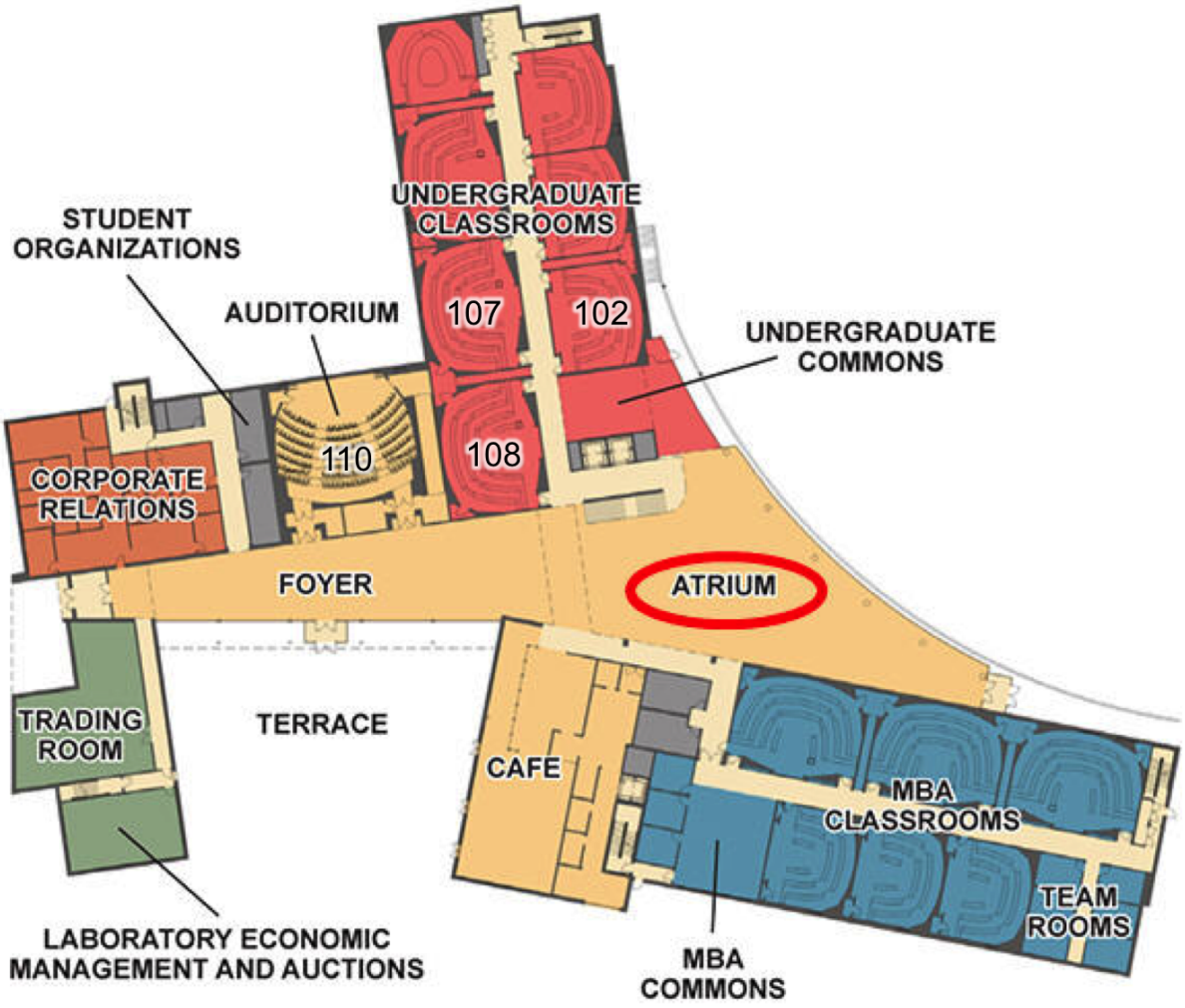
LIFE SCIENCE SYMPOSIUM

May 10, 2019

PennState



LIFE SCIENCE SYMPOSIUM

May 10, 2019

Organized by the Huck Graduate Student Advisory Committee

Chair: Di (Bruce) Chen, *Genetics (Molecular, Cellular, & Integrative Biosciences)*
Associate Chair: Jasmine Caulfield, *Neuroscience*
Secretary: Mehreen Mughal, *Bioinformatics & Genomics*

Allison Williams, *Biochemistry, Microbiology, & Molecular Biology*
Kelly Rios, *Biochemistry, Microbiology, & Molecular Biology*
Lila Rieber, *Bioinformatics & Genomics*
Dominika Dec, *Ecology*
Neha Oli, *Physiology*
Christopher Benson, *Plant Biology*
Dakota Brockway, *Neuroscience*
Amanda Van Buskirk, *Ecology*

Sponsors

The Huck Institute of the Life Sciences
Penn State Eberly College of Science
Penn State College of Health and Human Development
Penn State College of Agricultural Sciences
Penn State College of Nursing
Penn State Graduate School
American Society for Microbiology

SCHEDULE AT A GLANCE

Time	Event	Location*
8:30 am	Breakfast and Registration	Atrium
9:00 am	Introduction and Welcome	Rm 110
9:05 am	**Keynote Presentation I:** Nina Jablonski, PhD Evan Pugh University Professor of Anthropology *The evolution and meanings of human skin pigmentation*	Rm 110
10:05 am	Coffee Break	Atrium
10:15 am	Student Research Talks	Track A: Rm 107 Track B: Rm 108
11:45 am	**Poster Session,** *Lunch Served*	Atrium
1:45 pm	Invited Student Seminar: **Kelly Ness**, *Sleep restriction increases fat metabolism and alters lipid trafficking, changes that are not fully restored with two nights of recovery sleep: implications for cardiometabolic disease risk*	Rm 107
1:45 pm	Invited Student Seminar: **Mengyuan Jia**, *Identification of new late blight resistance genes using Genotyping-by-sequencing and RNA-sequencing approaches*	Rm 108
2:15 pm	Invited Student Seminar: **Zhi Chai**, *RNAseq studies reveal distinct transcriptional response to vitamin A (VA) deficiency in small intestine (SI) versus colon, discovering novel VA-regulated genes*	Rm 107
2:15 pm	Invited Student Seminar: **Nathan Johnson**, *Sequence divergence among trans-species small RNAs in parasitic plant genus Cuscuta compensates for target-site diversity in hosts*	Rm 108
2:45 pm	Coffee Break	Atrium
3:00 pm	**Keynote Presentation II**: Douglas Cavener, PhD Professor and Verne M. Willaman Dean, Eberly College of Science *Title TBA*	Rm 110
4:00 pm	Closing Remarks and Awards	Rm 110

*All events held at Smeal College of Business Building

TRACK A: BIOCHEMISTRY & MOLECULAR BIOLOGY

10:15 am **Ccr4–Not maintains genomic integrity by controlling the ubiquitylation and degradation of arrested RNAPII**
Haoyang Jiang, Marley Wolgast, Laura M. Beebe, Joseph C. Reese.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences

10:30 am **Quantifying differential enhancer activity in CNV models using novel modified STARR sequencing**
Maitreya Das, Mathew Jensen, Santhosh Girirajan.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences

10:45 am **CsrA-mediated translational activation in *Escherichia coli***
Stephanie Poly, Phil Bevilacqua, Tony Romeo, Paul Babitzke, Andrew Renda.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology
Poster 21

11:00 am **Use of CRISPR/Cas9-mediated genome editing to examine the role of S-locus F-box protein-containing SCF complexes in S-RNase-based self-incompatibility in *Petunia inflata***
Linhan Sun, Justin S. Williams, Shu Li, Lihua Wu, Wasi A. Khatri, Patrick G. Stone, Matthew D. Keebaugh, Teh-hui Kao.
Presenter affiliation: Plant Biology
Poster 19

11:15 am **A novel *Arabidopsis thaliana* root hair mutant provides a platform for studying expansin function in vivo**
Nathan K. Hepler, Moyan Jia, Daniel J. Cosgrove.
Presenter affiliation: Plant Biology
Poster 20

11:30 am **CNGC6 and CNGC14 are important for FER-dependent mechanical signaling, but not FER-dependent RALF1 signaling**
Aditi Bhat, Gabriele Monshausen.
Presenter affiliation: Plant Biology
Poster 7

TRACK B: PHYSIOLOGY & INFECTIOUS DISEASE

10:15 am **Sex-specific responses of mosquitoes to a mosquito-borne viral infection**
Karen Kemirembe, Jason L. Rasgon.
Presenter affiliation: Entomology

10:30 am **Adolescent social stress alters μ-opioid signaling in mice**
Dakota Brockway.
Presenter affiliation: Neuroscience
Poster 35

10:45 am **Impacts of immune challenge on thermoregulation by *Bombus impatiens* queens**
Hannah Stewart, Ruud Schilder.
Presenter affiliation: Entomology

11:00 am **Evaluating tick distribution and abundance on the American black bear (*Ursus americanus*) in Pennsylvania**
Hannah S. Greenberg, Erika T. Machtinger, Mark Ternent, Justin D. Brown.
Presenter affiliation: Entomology
Poster 6

11:15 am **Development of a peptide-based diagnostic test for bovine tuberculosis**
Sreenidhi Srinivasan, Gareth Jones, Maroudam Veerasami, Gobena Ameni, Martin Vordermeier, Vivek Kapur.
Presenter affiliation: Animal Science

11:30 am **Pharmacological disruption of an ApiAP2 transcription factor in the human malaria parasite *Plasmodium falciparum***
Timothy Russell, Erandi DeSilva, Gabrielle Josling, Gianni Panagiotou, Manuel Llinás.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology
Poster 18

POSTERS

1 **OpenSimRoot/Sorghum: a novel tool for in silico analysis of a stress tolerant cereal crop**
Miranda D. Niemiec, Xiyu Yang, Jonathan P. Lynch.
Presenter affiliation: Plant Biology

2 **Fungal root microbiome dynamics: species, sex, and genotype-specific transmission affecting tropical tree seedling performance**
Alyssa L. Decker, Jenalle L. Eck, Liza S. Comita, Molly A. Robertson, Scott A. Mangan, Howard W. Fescemyer, James H. Marden.
Presenter affiliation: Biology

3 **Genomic methylation analysis to investigate phenotypic instability in *Poa annua***
Christopher Benson, David R. Huff.
Presenter affiliation: Plant Biology

4 **Effects of feeding a flaxseed supplement in the transition period on milk production, fatty acid concentration in milk and plasma, incidence of disease postpartum and reproductive function in dairy cows and heifers.**
Francesca A. Gambonini, Devin M. Cunningham, R. C. Fry, Kevin J. Harvatine, Joy L. Pate, J. Moats, Troy L. Ott
Presenter affiliation: Animal Science

5 **Acquiring deep water during drought: rice root traits for drought tolerance**
Jenna E. Reeger, Kathleen M. Brown.
Presenter affiliation: Plant Biology

6 **Evaluating tick distribution and abundance on the American black bear (*Ursus americanus*) in Pennsylvania**
Hannah S. Greenberg, Erika T. Machtinger, Mark Ternent, Justin D. Brown.
Track B
Presenter affiliation: Entomology

7 **CNGC6 and CNGC14 are important for FER-dependent mechanical signaling, but not FER-dependent RALF1 signaling**
Aditi Bhat, Gabriele Monshausen.
Presenter affiliation: Plant Biology

8 **Management practices and age cohorts that contribute to increased Peste des petits ruminants seroprevalence in sheep, goats, and cattle in northern Tanzania**
Catherine M. Herzog, William de Glanville, Brian J. Willett, Tito Kibona, Isabella M. Cattadori, Vivek Kapur, Peter J. Hudson, Joram Buza, Sarah Cleaveland, Ottar N. Bjørnstad.
Presenter affiliation: Biology

POSTERS

9 **Wildflower meadow restoration on surface mines**
Sarah Rothman, Andy Cole, Mary Ann Bruns, Marvin Hall.
Presenter affiliation: Ecology

10 **Identification and mapping of late blight resistance QTLs in the wild tomato accession PI 224710 (*Solanum pimpinellifolium*)**
Sihui Gao, Hamid Ashrafi, Majid R. Foolad.
Presenter affiliation: Plant Biology

11 **The effects of neonicotinoid seed treatments on cotton extrafloral nectar**
Asher G. Jones, Kelli Hoover, Gary W. Felton
Presenter affiliation: Entomology

12 **The importance of the chlorophyte *Ostreobium* in the coral-dinoflagellate symbiosis**
Claudia Tatiana Galindo Martinez, Viridiana Ávila-Magaña, Mónica Medina, Roberto Iglesias-Prieto.
Presenter affiliation: Biology

13 **Investigating persistent measles dynamics in Niger and associations with temperature and rainfall variation**
Alexandre Blake, Nita Bharti.
Presenter affiliation: Biology

14 **Learning the properties of adaptive regions with functional data analysis**
Mehreen Mughal, Michael DeGiorgio.
Presenter affiliation: Bioinformatics & Genomics

15 **FRO3 plays an integral role in whole plant iron homeostasis in *Arabidopsis***
Brendon Juengst, Anshika Jain, Erin Connolly.
Presenter affiliation: Plant Biology

16 **Receptor tyrosine-kinase ROR is required for dendrite regeneration in *Drosophila* peripheral neurons**
Derek M.R. Nye, J. Ian Hertzler, Alex.T. Weiner, Richard M. Albertson, Melissa M. Rolls.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences

17 **Proximity-dependent biotin labeling reveals the spatial organization of the *Plasmodium* DOZI/CITH/ALBA complex**
Kelly T. Rios, Scott E. Lindner.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology

POSTERS

18 **Investigating paralogous ApiAP2 proteins with similar DNA binding specificities in *Plasmodium falciparum***
Victoria A. Bonnell, Gabrielle A. Josling, Timothy J. Russell, Heather J. Painter, Manuel Llinás.
Track B
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology

19 **Use of CRISPR/Cas9-mediated genome editing to examine the role of S-locus F-box protein-containing SCF complexes in S-RNase-based self-incompatibility in *Petunia inflata***
Linhan Sun, Justin S. Williams, Shu Li, Lihua Wu, Wasi A. Khatri, Patrick G. Stone, Matthew D. Keebaugh, Teh-hui Kao.
Track A
Presenter affiliation: Plant Biology

20 **A novel *Arabidopsis thaliana* root hair mutant provides a platform for studying expansin function in vivo**
Nathan K. Hepler, Moyan Jia, Daniel J. Cosgrove.
Track A
Presenter affiliation: Plant Biology

21 **CsrA-mediated translational activation in *Escherichia coli***
Track A
Stephanie Poly, Phil Bevilacqua, Tony Romeo, Paul Babitzke, Andrew Renda.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology

22 **RNA G-quadruplex form “microaggregates” that are temperature sensitive in biologically relevant spermine conditions**
Allison Williams, Philip Bevilacqua.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology

23 **A study of comparative genomics in the *Orbicella* sister species**
Ana M. González, Mónica Medina.
Presenter affiliation: Biology

24 **Conversion of human glioblastoma cells into neurons by neuronal transcription factors**
Xin Wang, Zifei Pei, Aasma Hossain, Tania Tsila Barnatan, Yuting Bai, Gong Chen.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences

25 **Transcriptome analysis of direct astrocyte-to-neuron conversion**
Ningxin Ma, Brendan Puls, Jiuchao Yin.
Presenter affiliation: Neuroscience

POSTERS

26 **Understanding muscle dysfunction associated with purine nucleotide cycle deficiency**
Latisha Franklin.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology.

