purpose was to evaluate whether parrots exhibited a set of complex mammalian-like sleep traits previously identified in songbirds.

We collected sleep data from 5 budgerigars using EOG, multichannel EEG, and behavioral recordings. Sleep was characterized using both manual and automated techniques, including automated detection of slow waves and eye movements.

We found that parrots have substantial amounts of REM and SWS comparable to humans, a clear stage 2-like sleep state, and a pattern of SWS decrease and REM increase across the night. We also showed that experimental conditions commonly used in older avian sleep studies can distort sleep architecture.

Our findings suggest that the common ancestor of amniotes (mammals, birds, and reptiles) possessed the precursors of REM and SWS. These results also motivate continued re-examination of avian sleep and the phylogenetic correlates of sleep traits across species.

Ben Casterline (G4, Immunology/Microbiology)

Vertical acquisition of the human symbiont *Bacteroides fragilis* patterns disease susceptibility in later life

Benjamin W. Casterline, Wei Ping Teoh, and Juliane Bubeck Wardenburg

The gut microbiome is increasingly recognized to mediate both enteric and systemic diseases. Thus, the acquisition of particular strains during microbiome development in early life may govern future disease susceptibility. Strains of enterotoxigenic *Bacteroides fragilis* (ETBF), a common commensal anaerobe, have been implicated in both lethal sepsis and inflammatory bowel disease. We developed a mouse model of ETBF inheritance to investigate whether early life acquisition patterned susceptibility to these diseases in later life. We found that ETBF was acquired by neonatal animals at a specific stage of enteric development. ETBF exposure from the dam at this stage led to stable enteric colonization and predisposed colonized animals to colitis. However, ETBF colonized animals were highly protected from lethal sepsis. Selective deletion of the *Bacteroides fragilis* enterotoxin (BFT), a metalloprotease associated with epithelial injury, protected animals from colitis but eliminated the protective effect of ETBF colonization on sepsis. Protection from sepsis was associated with serum neutralizing antibody against BFT, which was potently induced by ETBF but not toxin-deficient ETBF (*Δbft*) colonization. These results demonstrate the importance of immunological priming against enteric microbes during early life acquisition to protection from systemic disease. Probiotic therapy targeted to key inflection points during microbiome development may permit strategic modification of disease susceptibility in later life.
Justin Chew (G5, Genetics, Genomics and Systems Biology)

Vulnerability to Molecular Noise Constrains Cyanobacterial Clock Architecture

Justin Chew and Michael Rust

Circadian clocks generate precise 24-hour rhythms to anticipate the day/night cycle. This precision is achieved despite the fact that biological clocks are based on fundamentally stochastic biochemical reactions. We show that the cyanobacterium *Synechococcus elongatus* suppresses timing error through high expression of Kai oscillator proteins, and that single cell oscillations become erratic at reduced protein copy number. Stochastic modeling shows that the negative feedback loop necessary for oscillations amplifies noise, which can nevertheless be suppressed over many molecules. In the tiny cyanobacterium *Prochlorococcus*, where Kai protein copy numbers are naturally low, the feedback loop has been lost, resulting in a simplified system that no longer free-runs but is more resistant to molecular noise, suggesting that noise tolerance is a fundamental design constraint for biological oscillators.

Michael Clark (G3, Biochemistry & Molecular Biology)

On the structural basis of electromechanical coupling

Michael Clark, Pedro Rodriguez, Shane Gonen, Tamir Gonen, Eduardo Perozo

The voltage-gated ion channel (VGIC) constitutes the molecular basis of cellular excitability and intercellular electrical communication. Structurally, VGICs comprise two essential domains: (1) a voltage-sensing domain (VSD) which undergoes a conformational change in response to changes in the membrane potential, and (2) a pore domain which allows conductance of ions across the membrane. We seek to understand how a conformational change in the VSD opens or closes the pore domain; a process termed electromechanical coupling. We use as a model system an archaeal potassium channel that is activated by membrane hyperpolarization, i.e., activated with the opposite polarity to the majority of ion channels of known structure. Here we present our progress in elucidating the structure of this channel, as well as discuss a possible activation mechanism for this channel.
**John Coukos (G2, Chemical Biology)**

*Regulation of post-translational modifications formed by reactive glycolytic metabolites*

John Coukos, Gihoon Lee, Jae Won Chang, Raymond Moellering

The covalent modification of proteins by small molecules is a well-established regulatory mechanism in cell signaling. These post-translational modifications (PTMs) increase the chemical diversity of proteins from an estimated 20,000-25,000 gene products to over a million distinct functional protein states. While most known PTMs are thought to be installed primarily enzymatically, our lab has discovered several non-enzymatic PTMs formed by the interaction between proteins and reactive glycolytic metabolites. These modifications represent a hitherto uncharacterized and direct link between primary metabolic flux and protein function.

Through the development of novel metabolomic and proteomic platforms, we are studying the formation and regulation of reactive metabolite PTMs and hope to gain insight into the landscape of these modifications within the proteome. Additionally, we are interested in how specific sites of these PTMs integrate glycolytic flux with cell signaling within the context of both normal biological function as well as metabolic and age related disease.

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**Wenli Dai (G2, Biophysics)**

*Cardiomyocyte ZO-1 regulates intercalated disc organization and whole heart physiology*

Wenli Dai, Le Shen, Rangarajan Nadadur, Leonid Tyan, Kaitlyn Shen, Margaret Gadek, Michael T. Broman, Ivan Moskowitz, Christopher Weber

Intercalated discs (IDs) in the heart share similarities with apical junctional complexes (including tight junctions) in simple epithelium; proteins such as ZO-1 (*Tjp1*) are found in both. Although ZO-1 can bind to multiple ID proteins, its contributions to ID organization and heart function remain largely undefined. We aim to understand if and how the tight junction protein ZO-1 contributes to ID structure and heart physiology.

Tamoxifen inducible cardiomyocyte specific ZO-1 knockout mouse (ZO-1 KO) was generated by crossing *Tjp1* floxed mice with myosin heavy chain 6-CreERT2 mice. Protein localization and ID organization were determined by immunofluorescent staining and immuno-gold labeling of ventricular tissue sections. Whole heart physiology was determined by surface electrocardiogram (ECG), echocardiogram, and intra-cardiac electrogram. Cardiomyocyte action potentials were measured by whole cell current clamp. Immunofluorescent staining confirmed ID associated ZO-1 is significantly reduced (44±13%) in ZO-1 KO mice, and showed decreased Coxsackie and adenovirus receptor (CAR) (56±2%), and connexin 43 (67±3%). Surface ECG showed ZO-1 KO caused increased PR interval (28.0 vs. 45.3ms) and 3rd degree heart block. Whole cell current clamp studies showed action potential prolongation in both ventricular and atrial cardiomyocytes, (APD90 86.8±21 vs. 322.8±38.5ms, 94.4±9.9 vs. 190.4±25.5ms respectively). Furthermore, RNA-sequencing showed ZO-1 expression decrease in patients with paroxysmal atrial fibrillation (81±9% of control, P=0.03). We propose a model in which ZO-1 stabilizes connexins and CAR to allow efficient cell-cell communication, and loss of ZO-1 contributes to the pathogenesis of heart disease.
**Reem Elorbany (G2, Genetics, Genomics and Systems Biology)**

