5th Annual University of Colorado MSTP Retreat

Anschutz Health Sciences Building

February 2nd, 2023

Table of Contents

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University of Colorado Cancer Center

Dr. Vineet Chopra and the Department of Internal Medicine

Cancer Center

NCI-DESIGNATED COMPREHENSIVE CANCER CENTER

University of Colorado
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Department of Medicine

Retreat Schedule

Time	Session	Location
8:30-9AM	**Registration and Coffee**	Anschutz Health Science Building Donald M Elliman Conference Center (AHSB 2010/2011)
9-9:05AM	**Opening remarks and Welcome** Kelsey Kines	AHSB 2010/2011
9:05-9:30AM	**State of the program address** Cara Wilson, MD	AHSB 2010/2011
9:30-10:30AM	**Student oral abstract presentations** 9:30-10:00 Brian Lloyd 10:00-10:30 Nickole Moon	AHSB 2010/2011
10:30-10:45AM	**Student Flash Talks** Amita Kashyap Meghan Kellett Nk Egbukichi Varuna Nangia Laurel Darragh Keith Dodd	AHSB 2010/2011
10:45-11AM	Break	
11:00-12:15PM	**Student poster session**	AHSB rooms 2200 and 2201
12:15-1:00PM	Lunch	
1:00-2:00PM	Keynote	AHSB 2010/2011
2:00-3:05PM	**information to what session you will attend first will be given in the opening remarks** Breakout Session 1:Science Communication in the Clinic and in the Community with Dr. Nicole Kelp Breakout Session 2: CU MSTP Trivia	Breakout 1: AHSB 2002 Breakout 2: AHSB 2004
3:05-3:15PM	Break	
3:15-4:15PM	**Student oral abstract presentations** 3:15-3:45 Emily King 3:45-4:15 Brigit High	AHSB 2010/2011
4:15-4:40PM	**Wrap Up/MSTP Service Awards**	AHSB 2010/2011
5:00PM	**Gather at T-street Kitchen for happy hour**	T-street Kitchen

Retreat Speakers

Angelo M De Marzo MD, PhD

Professor of Pathology, Urology, and Oncology
The Johns Hopkins University School of Medicine

Dr. De Marzo received his B.A. in Molecular, Cellular & Developmental Biology (MCDB) from the University of Colorado at Boulder. He earned his M.D. and Ph.D. in Experimental Pathology from University of Colorado Health Sciences Center, and completed a residency in Anatomic Pathology at the Johns Hopkins University School of Medicine/Johns Hopkins Hospital in Baltimore. He completed a research fellowship at the Brady Urological
Institute at Johns Hopkins and joined the Johns Hopkins faculty to start his independent laboratory in 1998. The lab primarily uses human pathology tissue samples to make clinical observations to form the basis of testable hypotheses regarding disease mechanisms and pathogenesis. These hypotheses are tested using molecular pathology and genomic approaches using human clinical pathology tissues, cancer cell lines and animal models.

Dr. De Marzo and colleagues described a new risk factor/precursor lesion (termed proliferative inflammatory atrophy or PIA) and model for the molecular pathogenesis of prostate cancer. These microscopic lesions comprise areas of chronic inflammation and associated epithelial cell damage and regeneration. Over time, some luminal epithelial cells in PIA aberrantly and progressively overexpress the oncogene c-MYC (MYC), leading at times directly into invasive cancer, or more commonly to high grade prostatic intraepithelial neoplasia (PIN), the main direct precursor of invasive carcinoma. A key focus of the lab is to elucidate the molecular mechanisms by which MYC drives the development of PIN, invasive adenocarcinoma and progression to castration resistant metastatic disease. Lab members have demonstrated that MYC overexpression drives the hallmark prostate cancer cell change of increased nucleolar size and activity, as well as increased telomerase RNA (TERC) expression. Most recently the lab has shown that MYC overexpression drives increased mitochondrial DNA copy number via upregulation of mitochondrial DNA replication in PIN and prostate cancer lesions. Along with colleagues, including Srinivasan Yegnasubramanian M.D. Ph.D., his lab uses genomic and multiplex *in situ* approaches to study all stages of prostate cancer and precursor lesions. De Marzo is currently co-leading a U54 Project at Johns Hopkin as part of the NIH TBEL Program exploring the role of chronic inflammation, as well as immune evasion in driving prostatic cancer formation and progression and the synergy between MYC activation and PTEN loss in prostate cancer. In addition to characterizing genome-wide genetic, epigenetic and transcriptomic changes in human tissues, this project involves designing and working with a number of novel genetically engineered mouse models, constructed by collaborator Charles Bieberich, Ph.D.