27 **The role of synonymous mutation in cancer**
Yiyun Rao, Nabeel Ahmed, Scott Leighow, Justin Pritchard, Edward O'Brien.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences

28 **The mechanism of reiterative transcription at the pyrG promoter**
Yeonoh Shin, Katsuhiko Murakami.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology

29 **Design and construction of a donor plasmid to create anti-GD2 CAR T cells by CRISPR/Cas9**
Ángel Alvarado Toro.
Presenter affiliation: University of Puerto Rico - Ponce, Biology

30 **Prostaglandin E2 and PERK signaling pathways regulate differentiation of stress erythroid progenitors**
Yuanting Chen, Jie Xiang, Robert Paulson.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences

31 **The postprandial effect of spice consumption in a high-fat meal on proinflammatory cytokine secretion in overweight/obese men**
Ester S. Oh, Kristina S. Petersen, Penny M. Kris-Etherton, Connie J. Rogers.
Presenter affiliation: Nutritional Sciences

32 **The aryl hydrocarbon receptor mediates resistance to a chemotherapeutic agent in head & neck cancer**
Brandon A. Yusko, Iain A. Murray, Gary H. Perdew.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences

33 **Investigating paralogous ApiAP2 proteins with similar DNA binding specificities in *Plasmodium falciparum***
Victoria A. Bonnell, Gabrielle A. Josling, Timothy J. Russell, Heather J. Painter, Manuel Llinás.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology

34 **The effects of chronic peri-adolescent asthma on acute brain and peripheral immune responses**
Jasmine I. Caulfield, Kerri J. Schopf, Sonia A. Cavigelli.
Presenter affiliation: Neuroscience

35 **Adolescent social stress alters μ-opioid signaling in mice**
Dakota Brockway.
Track B
Presenter affiliation: Neuroscience

36 **Changes in proportion and functions of circulating immune cells during early pregnancy in dairy heifers**
Neha Oli, Joy L Pate, Troy L Ott.
Presenter affiliation: Physiology

37 **The optimization of butyrate production by resistant starch**
June Teichmann, Darrell Cockburn
Presenter affiliation: Food Science

38 **Vitamin D regulates the microbiota to induce RORɣt/FoxP3+ regulatory T cells**
Juhi Arora, Margherita T. Cantorna.
Presenter affiliation: Pathobiology

39 **Dual inhibition of SHIP1 and SHIP2 in the treatment of diet induced obesity in mice**
Shamara Lawrence, Sandra Fernandes, William G. Kerr.
Presenter affiliation: University of Arkansas at Pine Bluff

40 **Stress-induced effects on endometriosis and tight junction protein expression are counteracted by VSL#3 administration in an animal model**
Adriana C. Hernández Santini, Myrella L. Cruz, Gerardo A. Arroyo, Raquel Rivera-Méndez, Gladys Chompre, Caroline B. Appleyard.
Presenter affiliation: Biology, University of Puerto Rico - Ponce

41 **Inflammation of the brain in Tmem 135 mutant mice**
Karla Anaya, Wei-Hua Lee, Akihiro Ikeda.
Presenter affiliation: Cell, Molecular, & Developmental Biology, UC Riverside

42 **Diet and exercise-induced weight maintenance, alone and in combination with a whole tumor cell vaccine, delays mammary tumor growth and reduces tumor-infiltrating MDSCs expressing PD-L1 and IDO**
Yitong Xu, William J. Turbitt, Andrea M. Mastro, Connie J. Rogers
Presenter affiliation: Physiology

KEYNOTE SPEAKERS

Douglas R. Cavener

Douglas R. Cavener is internationally recognized for his research in molecular biology, genetics, and evolutionary biology. His recent work has focused on the etiology of human diseases including diabetes and neurodegenerative disorders.

Dr. Cavener joined Penn State in 2000 and has served as the department head of Biology over the past 15 years. In 2012, he was also appointed adjunct professor of Life Sciences at the Nelson Mandela African Institute of Science and Technology in Tanzania. Dr. Cavener was appointed the dean of the Eberly College of Science on July 18, 2015.

Dr. Cavener began his academic career in 1982 as an assistant professor of Molecular Biology at Vanderbilt University and advanced to associate professor and then professor. At Vanderbilt, he was a leader in graduate education and programs in molecular biology and biomedical sciences. Over his tenure at Vanderbilt and Penn State, Dr. Cavener has trained 24 Ph.D. students and continues to mentor graduate and undergraduate students in his research lab located in the Huck Life Science Building.

Dr. Cavener earned his B.A. in Biology in 1973 from Pasadena College, M.S. in Genetics in 1977 from Brown University, and Ph.D. in Molecular and Population Genetics in 1980 from the University of Georgia. He pursed postdoctoral studies at Cornell University for two years prior to his first academic appointment. Based on his earlier research Dr. Cavener won the prestigious Theodosius Dobzhansky Prize from the International Society for the Study of Evolution. He was recently elected a Fellow of the American Association for the Advancement of Science.

KEYNOTE SPEAKERS

Nina Jablonski

Nina G. Jablonski is Evan Pugh University Professor of Anthropology at Penn State. A biological anthropologist and paleobiologist, she studies the evolution of adaptations to the environment in Old World primates including humans. Her research program is focused in two major areas. Her paleoanthropological research concerns the evolutionary history of Old World monkeys, and currently includes an active field project in China. Her research on the evolution of human adaptations to the environment centers on the evolution of human skin and skin pigmentation and includes an active field project examining the relationship between skin pigmentation and vitamin D production.

Dr. Jablonski is currently collaborating on the development of new approaches to science education in the United States. These approaches have the dual aims of improving the understanding of evolution and human diversity, and stimulating interest among students in pursuing STEM courses and careers. With the support of NESCent (the National Evolutionary Synthesis Center) and active collaboration of Henry Louis Gates, Jr., she is leading a group of 30 scholars in the development of “genetics and genealogy” curricula for K-12 and undergraduate university students.

Dr. Jablonski also leads a major new scholarly initiative aimed at studying the effects of race in South African society. With the support of the STIAS (the Stellenbosch Institute for Advanced Study), she is the convener of the “Effects of Race” (EOR) program, which will bring together a select group of senior and junior scholars yearly to formulate new approaches to the study of race and the mitigation of racial discrimination

INVITED STUDENT SPEAKERS

Kelly Ness

Sleep restriction increases fat metabolism and alters lipid trafficking, changes that are not fully restored with two nights of recovery sleep: implications for cardiometabolic disease risk

Kelly earned her bachelor's degree from Washington University in Saint Louis in 2011, double majoring in Biology and Environmental Studies. After graduating, she participated in the junior scientist training program at the National Institutes of Health and worked as a medical technologist at Medstar Washington Hospital Center. Kelly joined the Integrative and Biomedical Physiology program at Penn State in 2014 and is advised by co-mentors Gregory C. Shearer and Orfeu M. Buxton. She is the recipient of a T32 Ruth L. Kirschstein National Research Service Award (NRSA) and served as chair of the Huck Graduate Student Advisory Committee (HGSAC) from 2017-2018. Kelly has two first-author publications, one in press and one under review, with a third in preparation.

Mengyuan Jia

Identification of new late blight resistance genes using Genotyping-by-sequencing and RNA-sequencing approaches

Mengyuan Jia received her bachelor's degree in biology from the College of St. Scholastica and her master's degree at University of Minnesota in 2014, conducting genetic and molecular research of nectar production and regulation. She joined the Plant Biology program as a PhD candidate in 2014,and has been working with Dr. Majid Foolad on mapping and breeding new late blight resistance genes in tomato. She received the Huck Braddock/Robberts endowment funds, the College of Ag graduate student competitive grant, the J. Franklin Styer Grad Fellowship, and the Huck travel grant. She has given several oral and poster presentations on campus and at the 2019 International Plant and Animal Genome Conference. She co-authored one publication in 2018, and two first-author manuscripts are in preparation.

INVITED STUDENT SPEAKERS

Zhi Chai

RNAseq studies reveal distinct transcriptional response to vitamin A (VA) deficiency in small intestine (SI) versus colon, discovering novel VA-regulated genes

Zhi received his bachelor's degree in Animal Sciences from Zhejiang University in 2013. Since then he has been working towards his PhD in Physiology with Dr. Catharine Ross in Nutritional Sciences. Joining force with researchers in Immunology and Bioinformatics, his project studies the effects of vitamin A deficiency and *Citrobacter rodentium* infection on the transcriptomes in mice intestine. He has gained familiarity with the pipeline of RNAseq study, from performing animal studies to differential expression and WGCNA analyses. He received a Huck Graduate Fellowship in 2013 and a NIH-NRSA T32 Grant in 2014. During the ASN conference in 2018, he won two travel awards through poster competitions, one titled "Emerging Leaders in Nutrition Science" and the other "Carotenoid and Retinoid Interactive Group."

Nathan Johnson

Sequence divergence among trans-species small RNAs in parasitic plant genus *Cuscuta* compensates for target-site diversity in hosts

Nate is a PhD candidate in Plant Biology, working with Mike Axtell. His current work focuses on the intersection of small RNAs and parasitic plants, investigating the recent discovery of *trans*-species gene-regulation in *Cuscuta*. He completed his bachelor's degree in Plant Biology from Michigan State University in 2011, where he then continued work on cell wall biosynthesis as a part of the Great Lakes Bioenergy Research Center. As a part of the Axtell lab, Nate has published work in the journals G3, Current Opinion in Plant Biology, and Nature and received funding from the Hill Memorial travel grant as well as the Huck Graduate Research Innovation Grant.

ABSTRACTS

Design and construction of a donor plasmid to create anti-GD2 CAR T cells by CRISPR/Cas9

Ángel Alvarado Toro.
Presenter affiliation: University of Puerto Rico - Ponce, Biology
Poster 29

In the field of cancer immunotherapy, chimeric antigen receptor (CAR) T cells have been a promising tool for cancer therapy. The mechanism of CAR T cell therapy is by filtering the patient's blood to separate the white blood cells from the red blood cells to isolate T cells. Once these T cells have been genetically modified to express the synthetic chimeric antigen receptor, the receptor binds to antigen recognition domains of the desired specificity connected to other T cell costimulatory domains, giving rise to induced CAR T cell cytotoxicity towards the target cancer cell. However, studies show this therapy has restricted cytotoxic activity against solid tumors largely due to high rates of T cell exhaustion. T cell exhaustion is an abnormal state of differentiation that is characterized by T cell malfunction. I propose to use CRISPR/Cas9 to create anti-GD2 CAR T cells at the targeted locus due to its correlation to reducing exhaustion and inducing cytotoxicity to cancer cells. To create these CAR T cells, we will use CRISPR/Cas9 to make a homology repair template that encodes homology to the targeted locus, flanking an anti-GD2 CAR construct. Eyquem et al. (2017) showed that targeting the CAR to the TRAC locus creates an efficient internalization and re-appearance of the CAR following single or repeated exposure to antigen, resulting in terminal T-cell differentiation and exhaustion. Viral vectors to transfer CAR DNA are efficient but tend to insert the sequence in random areas of the genome and may lead to off-target effects. CRISPR/Cas9 incorporates the desired DNA in the vector into a specific region of the genome. Creating this plasmid will induce more T cell memory formation, create more less exhausted T cells and induce more cytotoxicity towards cancer cell.