*Variation in Gene Regulatory Dynamics during Human Cardiac Development*

Reem Elorbany, Katie Rhodes, Yoav Gilad

Changes in gene regulation direct the development of a single cell into the diverse array of specialized tissues and organs in the human body. Although studies in model organisms have revealed many developmental control genes important for cell fate determination, much remains unknown about the dynamic changes in gene regulation that lead stem cells to their terminal cell types. To study this, we use human induced pluripotent stem cells, which can be generated from somatic cells of any individual and differentiated into a variety of cell types. In this project, we differentiate human iPSC lines into cardiomyocytes and measure gene regulatory phenotypes at regular time points throughout the differentiation. Using 70 Yoruban iPSC lines, we collect gene expression and chromatin accessibility data every day for 16 days of differentiation, from iPSC to cardiomyocyte. We will investigate the temporal patterns of gene regulation that specify cardiac cell fate and characterize the mechanisms underlying these patterns by identifying eQTLs and chromatin QTLs related to cardiomyocyte development.

**Blake Flood (G3, Immunology)**

*Tumor Cell Intrinsic STING Signaling in Cancer*

Blake Flood, Leticia Corrales, Seng-Ryong Woo, Thomas Gajewski

Our laboratory has previously shown that immunogenic tumors spontaneously activate the innate immune system through the STING pathway. The STING pathway senses cytosolic DNA, which activates a signal transduction pathway culminating in phosphorylated IRF3 that translocates to the nucleus where it acts as a transcription factor to induce several genes including IFN-β. STING-dependent IFN-β production by immune cells infiltrating the tumor, in turn, was required for spontaneous priming of CD8+ T cells against tumor antigens. Based on this notion, STING agonists were developed and tested as a pharmacologic approach to activate the pathway. As part of these studies, we recently have observed that tumor cells themselves frequently fail to produce IFN-β in response to STING agonists or cytoplasmic DNA, arguing that loss of activation of this pathway might occur regularly as a component of oncogenesis. Surprisingly we find that tumor cells retain expression of each gene in the STING pathway and STING signal transduction is in tact up to and including nuclear translocation of IRF3. ChIP assays clearly demonstrate IRF3 is unable to bind the IFN-β promoter but can still bind other sites in the genome. This suggests the defect in IRF3 DNA binding may be specific to the IFN-β locus. Sequencing of the locus shows no mutations in or around the binding site so we are currently investigating epigenetic mechanisms regulating IFN-β gene expression.
**Phillip Hsu (G3, Immunology)**

*Ythdc2 regulates spermatogenesis through affecting the translation of N6-methyladenosine-modified RNA*

Phillip J. Hsu, Yunfei Zhu, Honghui Ma, Xiaodan Shi, Yuanyuan Liu, Meijie Qi, Zhike Lu, Hailing Shi, Guanzheng Luo, Qing Dai, Mingxi Liu, Bin Shen, Chuan He

N^6^-methyladenosine (m^6^A) is the most common internal modification in eukaryotic mRNA. It is dynamically installed and removed, and acts as a new layer of mRNA metabolism, regulating biological processes including stem cell pluripotency, cell differentiation, and energy homeostasis. m^6^A is recognized by selective binding proteins; YTHDF1 and YTHDF3 work in concert to affect the translation of m^6^A-containing mRNAs, YTHDF2 expedites mRNA decay, and YTHDC1 affects the nuclear processing of its targets. The biological function of YTHDC2, the final member of the YTH protein family, remains unknown. We report that YTHDC2 selectively binds m^6^A along its consensus motif GGACU. YTHDC2 promotes translation of its targets, and associates with cellular fractions involved in translation initiation in HeLa cells. *Ythdc2* knockout mice are infertile and have significantly smaller testes compared to those of littermates. In the testes, *Ythdc2* is temporally expressed as meiosis begins, and germ cells of *Ythdc2* knockout mice do not develop past the zygote stage. Thus, YTHDC2 is an m^6^A binding protein that plays critical roles during spermatogenesis.

**Molly Imgruet (G2, Pathology)**

*Insufficient levels of the tumor suppressor, CUX1, may lead to the development of therapy-related myeloid neoplasms.*

Molly Imgruet, Ningfei An, Saira Khan, and Megan McNerney

The treatment of almost all primary tumor types with chemotherapy and/or radiation leaves patients with a risk of developing a therapy-related myeloid neoplasm (t-MN). t-MNs can present as therapy-related acute myeloid leukemia, myelodysplastic syndrome or myelodysplastic/myeloproliferative neoplasms. Patients with t-MN tend to have high-risk genomic abnormalities, with monosomy 7 being the most common. Deletion of part or all of chromosome 7 [-7/del(7q)] occurs in half of all t-MNs, and carries a prognosis of less than one year survival. It is unknown how this frequent -7/del(7q) abnormality leads to the development of t-MN.

The McNerney Lab has previously identified a haploinsufficient, myeloid tumor suppressor in the commonly deleted region of 7q22, *CUX1*. CUX1 is a transcription factor that has been shown to target genes in the mitotic cell cycle, and haploinsufficiency of the *CUX1* ortholog *cut* in *Drosophila* led to increased hemocyte proliferation and melanotic tumor formation. Our overall objective is to identify the biological pathways regulated by CUX1, and to understand how these pathways are perturbed in the context of treatment with alkylating agents. We hypothesize that CUX1 insufficiency leads to aberrant myeloid cell proliferation and differentiation in the context of alkylator chemotherapy, and we have generated an inducible, shRNA-transgenic, *Cux1*-knockdown mouse model to probe the role of *Cux1* in the pathogenesis of t-MN. Treating these *Cux1*-knockdown mice with an alkylating agent leads to rapid morbidity within five months, and the mice develop anemia, monocytosis and an increase in granulocytes. This early work suggests a driving role for Cux1 in the pathogenesis of these aggressive, treatment-resistant diseases.
David Koren (G5, Neurobiology)

Cross-compartmental modulation of dendritic signals for retinal direction selectivity

David Koren, James C. Grove, and Wei Wei

Compartmentalized signaling in dendritic subdomains is critical for the function of many central neurons. In the retina, individual dendritic sectors of a starburst amacrine cell (SAC) are preferentially activated by different directions of linear motion, indicating limited signal propagation between the sectors. However, the mechanism that regulates this propagation is poorly understood. Here, we find that metabotropic glutamate receptor 2 (mGluR2) signaling, which acts on voltage-gated calcium channels in SACs, selectively restricts cross-sector signal propagation in SACs, but does not affect local dendritic computation within individual sectors. mGluR2 signaling ensures sufficient electrotonic isolation of dendritic sectors to prevent their depolarization during non-preferred motion, yet enables controlled multicompartmental signal integration that enhances responses to preferred motion. We find that mGluR2-mediated dendritic compartmentalization in SACs is important for the functional output of direction-selective ganglion cells (DSGCs). Therefore, our results directly link modulation of dendritic compartmentalization to circuit-level encoding of motion direction in the retina.