Dr. De Marzo is an author on more than 400 papers, reviews and book chapters. He recently completed a term on the Editorial Board of the *Journal of Clinical Investigation*. He also serves on the Editorial Board for *Cancer Prevention Research* and *The Prostate*.

He has been elected to be a member of the Association of American Physicians and served as faculty for several years at the AACR-ASCO Methods in Clinical Cancer Research Workshop. He currently serves on the AACR Pathology in Cancer Research Task Force. In terms of classroom instruction, Dr. De Marzo directs a yearly course for graduate students on the Pathobiology of Cancer.

Dr. Cara Wilson, MD – MSTP Director, Program Address

Cara Wilson, M.D. is a Professor of Medicine in the Division of Infectious Diseases at University of Colorado at Denver and holds a secondary appointment in the Department of Immunology and Microbiology. She is the director of the Medical Scientist Training Program at the University of Colorado. She received her medical degree from the University of Virginia School of Medicine and completed her residency training in Internal Medicine at Johns Hopkins Hospital. She subsequently completed Infectious Diseases fellowship training at Massachusetts General Hospital. Her laboratory studies the human immune response to HIV-1 infection and the factors that drive HIV-1 pathogenesis, particularly in intestinal mucosal tissue. Her most recent studies have focused on understanding the complex interactions between virus, gut commensal bacteria, and intestinal immune cells that contribute to mucosal and systemic inflammation during HIV-1 infection. She also extensive experience in designing and implementing HIV clinical trials through her involvement in the national AIDS Clinical Trials Group (ACTG), with an emphasis on studies of HIV-associated immune activation and immune-based vaccines and therapies.

Breakout Sessions

Science Communication in the Clinic and the Community

In this session, students will learn about the fundamentals of science communication for health, both one-on-one with patients, in public health outreach, and in community advocacy. Students will practice communicating through scenarios and receive feedback from peers and the session leader (Dr. Nicole Kelp)

CU MSTP Trivia!

Come one, come all! Step on up to test your knowledge of how well you know the University of Colorado MSTP.

Student Oral Presentations

Brian Lloyd
Neurexin-3 subsynaptic densities are spatially distinct from Neurexin-1 and essential for excitatory synapse nanoscale organization
GS4, Pharmacology
Brian Lloyd*, Rebecca Roth, Jason Aoto
Neurexin-3 subsynaptic densities are spatially distinct from Neurexin-1 and essential for excitatory synapse nanoscale organization
Synaptic adhesion molecules are a diverse class of proteins that participate in synaptic formation, maintenance, and function which are critical for efficient synaptic transmission and plasticity. Recent evidence suggests that synaptic adhesion molecules allow for effective synaptic transmission via clustering and alignment of presynaptic active zones, where neurotransmitter is released, and postsynaptic receptors. Neurexins (Nrxns) are a class of essential, disease relevant presynaptic adhesion molecules which have been proposed to modulate synaptic nano-organization due to their known roles in regulating pre and postsynaptic structure via intracellular and transsynaptic signaling respectively. Nrxns are encoded by three evolutionarily conserved Nrxn genes (Nrxn1, 2, and 3) which were initially proposed to be redundant at all synapses; however, it is becoming increasingly apparent that individual Nrxns govern distinct aspects of synapse function. For example, Nrxn3 has been shown to control AMPA receptor strength but how Nrxn3 dependent nano-organization may contribute to this effect remain unknown. Here, I am investigating the role of Nrxn3 in synapse nano-organization using our Nrxn3 conditional knockout mouse, a novel epitope tagged Nrxn3 mouse, and 3D STORM to examine the clustering and alignment of proteins critical for synaptic transmission. 3D STORM shows that Nrxn3 is required for the nano-organization of excitatory synapses and that Nrxn3 forms nanoscopic signaling platforms that are distinct from Nrxn1. These data represent, to the best of our knowledge, the first evidence that neurexins, and more widely presynaptic adhesion molecules, are required for the nano-organization of excitatory synapses and provides further insight into the mechanism by which Nrxn3 controls AMPA receptor strength. Future studies will focus on defining the molecular composition of neurexin signaling platforms and determining if they are modulated by changes in synaptic activity.

