DMU MENTORED STUDENT RESEARCH PROGRAM

RESEARCH IS VITAL AND AT DMU STUDENTS ARE VITAL TO RESEARCH.

July 21, 2017

DES MOINES UNIVERSITY
OFFICE OF RESEARCH

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OFFICE OF RESEARCH

Mentored Student Research Program
July 21, 2017
Des Moines University, Des Moines, IA

Dear Mentored Research Students

On behalf of the Research and Grants Committee, welcome to the Des Moines University (DMU) Mentored Student Research Program closing program. This event represents and celebrates the culmination of your summer research experiences. We know you have worked hard over the last seven weeks; tackling challenges in the laboratory; learning new skills; and building new professional relationships. We were able to see firsthand the engagement, inquisitive minds, and commitment that each of you brought to this year's program and we are thoroughly impressed. Many of you will continue to work on your respective research projects over the coming academic year, and we encourage you to do so.

The goal of the DMU Mentored Student Research Program is to provide opportunities for students to develop their skills as researchers by receiving coaching and mentorship from faculty. Dissemination of new knowledge, by faculty and student researchers, supports Des Moines University's mission. You have contributed to the fulfillment of this mission by your participation in the Mentored Student Research Program. We encourage you to continue to develop as a researcher, and thank you for your hard work this summer.

This program would not be possible without the support of many individuals and departments across campus. The University has invested in this program financially, researchers across campus have taken the time to deliver research talks, and your mentors have invested time in your professional growth and education. Please take the opportunity to thank your mentors for their investment this past summer.

Keep asking questions and searching for answers! I wish you the best of luck in your future endeavors.

Sincerely,

Jeffrey Gray, PhD
Vice President for Research and Global Initiatives, Des Moines University
Jeffrey.Gray@dmu.edu

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Agenda

Time	Agenda	Location
8:30 am	**Registration, Breakfast, and Poster Viewing**	**SEC Square**
9 am	**Welcome** Jeffrey Gray, PhD *Vice President for Research and Global Initiatives*, *Des Moines University*	**SEC Auditorium**
9:15 am	**Keynote Address: It Takes a Village: A Translational Scientist's Journey** Alexandra J. Greenberg, PhD, MPH *Assistant Professor of Epidemiology, Center for Clinical and Translational Science, Mayo Clinic* • Describe the role of team science in translational biomedical research • Distinguish between cross-, multi-, inter-, and trans-disciplinary research • Evaluate what types of research teams individuals can participate in • Consider how to grow into an inter- or trans-disciplinary research team	
10:15 am	**Poster Viewing**	**SEC Square**
10:45 am	**Evidence of Different Growth Strategies in Phytosaurs from the American Southwest** *Robert Katz, Cooperstown Graduate Program* Mentor: Sarah Werning, PhD	**SEC Auditorium**
11 am	**The *Acinetobacter nosocomialis* Strain M2 T6SS Effector Ase1 Degrades Peptidoglycan** *James Dorosh, DO'20* Mentor: Michael Carruthers, PhD	
11:15 am	**Group Picture**	**Outside SEC Auditorium**
11:30 am	**Poster Viewing**	**SEC Square**
12:20 pm	**Lunch**	**SEC Auditorium**
12:30 pm	**Food Insecurity in Iowa: A Predictive Modeling Approach** *Christine Jackson, DO'20* Mentor: Simon Geletta, PhD	
12:45pm	**Mediterranean Diet Pattern in the Multi-Ethnic Study of Atherosclerosis** *Pooja Gottumukkala, DO'21* Mentor: Jun Dai, MD, PhD	
1 pm	**Adjourn**	

Keynote Speaker

Alexandra J. Greenberg, PhD, MPH

Assistant Professor of Epidemiology, Center for Clinical and Translational Science, Mayo Clinic

- **BA:** Grinnell College
- **MPH:** Quantitative Methods, Harvard T.H. Chan School of Public Health
- **PhD:** Mayo Graduate School of Biomedical Sciences
- **Postdoctoral Fellowship:** Cancer Epidemiology, Mayo Clinic
- **Cancer Prevention Fellowship:** Health Communication and Informatics Research Branch, Behavioral Research Program, and Outcomes Research Branch, Healthcare Delivery Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute

Dr. Greenberg indicated she has no financial relationships to disclose relevant to the content of this CME activity.