Victoria Lee (G4, Immunology)

Defining tolerance mechanisms regulating self-specific T cells

Victoria Lee, Christine Miller, Sharon Zeng, Jaime Chao, Nicholas Socci, Sven Malchow, Mary Schoenbach, Peter A. Savage

Although many autoreactive T cells are thought to be purged from the conventional T (Tconv) cell repertoire by clonal deletion or differentiation into innate-like lineages, available evidence suggests that this process is imperfect. Consistent with this, the systemic depletion of regulatory T (Treg) cells results in fatal autoimmunity, demonstrating that self-specific T cells exist within the T cell repertoire, and that such cells are pathogenic when left unchecked. However, little is known about the frequency, phenotype, and specificity of these self-reactive T cells, nor the prevailing tolerance mechanisms regulating these cells at steady state. Here, we utilize deep TCR sequencing to identify self-specific CD4+ Tconv clonotypes within the endogenous T cell repertoire that infiltrate the prostate following Treg cell ablation. Our studies reveal a number of recurrent TCRs that are expressed by Tconv cells infiltrating the prostate of Treg-depleted mice, suggesting that organ infiltration by these clones may be a TCR-driven process. Comparison of the prostate Tconv cell TCR dataset to that of a control organ (salivary glands) revealed that prostate-infiltrating clones are also found in the salivary glands, albeit at consistently lower frequencies. By tracking the fate of prostate-infiltrating Tconv clonotypes using a TCR retrogenic system, we aim to determine the nature of the self-antigens recognized by these cells, and define the tolerance mechanisms regulating these cells at steady state. This study is expected to yield new insights fundamental to our understanding of self-specific T cells and immune tolerance.
Katie Long (G3, Computational Neuroscience)

The neural basis of texture invariance

Katie Long, Justin Lieber, Hannes Saal, Zoe Boundy-Singer, and Sliman Bensmaia

Our sense of touch endows us with an exquisite sensitivity to surface texture. Coarse textural features are conveyed in afferents’ spatial pattern of activation, drawing analogies to vision. In contrast, fine textural features are conveyed in temporal spiking patterns, driven by skin vibrations elicited when the textured surface moves across the skin, and drawing analogies to audition. While nerve fiber responses are highly dependent on exploratory parameters, such as contact force and scanning speed, the perception of texture is highly invariant with respect to these parameters. Thus, neural signals must be interpreted in the context of how they are acquired. Nothing is known about how this is achieved. To address this question, we recorded the responses of neurons in the primary somatosensory cortex (S1) and peripheral nerves of rhesus macaques as we scanned textured surfaces across their skin at different speeds. To test the degree to which neuronal responses are speed dependent, we used machine learning to classify textures based on the neuronal responses they evoked, pooling responses evoked by each texture at different speeds. To the extent that neuronal responses to a given texture were similar across speeds, classification performance would be high. Indeed, we found that the responses of neurons in S1 are independent of scanning speed. In contrast, classification performance based on the responses of nerve fibers was poor. We conclude that the perceptual invariance of texture across speeds can be explained by neuronal responses at the earliest stages of cortical processing, namely S1.

Kaitlin McLean (G3, Development, Regeneration, and Stem Cell Biology)

The Role of Brwd1 in Chromatin Remodeling and Accessibility at the Igk Locus

Kaitlin McLean, Malay Mandal, Marcus Clark

Brwd1 is an epigenetic reader required for normal B cell development. Brwd1 is recruited to the histone marks H3K9Ac and H3S10pK14Ac. Additionally, Brwd1 is enriched at GAGA DNA repeats, and when Brwd1 is located at these GAGA motifs, marked epigenetic remodeling occurs in the form of nucleosome positioning or depletion, and enhanced DNA accessibility. Brwd1−/− mice display severely diminished Igk recombination. During normal Igk recombination, Brwd1 binds at the Jk gene cluster and positions nucleosomes relative to a GAGA motif located 5’ of each Jk segment, exposing the RSS. The RAG complex is then recruited and initiates recombination. By a poorly understood mechanism, the Igk locus then contracts, pulling the Vk gene cluster into the recombination center established at Jk. Vk transcription in Brwd1−/− small pre-B cells is severely diminished suggesting that Brwd1, despite not binding in the Vk gene cluster, controls accessibility of both Vk and Jk gene clusters. Overall, we hypothesize that Brwd1 assembles an accessibility center at Jk that performs several critical functions including positioning nucleosomes relative to GAGA motifs, locus contraction and Vk accessibility required for Igk recombination. We are testing these hypotheses using chromosome conformation capture in Brwd1−/− cell lines to assay for contraction in the absence of Brwd1. We are also testing the necessity and sufficiency of GAGA motifs in directing Jk function by editing these motifs using Crispr/Cas9 in pre-B cell lines. These and other experiments should improve our understanding of this recently identified epigenetic regulator.
Christine Miller (G2, Immunology)

Origins and Functional Characteristics of Memory Phenotype CD8 T Cells

Christine Miller, Victoria Lee, and Peter Savage

Memory phenotype CD8+ T cells exhibiting a CD44hiCD122hi phenotype (MP CD8 T cells) comprise a major population of T cells in mice, making up 15-20% of total peripheral CD8+ T cells. Despite the prevalence of this population, little is known about the nature of antigens recognized by these cells, their developmental origins, and the function of these cells in immune regulation and host defense. MP CD8 T cells are abundant in germ-free mice and specific pathogen free mice that have not been exposed to known pathogens, suggesting that these cells are reactive to endogenous self-ligands. To understand the diversity and antigen specificity of this population, we performed TCR repertoire profiling involving sequencing of TCR alpha chains expressed by naive (CD44loCD122lo) CD8 T cells and MP CD8 T cells isolated from TCR beta transgenic mice. We find that the MP CD8 TCR repertoire is largely distinct from that of naive CD8 T cells, suggesting that differentiation into the MP subset is a TCR-dependent, antigen-driven process. In preliminary studies, we find that bulk MP CD8 T cells do not infiltrate non-lymphoid organs following transfer into lymphopenic mice, suggesting that the antigen specificity or differentiation state of these cells preclude infiltration of peripheral organs. In ongoing work, we are reconstructing recurrent MP CD8 T cell clones by generating TCR "retrogenic" mice, and using T cells from these mice to determine precisely where and how this cell population arises, determine whether cognate antigen is widely distributed or tissue-restricted, and elucidate the functional role of these cells in the immune system.