Inflammation of the brain in Tmem 135 mutant mice

Karla Anaya, Wei-Hua Lee, Akihiro Ikeda.
Presenter affiliation: Cell, Molecular, & Developmental Biology, UC Riverside
Poster 41

Based on our lab previous findings, mice with a mutation on the Transmembrane protein 135 causes early ocular aging by showing Age-related Macular Degeneration phenotypes. The Tmem 135 mutation was discovered to be involved in the balance of mitochondrial fission and fusion, which lead to an increase in ROS levels making the mice more vulnerable to environmental stress. We analyzed if the Tmem 135 mutation would also cause early aging phenotypes by quantification of neuronal markers, such as microglia morphology (Iba1) and neurogenesis capacity (NeuN) . Given our biomarkers and

previous findings we hypothesized that transgenic mice would have more microglia activation, and a higher number of ameboid-like microglia, lower astrocyte activation and low levels of NeuN due to loss in ability to regenerate. Our preliminary results indicate that transgenic mice indeed seemed to have more activated and ameboid-like microglia which indicated a higher level of brain inflammation. With respect to NeuN, transgenic mice showed less NeuN positive cells, and uneven staining throughout various regions of the brain. Future directions of this project are statistical analysis of a bigger sample size, and further molecular testing to prove or disprove that Tmem 135 affects brain tissue and its mitochondria dynamics.

Vitamin D regulates the microbiota to induce RORɣt/FoxP3+ regulatory T cells

Juhi Arora, Margherita T. Cantorna.
Presenter affiliation: Pathobiology
Poster 38

The active form of vitamin D (1,25(OH)2D) suppresses experimental models of inflammatory bowel disease in part by regulating the microbiota. In this study, the role of vitamin D in the regulation of microbe induced ROR ɣt/FoxP3+ T regulatory cells (T regs) in the colon was determined. Vitamin D sufficient (D+) mice had significantly higher frequencies of FoxP3+ T regs and RORɣt/FoxP3+ T regs in the colon compared to vitamin D deficient (D-) mice. The higher frequency of RORɣt/FoxP3+ T regs in D+ colon correlated with higher numbers of bacteria from the *Clostridium* XI, *Clostridium* XIVa and *Clostridium* XVIII, and *Bacteroides* in D+ compared to D- cecum. D- mice with fewer RORɣt/FoxP3+ T regs were significantly more susceptible to colitis than D+ mice. Transfer of the cecal bacteria from D+ or D- mice to germfree recipients phenocopied the higher numbers of RORɣt/FoxP3+ T regs and the reduced susceptibility to colitis in D+ versus D- recipient mice. 1,25(OH)2D treatment of the D- mice beginning at 3 weeks of age did not completely recover RORɣt/FoxP3+ T regs or the *Clostridium* XIVa and *Clostridium* XVIII numbers to D+ values. Early vitamin D status shapes the microbiota to optimize the population of colonic RORɣt/FoxP3+ T reg cells important for resistance to colitis. Supported by NIH grant (R01AT005378), USDA National Institute of Food (PEN04605-1010021) and USDA (2914-38420-21822).

ABSTRACTS

Genomic methylation analysis to investigate phenotypic instability in *Poa annua*

Christopher Benson, David R. Huff.
Presenter affiliation: Plant Biology
Poster 3

Poa annua (annual bluegrass) displays a variety of morphologies ranging from one of agriculture's most noxious weeds to a highly valued putting surfaces in the golf industry. Despite the USA's $800 million turfgrass seed and $1.1 billion sod industries, there are currently no commercial varieties of *P. annua*. Fitting with its remarkable versatility and reluctance to produce valuable seed through traditional breeding, our research suggests that *P. annua* can pass memory of environmental conditions to its offspring via epigenetic mechanisms. In this study, we use methylation sensitive amplification polymorphism (MSAP), enzyme-linked immunosorbent assays (ELISA), and plant phenotyping to study transgenerational inheritance and epigenetic modification with the hopes of providing breeders and turfgrass managers the foundational knowledge to improve breeding efforts in adaptable crop species like as *Poa annua*.

CNGC6 and CNGC14 are important for FER-dependent mechanical signaling, but not FER-dependent RALF1 signaling

Aditi Bhat, Gabriele Monshausen.
Presenter affiliation: Plant Biology
Poster 7

In their natural environment, plants are constantly under a wide range of biotic and abiotic stresses which contribute to shaping plant growth. It is well established that plant cell expansion is controlled by a combination of cell wall loosening and cell turgor, but despite a wealth of research, many questions about the precise mechanisms regulating these processes remain. Vacuoles, which typically occupy 90% of the volume in fully differentiated plant cells, are essential organelles that help maintain turgor pressure. However, our understanding of the role of vacuoles in cellular signaling and their contribution to fine-tuning cellular growth responses to external stimuli is still quite limited. Vacuoles are highly complex organelles with a convoluted organization characterized by the presence of transvacuolar strands (TVS) and dynamic tubular protuberances. The morphology of the vacuole is regulated by the actin cytoskeleton, which is also involved in growth control. To investigate the role of the vacuole in rapid growth adjustments, we examined vacuolar dynamics in Arabidopsis roots treated with RALF1 (Rapid Alkalinization Factor 1), a small secreted peptide that is the ligand of the receptor-

like kinase FERONIA. RALF1 is involved in growth regulation and in roots inhibits growth in a FER-dependent manner. It has previously been established that binding of the RALF1 ligand by FER triggers a rapid increase in cytosolic Ca2+ levels, extracellular alkalization and protein phosphorylation. How this signal transduction pathway contributes to growth arrest is currently not known. Here, we present evidence exogenous RALF1 treatment leads to a Ca2+- and FER-dependent changes in vacuolar morphology in roots, which however, is not essential for the growth inhibition.

Cytosolic free Ca2+ serves as a ubiquitous secondary messenger for an intricate network of signaling pathways occurring in response to various biotic and abiotic stresses, physiological processes such as gravitropism and tip growth, as well as in response to various hormones and elicitors such as auxin, RALF1 etc. Similar to exogenous RALF1 and auxin treatments, mechanical bending also leads to an instantaneous increase in cytosolic Ca2+ levels. However, the identity of Ca2+ permeable channels involved in the rapid influx of Ca2+ is still unknown. Previous studies conducted in our lab have shown FERONIA to be essential for regulating mechanical signal transduction in *Arabidopsis* roots. Furthermore, it has been established that CNGC14 is required for Ca2+ influx in response to auxin. Here, we present evidence that CNGC6 and -14 are important mediators of FER-dependent mechanical ion signaling, although not for FER-dependent RALF1 signaling.

Investigating persistent measles dynamics in Niger and associations with temperature and rainfall variation

Alexandre Blake, Nita Bharti.
Presenter affiliation: Biology
Poster 13

The regular, defined spatio-temporal patterns of measles that were documented in settings like England and Wales in the pre-vaccination era, are not necessarily seen today in low-income countries where measles persists, such as Niger. Further investigations of mechanisms underlying measles dynamics in current settings could provide valuable insights to these persistent measles hotspots to improve surveillance systems and support targeted interventions.

A large part of Niger follows a seasonal pattern with the variation of population density between rural and urban areas because of agricultural migration. Environmental factors such as temperature and rainfall could then be valuable indicators of drivers of measles transmission. Simultaneously, a heterogeneous vaccination coverage, and the possibility of re-introductions due to contiguity with

neighboring countries could lead to chaotic measles dynamics. We investigated weekly measles spatio-temporal patterns in Niger surveillance data from 1995-2001 in association with temperature and rainfall variation.

We realized a wavelet analysis on weekly measles surveillance data at the health district level. We completed a descriptive analysis using the power spectrum of the 38 health districts. We also interpolated temperature and rainfall using spatio-temporal kriging with external drift and then aggregated them at the same spatio-temporal scale as the surveillance data to look for associations. A better understanding of some of the drivers of measles in Niger could improve preparedness to those recurrent outbreaks and help optimizing public health interventions.

Investigating paralogous ApiAP2 proteins with similar DNA binding specificities in *Plasmodium falciparum*

Victoria A. Bonnell, Gabrielle A. Josling, Timothy J. Russell, Heather J. Painter, Manuel Llinás.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology
Poster 33

Gene expression during the *P. falciparum* intraerythrocytic developmental cycle (IDC) is highly coordinated and is thought to be largely regulated by the Apicomplexan AP2 (ApiAP2) family of sequence-specific DNA binding proteins. In this work, we focus on the functional characterization of four ApiAP2s (PF3D7_0420300, PF3D7_0802100, PF3D7_1305200, PF3D7_1456000) that bind a similar CACACA DNA sequence motif in vitro. These four proteins are expressed at different times during the IDC and contain paralogous AP2 DNA binding domains. Although these proteins all bind the CACACA motif, we predict that they regulate distinct subsets of target genes. Using both in vitro and in vivo approaches, we seek to define how these gene target preferences are established. To determine the comprehensive genome-wide targets for these four ApiAP2s, we are using chromatin immunoprecipitation followed by high throughput sequencing (ChIP-seq). As a complementary approach, we have measured the differential binding specificities against all intergenic instances of the CACACA motif across the *P. falciparum* genome using a recently developed genomic context protein binding microarray (gcPBM). This in vitro experiment tests the relevance of the sequence context in which CACACA motifs are found across the genome, which may impart differential target specificities. Our ChIP-seq results point to PF3D7_0802100 playing a role in activation of late stage genes, while gcPBM results suggest that paralogous AP2 DNA binding domains interact with different flanking regions surrounding the CACACA motif. Using immunoprecipitation coupled with mass spectrometry

(IP-MS) we will also identify potential ApiAP2 protein interacting partners. Further work into identifying gene targets and binding preferences will not only shed light on the mechanisms underlying *P. falciparum* gene regulation but will also determine specific DNA sequence elements that govern differential binding of paralogous transcription factors.

Adolescent social stress alters μ-opioid signaling in mice

Dakota Brockway.
Presenter affiliation: Neuroscience
Poster 35

Adolescence is a particularly vulnerable period of development and stress during adolescence can contribute to the development of anxiety and substance use disorders later in life. Many adolescents experience social stress, for example those in families who frequently relocate. Despite this, very little is known about how social stress during adolescence alters neurobiology later in life. To model the effects of social stressors during adolescence, mice were subjected to a protocol of adolescent chronic variable social stress (CVSS) consisting of social isolation followed by social reorganization in repeating cycles for 4 weeks. Adolescent CVSS has been shown to cause increased anxiety like behavior and increased ethanol consumption in males and females. The current study used slice electrophysiology to investigate the effects of CVSS on μ-Opioid signaling in the nucleus accumbens. The results indicate that adolescent CVSS mice display evidence for altered endogenous endorphin tone in the nucleus accumbens in females. Further, female adolescent CVSS mice exhibit increased inhibitory input in the nucleus accumbens in response to μ-Opioid receptor agonists. Ultimately these results provide a better understanding of the neurobiological changes associated with social stress during adolescence and how these may contribute to substance use disorders later in life.

The effects of chronic peri-adolescent asthma on acute brain and peripheral immune responses

Jasmine I. Caulfield, Kerri J. Schopf, Sonia A. Cavigelli.
Presenter affiliation: Neuroscience
Poster 34

Asthma is a common adolescent chronic health challenge affecting 9% of U.S. adolescents and is often comorbid with anxiety and depression. Little is known about the neurobehavioral impacts of chronic adolescent asthma. Microglia, the immune cells of the brain, become activated after peripheral insult,

and their over-activation is implicated in development of neuropsychiatric disorders. The mechanism underlying asthma and internalizing disorder comorbidity, and the involvement of microglia, are unknown. To determine these mechanisms, we developed a BALB/c mouse model of chronic developmental asthma to individually manipulate airway inflammation (via repeated exposure to house dust mite extract, HDM) and labored breathing (via repeated exposure to methacholine, MCH). We have previously demonstrated that mice exposed to adolescent MCH had significantly higher adult anxiety-related neurobiological and behavioral symptoms than unexposed mice. Here, we examined the acute effects of HDM and MCH on lung immune function, circulating corticosterone concentration, and microglia activation at postnatal day (P) 56 at 0, 1, 2, 4, 8, or 24 hours after final asthma treatment (HDM or MCH). At P56, lung IL-1β and IL-5 gene expression peaked at 4 hours after final HDM treatment. Alveolar macrophages were significantly higher and serum corticosterone concentration was blunted in HDM animals compared to other groups. Based on Cd11b expression, hippocampal microglia did not respond acutely in a time-dependent manner. However, preliminary data suggest that there may be a chronic impact on baseline microglia activity following this asthma paradigm. These results provide preliminary background on the potential role of microglia in asthma-anxiety comorbidity.

Prostaglandin E2 and PERK signaling pathways regulate differentiation of stress erythroid progenitors

Yuanting Chen, Jie Xiang, Robert Paulson.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences
Poster 30

In response to tissue hypoxia caused by anemia, hemorrhage or infection, the process termed stress erythropoiesis restores tissue oxygenation by rapid production of erythrocytes. In contrast to steady-state erythropoiesis, stress erythropoiesis give rise to bulk erythrocytes depends on specialized progenitors and distinct series of signals. During stress erythropoiesis, the early stress erythroid progenitors are rapidly expanded without differentiation. In response to transition signals, these early progenitors change from proliferating progenitors to differentiating stress erythroid progenitors. Previous work in our lab identified erythropoietin (Epo) as the one of the key transition signals. Here we show that prostaglandin E2 (PGE2) signaling dependent protein kinase RNA-like endoplasmic reticulum kinase (PERK) act as downstream effector of Epo. PERK kinase belongs to the integrated stress response kinase family. We found that mutation of PERK or inhibition of PERK kinase activity causes severe defects in stress erythropoiesis. Interference with PERK blocks the transition from

amplifying progenitors to differentiating stress burst forming units-erythroid (BFU-Es) in both mouse and human cell cultures. We will present data showing that the Epo dependent increase in PGE2 activates PERK signaling activities by regulating intracellular Ca2+ flux in response to anemic stress. We will also demonstrate a novel role of PERK signaling in global translational control through communicating with mammalian target of rapamycin complex 1 (mTORC1) signaling during erythroid differentiation.