Continuing Education Credit

- **DO:** Des Moines University (DMU) is accredited by the American Osteopathic Association (AOA) to provide osteopathic continuing medical education for physicians. DMU designates this program for a maximum of 3.0 AOA Category 2-A credits and will report CME and specialty credits commensurate with the extent of the physician's participation in this activity.
- **DPM:** Des Moines University (DMU) is approved by the Council on Podiatric Medical Education as a provider of continuing education in podiatric medicine. DMU has approved this live activity for a maximum of 3.0 continuing education contact hour(s).
- **MD:** This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Iowa Medical Society (IMS). Des Moines University (DMU) is accredited by the IMS to provide continuing medical education for physicians. DMU designates this live activity for 3.0 *AMA PRA Category 1 Credit(s)™.* Physicians should claim only the credit commensurate with the extent of their participation in the activity.
- **Other:** This live activity is designated for 3.0 *AMA PRA Category 1 Credit(s)™.*

Keynote Speaker Presentation Slides

It Takes A Village:
A Translational Scientist's Journey

Alexandra J. Greenberg, PhD, MPH
Assistant Professor of Epidemiology, Center for Clinical and Translational Science, Mayo Clinic
Translational Integrator, Mayo Clinic Center for Regenerative Medicine

Des Moines University Mentored Student Research Program
Friday, July 21, 2017

Overview

- What is team science?
- What are the different types of research teams?
- Case Study
  - Personalizing Multiple Myeloma Treatment
- Summary
- Acknowledgements
- Questions

Disclosures

- I have no financial relationships to disclose relevant to the content of this CME activity.

What is team science?

- **Team science**
  - "Scientific collaboration, i.e., research conducted in an interdependent fashion by more than one individual, including research conducted by small teams and larger teams"
- **Science Teams**
  - Team science conducted by a group of 2-10 individuals; groups bigger than that are referred to as "larger groups"

"Enhancing the Effectiveness of Team Science," The National Academics of Science, 2015.

Intended Learning Objectives

- Describe the role of team science in translational biomedical research
- Distinguish between cross-, multi-, inter-, and trans-disciplinary research
- Evaluate what types of research teams individuals can participate in
- Consider how to grow into an inter- or trans-disciplinary research team

What is team science?

- **Team effectiveness**
  - "A team's capacity to achieve its goals and objectives… leading to improved outcomes for team members"
- **The Science of Team Science**
  - "Interdisciplinary field that empirically examines the processes by which large and small scientific teams, research centers, and institutes organize, communicate, and conduct research"

"Enhancing the Effectiveness of Team Science," The National Academics of Science, 2015.

Overview

- What is team science?
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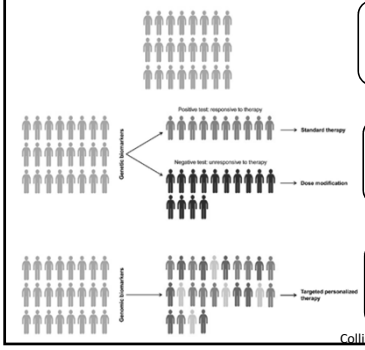
Case Study: Personalizing Myeloma Treatment
Defining Personalized Medicine



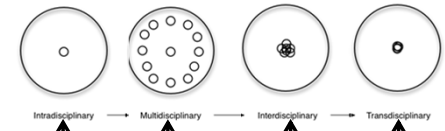
Current Standard of Care: Treatments designed for "average" patient

Stratified Medicine: Tailors treatment to patients based on genetics and other biomarkers

Personalized Medicine: Tailors treatment to patients based on genetics, environment, and lifestyle

Collins and Varmus, NEJM, 2015

What are the different types of research teams?



Transdisciplinary: Experts work jointly to develop new framework and paradigm extending beyond that existing in their field

Stokols *et al*., Am J Prev Med. 2008. 35(2s):S77-S89)
http://www.arj.no/wp-content/2012/03/interdisciplinary.png

Case Study: Personalizing Myeloma Treatment
Defining Personalized Medicine

"The right treatment for the right patient at the right time"

- Also known as "individualized medicine" or "personalized medicine"
- Not a new concept
- Large-scale application of individual patient characteristics not previously feasible…