Rangarajan Nadadur (G5, Development, Regeneration, and Stem Cell Biology)

Differential Enhancer Transcription Defines a Gene Regulatory Network


Transcription factors (TFs) determine context-dependent gene expression by binding and modulating enhancers. Defining functional TF-dependent enhancers from the thousands of TF binding locations genome-wide remains a fundamental challenge for understanding TF-dependent gene regulatory networks. Based on evidence that non-coding RNA (ncRNA) is transcribed from enhancers, we hypothesized that TF-dependent ncRNA transcriptional profiling would identify functional TF-dependent enhancers. We defined TF-dependent ncRNAs for TBX5, a critical cardiac TF, by deep sequencing ncRNAs from wildtype versus Tbx5 mutant mouse atrium. Genome-wide, Tbx5-dependent ncRNAs were enriched for chromatin accessibility and tissue-specific marks of active enhancers. Tbx5-dependent ncRNA-defined enhancers were enriched for TBX5 binding and demonstrated robust Tbx5-dependent activity in-vitro. The direction and magnitude of Tbx5-dependent enhancer transcription correlated positively with that of Tbx5-dependent target gene expression, providing a quantitative metric for Tbx5-dependent enhancer function. Tbx5-dependent atrial ncRNAs identified enhancers required for expression of a calcium-handling network previously associated with Tbx5 function in the atrium, elucidating a physiologically relevant gene regulatory network. Application of TF-dependent enhancer transcription may allow broad elucidation of TF-dependent gene regulatory networks.
Victoria Okuneye (G3, Behavioral Neuroscience)

Hallucination Severity Predicted by Auditory Cortex Resting State Connectivity in Bipolar & Schizophrenia Network on Intermediate Phenotypes Study

Victoria T Okuneye, Shashwath A Meda, Matcheri S Keshavan, Carol A Tamminga, John A Sweeney, Elliot S Gershon, Godfrey D Pearlson, Sarah K Keedy

Hallucinations are a prevalent and often highly distressing feature of psychosis. Auditory hallucinations are the most common form of hallucination and are observed across the psychotic disorder spectrum. Previous functional imaging studies of auditory hallucinations in psychosis patients have demonstrated abnormal activation patterns in the primary auditory cortex. In order to investigate the mechanisms that predispose hallucinations, we examine if alterations in resting connectivity to auditory cortex predict hallucination severity in a large sample of psychosis patients.

Whole brain resting state connectivity to primary and secondary auditory cortex defined as Brodmann Areas 22, 41, and 42 were evaluated for 392 psychosis subjects and 219 healthy controls. Subjects were recruited as part of the multisite Bipolar & Schizophrenia Network on Intermediate Phenotypes (BSNIP1) study. Univariate multiple regression analysis evaluated where brain resting state connectivity to the auditory cortex was a significant predictor of hallucination severity as measured by the hallucination item in the PANSS clinical rating scale.

Significant negative associations were found in right orbitofrontal cortex and right cerebellum. A significant positive association was also found in left middle temporal cortex. Positive mean connectivity was found in these areas for both psychosis and healthy subjects.

Our findings suggest that increased connectivity of auditory cortex with upstream language and auditory processing areas coupled with reduced connectivity in frontal top down control areas are associated with increased hallucination severity. Furthermore, the results demonstrate a possible common pathway across psychotic disorders of hallucination propensity that is related to connectivity dysfunction of the auditory cortex.

Ramy Parameswaran (G5, Biophysical Sciences)

Flexible semiconductor-cell hybrid constructs for the optical training of cardiomyocytes

Ramy Parameswaran*, Kelliann Koehler*, Hemi Rotenberg, Michael Burke, Barbara Hissa de C V Couto, Kiela Moreno, Michael Paul, Bozhi Tian

Interfacing electronic devices with biological systems for clinical therapeutics has been of interest for many decades now. Traditionally, devices for such applications have involved the use of mechanical or chemical tissue adhesives and stimulators with bulky and rigid designs. Here, we use a polymer-semiconductor hybrid material to act as wireless stimulation substrate for target cells and tissues. More specifically, we demonstrate that primary rat neonatal cardiomyocytes can be cultured onto a polymeric SU8-Silicon nanowire mesh and can be trained to beat at a desired target frequency upon 514 nm light stimulation via a photovoltaic mechanism. We also demonstrate via a Langendorff perfused heart model the efficacy of this device in pacing rat adult hearts ex vivo. These findings can provide us with a platform to optimize therapeutic strategies for patients who suffer from cardiac arrhythmias.
**Sylvia Ranjeva (G4, Ecology and Evolution)**

Recurring infection with ecologically distinct human papillomavirus (HPV) types explains high population-level HPV prevalence and diversity

Sylvia Ranjeva, Anna Giuliano, Sarah Cobey, and Greg Dwyer

Human papillomavirus (HPV) is the most common sexually transmitted infection in the USA, with a prevalence of 39% in women and 45% in men. Beyond its role as the etiological agent of cervical cancer, HPV is responsible for various genital and oropharyngeal cancers in men and women, as well as genital warts. The high prevalence of HPV results from the coexistence of over 200 low-prevalence HPV types. Despite the public health burden posed by HPV-associated disease, it is unclear how HPV natural history, including host immunity and immune-mediated competition, and differences in the host environment of each HPV type contribute to its population-level prevalence and diversity. To test hypotheses about the dynamics of HPV natural infection, we fit mechanistic models to longitudinal data describing HPV infection in a cohort of unvaccinated men. We find that the dynamics are characterized by a lack of competition, whether through homologous immunity or competition between types, and high rates of reinfection or persistence. Slight differences in the high-risk subpopulations that sustain each HPV type, which signal resource partitioning, combined with high rates of reinfection or persistence within individuals, support HPV type prevalence and coexistence.