Nickole Moon
Sensing Stress: Extracellular Vesicles as Communicators of Stress-Mediated Cellular Allostasis
GS3, Neuroscience
Nickole Moon, Jennifer Chan, Christopher Morgan, Tracy L. Bale
Cellular reprogramming at reproductive tissues following chronic parental stress influences offspring neurodevelopment. In males, mechanistic studies identified lasting changes following chronic stress at epididymal epithelial cells (EECs) that provide sperm with essential maturation signals. While the mechanisms regulating the cellular allostatic set point following stress are unclear, the glucocorticoid receptor (GR) is a known mediator of stress and key target orchestrating allostasis. To examine the hypothesis that stress initiates GR-dependent programming, we reduced EEC GR expression in our mouse model of chronic paternal stress. To assess GR dependent processes regulating allostasis, we analyzed the active EEC translatome and detected two clusters of co-regulated genes related to chromatin and mitochondrial processes. Moreover, CUT&RUN sequencing revealed that stress increased binding by the transcriptional repressor,

H3K27me3, and that associated genes influence mitochondrial processes. As stress-responsive modulators of cellular energy, mitochondria are likely allostatic mediators. Using cell-based respirometry, we found that prior stress decreased basal mitochondrial respiration, and that GR knockdown protected against this effect. Furthermore, extracellular vesicles (EVs) secreted by EECs convey cargo necessary for sperm maturation, and stress alters that content. Therefore, we assessed EVs as coordinators of mitochondrial respiration, and found reduced respiration following EEC incubation with stress EVs. Together, these studies demonstrate a role of GR in programming the chromatin landscape after chronic stress to impact cellular energy requirements, and of EVs to maintain this new set point. These regulatory mechanisms of allostasis broadly apply to stress-vulnerable cells and are important to understand the enduring pathophysiology of trauma and potential interventions.

Emily King
Prolonged lung inflammation is characterized by early recruitment of monocytes to the airspace and pulmonary interstitium with proliferation driving elevated macrophage numbers and persistence
GS3, Immunology
Emily M. King*, Alexandra L. McCubbrey, Thienthanh Trinh, Jazalle McClendon, Peter M. Henson, and William J. Janssen
Rationale: During inflammation, blood monocytes migrate to the lung and differentiate into recruited macrophages in the airspace (AMs) and the interstitium (IMs). In self-limited injury, macrophage numbers increase but return to baseline within days. In prolonged injury their numbers are persistently elevated, mediating ongoing inflammation and fibrosis. The mechanism of this persistent elevation is unknown. Defining the role of monocyte recruitment versus local macrophage proliferation will inform future therapeutic strategies.
Methods: Mice received intra-tracheal (i.t.) LPS or bleomycin to initiate injury. 5-ethynyl-2-deoxyuridine (EdU) was given to label blood monocytes and lungs were harvested 3 days later to measure monocyte recruitment. Proliferation was measured by collecting lungs 6 hours after EdU. Macrophage EdU labeling was analyzed by flow cytometry.
Results: At homeostasis resident IMs and AMs have low proliferation and no monocyte recruitment. In self-limited injury (LPS), monocytes are recruited in the first 1-3 days after LPS and local macrophage proliferation peaks at day 3, with both recruitment and proliferation ceasing by day 6 and injury resolving by day 12. In prolonged injury (bleomycin), early monocyte recruitment is followed by increased proliferation of AMs and IMs that continues as macrophage numbers increase and fibrosis occurs at day 14.
Conclusions: Our data show that LPS injury causes monocyte recruitment primarily in the first 3 days and a brief increase in macrophage proliferation at day 3. In contrast, early monocyte recruitment is followed by sustained proliferation of AMs and IMs in bleomycin injury. These data indicate that the persistence of elevated macrophage numbers is driven by proliferation and not ongoing monocyte recruitment. These findings have important implications for the timing and targeting of interventions for prolonged and fibrotic lung injury.