Collins and Varmus, NEJM, 2015

Overview

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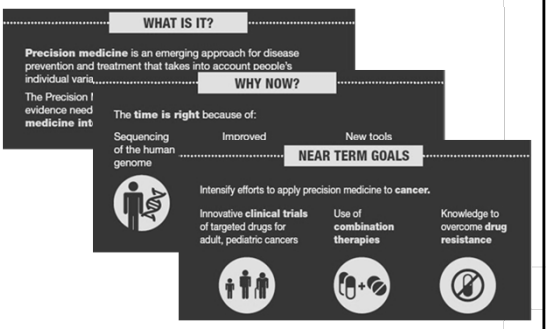
Case Study: Personalizing Myeloma Treatment
Defining Personalized Medicine

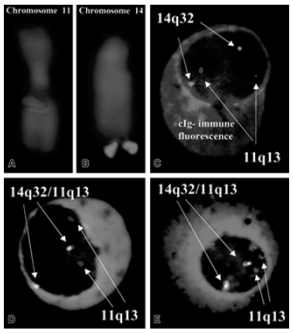
- New technologies can now make this possibility a reality
  - Large-scale biologic databases
    - Sequencing of the human genome
    - 1000 Genomes Project
    - The Cancer Genome Atlas
  - Highly sensitive and specific methods for characterizing patients
    - Genomics, proteomics, metabolomics
    - Increasingly diverse cellular assays
    - Mobile health technology
  - Computational tools
    - "Big Data"

Case Study: Personalizing Myeloma Treatment
Defining Personalized Medicine



Collins and Varmus, NEJM, 2015

Case Study: Personalizing Myeloma Treatment
Multiple Myeloma Cytogenetics



http://www.londonhaematology-oncology.co.uk/myeloma/

Case Study: Personalizing Myeloma Treatment
Multiple Myeloma

SEER Incidence and U.S. Mortality age-adjusted rates and trends by race/ethnicity (2005-2009).

Race/Ethnicity	Incidence rate per 100,000	Morality rate per 100,000
All races	5.8	3.4
White	5.3	3.2
Hispanic	5.4	2.8
Non-hispanic	5.3	3.2
Black	11.7	6.4
Asian/Pacific Islander	3.5	1.7
Amer Ind/Alaska Nat	4.5	2.4
Hispanic	5.4	2.7

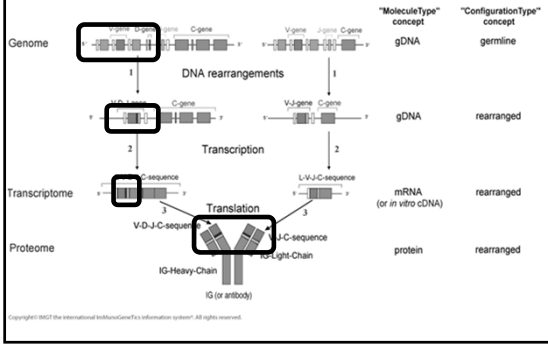
Kyle, RA *et al.*, 2003. Mayo Clin Proc 78(1): 21-33.
Jemal, A. *et al.* 2010. CA Cancer J. Clin. 60(5): 277-300.

Case Study: Personalizing Myeloma Treatment
Research Objectives

Cytogenetic Type	Cytogenetic Abnormality	Frequency (%)	Myeloma Risk Type
Hyperdiploid MM	Hyperdiploid	45	Standard
t(11;14) MM	t(11;14)(q13;q32)	25	Standard
t(4;14) MM	t(4;14)(p16;q32)	15	Intermediate
t(14;16) MM	t(14;16)(q32;q23)	5	High
t(6;14) MM	t(6;14)(p21;q32)	3	Standard
t(14;20) MM	t(14;20)(q32;q11)	2	High
Unclassified MM	All others	5	Standard

Objective: Is the distribution of the four most clinically assessed myeloma-associated abnormalities [t(11;14), t(4;14), del13q and del17p] different in black patients compared with white patients?

Case Study: Personalizing Myeloma Treatment
Multiple Myeloma



Case Study: Personalizing Myeloma Treatment
Building the team…

- **Objective:** Is the distribution of the four most clinically assessed myeloma-associated abnormalities [t(11;14), t(4;14), del13q and del17p] different in black patients compared with white patients?
- **What expertise is needed to conduct this study?**

Dr. Rajkumar Hematology/ Oncology

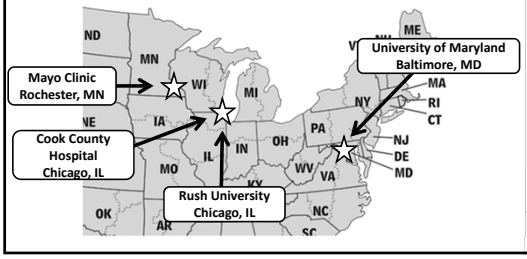
Dr. Vachon Epidemiology

Dr. Ketterling Cytogenetics

Dr. Greenberg Translational Science

Case Study: Personalizing Myeloma Treatment
Expanding the team…

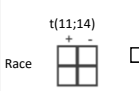
- **Challenge:** Not a great range of diversity of patients in our area
- Needed to partner with experts with access to racially and ethnically diverse patients



