7th Annual CU MSTP Retreat

Friday April 18th, 2025
Krugman Conference Hall

Retreat Schedule

Time	Session
8:30-9:00 AM	**Registration & Breakfast**
9:00-9:30 AM	**Welcome & Program address** *Cara Wilson, MD*
9:30-9:45 AM	**Break**
9:45-10:45 AM	**Student Oral Presentations I** *Ira Fleming* *Annika Gustafson*
10:45-11:00 AM	**Break**
11:00-11:45 AM	**Poster Session A**
11:45-12:45 PM	**Lunch & Excellence in Service Award**
12:45-1:45 PM	**Keynote Address** *Melanie Cree, MD, PhD*
1:45-2:30 PM	**Poster Session B**
2:45-3:45 PM	**Student Oral Presentations II** *North Foulon* Jackson Stocking
3:45-4:00 PM	**Lightning Talks**
4:00-4:15 PM	**Break & Student Voting**
4:15-4:25 PM	**Final Remarks & Awards**
4:30-5:45 PM	**T-Street Happy Hour**

Keynote Speaker

Dr. Melanie Cree, MD, PhD is a Physician Scientist, Pediatric Endocrinologist and Associate Professor at the University of Colorado Anschutz and Children's Hospital Colorado. Dr. Cree's clinical practice is focused on treating adolescents with polycystic ovary syndrome. She founded and directs the Children's Hospital Colorado multi-disciplinary PCOS clinic, published on this clinic model and guided the creation of similar clinics at multiple centers within the United States. Dr. Cree's research program is focused on translational research in disorders of insulin resistance that affect the reproductive axis and cardiometabolic health. She recently completed 2 clinical trials to treat steatoic liver disease in girls with PCOS with an amino acid supplement and 4 months of oral semaglutide. She is currently conducting an NIH funded clinical trial to assess the effect of injectable semaglutide on rates of ovulation in females with PCOS and obesity.

Dr. Cree is committed to collaborative research and initiated a multi-site data base study in 2017 to collect data in adolescents with PCOS and has obtained grant funding to expand this to 20 sites across the United States. She is also working with the Centers for Disease Control and National investigators to standardize testosterone assay ranges for women. Dr. Cree is dedicated to professional education and mentorship in PCOS giving presentations across the globe and mentoring all levels of trainees. Dr. Cree is a leader within professional organizations; she founded and was the former chair of the Pediatric Endocrine Society PCOS special interest group and is currently a board member for the Androgen-Excess PCOS Society. Dr. Cree regularly works with patient organizations, primarily PCOS Challenge.

Student Oral Presentations

Stromal cells are targets for delivery of vaccine mRNA and can be leveraged for stable retention of foreign nucleic acid

Ira Fleming*, Robert Belfon, Valerie Olsen, Erika Lasda, PhD, Jay Hesselberth, PhD, Beth Jirón Tamburini, PhD

Following vaccination, antigen is transported through the lymphatics to the draining lymph node either passively or via migratory cells that traffic antigens from the site of injection. Our prior work outlined a process by which lymphatic endothelial cells (LECs) of the lymph node capture and archive protein antigens for six or more weeks after vaccination or viral infection. Antigen archiving results in a positive effect on cellular immune memory and enhanced protection against pathogenic re-challenge. To address whether LECs also may participate in vaccine retention and immune responses following mRNA vaccination, we used an mRNA-encoded Cre recombinase “vaccine” to activate a fluorescent reporter system in-vivo. Out of all measured cell types, stromal and hematopoietic, LECs were converted most efficiently (~70% produce fluorescent reporter). We also demonstrate that while protein antigens can be archived by LECs, mRNA vaccine delivered by lipid nanoparticle (LNP) is rapidly degraded or discarded. To better address whether the protein-stable environment in archiving LECs can be leveraged for RNA retention, we designed a protein-DNA/RNA hybrid molecule biosensor compatible with single cell sequencing platforms. We found that lymph node LECs acquire and retain these protein-oligo conjugates with high efficiency relative to other cell types and maintain the biosensor in an RNA stable environment. We predict that by using a protein carrier to direct translate-able RNA vaccine to protected compartments with LECs for extended periods we could, as in the case of protein antigen archiving, improve immune memory.