Quantifying differential enhancer activity in CNV models using novel modified STARR sequencing

Maitreya Das, Matthew Jensen, Santhosh Girirajan.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences

Neurodevelopmental Disorders though studied extensively still possess a large amount of uncertainty accompanying them. Not only do they encompass a large number of symptoms and phenotypes, but also these phenotypes show extensive heterogeneity among patients. A niche field involve the study of CNVs (Copy Number Variants) associated with neurodevelopmental disorders such as in chromosome 16p12.1. These include large deletions or duplications that have been observed to be inherited in patients from parent generations and have also shown strong association with phenotypes associated with neurodevelopmental disorders, in various disease models. The gene regulatory aspect of CNVs however are yet to be widely studied. Since enhancers and promoters play a major role in gene expression, it is highly important to understand differential activity of these factors among patients and non-patients. We attempt to utilize a novel modified version of STARR Sequencing to quantify differential enhancer activity in wild type and CNV models in immortalized cell culture systems. STARR sequencing is traditionally used to discover and quantify enhancer property of randomly sheared genome fragments cloned into a specialized vector transfected into a host cell culture system. If the fragment possesses enhancer property, it transcribes itself which is quantified using RNA sequencing. We hope to compare enhancer activity in wild type host cells and cells carrying CNV deletions to better understand the role played by enhancers in neurodevelopmental disorders.

ABSTRACTS

Fungal root microbiome dynamics: species, sex, and genotype-specific transmission affecting tropical tree seedling performance

Alyssa L. Decker, Jenalle L. Eck, Liza S. Comita, Molly A. Robertson, Scott A. Mangan, Howard W. Fescemyer, James H. Marden.
Presenter affiliation: Biology
Poster 2

Tropical trees in Panama are negatively affected by soil from conspecific trees, apparently because of shared susceptibility to pathogens. Interactions in the soil between fungi and plant roots drive community dynamics and diversity. Here, we test the hypothesis that root microbiomes that establish in *Virola surinamensis* seedlings vary depending on relatedness to the soil inoculum source and affect seedling growth performance. In a greenhouse experiment, seedlings were grown in soil with mother, male, other female (conspecific) and heterospecific inocula. Data were gathered on the fungal microbiome using the sequenced ITS2 region of 158 *V. surinamensis* seedling roots. A custom pipeline, using QIIME, MOTHUR, and other bioinformatics tools, was used to assign taxonomy and relative abundances of fungal species present in the root microbiome. The abundance of specific fungal taxa within the community, including *Rhizophagus clarus*, *Chaetothyriales* and *Sordariomycetes*, were significantly elevated in particular source inocula. Abundances of some possibly pathogenic fungi (e.g., *Sympoventuriaceae*, *Fusarium* sp.,) were positively associated with maternal soil and hence candidates for negative effects of growing near a parent tree. Multiple fungal species were identified as being transmitted in a species-specific and/or sex-specific fashion. Abundance of certain fungal taxa was positively associated with the microbiome diversity and seedling growth performance (as was microbiome diversity itself). We identified one interaction between a plant resistance gene haplotype and a fungal strain in the root microbiome, which appears to have strong effects on the overall microbiome composition and plant growth. Overall, these data indicate a number of connections between fungal transmission, genotype-specific interactions, and seedling performance that may affect community dynamics of tropical trees.

ABSTRACTS

Understanding muscle dysfunction associated with purine nucleotide cycle deficiency

Latisha Franklin.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology.
Poster 26

Adenylosuccinate Lyase (ADSL) Deficiency is a disorder caused by a decrease in ADSL function resulting in cognitive dysfunction, delayed development, muscle dysfunction, autistic like behaviors, and seizures. Inborn errors of purine metabolism, such as ADSL or AMPD Deficiency, result in muscle dysfunction, however the cascade of molecular mechanisms is unknown. Purine metabolism consists of the de novo biosynthetic pathway and the purine nucleotide cycle (PNC). These processes aid in muscle function by generating and maintaining optimal purine levels as well as facilitating energy metabolism. Metabolically, decreasing ADSL affects purine metabolism by reducing the conversion of de novo synthesis metabolite SAICAR to AICAR and PNC metabolite S-AMP to AMP. Decreasing AMPD impacts the AMP/ADP/ATP ratio. Due to purine metabolism conservation, we can model ADSL Deficiency using RNAi in *Caenorhabditis elegans*. *C. elegans* with impaired expression of adsl-1 results in muscle dysfunction that is positively correlated with SAICAR accumulation. RNAi of adss-1 and ampd-1, enzymes solely acting in the PNC, results in abnormal muscle function. I hypothesize adss-1 maintains optimal metabolic flux through purine metabolism, adsl-1 prevents the toxic accumulation of SAICAR and provides fumarate to the TCA cycle, and ampd-1 maintains optimal AMP/ADP/ATP ratio which each allow for appropriate muscle function. I have used behavioral assays, imaging, and a comparative metabolic approach to define physiological and metabolic differences driving muscle dysfunction in RNAi of adsl-1, adss-1, and ampd-1. GFP labeled mitochondrial imaging reveals ampd-1 knockdown animals have an abnormal array of mitochondria, while adsl-1 and adss-1 knockdown animals do not appear to be affected. Metabolic analysis using liquid chromatography/mass spectrometry (LC/MS) and Metaboanalyst shows RNAi of adsl-1 and ampd-1 largely has the same metabolic profile. Behavioral analysis using the Wormlab software reveals ranging muscle dysfunction in adsl-1, adss-1, and ampd-1 RNAi animals, from most to least deficit respectively. I conclude the metabolic mechanism resulting in muscle dysfunction in adsl-1 RNAi animals is the result of multiple factors including the accumulation of SAICAR, disruptions in TCA cycle, and altered mitochondrial function. This knowledge will elucidate the molecular differences specific to causing muscle dysfunction associated with ADSL and AMPD Deficiency.

ABSTRACTS

The importance of the chlorophyte *Ostreobium* in the coral-dinoflagellate symbiosis

Claudia Tatiana Galindo Martinez, Viridiana Ávila-Magaña, Mónica Medina, Roberto Iglesias-Prieto.
Presenter affiliation: Biology
Poster 12

The scleractinian coral symbiosis with dinoflagellates confers corals the capacity to build reefs in oligotrophic environments. The optical properties of the coral skeleton allow the coral to be one of the most efficient light collectors in nature. With three to four-fold lower chlorophyll a density than terrestrial plants, corals are able the absorb the same percentage of irradiance. The multiple light scattering by the coral skeleton creates a diffuse light field within the coral tissue, reducing the dinoflagellate self-shading and increasing the probability of light absorption. However, the solar irradiance and the coral high light absorption efficiency make corals vulnerable during stressful conditions. A natural response in photosynthetic organisms exposed to stressful high light conditions is a reduction in the optical cross-section. However, in corals, any reduction in the optical cross-section produces a large increase in the light availability due to the multiple light scattering by the coral skeleton. Consequently, when corals have a considerable reduction in the optical cross section, they reach the limits of tolerance for the coral-dinoflagellate symbiosis by beginning a positive feedback loop that only ends in the breakdown of the coral-dinoflagellate symbiosis (i.e. coral bleaching). Within this positive feedback loop, the excessive light stress makes dinoflagellate recovery impossible within the coral tissue. This raises the question about how the coral-algae symbiosis can recover after a bleaching event. In this research, I will explore how endolithic algae *Ostreobium* sp. within the coral skeleton helps the coral to exit the positive feedback loop and to recover from bleaching. The reduction in the dinoflagellate population within the coral tissue during a bleaching event increases the light availability within the coral skeleton and allows the chlorophyte *Ostreobium* to bloom near the coral skeleton surface. As a result, the *Ostreobium* population within the coral skeleton reduces the multiple light scattering effect allowing the repopulation of the coral tissue by the dinoflagellates.

ABSTRACTS

Effects of feeding a flaxseed supplement in the transition period on milk production, fatty acid concentration in milk and plasma, incidence of disease postpartum and reproductive function in dairy cows and heifers.

Francesca A. Gambonini, Devin M. Cunningham, R. C. Fry, Kevin J. Harvatine, Joy L. Pate, J. Moats, Troy L. Ott
Presenter affiliation: Animal Science
Poster 4

During the transition period, cows exhibit reduced immune function that can lead to postpartum disease and reduced fertility. Dietary fatty acids (FA) modulate immune function. This study determined the effects of feeding a supplement high in omega-3 FA on milk production, FA concentration in milk and plasma, postpartum disease and fertility. Six sequential, 60-day periods (n=3 control (C), n=3 treated (FL)) were conducted over 12 months on a commercial dairy. A subset of cows (2+ lactations) and heifers (1st lactation) receiving the C (n=292) or FL (n=271) diets for the entire transition period were used. Diets were fed starting ~3 weeks pre-calving and for ~3 weeks after calving. The C diet was isonitrogenous and isocaloric to the FL diet, which contained a commercial flaxseed supplement (LinPRO™R) formulated to 3% of dry matter intake. Individual cow production, health and fertility data were collected. Blood was taken from a subset of cows and heifers (n=12/period) at entrance into the close-up pen, the week of calving and for 2 following weeks. Plasma and milk were analyzed for FA content. Data were analyzed using the MIXED procedure of SAS with repeated measures or proc GLIMMIX, with fixed effects of treatment and lactation and random effects of cow within treatment. Seasonal effects were accounted for by blocking. Both milk and plasma total omega-3 concentration was greater ($P<0.01$) in the FL group, while the omega-6:omega-3 ratio was lower ($P<0.01$). Milk yield tended to be greater in the FL group at 5 ($P=0.06$) and 10 weeks ($P=0.1$) postpartum. Milk fat and protein percent were greater ($P<0.01$) in the FL group during the first month of lactation. First service conception rates in cows (C 54% vs. FL 55%) and heifers (57% vs. 67%) did not differ nor did pregnancy loss. Incidence of postpartum disease did not differ between groups. In summary, the FL diet increased omega-3 FA in milk and plasma and tended to increase milk yield while having no detrimental effect on conception rates, embryo loss or disease postpartum.

ABSTRACTS

Identification and mapping of late blight resistance QTLs in the wild tomato accession PI 224710 (*Solanum pimpinellifolium*)

Sihui Gao, Hamid Ashrafı, Majid R. Foolad.
Presenter affiliation: Plant Biology
Poster 10

Late blight (LB), caused by the oomycete *Phytophthora infestans*, is one of the most destructive diseases of the cultivated tomato (*Solanum lycopersicum L*.) worldwide. As new and more aggressive clonal lineages of *P. infestans* have continued to emerge, it is of great importance to identify and characterize new sources of host resistance. Recently, we identified Solanum pimpinellifolium accession PI 224710 to be highly resistant to several *P. infestans* clonal lineages in the United States, including the prevalent lineage US-23. The goals of the present study were to identify, map and characterize LB resistance genes in PI 224710. An F2 population (n = 1721), derived from a cross between this accession and a LB-susceptible tomato breeding line, was screened for LB resistance under greenhouse conditions. A total of 43 resistant and 27 susceptible plants were selected, based on the disease performance of F2 individuals and their corresponding F3 progeny families. Using SolCAP Illumina Infinium Array, 1,769 polymorphic SNP markers were identified between parental lines, of which 469 non-redundant markers were used to construct a genetic linkage map. A trait-based QTL analysis resulted in the identification of three major QTLs on chromosomes 6, 9, and 10 that were associated with LB resistance in PI 224710. This information may facilitate marker-assisted transfer of resistance from PI 224710 to the cultivated tomato. Near-isogenic lines (NILs) are being developed and differential gene expression analysis and RNA-seq experiments conducted towards identification and characterization of the underlying resistance genes.

A study of comparative genomics in the *Orbicella* sister species

Ana M. González, Mónica Medina.
Presenter affiliation: Biology
Poster 23

Speciation is the process in which change overtime results in discrete taxa with certain natural history peculiarities including particular reproductive strategy and ecological niche usage. Here we studied the genomes of the Caribbean coral species, *Orbicella*, to assess if different gene family expansions associate with *Orbicella*'s reproductive strategies and niche ecology. We hypothesized that genes responsible for local adaptation to different environments (based on depths) and genes responsible for

temporal prezygotic isolation should be overrepresented in these species. We compared the genomes of the three sister *Orbicella* species among each other to assess individual differences and compared against the Caribbean corals *Acropora palmata* and *A. cervicornis*. In addition, we used genomic data from the closest living relative to *Orbicella*, namely *Cyphastrea serailia* and *C. microphtalma*, which live in the Indo-Pacific. Preliminary data indicate species-specific differences in the genome content and family enrichments.

Evaluating tick distribution and abundance on the American black bear (*Ursus americanus*) in Pennsylvania

Hannah S. Greenberg, Erika T. Machtinger, Mark Ternent, Justin D. Brown.
Presenter affiliation: Entomology
Poster 6

The abundance of ticks has been increasing in the United States in recent years, as has the number of diagnosed cases of tick-borne diseases. American black bear (*Ursus americanus*) populations have also been increasing in the Eastern United States. As a competent host of several species of ticks and a mammal capable of traveling great distances, the influence of black bears as hosts of tick vectors requires evaluation. Ectoparasite surveys were conducted on black bears in Pennsylvania to determine abundance and distribution of tick species on this host. These surveys were conducted using standardized 4” x 4” squares placed on sixteen pre-designated body regions on live and hunter-harvested black bears from June – December 2018. In total, 171 I*xodes scapularis* adults, 1 *Dermacenter variabilis* adult, 58 nymphs, and 9 larvae were found on black bears using the tick squares. Tick density differed by body region and by month, with highest numbers found between the toes in August on live trapped bears, and on the ears, front under-arms, and chest in November on hunter-harvested bears. Additional ticks were found outside the standardized body region squares and all ticks were submitted for pathogen testing to the East Stroudsburg University Northeast Wildlife DNA Laboratory. This data demonstrates that tick congregation on specific body regions on black bears has much greater variability compared to other mammals, such as white-tailed deer, and may be related to time of year and tick life-cycles.