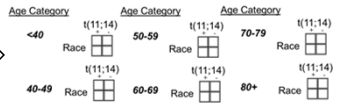
Case Study: Personalizing Myeloma Treatment
Methods

- All analyses conducted using R Statistical Software
- Differences for each cytogenetic abnormalities were compared individually by race using Chi-squared tests
- Cochran–Mantel–Haenszel tests were conducted to determine whether there were significant differences in cytogenetic abnormality by age and race

Chi-squared test



Cochran-Mantel-Haenszel Test



Case Study: Personalizing Myeloma Treatment
Methods

- Multi-center study
  - Mayo Clinic (Rochester, MN, USA)
  - Three major institutions with large African American clinical practices:
    - University of Maryland at Baltimore, MD, USA
    - Cook County Hospital, Chicago, IL, USA
    - Rush University Medical Center, Chicago IL, USA.
- Patient data were collected according to a standardized case report form developed at Mayo Clinic
- All patient data were de-identified and replaced with a study code

Case Study: Personalizing Myeloma Treatment
Results

Demographics	Black		White		P-value
Total, n (%)	292		471		
Cook County Hospital	71	24.3%	0	0.0%	
Rush University Medical Center	50	17.1%	0	0.0%	
University of Maryland	121	41.4%	0	0.0%	
Mayo Clinic	50	17.1%	471	100.0%	
Gender, n (%)					<0.001
Male	130	44.5%	283	60.1%	
Female	162	55.5%	188	39.9%	
Age, n (%), years					<0.001
<40	14	4.8%	9	1.9%	
40–49	44	15.1%	34	7.2%	
50–59	93	31.8%	121	25.7%	
60–69	94	32.2%	169	35.9%	
70–79	35	12.0%	118	25.1%	
80+	12	4.1%	20	4.2%	

Greenberg *et al*, Blood Cancer Journal, 2015

Case Study: Personalizing Myeloma Treatment
Methods

- Inclusion criteria
  - Newly diagnosed (not relapsed)
  - Diagnosed between 1 January 2006 and 31 January 2013
  - Had clinical cytogenetic and FISH analyses available in the medical record within year before or 6 months after diagnosis
- Information regarding probes and clinical results for t(11;14), t(4;14), monosomy 13/del13q and del17p on FISH testing was abstracted
- Patients categorized based on the presence/absence

Case Study: Personalizing Myeloma Treatment
Results

Demographics	Black		White		P-value
Primary cytogenetic abnormality, n (%)					
t(11;14)	19	6.5%	83	17.6%	<0.001
t(4;14)	16	5.5%	47	10.0%	=0.04
Monosomy 13/del 13q	85	29.1%	223	47.3%	<0.001
Monosomy 17/del17p	23	7.9%	61	13.0%	=0.032
None of the studied abnormalities	185	63.4%	163	34.6%	<0.001

Greenberg *et al*, Blood Cancer Journal, 2015

Case Study: Personalizing Myeloma Treatment
Results

Cytogenetic abnormalities	Black		White		P-value (within race, by age)	P-value (within age, by race)
	Total	%	Total	%		
t(11;14)					0.93	<0.001
<60 years of age	151	5.3%	165	18.8%		
60+ years of age	141	7.8%	307	16.9%		
t(4;14)					0.81	0.04
<60 years of age	151	4.6%	165	11.5%		
60+ years of age	141	6.4%	307	9.1%		
Monosomy 13/del 13q					0.58	<0.001
<60 years of age	151	30.5%	165	44.2%		
60+ years of age	141	27.7%	307	48.9%		
Monosomy 17/del17p					0.3	0.027
<60 years of age	151	9.9%	165	13.9%		
60+ years of age	141	5.7%	307	12.4%		
None of the studied abnormalities					0.95	<0.001
<60 years of age	151	62.9%	165	34.5%		
60+ years of age	141	63.8%	307	34.5%		

Case Study: Personalizing Myeloma Treatment
What kind of team was this?