Dissecting the role of SIX1 in the rhabdomyosarcoma core-regulatory circuit demonstrates new potential approaches to targeted therapy

Annika L. Gustafson*, Jessica Hsu, Stephanie Nance, Brian J. Abraham, Kristin Artinger, Adam D. Durbin, Heide Ford

Rhabdomyosarcoma (RMS) is a high-risk pediatric sarcoma that resembles developing skeletal muscle. RMS depends on the myogenic transcription factors, MYOD1 and MYOG, whose expression is regulated by SIX1 and its obligate cofactor, EYA. Knock-down (KD) of SIX1 in muscle progenitors decreases MRF expression and abrogates muscle differentiation. In contrast, in RMS, KD of SIX1 increases expression, and skeletal muscle gene occupancy, of MYOD1 and MYOG, resulting in tumor cell differentiation and cessation of growth. The mechanism of how SIX1 mediates a differentiation program in myogenesis but maintains a progenitor-like state in RMS is unknown. To address this question, I analyzed SIX1 genome-wide occupancy and found that SIX1 binding is enriched at stem loci in myoblasts and redistributes to differentiation loci in myotubes. Further, we found that SIX1 KD in RMS results in SIX1 loss at enhancers of proliferation genes and residual SIX1 protein is increased at myogenic differentiation enhancers. We found through analysis on H3K27ac ChIPseq and dependency map data that in RMS, SIX1 participates in a feedforward, autoregulatory transcriptional core-regulatory circuit (CRC) that establishes the transcriptional baseline of RMS. SIX1 binds genome wide with c-MYC, MYCN, TCF12, ZEB2, MYOD1, and SOX8 to regulate RMS proliferation. To identify co-factors associated with SIX1 that may be therapeutically targetable, I performed co-immunoprecipitation for SIX1, and observed enrichment for EYA2. As EYA2 has an intrinsic tyrosine phosphatase activity linked to c-MYC stability, we assessed the ability of EYA2 inhibition to destabilize CRC expression. Treatment of RMS cell lines with a novel EYA2 tyrosine phosphatase inhibitor causes RNA and protein-level destabilization of the RMS CRC. This work provides a novel mechanism for targeting a CRC through an obligate co-factor of SIX1, and provides new insight into individual regulatory functions of SIX1 in RMS and myogenesis.

How does the ER protein Lyric promote cancer?

North Foulon*, Sylas Anderson, Eric Sawyer, Rob Abrisch, Janet Fox, Gia Voeltz

The oncoprotein Lyric overexpresses in almost every studied solid and hematologic malignancy and drives tumorigenesis in vivo. Patients bearing tumors with high levels of Lyric suffer more metastases and carry worse prognoses than those with low levels. However, despite the mounting evidence of its clinical impact, Lyric's cellular function remains unclear. Hundreds of thousands of cancer patients die due to treatment failure each year in the US, and there is a desperate need for novel cancer treatments; juxtaposed with these facts, the knowledge gap surrounding Lyric's molecular behavior becomes unacceptable.

Our preliminary results show that Lyric is an integral endoplasmic reticulum (ER) membrane protein which binds to mRNA and expands the translationally-active rough "sheet" domain of the ER when overexpressed. We have also found that Lyric associates with the Sec61 translocon, the complex responsible for co-translational translocation on the ER. These initial findings suggest Lyric may play a role in ER-localized translation, providing a potential mechanism for Lyric's tumorigenicity across a diverse set of malignancies. We will support this hypothesis using super-resolution live-cell imaging and translational assays including polysome profiling.