**Ian Roundtree (G5, Chemistry/Biochemistry and Molecular Biology)**

N6-methyadenosine Promotes Rapid Transcriptome Turnover throughout the Cell Cycle

Ian Roundtree, Qili Fei, and Chuan He

The cellular transcriptome is a dynamic population of thousands of mRNAs, each of which is regulated at the transcriptional and post-transcriptional level. Recently, reversible RNA modification has emerged as an epigenetic determinant of gene expression, imparting additional regulatory information to modified RNAs. The most abundant internal modification in eukaryotic mRNA, N6-methyladenosine (m6A), contributes to transcript processing, transport, translation initiation, and stability, and is required for responses to environmental and developmental stimuli. m6A-specific RNA-binding proteins of the YTH-family mediate many properties of m6A-modified transcripts, as first defined by the role for YTHDF2 in mediating decay of methylated mRNAs. In this study, we show that YTHDF2 contributes to rapid turnover of the cellular transcriptome throughout stages of the cell cycle. In the absence of YTHDF2, stage-specific transcripts exhibit delayed clearance, resulting in prolonged progression through mitosis and decreased cellular proliferation. This study represents an example of reversible RNA methylation rapidly shaping the cellular mRNA pool and expands the known utility of post-transcriptional in gene expression regulation.
Gabriel Salzman (G5, Biophysics)

Structural basis for regulation of adhesion G protein-coupled receptors by their extracellular domains

Gabriel Salzman, Sarah Ackerman, Chen Ding, Shu Zhang, Akiko Koide, Shohei Koide, and Demet Araç

Characterized by their large and diverse extracellular regions (ECRs), adhesion G protein-coupled receptors (aGPCRs) play roles in both cell adhesion as well as conventional G protein signaling. To better understand these roles independently and in concert, we characterized the ECR of GPR56 (ADGRG1), an aGPCR involved in central nervous system (CNS) myelination, development of the cerebral cortex, and several types of cancer. Using biochemistry, protein engineering, structural biology and in vivo assays, we set out to identify the mechanisms underlying the physiological and pathophysiological functions of GPR56. First, we engineered a small protein, termed monobody (Mb), which binds tightly and specifically to the ECR of GPR56. We solved the crystal structure of the ECR of GPR56 bound to this Mb at 2.5Å resolution, revealing for the first time the domain architecture and atomic structure of a complete aGPCR ECR. The structure reveals two domains in the ECR of GPR56: a previously unidentified ‘PLL’ domain at the N-terminus and an unusually short, but autoproteolytically active GPCR-Autoproteolysis INducing (GAIN) domain. Using in vitro and in vivo functional approaches, we observed the effects of several structure-guided mutations and identified a surface-exposed conserved patch on the PLL domain necessary for GPR56-mediated CNS myelination in zebrafish. Finally, we measured the effect of Mb binding on GPR56 signaling in vitro and observed a decrease in basal activity, classifying the Mb as an allosteric inverse-agonist. Our results suggest that the GPR56 ECR has an essential role in regulating receptor function in an intricate and multifaceted manner.

Nicelio Sanchez-Luege (G5, Development, Regeneration, Stem Cell Biology)

The Abelson kinase regulates passage of Notch through the endocytic pathway to stabilize photoreceptor differentiation

Nicelio Sanchez-Luege and Ilaria Rebay

The signals and mechanisms that drive photoreceptor differentiation in the retina remain elusive and poorly understood. We have uncovered a novel paradigm in the Drosophila eye, in which a cytoplasmic kinase actively silences Notch signaling to stabilize photoreceptor differentiation. The foundational observation is that loss of the Abelson kinase (Abl) causes differentiating photoreceptors to aberrantly enter the optic lobe of the brain. How does Abl mechanistically stabilize the differentiation program? Our model is that Abl actively silences Notch by interacting with a network of ubiquitin ligases that are known to regulate Notch trafficking and signaling, namely Deltex (Dx) and Suppressor of Deltex (Su(dx)). Supporting this model, we have found that the Notch (N) receptor accumulates into large endocytic puncta in abl mutant retinas. Many of these N puncta localize to Hrs+ vesicles, suggesting that Abl is required for N's progression from the endosome to the lysosome for degradation. Consistent with prior work from other labs showing that Notch signaling can be ectopically activated by aberrant trafficking, genetically reducing Notch dominantly suppresses the loss of photoreceptors from abl mutant retinas. Ongoing experiments employ a N-responsive transcriptional reporter to directly assay the increased Notch signaling activity under Abl loss. We also find that overexpression of Su(dx), which promotes N endocytosis into the degradation pathway, enhances the size of N puncta in abl mutant retinas. This result suggests an interaction between Abl and the ubiquitin ligase network. Therefore, we are currently using a mutagenic approach, along with a Notch-responsive reporter system in Drosophila S2 cells, to screen tyrosines in Su(dx) and Dx as potential Abl kinase targets, which may uncover the biochemical basis of Abl's interaction with the Notch pathway.
**Mathew Schnorenberg (G3, Institute for Molecular Engineering)**

*Phospholipid-Based Drug Delivery Systems are Susceptible to Fatty Acid Ester Hydrolysis During Conjugation, Purification, and Formulation Processes*

Mathew R. Schnorenberg, Sang Pil Yoo, Matthew V. Tirrell, James L. LaBelle

Phospholipids are promising tools for nanoparticle drug delivery. As natural components of cell membranes, phospholipids are biocompatible, and their hydrophobic “tails” can drive self-assembly of various nanostructures such as micelles and liposomes. These nanoparticles can be functionalized with therapeutic, diagnostic, and targeting elements, and they can be PEGylated to extend circulation half-life. However, chemically modifying and purifying functionalized phospholipids, such as with drug, targeting ligand, or PEG, can expose them to harsh chemical conditions unlike their native physiological environment. Consequently, the main obstacles to clinical translation of lipid-based nanocarriers are quality assurance and consistency in self-assembly formulations.

Peptides are one type of molecule that can be conjugated to lipid-based carriers, either as therapeutics or targeting ligands. Because peptides can be conveniently synthesized using solid-phase peptide synthesis (SPPS) and purified by high-performance liquid chromatography (HPLC), it is tempting to conjugate phospholipids to peptides while on solid-phase support. However, SPPS requires strong aqueous acid to remove the molecules from solid-phase support, and the buffer for HPLC purification is commonly acidic water. While peptides are constructed of amide bonds that are stable in these SPPS and HPLC conditions, phospholipids have ester bonds, which are known to undergo acid-catalyzed hydrolysis. Here we tested the stability of a water-soluble, PEGylated phospholipid commonly used for liposome and micelle formulations, distearoyl-phosphoethanolamine-PEG (DSPE-PEG), in various solvents, temperatures, and timescales relevant for SPPS and HPLC. We monitored the hydrolysis of DSPE-PEG using (1) Matrix Assisted Laser Desorption/Ionization Time of Flight (MALDI-TOF) and (2) Electrospray Ionization (ESI) mass spectrometry.