Dr. Rajkumar Hematology/ Oncology | **Dr. Vachon** Epidemiology | **Dr. Ketterling** Cytogenetics | **Dr. Greenberg** Translational Science

- But wait… how do we know what treatments might work best for each cytogenetic subgroup?

… TO THE LAB!

Case Study: Personalizing Myeloma Treatment
Conclusions

- Frequency of the t(11;14) translocation is significantly lower in blacks compared with whites; difference was similar across age
- Lower rate of the t(4;14) translocation
- 63.4% of black patients did not have any of the four abnormalities that we studied compared to 34.6% of whites patients
- Hypothesize that MM in black patients is associated with either excess prevalence hyperdiploidy

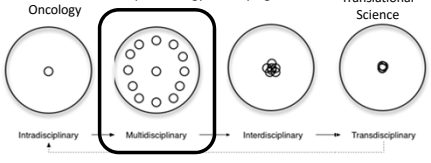
Case Study: Personalizing Myeloma Treatment
What kind of team was this?

Dr. Rajkumar Hematology/ Oncology | **Dr. Vachon** Epidemiology | **Dr. Ketterling** Cytogenetics | **Dr. Greenberg** Translational Science

Dr. Jelinek Immunology

Case Study: Personalizing Myeloma Treatment
What kind of team was this?

Dr. Rajkumar Hematology/ Oncology | **Dr. Vachon** Epidemiology | **Dr. Ketterling** Cytogenetics | **Dr. Greenberg** Translational Science



http://www.arj.no/wp-content/2012/03/interdisciplinary.png

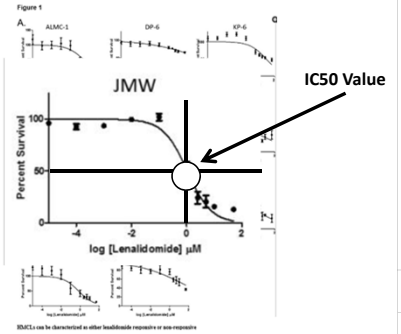
Case Study: Personalizing Myeloma Treatment
Back to the lab…

- **Objective 2:** Is there an association between response to immunomodulatory agents (such as lenalidomide) and cytogenetic subtype of multiple myeloma?

- **Methods (in brief)**
  - Human cell lines representative of the major cytogenetic subtypes of myeloma cultured
  - Variety of doses of lenalidomide administered at hour 0, along with IL-6
    - Doses ranged from 0.00001 to 50 uM
  - Tritiated thymidine added at 80 hours post-plating
  - Cells harvested and measured using scintillation counter

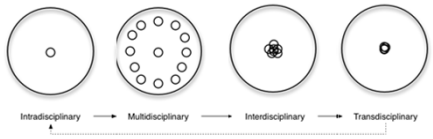
Greenberg AJ *et al*, Eur J Haematol. 2013. 91(6):10.1111/ejh.12192

Case Study: Personalizing Myeloma Treatment
Back to the lab…



Greenberg AJ *et al*, Eur J Haematol. 2013. 91(6):10.1111/ejh.12192

What kind of team are you on?



Intradisciplinary: Within a single discipline

Multidisciplinary: Sequential process; experts work independently and then combine efforts in end

Interdisciplinary: Interactive process; work jointly and draw from their area of expertise to address a common problem

Transdisciplinary: Experts work jointly to develop new framework extending beyond that existing in their field

Case Study: Personalizing Myeloma Treatment
Back to the lab…

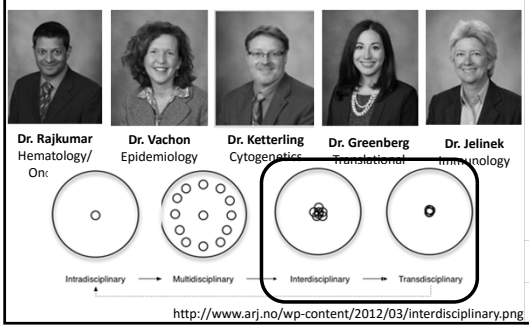
Cytogenetic Subtype	Cell Line	Calculated IC50 with IL-6 (μM) (95% C.I.)	Response Classification
Hyperdiploid MM	KP-6	13.31 (6.297, 28.14)	UR
	DP-6	N/A	UR
	DT-6I	5.211 (1.338, 20.3)	UR
t(11;14) MM	RM43	N/A	UR
	U266	0.521 (0.318, 0.852)	R
t(4;14) MM	JMW	1.049 (0.734, 1.499)	R
t(14;16) MM	ANBL-6	3.036 (1.786, 5.163)	R
t(6;14) MM	KMM-1	N/A	UR
t(14;20) MM	ALMC-1	2.608 (1.074, 6.332)	R
	ALMC-2	1.199 (0.799, 1.801)	R