Investigating the impact of Purkinje cell degeneration on motor coordination

Jackson Stocking*, Abigail Person

Individuals with ataxia present with discoordination of movements such as dysmetria, the over- or under-shooting of targets during movement. Ataxic patients often exhibit Purkinje cell (PC) degeneration, but the mechanistic relationship between PC loss and coordination deficits is not well understood. Insight into this mechanism can be gained by considering cerebellar coordination of reaching in healthy animals. Recent work from our lab studying coordination of skilled reaching has revealed a population rate code in PCs that inversely correlates with reach velocity, while cells in the anterior interposed (IntA) cerebellar nucleus exhibit scaled rate increases during reach deceleration. In addition, stimulation revealed a causal role of IntA in limb deceleration. Together, these findings suggest a cerebellar reach coordination module in which PCs pause firing proportionally to early reach velocity, disinhibiting IntA to cause appropriate bursting to induce accurate reach deceleration. To investigate the possible contribution of this coordination module to the development of ataxia, I am combining PC ablation with in vivo electrophysiologic, electromyographic, and kinematic analysis during skilled reaching. Initial kinematic analyses reveal a disruption in the tuning of the gain of reach deceleration relative to velocity after PC ablation. Simultaneous recordings in IntA reveal a decrease in reach-related modulation. These results suggest a breakdown in the coordination of reach deceleration, due to a loss of scaled IntA bursting following the loss of upstream PCs.

Flash Talk

Are you Y(e)ARNing for a new hobby?
Ashlyn Stahly

Poster Session A

Assessing Systemic Delivery of Galectin-3-Targeting Therapies for Retinal and CNS Uptake
Elena Esch*, Yuhuan Luo, Joe Barreto, Zhaoui Wang

Programmed death ligand-1 signaling within dendritic cells facilitates T cell responses during vaccinia infection
Uma Kantheti*, Erin D. Lucas, Beth A. Jirón Tamburini

Transcriptional Insights into KIR-educated NK cells
Sofia I. Celli*, Ana C. Codo, Cameron Manes, Christopher Collora, Katherine M. Kichula, Noah Cline, Neus Font-Porterias, Tonya Brunetti, Laurent Gapin, Karl-Johan Malmberg, Paul J. Norman, Liyen Loh

Using phylogenies to evaluate dengue fitness in Thailand
Douglas Fritz*, Leah Katzelnick, Henrik Salje

Dissection of the Mechanisms that Drive Loss of B Cell Anergy During Development of Autoimmunity
Brandon Hilliard*, Christopher Hill, Kristen Wells, Mia Smith

Accumbal calcium-permeable AMPA receptors orchestrate social attachment
Mostafa M. El-Kalliny*, William M. Sheeran, Liza E. Brusman, Olivia E. Neilly, Kelly E. Winther, Michael A. Kelberman, Zoe R. Donaldson

Poster Session B

PARP1 and PARP2 are dispensable for DNA repair by microhomology-mediated end-joining during mitosis
Raquel Ortega*, Erin Taylor, Sophie M. Whitehead, Thomas Danhorn, Benjamin G. Bitler, Nausica Arnoult

Stress causes sex-specific adaptations to ventral subiculum synapses, circuitry, and anxiety-like behaviors
Carley N. Miller*, Yuan Li, Kevin T. Beier, Jason Aoto

Impact of protein synthesis and inflammation on the metabolism of myelodysplastic syndrome stem cells
Daniel R. Moskop*, Sweta B. Patel, Brett M. Stevens, Austin E. Gillen, Daniel A. Pollyea, Craig T. Jordan, Eric M. Pietras

Uncovering the Role of HIF in Intestinal Epithelial IFNg Homeostasis
Rachel Cohen*, Liheng Zhou, and Sean Colgan

Elucidating the role of estrogen signaling in the HNSCC TME
Jessica Beynor*, Michael Knitz, Laurel Darragh, Thomas Bickett, Tyler Weiskopf, Sana Karam

Inducing Innate Immunity in High-Grade Serous Ovarian Carcinoma via Inhibition of EHMT1/2
Scott Lin*, Lily Nguyen, Zachary Watson, Elizabeth Woodruff, Benjamin Bitler

Non-Categorical Spectral Tuning in the Mouse Early Visual System
Juan Santiago Moreno*, Daniel J. Denman

Thank you to the 2024 Retreat Planning Committee!

Carley Miller
Brandon Hilliard
Nickole Moon
Dustin Fykstra
Jacob Cox
David Beltran-Cardona
Siddhu Maligireddy
Rachel Cohen
Erin Fish
Matthew Mardo
Selin Ekici
Alex Camai
Bruce Kirkpatrick
Isabelle Hua

Thank you to our faculty poster judges!

Alberto Cruz-Martin, PhD
Joe Hurt, MD, PhD
Justin O'Hare, PhD
Melanie Cree, MD, PhD
Bryan Haugen, MD
Brian Russo, PhD
Jennifer Richer, PhD
J. David Port, PhD