Brigit High
Structural comparisons of human and mouse fungiform taste buds
GS5, Neuroscience
Brigit High*, Thomas E. Finger
The morphology of taste buds in fungiform papillae is generally conserved across mammalian species, but significantly more is known about murine taste buds than human

taste buds. Both mouse and human taste buds contain elongate taste receptor cells as well as gustatory nerve fibers which share structural and molecular features. However, a recent finding that the composition of the purinergic receptor subunits differs between mice and humans suggests that while major features of fungiform taste buds may be preserved between species, other features may differ. Using immunofluorescent image stacks, we compared morphological characteristics of mouse and human fungiform taste buds. Our results indicate similarities in certain aspects, such as average taste bud diameter and number of cells within the taste bud. However other features differ significantly. For instance, human taste buds are 42% taller and 60% larger in volume than those of mice. Human taste buds also have a 33% higher innervation density by nerve fibers expressing the purinergic receptor P2X3. Additionally, as in mice, a subset of human taste cells are immunoreactive for PLCβ2 and contain CALHM1-immunoreactive punctae apposed to gustatory nerve afferents indicative of channel-type synapses (Taruno et al., 2021). These CAHLM1 puncta are, however, significantly larger in humans than in mice. Overall, these findings suggest that while many similarities exist in the morphology and innervation of mouse and human fungiform taste buds, there are also significant differences that may impact gustatory signal transmission.

Student Lightning Talks

Amita Kashyap
Mechanism of Migration and Fate of Pulmonary iILC2s in Helminth Infection
GS2, Immunology

Meghan Kellett
Nuclear FAK drives thyroid cancer growth and survival
GS5, Cancer Biology

Laurel Darragh
Elective nodal irradiation mitigates local and systemic immunity generated by combination radiation and immunotherapy in head and neck tumors
GS4, Immunology

Keith Dodd
Relationship Between Functional Connectivity and Weight-Gain Risk of Antipsychotics in Schizophrenia
GS2, Bioengineering

Nk Egbukichi
Thyroid Cancer: Standard of Care
GS2, Cancer Biology

Varuna Nangia
Investigating melanoma cell-cycle fate in the presence of MAPK inhibition
GS2, Biochemistry

Poster Session

1. **Austin Jolly, GS5, Pharmacology**
   Austin Jolly*, Sizhao Lu, Allison Dubner, Tysen Noble, Mary Weiser-Evans
   The Chromatin Remodeler Brg1 Directs Vascular Stem Cell Differentiation into Myofibroblasts and Drives Vascular Fibrosis

2. **Raquel Ortega, GS2, Molecular, Cellular, and Developmental Biology**
   Raquel Ortega*, Hubert Fleury, Nausica Arnoult, Ben Bitler
   Determining the role of H3K9me2 on MMEJ and PARPi resistance

3. **Jacqueline Turner, GS3, Pharmacology**
   Jacqueline Turner*, Lisa Katsnelson, Marc D'Antonio, Kasey Couts, Richard Tobin, Raul Torres
   Lysophosphatidic acid is a lipid-regulated immune checkpoint

4. **Hei-Yong Lo, GS4, Molecular Biology**
   Hei-Yong Lo, Chad Pearson, Matthew Taliaferro
   Where does ASPM RNA go and How does it get there anyways?