ABSTRACTS

A novel *Arabidopsis thaliana* root hair mutant provides a platform for studying expansin function in vivo

Nathan K. Hepler, Moyan Jia, Daniel J. Cosgrove.
Presenter affiliation: Plant Biology
Poster 20

The plant cell wall is a complex architectural structure composed of multiple polysaccharides. Noncovalent interactions between wall polysaccharides provide the mechanical strength necessary to support plant growth; however, modification of these interactions is also critical for plant development. One important class of proteins which mediate irreversible cell wall loosening (“creep”) are expansins. Despite their discovery nearly three-decades ago, research on expansin function has been limited, due in large part to extensive functional redundancy and difficulty to express recombinantly. In order to develop a platform for studying expansin function in vivo, we targeted Arabidopsis thaliana (Col-0) paralogs AtEXPA7 and AtEXPA18 for knockout using CRISPR/Cas9. Phylogenetically, AtEXPA7 and AtEXPA18 form a monophyletic group (‘clade’) named EXPA-X, and expression analyses indicate the two localize to root hair progenitor cells and elongated root hairs. Root hairs are a useful and commonly utilized tissue for studying gene function, as they are easily observable structures and aberrations in root hair development are not detrimental to plant growth. While single gene knockouts atexpa7 and atexpa18 still produce elongated root hairs, atepxa7/atexpa18 seedlings fail to exhibit any root hair elongation. Complementation using either EXPA-X paralog restores root hair elongation to that observed for single gene knockouts, confirming the loss of EXPA-X as the reason for ablated root hair development. Failure to produce elongated root hairs in atexpa7/atexpa18 mutants was not time dependent and all attempts at stimulating elongation were unsuccessful, further illustrating the importance of EXPA-X in root hair elongation. To our knowledge, this is the first demonstration of an expansin clade being critical for a specific plant developmental process, and definitively confirms the role of EXPA-X in root hair development, which up until now has been more speculation than demonstration. Lastly, as a proof of concept for our platform, we transformed three EXPA genes (AtEXPA10, AtEXPA11, AtEXPA12) into atexpa7/atexpa18 mutants, all under control of the AtEXPA7 promoter in order to ensure root hair-specific expression. All three genes restored root hair elongation within the range of single gene complements or wild-type lengths. These results reveal a deeply conserved function for α-expansin, as well as demonstrate the usefulness of our platform for exploring expansin function. Future work will include: 1. targeted mutagenesis assays designed to elucidate the biochemical function of expansins, and 2. additional exploration of functional conservation among more diverse expansin genes.

ABSTRACTS

Stress-induced effects on endometriosis and tight junction protein expression are counteracted by VSL#3 administration in an animal model

Adriana C. Hernández Santini, Myrella L. Cruz, Gerardo A. Arroyo, Raquel Rivera-Méndez, Gladys Chompre, Caroline B. Appleyard.
Presenter affiliation: Biology, University of Puerto Rico - Ponce
Poster 40

Introduction: Endometriosis is a gynecological disorder in which tissue that normally lines the endometrium grows outside the uterus and commonly results in peritoneal inflammation and infertility. Our previous studies show that stress exacerbates the development of endometriosis symptoms with worsening of colonic damage, and probiotic administration can decrease lesion size. Tight junction proteins are important to maintain the integrity of the intestinal barrier, and their disturbance can contribute to a variety of pathological conditions. It is possible that in our model stress contributes to the intestinal effects via modulation of tight junction proteins, but it is unclear whether probiotic use could counteract any of these effects. In this project we focused on tight junction protein expression intensity using the specific integral membrane proteins occludin and claudin-2 to investigate how probiotics might alleviate endometriotic damage in the colon. Downregulation of occluding can enhance paracellular permeability, while claudin-2 overexpression has been linked to intestinal pathophysiology by decreasing barrier function of other claudins.

Hypothesis: Probiotic administration will reverse the effects of stress on colonic tight junction protein expression in an animal model of endometriosis.

Methods: Endometriosis was induced by suturing uterine horn tissue next to the intestinal mesenteries in female Sprague-Dawley rats (11-12/group) on day 0. One-week later, rats were given the probiotic mixture VSL#3 or placebo in their drinking water before subjecting to 7 days of water avoidance stress (60 mins/day; days 14-20). Non-stressed controls also received VSL#3 or placebo. On day 60 the rats were sacrificed, the vesicles were retrieved and measured, and the tissues collected before paraffin embedding. Colonic damage was measured and immunofluorescence for claudin-2 and occludin was performed.

Results: The vesicle area from rats exposed to stress were significantly larger in size ($p<0.05$) while after probiotic administration, size was reduced ($p<0.01$). Colonic macroscopic damage had a trend to increase in endometriosis animals and was reduced after probiotic administration ($p<0.05$). Colonic

occludin expression showed a trend to increase when probiotic was administered after stress, while claudin-2 expression was downregulated after stress ($p<0.01$) and probiotic administration ($p<0.01$).

Conclusion: Stress aggravates endometriosis symptoms with larger vesicles and increased colonic damage. After probiotic administration, these symptoms are reversed and integrity of the tight junctions in colonic tissue is increased. This tendency provides further support for the potential use of probiotics as a complementary treatment to reduce the effects of inflammation in this condition.

Supported in part by P20 GM103475-15, R25GM096955 & R25GM082406.

Management practices and age cohorts that contribute to increased Peste des petits ruminants seroprevalence in sheep, goats, and cattle in northern Tanzania

Catherine M. Herzog, William de Glanville, Brian J. Willett, Tito Kibona, Isabella M. Cattadori, Vivek Kapur, Peter J. Hudson, Joram Buza, Sarah Cleaveland, Ottar N. Bjørnstad.
Presenter affiliation: Biology
Poster 8

Peste des petits ruminants virus (PPRV) causes a contagious disease of high morbidity and mortality in global sheep and goat populations and has spread to more than 70 countries in Asia, the Middle East, and Africa. PPRV threatens 80% of the global small ruminant population of nearly 2 billion animals and the livelihoods of over 330 million farmers who rely directly on small ruminants. PPRV, which is a *Morbillivirus* similar to rinderpest and measles, is spread by direct contact with infected hosts, aerosols, or fomites. Following the eradication of rinderpest, PPRV has also been shown to elicit seroconversion in cattle and few studies have explored PPRV epidemiology in cattle. Overall, current knowledge of PPRV epidemiology in sub-Saharan Africa is lacking and this study addresses this gap.

In our previous work, data generated from cross sectional studies involving household surveys and livestock sampling (n = 7,538) in nine agropastoral and eleven pastoral villages in northern Tanzania were used to investigate PPRV epidemiology. We found the overall observed seroprevalence was 21.1% and differed with management practice (agropastoral: 5.8%, pastoral: 30.7%). Seroconversion varied significantly by sex, species, and management system.

Using the same serosurvey, we investigated PPRV age-seroprevalence and household survey data to determine specific management risk factors for increased PPRV circulation, to explore spatial variation

in the force of infection at multiple scales, and to identify the age cohort(s) responsible for PPRV transmission among sheep, goats, and cattle. We used generalized linear mixed models within a catalytic framework to calculate the force of infection (FOI, per capita infection rate of susceptible hosts) and reproductive numbers using both an age constant and piecewise constant model. We used a machine learning approach to identify specific management risk factors for PPRV seroconversion such as confinement and grazing practices, seasonal camp and market attendance, herd size, and demographics. We found the dentition-based age group with the highest FOI for sheep and goats was 1.5-2 years of age, and 3.5-4.5 years of age for cattle. Pastoral management systems had higher FOI and a wider range of ages with a higher FOI than agropastoral systems. Insights from this investigation of specific management practices will lead to improved control strategies through feasible changes in non-vaccination practices, geographical areas and host species to target, and discovery of additional ecological mechanisms driving PPRV seroconversion.

Ccr4–Not maintains genomic integrity by controlling the ubiquitylation and degradation of arrested RNAPII

Haoyang Jiang, Marley Wolgast, Laura M. Beebe, Joseph C. Reese.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences

The Ccr4–Not complex regulates essentially every aspect of gene expression, from mRNA synthesis to protein destruction. The Not4 subunit of the complex contains an E3 RING domain and targets proteins for ubiquitin-dependent proteolysis. Ccr4–Not associates with elongating RNA polymerase II (RNAPII), which raises the possibility that it controls the degradation of elongation complex components. Here, we demonstrate that Ccr4–Not controls the ubiquitylation and turnover of Rpb1, the largest subunit of RNAPII, during transcription arrest. Deleting NOT4 or mutating its RING domain strongly reduced the DNA damage-dependent ubiquitylation and destruction of Rpb1. Surprisingly, in vitro ubiquitylation assays indicate that Ccr4–Not does not directly ubiquitylate Rpb1 but instead promotes Rpb1 ubiquitylation by the HECT domain-containing ligase Rsp5. Genetic analyses suggest that Ccr4–Not acts upstream of RSP5, where it acts to initiate the destruction process. Ccr4–Not binds Rsp5 and forms a ternary complex with it and the RNAPII elongation complex. Analysis of mutant Ccr4–Not lacking the RING domain of Not4 suggests that it both recruits Rsp5 and delivers the E2 Ubc4/5 to RNAPII. Our work reveals a previously unknown function of Ccr4–Not and identifies an essential new regulator of RNAPII turnover during genotoxic stress.

ABSTRACTS

The effects of neonicotinoid seed treatments on cotton extrafloral nectar

Asher G. Jones, Kelli Hoover, Gary W. Felton
Presenter affiliation: Entomology
Poster 11

Extrafloral nectar (EFN) is a sugary substance produced by many plants from non-floral structures. Rather than facilitating pollination like its floral counterpart, EFN is thought to play a role in plant indirect defence by providing sustenance for natural enemies such as ants and parasitoid wasps. EFN production is often strongly upregulated in response to plant damage and evidence suggests that it is regulated by the plant hormone jasmonic acid. There is currently little known about how human activities such as the use of pesticides could affect plant regulation of this resource. Neonicotinoids are the most widely used class of insecticides globally. These nicotine-like chemicals are often applied prophylactically as seed treatments (NSTs) to crops including maize, soybean and cotton. The active ingredients are taken up systemically and translocated throughout the plant to provide protection against insect pests. Neonicotinoids and their metabolites can also affect plant hormone signalling pathways or act as plant hormone mimics (1), and NSTs may alter the expression of plant defence compounds (2). Whether NSTs could also alter plant indirect defences such as EFN has received little attention. In this study we measured the effects of imidacloprid and clothianidin NSTs on the quantity and composition of cotton (*Gossypium hirsutum*) EFN. We found no effect of seed treatment on the quantity of soluble solids produced by nectaries in either undamaged or damaged plants. Untargeted metabolomics analysis using gas chromatography-time of flight-mass spectrometry of carbohydrates and amino acids will inform whether NSTs affect the composition of cotton EFN. The active ingredients of imidacloprid and clothianidin were detected in cotton EFN using enzyme-linked immunosorbent assays at 122 ± 11 and 77 ± 17 ppb, respectively. Bioassays using the parasitoid wasp *Cotesia marginiventris* will investigate how feeding on EFN from NST plants affect longevity and parasitisation success. This study provides insight into how systemic insecticides may affect plant resources and natural enemies of herbivores.

ABSTRACTS

FRO3 plays an integral role in whole plant iron homeostasis in *Arabidopsis*

Brendon Juengst, Anshika Jain, Erin Connolly.
Presenter affiliation: Plant Biology
Poster 15

Iron deficiency is a major nutritional problem for human populations throughout the developing world and the majority of people acquire iron primarily from plant sources. Additionally, iron bioavailability is a major limiting factor in about 30% of arable croplands worldwide. An improved understanding of iron uptake and homeostasis is necessary to help combat both issues. We are focused on understanding the role of a mitochondrially-localized ferric iron reductase (FRO3) in cellular iron dynamics and whole plant iron homeostasis. While FRO3 is expressed throughout the plant, its expression is greatest in the vasculature. Knockout of FRO3 causes a 50% reduction in mitochondrial iron content and also alters whole plant iron sensing. fro3 lines accumulate 1.2X as much iron as WT plants do, while showing an increased iron deficiency response compared to WT suggesting that while accumulating more total iron, they sense some level of iron deficiency. Furthermore, RNA-seq data suggests that fro3 lines have an altered genomic response to iron deficiency, and sense a greater iron deficiency than WT. These data show that loss of FRO3 disrupts Fe homeostasis and suggest that vascular mitochondrial iron content may play an important role in whole plant iron homeostasis.

Sex-specific responses of mosquitoes to a mosquito-borne viral infection

Karen Kemirembe, Jason L. Rasgon.
Presenter affiliation: Entomology

In humans, hormone-related sex differences dictate various health aspects. For example, they affect how we metabolize medications, sex-specific treatment outcomes, and disease symptoms. In mosquitoes, sex differences are integral in important aspects of their biology, such as female blood-feeding, reproduction, and pathogen transmission making females, and not the males, the primary focus of most research. Male mosquitoes, in contrast, only feed on sugar. Because male mosquitoes can acquire some virus pathogens from their infected mothers by vertical transmission and pass these on to their female counterparts during mating, it is important not to ignore their potential role in disease transmission. Since female mosquitoes are more likely to encounter viral pathogens during blood feeding, we hypothesize that there will be sex-specific differences in the response of mosquitoes to pathogen infection. My research therefore aims to compare responses of male and female Anopheles gambiae mosquitoes to a mosquito- borne alphavirus (O'Nyong Nyong Virus [ONNV]). Preliminary

results on survival comparisons, within- host virus multiplication, and modes of transmission will be discussed. My results will inform on the overlooked possible contributions of male mosquitoes to virus persistence in the environment, help inform research efforts to use male mosquitoes, rather than just the females, as tools to reduce mosquito borne infections, and help predict the potential drawbacks of recently developed techniques such as mosquito sex ratio distortion for controlling vector-borne diseases.