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**Dustin Shaw (G2, Immunology)**

*Human intestinal plasma cells in health and disease*

Dustin Shaw, Kelli Williams, Matthew Dimaano, Katherine Meckel, Patrick Wilson, Bana Jabri

Human intestinal plasma cells reside in the lamina propria and secrete several grams of antibody into the lumen daily. Secreted antibody, in the form of IgA, shapes and maintains our commensal bacteria while also protecting against potential pathogens. Surprisingly, patients deficient in IgA have only a modest increase in rates of intestinal infections. However, they do have an increased risk for Celiac Disease and Inflammatory Bowel Disease (IBD), suggesting that plasma cells may play a role in the pathogenesis of intestinal disease. Both IBD and the often-associated autoimmune disease Primary Sclerosing Cholangitis (PSC) have strong HLA-II associations on GWAS, which suggests B cell involvement in pathogenesis. Surface markers shows that intestinal plasma cells from PSC and IBD subjects differs by B cell receptor isotype. Additionally, RNA sequencing of colon biopsies revealed differential expression of IgG1 heavy chain, IGHG1. We propose performing a single cell RNA sequencing and simultaneous cloning of the antibody receptor from each individual cell. By this approach, we will be able to link antibody specificity, surface phenotype, and the transcriptional profile of the cell. This information will help identify and characterize the plasma cell subsets involved in the pathogenesis of PSC and IBD. Data from this study may lead to more targeted therapies for IBD and PSC, most of which are currently ineffective, or rely on broad immunosuppression.
Sophia Uddin (G4, Computational Neuroscience)

ERP Signatures of Environmental Sound Processing in Language Context

Sophia Uddin, Shannon LM Heald, Howard C Nusbaum

Despite the fact that environmental sounds are acoustically distinct from speech, we have found that they are quickly and easily processed in sentence context. Behavioral studies suggest that listeners can understand the meaning of environmental sounds and use linguistic context to aid in understanding these sounds in much the same way as for spoken words. However, similar behavior can arise from different neural mechanisms. We conducted an ERP study in which listeners heard sentences ending in either an environmental sound or a spoken word. In half the sentences, the last item made sense with the preceding context (“sense”), and in half it did not (“nonsense”). We used bootstrapping to test for significant scalp topography differences between conditions after last item onset. Nonsense sentences ending in words produced a stronger central negativity corresponding to the typical N400 than meaningful sentences (consistent with previous literature). The N400 is thought to index recognition or integration processes that are more difficult for nonsensical stimuli. By comparison, environmental sounds elicited two phasic ERP responses with similar scalp distribution in the same time window. The earlier varied with meaningfulness, with a stronger negativity for nonsense sentences. The fact that the N400 is not higher-amplitude for sounds than for words suggests that listeners do not automatically treat the sounds as nonsense. Our data suggest that mechanisms for word processing may be more flexible than thought previously; differences between sounds and words may reflect relative unfamiliarity with recognizing environmental sounds in spoken sentence context.

Frank Wen (G3, Ecology and Evolution)

Vaccination and the evolution of seasonal influenza

Frank Wen, Anup Malani, and Sarah Cobey

Although vaccines against seasonal influenza are designed to protect against currently circulating strains, they may also affect the emergence of antigenically divergent strains and thereby change the rate of antigenic evolution. Such evolutionary effects could change the benefits that vaccines confer to vaccinated individuals and to the host population (i.e. the private and social benefits of vaccination). To investigate the potential evolutionary impacts of vaccination, we simulated the dynamics of an influenza-like pathogen in a host population receiving annual vaccines. On average, increasing vaccination rates decreased the cumulative amount of antigenic evolution of the viral population and the incidence of disease. These effects were mediated by the breadth of immunity conferred by the vaccine. To understand how the evolutionary effects of vaccination might affect its private and social benefits over multiple seasons, we fit linear panel models to simulated longitudinal infection and vaccination histories. Including the evolutionary effects of vaccination lowered the private benefits but increased the social benefits compared to when evolutionary effects were ignored. Thus, in the long term, vaccines' private benefits may be lower and social benefits may be greater than predicted by current measurements of vaccine impact, which do not capture for long-term evolutionary effects. These results suggest that conventional vaccines against seasonal influenza could greatly reduce the burden of disease by slowing antigenic evolution like universal vaccines. Furthermore, vaccination's evolutionary effects compound a collective action problem, placing greater importance on policies to encourage vaccination.
Alyson Yee (G3, Microbiology)

_Microbiome determinants of health outcomes in preterm infants_

Alyson Yee, Maureen Groer, Larry Dishaw, Ming Ji, Jack Gilbert

Preterm infants are a unique population with abnormal early life microbiome colonization. Compared with term infants, those born preterm are at higher risk for microbial insult. First, they are often delivered via emergency Caesarean section, which reduces their exposure to maternal vaginal and enteric microbes. Furthermore, they are subject to higher rates of formula feeding, invasive procedures, and antibiotics, all of which contribute to the assembly of the microbial community. Finally, preterm infants who stay in the NICU can develop a flora dominated by microbes associated with the NICU environment and high levels of antibiotic resistance. Few prospective studies focus on the preterm gut microbiome over the NICU stay. We enrolled 78 preterm infants (born <37 weeks’ gestational age) and collected weekly stool microbiome samples over their NICU stay. We analyzed the samples by 16S rRNA amplicon sequencing. For each infant, we also collected parental demographic data, characteristics such as gestational age, weight, APGAR scores, morbidities, and recorded volumes of milk consumed. Consistent with the literature, we found that preterm infants’ gut microbiomes increase in diversity and show reduced time-to-time variability over the course of their hospitalization. We hypothesized that microbial community structure correlates with birth mode, gestational age, length of stay, feeding status, human milk cytokines, fecal calprotectin, and adverse prenatal events. For 14 infants, we also obtained stool microbiome samples and growth and development outcomes at 2 years of age. Our goal is to identify patterns of microbial succession during the NICU stay that may predict health outcomes as toddlers.

Katherine Zhou (G5, Biochemistry and Molecular Biology)

_Granule formation by the RNA binding protein heterogeneous nuclear ribonucleoprotein G (hnRNPG)_

Katherine Zhou and Tao Pan

Heterogeneous nuclear ribonucleoprotein G (hnRNPG) is a nuclear RNA binding protein that regulates diverse processes including transcription, alternative splicing, DNA repair, and sister chromatid cohesion. The domain structure of hnRNPG consists of an N-terminal RNA recognition motif and ~300 amino acids of low-complexity region rich in serine, arginine, glycine, and proline. We have previously shown that hnRNPG preferentially binds to RNAs containing N6-methyladenosine (m6A) using its low-complexity region, and that hnRNPG regulates the transcription and alternative splicing of hundreds of hnRNPG-bound transcripts containing m6A (Liu and Zhou et al., N6-methyladenosine alters RNA structure to regulate binding of a low-complexity protein, Nucleic Acids Res., 2017 Feb, doi: 10.1093/nar/gkx141). We further investigated the formation of large complexes by hnRNPG in vitro and in vivo. In vitro, full-length hnRNPG protein forms large round particles with a diameter of 50–100 nm. RNA binding influences the size and conformation of hnRNPG complexes. In addition, a 58-residue segment of the low-complexity region of hnRNPG is sufficient to form complexes of similar shape but smaller size. In HEK293T cells, endogenous hnRNPG localizes to small nuclear granules. The cellular localization of hnRNPG depends on active transcription, and our results suggest that hnRNPG interacts with RNA polymerase II. The influence of RNA binding on the size and conformation of large hnRNPG complexes could have implications for the function of hnRNPG in transcriptional regulation.
The Medical Scientist Training Program at the University of Chicago obtained federal funding in 1967, making it one of the oldest programs in the country. Since that time, the program has graduated nearly 300 alumni. These alumni now represent nearly every specialty in medicine and biomedical research with careers that range from clinicians to leaders in the biomedical industry. We give an overview of the wide range of trajectories alumni of the program have pursued with their degrees. Measures such as the proportion of women represented in programs such as MSTP are often considered by funding sources for biomedical research as markers for program growth and progression. We also review trends and changes in the student composition over the course of the last five decades.
<table>
<thead>
<tr>
<th>Name</th>
<th>PhD Specialization</th>
<th>Mentor</th>
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<tbody>
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</table>
Mary Frith