5. **Lily L. Nguyen, GS4, Molecular, Cellular, and Developmental Biology**
   Lily L. Nguyen*, Zachery L. Watson, Haley Aud, Benjamin G. Bitler, Edward B. Chuong
   Combination PARP and EHMT1/2 inhibition induces viral mimicry in PARPi-resistant ovarian cancer

6. **Joseph Joe, Hsieh, GS4, Cancer Biology**
   Joseph (Joe) Hsieh*, Lays Sobral, Nathan Nowling, and Paul Jedlicka
   Chromatin Regulation of PAX3-FOXO1 and Key Co-Factors in Driving Fusion-Positive Rhabdomyosarcoma

7. **Connor J. Hughes, GS5, Pharmacology**
   Hughes, C.J.*, Rosenbaum, S., Vartuli, R.L., Fields, K., Zhou, H., Gustafson, A., Kong, D., Slansky, J., Zhao, R., and Ford, H.L.
   Eya3 regulates NF-kB signaling, alters the pre-metastatic niche, and promotes tumor progression in Triple Negative Breast Cancer

8. **Uma Kantheti, GS2, Immunology**
   Uma Kantheti*, Erin D. Lucas, Beth A. Jirón Tamburini
   Programmed Death Ligand-1 interactions in the regulation of DC migration and T cell priming

9. **Frances Li, GS4, Microbiology**
   Frances S. Li*, Kathryn S. Carpentier, and Thomas E. Morrison
   Defining MARCO-Virus Interactions Important for Chikungunya Virus Clearance from the Circulation

10. **Mostafa M. El-Kalliny, GS2, Molecular, Cellular, and Developmental Biology**
    Mostafa M. El-Kalliny*, Kelly E. Winther, Makenzie Maker, Zoe R. Donaldson

Investigating the role of inhibitory interneurons of the nucleus accumbens in social attachment

11. **Juan Santiago Moreno, GS3, Neuroscience**
    Juan Santiago Moreno*, Daniel J. Denman
    COMPARISON OF HIGH THROUGHPUT RECEPTIVE FIELD MAPPING APPROACHES FOR HIGH DENSITY ELECTROPHYSIOLOGY IN MICE

12. **Jordan Hickman, GS2, Neuroscience**
    Jordan Hickman*, Grant Hughes, Daniel Denman
    Using Electrical Brain Stimulation to Encode Reliable and Discriminable Information in Primary Visual Cortex

13. **Bruce E. Kirkpatrick, GS3, Chemical & Biological Engineering**
    Bruce E. Kirkpatrick*, Joshua T. Kamps, Grace K. Hach, Laura J. Macdougall, Kristi S. Anseth
    Redshifted tetrazole-ene PEG networks for self-reporting fluorogenic hydrogelation

14. **Brenda Seymour, GS3, Immunology**
    Brenda Seymour*, Brandon Trent, Brendan Allen, Adam Berlinberg, Kristine Kuhn
    Bacterial indole is required for collagen-induced arthritis through enhanced Th17 immunity

15. **Annika Gustafson, GS2, Molecular Biology**
    Annika Gustafson*, Jessica Hsu, Lomeli Shull, Adam Durbin, Kristin Artinger, Heide Ford
    Assessing the role of SIX1 in dynamic gene expression throughout myogenesis and in FN-RMS

16. **William Sheeran, GS3, Molecular, Cellular, and Developmental Biology**
    William Sheeran*, Kelly Winther, Julie Sadino, Jayme Temple, & Zoe Donaldson
    Hippocampal substrates of social identity in monogamous prairie voles

17. **Nathaniel P. Skillin, GS3, Chemical & Biological Engineering**
    Nathaniel P. Skillin,* Katie M. Herbert, Bruce E. Kirkpatrick, Benjamin R. Nelson, Grace K. Hach, Kemal A. Günay, Frank W. DelRio, Ryan M. Khan, Kristi S. Anseth, Timothy J. White
    Collective Cellular Dynamics Drive Nematic Ordering of C2C12 Myotubes on Anisotropic Liquid Crystalline Polymer Networks

18. **Anagha Inguva, GS5, Cancer Biology**
    Anagha Inguva*, Krysta Engel, Hunter Tolison, Jordan Althoff, Shanshan Pei, Maria L. Amaya, Anna Krug, Mohammad Minhajuddin, Courtney Jones, Austin Gillen, Monica Ransom, Sarah Staggs, Daniel A. Pollyea, Clayton A. Smith, Brett M. Stevens, Craig T. Jordan
    Intracellular Calcium Localization Mediates the Activity of Venetoclax in Targeting Acute Myeloid Leukemia Stem Cells

Acknowledgments

Thank you to the 2023 Retreat Planning Committee!

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