Dual inhibition of SHIP1 and SHIP2 in the treatment of diet induced obesity in mice

Shamara Lawrence, Sandra Fernandes, William G. Kerr.
Presenter affiliation: University of Arkansas at Pine Bluff
Poster 39

Chronic low-grade inflammation in the visceral adipose tissue promotes the onset of obesity. Recent therapeutic approaches have revealed that specific targeting of the inflammatory pathway involved in the immune response in adipose tissue could oppose the effect of inflammatory stressors. Srivastava et al. show that inhibition of the phosphatase SHIP1 (SH2-containing inositol polyphosphate 5-phosphatase) using a small-molecule inhibitor increases the anti-inflammatory response of immunoregulatory cells, which promotes a lean-body state. Because SHIP exists in two paralogs, we would like to determine if specific targeting of both SHIP1 and SHIP2 permits control of diet-induced obesity. Here we examined the effect of dual inhibition of SHIP1 and SHIP2 during excess caloric intake in mice, by treating them with specific target inhibitor, namely 3AC (SHIP1) and As1949490 (SHIP2) for 4 weeks.

We hypothesize that the inhibitors will increase the proliferation of the immunoregulatory cells in adipose tissue, which would promote lean body physiology. We found that treated mice had reduced body weight and fat content. Therefore, the findings suggest that blocking both SHIP1 and SHIP2 will tamper with the inflammatory pathway that perpetuates obesity, causing the mice to not accumulate body fat.

ABSTRACTS

Transcriptome analysis of direct astrocyte-to-neuron conversion

Ningxin Ma, Brendan Puls, Jiuchao Yin.
Presenter affiliation: Neuroscience

Our lab has previously demonstrated direct astrocyte-to-neuron conversion through either overexpression of a single neural transcription factor NeuroD1 (Guo et al., 2014, Cell Stem Cell) or a cocktail of small molecules (Zhang et al., 2015, Cell Stem Cell; Yin et al., 2019, Stem Cell Reports). Such direct reprogramming technology represents a potential remedy for neuronal loss in neurodegenerative diseases and brain injuries. Despite the high conversion efficiency and fast procedure, the molecular events and downstream effectors during the astrocyte-to-neuron conversion are not well understood. To tackle these questions, we used time series analysis of RNA-seq data to characterize the transcriptome dynamics before, during, and after conversion, in order to understand the critical factors mediating such cell transition process. Administration of small molecules (core drugs: CHIR99021, DAPT, SB431542, LDN193189) significantly modified signaling pathways such as hedgehog, Wnt / β-catenin, SMAD and JAK / STAT. These signals rapidly elicited the neurogenic transcription factor network, including the members of bHLH family, and activated both excitatory and inhibitory neuronal genes. Meanwhile, converted cells exhibited a metabolic transition from glycolysis to oxidative phosphorylation, and reduced proliferation rate. Within two weeks, the gene ontology terms associated with neuronal functions became highly expressed. Moreover, we investigated the similarity and difference between chemical reprogramming mediated by core drugs and transcription factor NeuroD1 mediated cell conversion. Although both schemes turned on neurogenic programs, NeuroD1 overexpression showed more specific targeting and expedited conversion process, while core drugs had much broader effects. Together, these findings provide insights into the molecular mechanism of astrocyte-to-neuron reprogramming and may help develop efficient therapy for clinical applications.

Learning the properties of adaptive regions with functional data analysis

Mehreen Mughal, Michael DeGiorgio.
Presenter affiliation: Bioinformatics & Genomics
Poster 14

Identifying regions of positive selection in genomic data remains a challenge in population genetics. Most current approaches rely on comparing values of summary statistics calculated in windows. We present an approach termed SURFDAWave, which translates measures of genetic diversity calculated

in genomic windows to functional data. By transforming our discrete data points to be outputs of continuous functions defined over genomic space, we are able to learn the features of these functions that signify selection. This enables us to confidently identify complex modes of natural selection such as adaptive introgression. We are also able to predict important selection parameters that are responsible for shaping the inferred adaptive introgression events. By applying our model to human population-genomic data we recapitulate signals of adaptive introgression, such as the signal across BNC2 that overlaps with high-probability Neanderthal ancestry tracts, and predict that the split between the donor and recipient population for this region is consistent with the hypothesized Neanderthal-human split.

OpenSimRoot/Sorghum: a novel tool for in silico analysis of a stress tolerant cereal crop

Miranda D. Niemiec, Xiyu Yang, Jonathan P. Lynch.
Presenter affiliation: Plant Biology
Poster 1

Root architectural and anatomical phenes have proven to play an important role in edaphic stress tolerance in plants. SimRoot is a functional model used to simulate 3D root system architecture and nutrient acquisition in crops. Simulating how root phenotypes interact with the soil environment allows for identification of root traits responsible for increased stress tolerance. Sorghum is a crop that has shown to be relatively drought tolerant due to greater rooting depth. Development of a SimRoot sorghum model will aid in identifying synergistic phenes responsible for greater rooting depth and increased drought tolerance in sorghum.

Receptor tyrosine-kinase ROR is required for dendrite regeneration in *Drosophila* peripheral neurons

Derek M.R. Nye, J. Ian Hertzler, Alex.T. Weiner, Richard M. Albertson, Melissa M. Rolls.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences
Poster 16

While many regulators of axon regeneration have been identified, very little is known about mechanisms that allow dendrites to regenerate after injury. Using a *Drosophila* model of dendrite regeneration, we performed a candidate screen of receptor tyrosine kinases (RTKs) and found a requirement for RTK-like Orphan Receptor, dRor. In contrast, reduction of dRor using RNAi and null mutants had no effect on axon regeneration or normal dendrite development suggesting a specific role

in dendrite regeneration rather than general cell health or growth. Further characterization of the dendrite regeneration phenotype in null mutants indicated dRor is required at early stages of regeneration, and at later timepoints dendrites partially recovered. In mammals, Ror can act as a Frizzled (fz) co-receptor. Accordingly, we tested the role of fz and downstream wnt signaling proteins. Consistent with a role for wnt signaling we found that knockdown of fz, dsh, Axin and CK1ɣ reduced dendrite regeneration. We have found fz signaling through Axin localizes microtubule nucleation machinery in dendrites. We therefore hypothesized that dendrite regeneration would be sensitive to levels of microtubule nucleation proteins. Axon regeneration is not impaired by partial reduction in ɣ-Tubulin, the core nucleation protein. In contrast, we found that partial reduction of ɣ-Tubulin impairs dendrite regeneration. In concert, these data suggest that dRor and fz may work to promote dendrite regeneration by localizing nucleation sites.

The postprandial effect of spice consumption in a high-fat meal on proinflammatory cytokine secretion in overweight/obese men

Ester S. Oh, Kristina S. Petersen, Penny M. Kris-Etherton, Connie J. Rogers.
Presenter affiliation: Nutritional Sciences
Poster 31

Objectives: Postprandial lipidemia is a risk factor for cardiovascular disease. The postprandial inflammation that occurs concurrently with lipidemia following ingestion of a high-fat meal (HFM) may contribute to this association. Numerous individual spices have anti-inflammatory properties in vitro and in vivo in animal models and humans. However, the effect of consumption of a spice blend on inflammatory mediators has not been examined in humans in a randomized controlled trial. The objective of this study was to investigate the postprandial effect of spice consumption delivered in a HFM on inflammatory cytokine responses.

Methods: Overweight/obese (BMI ≥ 25 and ≤ 35 kg/m2), nonsmoking, men (40-65 years old) with elevated waist circumference (≥ 94 cm) and at least one other risk factor for cardiovascular disease were recruited for a 3-period crossover study (n=12). In random order, participants consumed the following dietary interventions: 1) a HFM (1076 kcal, 39% kcal from saturated fat), 2) a HFM containing 2 g of spice blend, or 3) a HFM containing 6 g of spice blend with a ≥ 3-day washout period between each test meal. The spice blend consisted of black pepper, basil, bay leaf, cinnamon, coriander, cumin, ginger, oregano, parsley, rosemary, red pepper, thyme and turmeric. Participants fasted overnight and blood was collected before, and hourly for four hours after the HFM. Peripheral blood

mononuclear cells (PBMCs) were isolated at each time point, and the number of monocytes (CD14+/HLA-DR+) were quantified by flow cytometry. PBMCs were stimulated with lipopolysaccharide (LPS) and pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, IL-8, MCP-1) were quantified by ELISA in the supernatants.

Results: Monocyte number (p=0.001), and the secretion of IL-1β (p=0.036) and TNF-α (p=0.046) from LPS-stimulated PBMCs were significantly elevated during the four-hour time period after HFM consumption compared to the baseline. However, the presence of 6g of spice in the HFM reduced the secretion of IL-6 (p=0.046), IL-8 (p=0.031), TNF-α (p=0.001) and MCP-1 (p=0.063) from PBMCs at 60 min after the meal.

Conclusions: Consumption of a HFM containing a spice blend attenuated postprandial inflammation in overweight/obese men.

Future Studies: Given that spices reduce postprandial inflammation, and chronic low grade systemic inflammation can be alleviated by reducing postprandial inflammation, long-term exposure to spices may reduce chronic low-grade inflammation. We are currently conducting on a 3-period, crossover, randomized, controlled-feeding study designed to investigate the effect of chronic spice consumption (4 weeks) on inflammatory mediators in overweight/obese adults at risk for cardiovascular disease. Our goal is to determine if phenotypic and/or functional changes of monocytes underlie the potential anti-inflammatory effect of spice consumption.

Funding Sources: McCormick Science Institute, Penn State Clinical and Translational Science Institute

Changes in proportion and functions of circulating immune cells during early pregnancy in dairy heifers

Neha Oli, Joy L Pate, Troy L Ott.
Presenter affiliation: Physiology
Poster 36

Introduction: Pregnancy affects immune cell populations in the uterus and peripheral blood of all placental mammals. Because the embryo is an allograft (half DNA from another organism), it could elicit an immune response from the mother that would result in pregnancy termination. In most of the scenarios, the embryo survives, and the pregnancy is established. However, the immune system has

been implicated in early pregnancy losses. Most of these embryo losses occur during the initial days of pregnancy (peri-attachment period). Research from our lab implicated myeloid lineage and lymphoid lineage cells as being regulated during early pregnancy in dairy cattle. Monocytes differentiate into macrophages in tissues including the uterus and we showed that macrophage numbers and function in the uterus is affected by early pregnancy in the uterus. Expression of SIRP Alpha, a marker for tolerogenic cells also increased during the same time. An Increase in Cytotoxic T cells in the uterus during early pregnancy indicated their potential role in angiogenesis to facilitate placentation. All these findings emphasize that the maternal immune system is affected by signals from the embryo during early pregnancy to ensure its survival.

Ongoing research is aimed at further characterizing the changes in circulating monocytes and other blood immune cells during early pregnancy in dairy cows and heifers. Our objective is to determine if circulating monocytes contribute to the increase in uterine macrophages and whether their function is affected by early signals from the developing conceptus. Furthermore, we are comparing these changes between heifers and cows that exhibit reduced fertility.

Methods: Blood was collected from Holstein dairy heifers on Days 14, 17 and 20 of the estrous cycle and Days 14, 17, 20 and 23 of early pregnancy. Immune cells were isolated and labeled with antibodies against different cell surface proteins for flow cytometry to determine the relative proportions of various immune cell types in blood. Flow cytometry data was analyzed using FlowJo software (n=4 heifers/status/Day). Statistical analysis was done using MIXED procedures on SAS.

Results: There was a two-fold increase (P value <= 0.01) in proportion of CD11c+ (expressed on monocytes) cells on Days 14 and 17 of early pregnancy when compared to cyclic heifers. SIRP Alpha expression increased (P value= 0.01) on Day 14 and Day 17 of pregnancy indicating the presence of tolerogenic myeloid lineage cells in the blood. Cytotoxic T cells (CD8 Beta+) also increased (P value < 0.03) on Day 20 of pregnancy. The data here indicates that the proportion of immune cells in the blood are altering during early pregnancy. Increase in expression of immunomodulatory molecule like SIRP Alpha further supports the fact that establishment of pregnancy requires a balance between inflammatory and tolerogenic responses to make an environment more tolerant for survival of the embryo.

ABSTRACTS

The role of synonymous mutation in cancer

Yiyun Rao, Nabeel Ahmed, Scott Leighow, Justin Pritchard, Edward O'Brien.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences
Poster 27

Synonymous mutations change mRNA sequence but not protein sequence. Studies showed that synonymous mutations can affect protein translation efficiency, splicing process and even protein structure and function. In cancer, the role of synonymous mutation hasn't been fully studied. How synonymous mutations alter gene expression and function and whether they lead to cancer-related phenotype remain unsolved. From analyzing the COSMIC database, we identify synonymous mutations near translation start codon, splice site and elongation area, which are likely to affect protein expression, function and mRNA splicing. While they are recurrent in multiple patients, they are more likely to play a driven role in cancer. To test the role, we introduce synonymous mutant into cells to test the protein expression change and functional change. In the previous result, we identified 61 patients in COSMIC has mutation c. 1116 C > T in CHEK2. In protein expression assay, we detected a decrease in GFP fluorescence intensity of CHEK2 synonymous mutant when tagging CHEK2 with GFP on C terminus.