*Hey Mary, are you secretly a commissural fiber? You won’t stop crossing my mind.*

Like her science hero, Rita Levi-Montalcini, Mary is an aspiring neuroscientist. Hailing from Black Mountain, NC, she studied psychology at Davidson College. Her undergraduate thesis centered around spatial working memory and the limbic system. We’re sure she’ll get lots of personal experience studying the effects of coffee and lack of sleep on memory during first year. On the weekends, she enjoys reading, running and relaxing with friends. She hopes to learn to proficiently navigate Chicago, and hopes that she is not ill-prepared for the weather while doing so. Take it from us, Mary, google maps and layering will be your best friends. The best vacation she's ever been on is to her grandparents’ farm in rural Virginia; in other words, she needs to travel more. Finally, Mary is a direct descendant of Pocahontas! Welcome to the University of Chicago MSTP, Mary!

Hendrik Glauninger

*Hey Hendrik, you’re giving me a heavy isotope.*

A native of Gießen, Germany, Hendrik has traveled afar from the exotic lands of Indiana University to join us at the University of Chicago. He graduated with a degree in biochemistry, which he earned studying copper resistance in *S. pneumoniae*, as well was studying the effect of exercise training on pulmonary hypertension. In the latter, he seems to have used himself as a test subject by participating in the IU Dance Marathon (which we’re pretty sure is the only type of marathon in which any sane person should participate). At the University of Chicago, he plans to do research in biochemistry and biophysics, and someday become a pediatrician. When he’s not chillin’ out, maxin’, relaxin’ all cool, he enjoys shooting some b-ball outside of school. Hendrik is inspired by fellow German scientist Max Planck. His favorite vacation ever was a cruise in the Bahamas- he was on a boat, and it was going fast, and he sported a nautical-themed Pashmina afghan. Welcome to the University of Chicago MSTP, Hendrik!

Yifei Hu

*Hey Yifei, are you made of copper and tellurium? Because you’re CuTe!!*

Yifei hails from New York City, and joins the veritable army of Pritzker students who earned their bachelor’s degree from Washington University in St. Louis. There, he was famous for his anime wallpapers and mad chemistry skillz. He used the aforementioned skillz to study antibiotics and natural products biosynthesis. At the U of C, he hopes to study chemical biology and phage therapy, which he can eventually put to use as an infectious disease doc. At WUSTL, he was a member of the Asian Christian Fellowship by day, and pianist by night. Maybe you get him to play some sweet tunes for you by bribing him with Starbucks green tea frappuccino’s. He is a man of modest goals, hoping next year to earn his Nobel Prize in Medicine, and would like to accomplish this by watching anime, sleeping, and hanging with friends. He is looking forward to checking out the wardrobe in his new Chicago apartment to see if it leads to the magical land of his favorite author, C.S. Lewis. You may not find Narnia, but we think you’ll like Chicago even more. Welcome to the University of Chicago MSTP, Yifei!
Anthony Hung

Hey Anthony, if you were a triangle, you would be acute one!

Traveling from warm and sunny Pasadena, CA, Anthony joins us in the equally warm and sunny Chicago (just ignore October-April for now). He studied biology at Duke University, where he researched the nutritional control of development and metabolism in *C. elegans*, as well as the ethical, legal, and social implications of the spread of non-invasive prenatal testing. During undergrad, he also personally studied the social implications of joining the chess club. Like his science hero, Stephen Jay Gould, Anthony enjoys both research and writing, and wrote for a student science publication during undergrad. At the University of Chicago, he hopes to explore his interests in genetics, metabolism, and immunology. An intrepid explorer, he hopes to get to know Chicago and visit every park and museum in the city. In the course of these explorations though, he hopes not to get horribly lost. His friends agree that he is famous for his dry humor, which will certainly be in high demand during anatomy. You’re already in high demand to us. Welcome to the University of Chicago MSTP, Anthony!

Megan Kennedy

Hey Megan, call me DNA helicase because I’d love to unzip your genes.

Originally from Palatine, IL, Megan is returning to the Midwest after studying ecology and evolutionary biology at Princeton University. There she was also involved in band, club swimming, water polo, and triathlons. Her research during undergrad included studying immune priming in insects and the human microbiome. These experiences contributed to her burgeoning interest in microbial ecology and infectious disease. She hopes to survive next year, and make a bunch of rad new friends in the process. Her secret fear though is to discover that she’s lactose intolerant. While this seems unlikely, we’re pretty sure that everyone has had at least one sleepless night beleaguered by this terrifying prospect. So eat cheese, Megan. Eat cheese like there’s no lactase tomorrow. Megan, luckily, is famous amongst her friends for her immunity to hangovers, as well as for her baking enthusiasm. She likes to display that enthusiasm with friends on the weekend, maybe after a nice run or swim. Megan can also hold her breath for over three minutes, and will add a brand new instrument to the Pritzker music salon: the bagpipes. We can’t wait to see what other new talents she will bring to the table. Welcome to the MSTP, Megan!

Alexis Monical

Hey Alexis, if you were a Dementor, I’d become a criminal just to get your kiss. ;)

Alexis joins us from Marquette University, where she studied Biological Science. She grew up just outside of Chicago in Des Plaines, IL, where her love for science was fostered early by Bill Nye the Science Guy, who remains her scientific hero. The part of her heart that hasn’t been stolen by the heartthrob scientist belongs to cardiology (or neurology and maybe pediatrics). In undergrad, she was excited by neuronal excitability through calcium activated potassium channels in the hippocampus, and hopes to continue studying the contribution of ion channels to disease for her graduate research. She was famous on campus for her killer dance moves (well, actually they’re apparently not that great, but presumably no one has actually died yet). Next year, Alexis hopes to find a great research mentor, see a musical, and find the perfect hole-in-the-wall burger joint. On the weekend, you can find this enthusiastic crafter working on a craft project along with her favorite creative buddy, Netflix. She, like many a med student, can be bribed with the promise of a nap. In 8th grade, her family went on a road trip inspired by 39 clues books where the next location was dependent on solving a hint. She made it back, so presumably she’s a pretty good detective. The only thing crazier than that vacation are Christmas dinners- her grandma had 17 kids! At least that will have prepared her well for joining our crazy MSTP family. Welcome to the University of Chicago, Alexis!
Sara Saheb Kashaf

Hey Sara, life without you is like dereferencing a NULL pointer.