Proximity-dependent biotin labeling reveals the spatial organization of the *Plasmodium* DOZI/CITH/ALBA complex

Kelly T. Rios, Scott E. Lindner.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology
Poster 17

Plasmodium transmission between mammalian hosts and the mosquito vector is integral to the parasite's lifecycle and the spread of disease. The transmission stages represent major parasite population bottlenecks, and as such are ideal points of intervention for malaria eradication. A phenomenon that may be exploited for such intervention is the translational repression of specific transcripts, in which genes are proactively transcribed and selectively blocked from translation. These mRNAs are stored in membraneless cytosolic messenger ribonucleoprotein (mRNP) granules, until transmission occurs and translational repression is relieved. RNA-binding proteins of the DOZI/CITH/ALBA complex localize to distinct cytosolic mRNP granules in both asexual and sexual stage parasites. However, this complex is only known to be functionally important for translational repression in female gametocytes. Moreover, no mechanism for how this functional switch from

asexual to sexual stage parasites is appreciated. Therefore, I have leveraged the complementary strengths of conventional formaldehyde crosslinking-immunoprecipitation and proximity-dependent biotinylation (BioID) approaches coupled to LC/MS/MS to determine if the spatial organization of this complex correlates with its function. Here, I have C-terminally tagged (e.g. GFP-; BirA*::GFP-) two members of the DOZI/CITH/ALBA complex, PyDOZI and PyALBA4, that have been experimentally located to complexes found at the 5' and 3' ends of mRNAs, respectively. This strategy enables the determination of spatial interactions, from which changes in the subcellular organization of proteins within this complex may be inferred, and whether the extension/compaction of mRNA correlates with translational status in asexual blood stage parasites and gametocytes. Additionally, I will use single-molecule RNA Fluorescence in situ Hybridization (smFISH) to confirm mRNA compaction of translationally repressed transcripts in female gametocytes.

Acquiring deep water during drought: rice root traits for drought tolerance

Jenna E. Reeger, Kathleen M. Brown.
Presenter affiliation: Plant Biology
Poster 5

Drought causes huge yield losses each year in cereal crops, including rice. Developing rice lines with better root traits for drought tolerance is a sustainable way to increase rice production and promote food security. Root anatomy, comprising the internal tissues in roots, has not been well studied, especially in different classes of roots over time in response to stress. Two rice genotypes, IR64 (lowland, drought susceptible) and Azucena (upland, drought tolerant), were grown in greenhouse mesocosms and subjected to vegetative-stage drought stress by cessation of watering 2 weeks after germination, which resulted in increasingly dry upper soil layers but continued availability of moisture in deeper soil. Plants were harvested weekly from 2-6 weeks after germination, and root anatomical traits were measured for each root class using laser ablation tomography. Root classes included thick and thin deep (older) nodal roots, thick and thin shallow (younger) nodal roots, and lateral roots.

Azucena had fewer but deeper roots compared to IR64, allowing Azucena to access deep water to produce greater shoot biomass than IR64. Azucena showed more variation in anatomical root traits within root classes and greater response to drought compared to IR64, suggesting that greater plasticity contributes to its drought tolerance. Root class had a significant impact in both genotypes on all nodal root anatomical traits, with xylem traits least impacted. Both Azucena and IR64 reduced root cross-sectional area in all classes in response to drought, but Azucena maintained greater root cross-sectional

area overall compared to IR64 in both treatments. Under control conditions, Azucena had greater total and mean metaxylem area, metaxylem number, and theoretical axial hydraulic conductance (conductance) than IR64. Under drought stress, both genotypes had less total and mean metaxylem area and conductance, particularly in thick shallow roots, though Azucena still maintained larger vessels and greater conductance than IR64. In both genotypes, thick nodal roots had greater total metaxylem vessel area, metaxylem vessel number, and conductance at the base (shallow, old) than near the tip (deep, young). In general, nodal root anatomy was more responsive to drought treatment than lateral roots. Azucena performed better under drought stress than IR64 by accessing deep water and maintaining higher root axial hydraulic conductance. These results suggest a complex temporal, genotype-specific response of rice root classes to drought stress.

CsrA-mediated translational activation in *Escherichia coli*

Stephanie Poly, Phil Bevilacqua, Tony Romeo, Paul Babitzke, Andrew Renda.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology
Poster 21

Originally identified as a repressor of translation, CsrA is the primary component of the conserved global regulatory Csr network. This system regulates many cellular processes including biofilm formation, motility, carbon metabolism, stringent response, and cell envelope stress. CsrA represses translation of numerous genes by binding to its mRNA target, thereby inhibiting ribosome binding. However, no example of CsrA-mediated translational activation has been reported. From an integrated transcriptomics study, we identified ymdA as having the strongest CsrA-mediated activation across the E. coli transcriptome. Here, we investigated the mechanism of CsrA-mediated activation of ymdA and found that CsrA activates ymdA post-transcriptionally. Electrophoretic mobility shifts, RNase T1 footprinting, and in vitro coupled transcription-translation assays revealed two critical CsrA binding sites in the leader region of the ymdA transcript. In vivo reporter fusion assays showed that CsrA activates ymdA expression at the post-transcriptional level. Furthermore, loss of binding at either of the two critical CsrA binding sites abolished CsrA-dependent activation. Computational RNA structure prediction mapping revealed an RNA hairpin upstream of the start codon that sequesters the Shine Dalgarno sequence (SD), which would inhibit ribosome binding. This hairpin also contains of one of the two critical CsrA binding sites, with the other site just upstream. Our results are consistent with a model in which bound CsrA destabilizes the SD-sequestering hairpin such that ribosomes can bind and initiate translation. Although the function of YmdA is not established, we hypothesize that CsrA-mediated activation of ymdA expression inhibits biofilm formation.

ABSTRACTS

Wildflower meadow restoration on surface mines

Sarah Rothman, Andy Cole, Mary Ann Bruns, Marvin Hall.
Presenter affiliation: Ecology
Poster 9

We are investigating the influence of soil amendments on the success of a native wildflower seed mix (NWSM) in surface mine restoration. Restoring surface mines to the forested ecosystems present before mining is difficult due to rocky, nutrient-poor soils and intense competition from non-native species. Inactive surface mines often become grasslands dominated by few species and often show little sign of succession, even decades later. Native wildflowers could increase biodiversity and improve soil quality, thus rebuilding native communities and increasing time to succession; however, NWSM has not been shown to meet the legal minimum requirement of 70% vegetative coverage post-mining in unamended soil. We seek to determine if additional nutrient or organic matter inputs could increase NWSM success with regard to coverage and biodiversity while improving soil quality.

To do so, we seeded a NWSM in experimental plots on a surface mine in Philipsburg, PA. Plots were either treated with inorganic fertilizer, low or high levels of spent mushroom compost, or left untreated in a randomized complete block design to account for soil heterogeneity. Percent coverage for the entire plot and community composition within a central frame were assessed biweekly from June through November. Soil samples were collected at the beginning and end of the season to identify potential changes in pH, nitrate content, labile carbon, organic matter content, and bulk density.

Surprisingly, control plots surpassed or equaled amended plots in percent coverage, species richness, and proportion of seedlings from the mix, contradicting prior results by suggesting that a NWSM can meet coverage standards without amendment. While many species previously growing on the mine successfully invaded the experimental plots, contributing to overall coverage, non-composted plots have significantly higher proportions of seedlings from the NWSM than composted plots. If nutrient and organic matter inputs were not a significant factor in the NWSM success, it may be site-specific features that allowed vegetation to flourish; results from restoration projects in urban environments, which present similar problems such as compaction and low-nutrient content, support the conclusion that initial soil characteristics have more influence on vegetative growth than management action. Future research should focus on identifying soil characteristics that may allow mining companies, private landowners, and government agencies to successfully establish wildflower meadows on surface mines.

ABSTRACTS

Pharmacological disruption of an ApiAP2 transcription factor in the human malaria parasite *Plasmodium falciparum*

Timothy Russell, Erandi DeSilva, Gabrielle Josling, Gianni Panagiotou, Manuel Llinás.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology
Poster 18

Malaria is a disease caused by the replication of obligate intracellular parasites within the red blood cells of an infected host. The human malaria parasite *Plasmodium falciparum* has a complex life cycle that enables it to be transmitted between human hosts by a mosquito vector. Measurement of mRNA abundance during the parasite life cycle has revealed that precisely timed transcriptional control is necessary for successful replication and transmission. Remarkably, the parasite is predicted to control the transcriptional timing of 3000 or more protein coding genes using a family of only 27 sequence specific DNA binding transcription factors: the Apicomplexan AP2s (ApiAP2s). The ApiAP2s are named for their homology to the plant specific AP2 family of proteins, a feature which makes them an attractive target for intervention. To date, a handful of *Plasmodium* ApiAP2 proteins are known to be essential for the generation of developmental stages required for parasite transmission. Here, we report the in silico prediction, followed by genetic and biochemical interrogation, of a small molecule that disrupts the DNA binding of the ApiAP2 transcription factor PF3D7_1466400. The molecule, termed ‘Compound G’, has specific activity against PF3D7_1466400 DNA binding in vitro as measured by inhibition of its ability to bind its cognate DNA sequence in a gel shift assay. Addition of Compound G to cultured blood stage *Plasmodium falciparum* causes a growth arrest. Interrogation of the parasite transcriptome during growth arrest revealed that many downregulated genes are predicted to be bound in their promoter regions by PF3D7_1466400, suggesting that the observed growth phenotype is a result of PF3D7_1466400 being prevented from activating transcription at its cognate loci. A decreased occupancy of PF3D7_1466400 at specific genomic loci was demonstrated by chromatin immunoprecipitation followed by quantitative PCR. This provides evidence that disruption of PF3D7_1466400 DNA binding takes place in vivo. Molecular genetic work is underway to conditionally knock down the expression of PF3D7_1466400. We predict that this will phenocopy the growth defect and transcriptional phenotype observed following dosage of parasites with Compound G.

ABSTRACTS

The mechanism of reiterative transcription at the pyrG promoter

Yeonoh Shin, Katsuhiko Murakami.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology
Poster 28

Reiterative transcription is a non-canonical form of RNA synthesis in which a nucleotide specified by a single base in the DNA template is repetitively added to the nascent transcript. We previously determined the final stage of reiterative transcription complex (RTC) from the pyrG promoter, which showed a presence of 8 bases poly-G RNA and its 5' end of RNA directed toward the main channel of RNAP (1). Here, we report a series of the X-ray crystal structures of the RTC at the early stage of RNA synthesis and RTC with pyrG promoter variants containing base substitution at the template DNA -1 position to reveal how poly-G is guided toward the Rifampin-binding pocket followed by the main channel of RNAP. Additionally, we performed biochemical assays including the monitoring 2-AP fluorescence from the template DNA during transcript slippage (both equilibrate and kinetics) and the in vitro transcription assays for monitoring the length of RNA produced from the pyrG promoter variants. These structures together with biochemical studies presented here reveal the mechanism of the reiterative transcription at the pyrG promoter.

Development of a peptide-based diagnostic test for bovine tuberculosis

Sreenidhi Srinivasan, Gareth Jones, Maroudam Veerasami, Gobena Ameni, Martin Vordermeier, Vivek Kapur.
Presenter affiliation: Animal Science

Bovine tuberculosis (bTB) is a chronic inflammatory disease of zoonotic and economic significance caused by Mycobacterium bovis. Although the tuberculin skin test has been the primary ante-mortem diagnostic test for bTB since the 1890s, it has several limitations, including a high degree of variability in the manufacture and quality of tuberculin available, and interference with vaccination programs with Bacille Calmette–Guérin (BCG) strains by sensitizing immunized animals. Hence, it is increasingly recognized that reliable, easy to produce, fit-for-purpose diagnostic assays that can differentiate infected and vaccinated animals (DIVA) are an essential prerequisite for the implementation of future (vaccination based) control programs alongside conventional test and slaughter approaches.

Here, we evaluated the performance characteristics of a fusion protein and a novel peptide formulation as defined skin test antigens. We expressed M. bovis antigens ESAT-6, CFP10 and Rv3615c as a single fusion protein, and also synthesized a set of overlapping peptides representing each of these antigens was chemically synthesized. Both IFN-γ release assays (IGRAs) and skin tests on experimentally infected animals, field reactors and naïve animals were performed to determine diagnostic sensitivity and specificity. Data were analyzed using GraphPad Prism 7.

The peptide cocktail induced a stronger IFN-γ response compared to the fusion protein in Peripheral Blood Mononuclear Cells (PBMCs) collected from M. bovis-infected cattle (n = 10; P = 0.0004), while both antigens induced an equivalent skin test response in experimentally infected cattle (n = 24; P = 0.83). In contrast, no measurable skin test or in vitro IFN-γ response was observed in naïve control animals (n = 20) or BCG vaccinates (n = 10), suggesting that the response was highly specific. We followed this up with skin tests performed in naturally infected animals identified in Ethiopia, an endemic country for bTB. The results demonstrated that our peptide cocktail better than the current tuberculin skin test standard in field conditions.

Taken together, optimization of a novel peptide formulation provides proof-of-principle for the rational design of defined antigens for the development of reliable, cost-effective and BCG vaccination-compatible bTB diagnostics where conventional test and cull strategies are neither feasible nor practicable.

Impacts of immune challenge on thermoregulation by *Bombus impatiens* queens

Hannah Stewart, Ruud Schilder.
Presenter affiliation: Entomology

Bumblebees are extremely important pollinators; however, their populations are in decline. One potential contributor to this decline is parasitic infection. Infections induce an immune response, which is an energetic drain on many biological processes. Often this manifests as a decrease in energy allocation to reproductive output. However, for bumblebees, energetic input to reproduction extends beyond egg production. This includes significant investment in thermoregulation, which is an organism's ability to maintain a body temperature different than ambient temperature. Thermoregulation is essential to bumblebee flight and foraging ability, and, importantly, brood incubation of their developing larvae. Throughout the summer and fall, workers will forage and incubate the larvae as queens are solely laying eggs. In a previous study, we demonstrated that worker

immune responses are inversely correlated with thermoregulatory ability, i.e., these traits trade-off energetically. Specifically, immune challenged bumblebees are unable to recover from chill coma as quickly as their healthy counterparts. However, in newly established colonies, it is queens who are solely responsible for brood provisioning. Recovering from chill coma provides a proxy for exiting diapause, and also for foraging at low ambient temperatures, e.g., during cold mornings. Therefore, we here examine if immune challenge impacts gyne chill coma recovery, and if this is similar to the patterns exhibited by workers.

Use of CRISPR/Cas9-mediated genome editing to examine the role of S-locus F-box protein-containing SCF complexes in S-RNase-based self-incompatibility in *Petunia inflata*

Linhan Sun, Justin S. Williams, Shu Li, Lihua Wu, Wasi A. Khatri, Patrick G. Stone, Matthew D. Keebaugh, Teh-hui Kao.
Presenter affiliation: Plant Biology
Poster 19

Self-incompatibility (SI) is an intraspecific reproductive barrier, by which pistils reject self-pollen to prevent inbreeding, but accept non-self pollen to promote outcrossing. SI possessed by Petunia involves multiple polymorphic S-locus F-box (SLF) genes and a single polymorphic S-RNase gene. 17 SLF genes have been identified in both S2- and S3-haplotypes of P. inflata, and all their encoded proteins, S2-SLF1 to S2-SLF17, and S3-SLF1 to S¬3-SLF17, are assembled into similar SCF (Skp1–Cullin1–F-box) E3 ubiquitin ligase complexes in pollen. Each complex also contains pollen-specific Skp1-like protein (PiSSK1) and Cullin1 (PiCUL1-P), and a conventional RBX1 (PiRBX1). For a given S-haplotype, all paralogous SLFs are thought to collectively mediate ubiquitination and degradation of non-self S-RNases, but not self-S-RNase, resulting in cross-compatible, but self-incompatible, pollination. To address the role of SCFSLF complexes in SI, we used CRISPR/Cas9 to separately knockout PiSSK1 and S2-SLF1 in S2S3 plants, generating two frameshift indel alleles for each gene. We used bud-selfing to obtain progeny homozygous for each allele and free of the Cas9 transgene. S2 pollen carrying either indel allele of PiSSK1 was incompatible with pistils of seven otherwise compatible S-genotypes, but compatible with pistils of an S3S3 transgenic plant in which production of S3-RNase was suppressed by an antisense S3-RNase gene, and with pistils of immature flower buds, which produce little S-RNase. S2 pollen carrying either indel allele of S2-SLF1 was incompatible with pistils producing S3-RNase, but compatible with pistils producing S7-RNase or S12-RNase. These results are consistent with our finding that, among the 17 SLFs produced by S2 pollen, S2-SLF1 is the only one that interacts with S3-RNase, whereas, in addition to S2-SLF1, two other SLFs, S2-SLF2 and

S2-SLF5, interact with S7-RNase and S12-RNase, respectively. All these results taken together suggest that PiSSK1 and SLF proteins function specifically in SI and are essential for cross-compatibility.

The optimization of butyrate production by resistant starch

June Teichmann, Darrell Cockburn
Presenter affiliation: Food Science
Poster 37

A healthy gut microbiome has been linked to prevention of multiple inflammatory related diseases like inflammatory bowel disease, obesity, and colorectal cancer. One of the mechanisms at work is thought to be bacterial production of butyrate, a short chain fatty acid (SCFA) known to provide energy to colon cells and promote apoptosis in cancerous cells in addition to preventing inflammation. Resistant starch (RS) is an emerging fiber that has been shown to modify the SCFA profile in favor of butyrate production within the large intestine. This study uses a human fecal community in a batch fermentation to determine how multiple types (type 2, 3 and 4) and sources (whole food potato starch and pure potato, tapioca, high amylose maize, green banana, and tigernut starch) of RS and addition of primary degrading bacteria (*Ruminococcus bromii* and *Bifidobacterium adolescentis*) affect butyrate production. Briefly, samples containing a fecal inoculum and one of the above treatments were incubated at 37°C for 24h in an anaerobic chamber. All RS were predigested with pancreatin and amyloglucosidase and ethanol sterilized before use. Samples were analyzed for organic acid production (butyrate, acetate, propionate, lactate, formate, and succinate were being tracked in this study) and 16S and whole genome sequencing data. Preliminary experiments with the various RS showed that each produced a unique fermentation profile. RS within a whole food source (potato) proved to induce higher levels of butyrate compared to its purified counterpart (isolated potato starch). Addition of primary degraders *R. bromii* and *B. adolescentis* were shown to have positive and negative effects, respectively, on butyrate production. Results indicate that different fermentation pathways were activated by different RS sources and that butyrate production seems to be activated at the expense of lactate production, and vice versa. Results can vary depending on the initial community, so further experiments will repeatedly test these variables using different starting microbiomes. Sequencing data will also be collected to develop a deeper understanding of the fermentation profiles produced by each microbiome. Our research on RS and how to manipulate its effect on bacterial metabolomes can eventually be used to mitigate the growing number of illnesses tied to an unhealthy gut microbiome.

ABSTRACTS

Conversion of human glioblastoma cells into neurons by neuronal transcription factors

Xin Wang, Zifei Pei, Aasma Hossain, Tania Tsila Barnatan, Yuting Bai, Gong Chen.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences
Poster 25

Background: Glioblastoma is one of the most severe primary cancer types in the central nervous system. Because of genomic and epigenetic heterogeneity, GBM is infiltrative and resistant to conventional treatments such as radiation, chemotherapy and molecular targeting drugs. Glioblastoma often arises from astrocytes, which can be directly converted into neurons according to our earlier work, so we hypothesize that glioblastoma cells might also be converted into non-proliferating neurons. This trans-differentiation therapy might provide a unique approach for glioblastoma treatment.

Methods: NeuroD1 was chosen as one of the candidate factors in this study because we have shown its critical roles in astrocyte-to-neuron conversion. Neurog2 and Ascl1 were also tested to understand possible different conversion mechanisms. Single transcription factor or GFP was overexpressed via retrovirus in human glioblastoma cells. Twelve hours after virus infection, culture medium was changed into differentiation medium containing neurotropic factors for neuronal maturation. Immunostaining and other tests were conducted at different days post infection.

Results: Retrovirus yielded high infection efficiency in fast-proliferating glioblastoma cells. All three factors tested were capable of converting glioblastoma cells into neuron-like cells efficiently. Besides morphological change, robust pan-neuronal markers were expressed during the conversion, such as immature neuronal markers DCX, Tuj1 and mature neuronal makers MAP2, NeuN. Majority of the converted cells from glioma were immunopositive for glutamatergic neuron marker vGluT1 and hippocampal neuron marker Prox1. Reactive astroglial marker GFAP decreased after conversion, but cancer marker EGFR and IL13Ra2 remained during conversion. Cell proliferation was inhibited during conversion indicated by Ki67 and BrdU. Robust synaptic puncta along dendrites were found in glioma-converted cells, indicated by SV2 immunostaining. Patch-clamp recordings revealed that most of the converted neurons could fire multiple action potentials or single action potential.

Conclusion: Our data suggest that several neuronal transcription factors are capable to convert human glioblastoma cells into neuron-like cells efficiently. The converted cells obtained a variety of neuron-specific markers with functional synaptic networks and active electrophysiological properties. This neuronal conversion was also confirmed by reduction of reactive astroglial marker GFAP. Although

some cancer markers remain in the converted neurons, glioblastoma cells stopped proliferating once being converted. In summary, our study suggests that converting human glioblastoma cells into neurons could be a potential therapeutic approach for glioblastoma treatment to at least control cancer cell proliferation and inhibit tumor progression.

RNA G-quadruplex form “microaggregates” that are temperature sensitive in biologically relevant spermine conditions

Allison Williams, Philip Bevilacqua.
Presenter affiliation: Biochemistry, Microbiology, & Molecular Biology
Poster 22

G-quadruplex have been predicted to be globally unfolded in eukaryotes and depleted in prokaryotes, with the working hypothesis that helicases play a major role in their unfolding (1). However, prokaryotic and eukaryotic cells contain different small molecules and ions and these could contribute to these observations as well. We set out to investigate small biomolecules that might play a role in G-quadruplex destabilization at biological salt conditions. Utilizing a variety of RNA G-quadruplex-forming sequences with different numbers of tiers and different loop length, we conducted a variety of biophysical experiments such as size exclusion chromatography (SEC), UV thermal denaturation, dynamic light scattering (DLS), and circular dichroism (CD) spectroscopy to investigate the role of polyamines in G-quadruplex stability. We determined that the polyamine spermine (+4 biological charge) causes sequence specific “microaggregation” of G-quadruplex, which melt at a reduced temperature, just slightly above physiological temperatures. We hypothesize that these microaggregates could be biologically relevant and help to play a role in global destabilization of G-quadruplex structures in eukaryotes.
(1) Guo, J. U., Bartel, D.P. Science. 2016, 353(6306), aaf5371.

ABSTRACTS

Diet and exercise-induced weight maintenance, alone and in combination with a whole tumor cell vaccine, delays mammary tumor growth and reduces tumor-infiltrating MDSCs expressing PD-L1 and IDO

Yitong Xu, William J. Turbitt, Andrea M. Mastro, Connie J. Rogers
Presenter affiliation: Physiology
Poster 42

Purpose: Physical activity and the prevention of weight gain can reduce breast cancer risk and increase survival. However, whether the immune system plays an important role in mediating this cancer preventive effect remains unknown. We have previously shown that diet and exercise-induced weight maintenance (WM), in combination with a whole 4T1.2luc tumor cell vaccine (VAX), significantly reduced mammary tumor growth and metastases in the 4T1.2luc murine mammary tumor model. This occurred concurrently with an elevation in tumor antigen-induced splenic IFN-g production and a reduction in the accumulation of splenic myeloid-derived suppressor cells (MDSCs) at day 35 post-tumor implantation. The goal of the current study was to determine if WM+VAX alters the tumor microenvironment at an early stage of tumor progression (day 24 post-tumor implantation), which may contribute to reduced tumor growth and enhanced immune outcomes at day 35 post-tumor implantation.

Experimental Design: Female BALB/c mice were randomized into sedentary, weight gain (WG) or exercising (access to voluntary running wheel), weight maintenance (WM) groups (n=22-27/group). After 8 weeks on the intervention, all mice were orthotopically injected with 5x104 4T1.2luc cells into the fourth mammary fat pad and continued on their intervention. Once injected, both WG and WM mice were further randomized into vaccination (VAX) or vehicle control (VEH) groups (n=10-15/group) and administered 1x106 irradiated 4T1.2luc cells (VAX) or HBSS (VEH) at day 7, 14 and 21 post-tumor implantation. Mice were sacrificed at day 24 post-tumor implantation and tumor-infiltrating immune cells were isolated for analyses.

Results: Both WM+VEH and WM+VAX groups showed a significant reduction in primary tumor growth and splenomegaly compared to both WG groups ($p<0.001$). Flow cytometric analysis demonstrated that the combination of WM+VAX significantly reduced total tumor-infiltrating MDSCs and MDSCs expressing programmed death-ligand 1 (PD-L1) and indoleamine 2,3-dioxygenase (IDO) compared to WG+VEH ($p<0.05$). This finding was consistent with a 1.5-4.5 fold decrease in the gene expression level of Pdcd1, Ido1 and Ifng in the total tumor infiltrates.

Conclusions: These results suggest that the combination of weight maintenance and a whole tumor cell vaccine may be altering both the number and immunosuppressive capacity of tumor-infiltrating MDSCs, which may contribute to the reduction in tumor growth and metastasis observed in previous experiments.

Impact: Preventing weight gain through diet and exercise may induce beneficial changes in host immune response to cancer, and may be an important recommendation in combination with immune-based therapies to enhance efficacy and improve clinical outcomes.

The aryl hydrocarbon receptor mediates resistance to a chemotherapeutic agent in head & neck cancer

Brandon A. Yusko, Iain A. Murray, Gary H. Perdew.
Presenter affiliation: Molecular, Cellular, & Integrative Biosciences
Poster 32

Tumor relapse and concurrent metastasis arising from acquired chemotherapy resistance is a dominant factor in cancer morbidity and is associated with poor prognosis. Thus, novel treatment regimens aimed at combating acquired resistance and increasing therapeutic efficacy are required. The aryl hydrocarbon receptor (AHR), a soluble receptor activated by endogenous and exogenous low molecular weight compounds (e.g. dietary/microbiota tryptophan metabolites, environmental pollutants and tobacco-smoke carcinogens), is frequently associated with aggressive tumorigenesis and metastasis. Our recent work in both monolayer culture and 3-D spheroid culture has demonstrated that inhibition of AHR signaling limits head and neck squamous cell carcinoma (HNSCC) motility and pro-inflammatory gene expression, critical elements of metastasis. Furthermore, under the nutrient-deprived conditions associated with the tumor microenvironment, we have shown that activation of AHR in HNSCC by endogenous and exogenous ligands promotes HNSCC survival when challenged with standard chemotherapeutic agents (e.g. 5-fluorouracil). These data combined with the recent advent of potent AHR inhibitors, strongly indicate that attenuation of AHR signaling in HNSCC may enhance sensitivity to chemotherapy and thus limit tumor relapse. Additionally, these studies provide mechanistic insights in to how the AHR contributes to chemotherapeutic resistance.

NOTES