Sara hails from Chestnut Hill, MA, and attended Carnegie Mellon University for chemical engineering and biomedical engineering. While in undergrad, Sara found the perfect cover story to justify her true love of travel: research! Her research has been the perfect excuse to travel to the Universities of Cambridge and Oxford, Boston, the Pittsburgh Supercomputing Center, Thailand and Iran. Her travels to Thailand gave her a sweet tooth for Thai coconut sticky rice with mango. In the limited time that she was not traveling, Sara enjoyed rowing and volunteering, and was a part of Enactus, Tau Beta Pi, and Public Health Brigades. Sara is clinically interested in GI, and hopes to conduct research on the gut microbiome. We’re pretty confident that you want to be in her good favor, as she’s previously given a policy brief at the UK Houses of Parliament. Her hero, famous scientist and science advocate Carl Sagan, would be proud. She’s humble though, and doesn’t ask for much from this next year at the U of C- merely that she achieve personal fulfillment in life. Luckily, we solidly concur that sleeping in and brunch are both excellent steps to take on the road to personal fulfillment. Welcome, Sara!

Mario Shammas

Hey Mario, 9x−7i > 3(3x−7u) solve for i.

Mario joins us at the University of Chicago all the way from Baghdad, Iraq. But don’t worry, we’re sure that after studying neuroscience at the University of Michigan for undergrad, he’s up for whatever Midwestern weather wants to throw at him. In Ann Arbor, Mario studied neurodegeneration in the context of Parkinson’s and ALS as well as linguistics. He hopes to continue along this path in grad school, and plans to study Parkinson’s Disease and eventually go into neurology like his idol Oliver Sacks, or neurosurgery. At the University of Michigan, Mario was a member of the Arabic Language Club and Orthodox Christian Fellowship, and he also enjoys tennis. A player and a fan, Mario is keeping his fingers crossed that Novak Djokovic regains the #1 ranking in tennis. Watch out, Federer and Nadal fans! His friends assert that he is famous for his plans to restore the Roman Empire (et tu, Brute?). Mario has now lived in five different countries, but we’re thrilled that Chicago is the next place he’ll call home. Welcome to the University of Chicago MSTP, Mario!

Sarah Sun

Hey Sarah, I wish I were your coronary artery so that I could be wrapped around your heart.

Sarah comes to us from Houston, TX after studying chemistry and mathematics at Vanderbilt University. But don’t be blinded by her Southern charm- she was actually born in Norway and speaks fluent Norwegian. During undergrad, she studied the effect of depression on mRNA editing of the serotonin receptor transcript, as well as conducting research in the field of synthetic organic chemistry. She also participated in several science and outreach programs, including giving science demonstrations to elementary schools, tutoring, and research mentorship. At the University of Chicago, she plans to study the immune system. She hopes to make great new friends next year. She’s worried about getting lost while trying to get home after a long day on campus; after all, the only place Sarah wants to get lost is in a good book. But this and most other problems can be solved with an entire pint of her favorite food, Ben and Jerry’s Chocolate Fudge Brownie ice cream. Sarah is famous among her friends for her tendency to laugh at everything, so don’t be offended. She was laughing with you, not at you. A figure skater since age 7, we’re confident that she’ll feel right at home during Chicago winters. Welcome to the University of Chicago MSTP, Sarah!
Andrew Wang
Hey Andrew, I wish I were adenine so I could get paired with U.

Originally from Ellicott City, MD, Andrew joins the MSTP already a member of the U Chicago family, where he earned his undergraduate degree in biological chemistry. During this time, he studied synthetic and structural biology, as well as venturing to Caltech for peptide chemistry research and to the NIH for neuroscience research. He hopes to put these skills to use during graduate school by studying chemical biology, and eventually wants to practice medicine in the field of infectious disease or oncology. When not working in the lab, Andrew volunteered for an ESL program for Chinese adults, wrote for an undergraduate research journal, and was involved in an Intervarsity Christian Fellowship. Next year, Andrew is excited to get to know everyone in the MSTP, hear about cool research, and meet interesting scientists. Luckily, Andrew has chosen a contemporary science hero in David Baker, whom he has a significantly higher likelihood of meeting than Lavoisier or Madam Curie. He is famous amongst his friends for his utter devotion to fishing. Maybe it was while fishing that he made it to the top 150 of the Goodreads trivia challenge. Game on, Andrew. Game. On. Despite his admittedly formidable trivia skills, he is still concerned about failing too many anatomy exams. We’re not too worried though. We think he’ll still be able to find time to try out new recipes on the weekend and fail only an acceptable number of anatomy exams. Welcome to the MSTP, Andrew!

Compiled and written by Kaitlin McLean.
Saturday, June 24th

In Chicago

• 5:00 p.m. – 6:00 p.m.  Alumni Happy Hour at Davanti Enoteca
  30 E. Hubbard St. Chicago, IL 60611
  www.davantienoteca.com/rivernorth

At the Grand Geneva

• 9:00 p.m. – 11:00 p.m. Trivia in the Linwood Room
  *Pub-style team trivia competition covering a variety of subjects from history to pop culture. Drinks and prizes!*

Sunday, June 25th

At the Grand Geneva

• 1:00 p.m. – 3:00 p.m.  Lake Cruise with Lake Geneva Cruise Line
  *Drinks and snacks served*
  www.cruiselandgeneva.com
Ugo Campus Shuttles

The University provides shuttle service around campus and portions of Hyde Park. Attendees will be able to take advantage of this service free of charge for all Anniversary events on Friday, June 23rd.

53rd Street Express

This route is the most direct way to get to campus from the Hyde Park Hyatt. It picks up from Harper Court, just around the corner from the hotel, and stops at the Ellis Garage. From there you can walk two blocks to the Quadrangle Club or three blocks to the Gordon Center for Integrative Science.

This route runs approximately every 30 minutes, starting at Harper Court at the top (0:00) and bottom (0:30) of the hour, from 7 a.m. – 6 p.m.

Polsky Express

This route is the most direct from campus back to the Hyatt during the day. It has stops at the Ellis Garage and in front of the Main Quad on Ellis Ave. and drops off at the Polsky Exchange, across the street from the hotel.

This route runs approximately every 30 minutes, departing the Polsky Exchange on the :15 and :45 of the hour, from 8 a.m. – 7 p.m.

A map of these and other available daytime routes is provided on the next page.
Ugo NightRide Shuttles

For transportation after the Smart Museum Reception, the Central Route stops on 55th, in front of the Ellis Garage, approximately every 15 minutes and drops off within a block of the Hyatt from 5 p.m. – 6 a.m.

This and other nighttime routes are mapped on the following page.
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7036 Grand Geneva Way
Lake Geneva, WI 53147
1 (800) 558-3417
http://www.grandgeneva.com/

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