Greenberg AJ *et al*, Eur J Haematol. 2013. 91(6):10.1111/ejh.12192

Take-Home Messages

- Biomedical research is no longer a solo activity– must work with others to do meaningful work!
- The type of team you work with can determine how far the impact of your research can stretch
- Inter- and trans-disciplinary teams can result in quicker translation of findings to patients

Case Study: Personalizing Myeloma Treatment
What kind of team was this?



http://www.arj.no/wp-content/2012/03/interdisciplinary.png

Acknowledgements

- Vincent Rajkumar, MD
- Celine Vachon, PhD
- Diane Jelinek, PhD, and the Jelinek Lab
- Rhett Ketterling, PhD
- Joyce (Joy) Balls-Berry, PhD

Student Keynote Abstracts

♦ 10:45 am G ♦

Evidence of Different Growth Strategies in Phytosaurs from the American Southwest

Robert Katz[1] and Sarah Werning, PhD[2]

[1] Science Museum Studies, Cooperstown Graduate Program, Cooperstown, NY
[2] Department of Anatomy, Des Moines University, Des Moines, IA

Phytosaurs were an exclusively Triassic, globally-distributed group of reptiles and distant ancestors of crocodylians and birds. Despite their ubiquity, little is known about their biology other than what is broadly observed based on anatomy, such as size and diet. Their superficial resemblance to crocodylians has led to the hypothesis that their lifespan and physiology were also similar.

Histological studies of fossils yield valuable information on the life histories of extinct animals. These data can be used to test hypotheses about whether ecologically similar taxa share growth strategies. Despite the accessibility of phytosaur material, only one phytosaur specimen has previously been examined histologically.

We sampled eight femora and three tibiae from phytosaurs collected from the Chinle Formation (NM) and Dockum Group (TX). These contemporaneous formations represent inland river and coastal ecosystems, respectively. All sampled phytosaurs grew faster than similarly-sized modern crocodylians, contradicting the hypothesis that the two distantly-related taxa shared similar life histories due to ecological and anatomical convergence. However, within phytosaurs, there is a range of growth rates. They also vary in their cortical to spongy bone ratio (associated with diving depth in modern aquatic vertebrates), suggesting that niche partitioning occurred in areas where multiple taxa were present, or between different ages within a single taxon.

Our results establish higher variation in the growth rates of phytosaurs than previously hypothesized. Future studies will continue to explore links between age, size, and ecology in this group.

♦ 11 am G ♦

The *Acinetobacter nosocomialis* Strain M2 T6SS Effector Ase1 Degrades Peptidoglycan

James Dorosh, DO'20, Rachel Anderson, Michael Carruthers, PhD

Des Moines University, Des Moines, IA

Acinetobacter is a genus of gram-negative, aerobic bacteria that cause high mortality rate infections in susceptible individuals. *Acinetobacter nosocomialis* and *A. baumannii* are responsible for approximately 80% of *Acinetobacter* infections and frequently associated with multidrug resistance. Strain M2, an A. *nosocomialis* isolated from a 1996 hip infection, produces a functional type 6 secretion system (T6SS) that facilitates killing of adjacent bacteria thus conferring increased fitness. Previously, we have shown that mutants deficient in expression of Ase1, a candidate T6SS effector in M2, exhibit a reduction in T6SS mediated killing of *E. coli*. From this we sought to determine the function of Ase1. Based upon a conserved domain search, we hypothesized the Ase1 binds and degrades peptidoglycan. Herein, we used ligation independent cloning and other standard methods to facilitate the heterologous expression of Ase1 in *E. coli* and determine the ability of Ase1-HIS to degrade peptidoglycan via a zymogram assay. Our data indicate that Ase1 can be expressed in the cytoplasm of *E. coli* without overt cell death. In addition, our results suggest that Ase1 degraded peptidoglycan as visualized via zymogram assay. Overall, these data confirm our hypothesis that Ase1 is a M2 T6SS effector and these are the first data to indicate a function for a T6SS effector in any *Acinetobacter* species.

♦ 12:30 pm G ♦

Food Insecurity in Iowa: A Predictive Modeling Approach

Simon Geletta, PhD and **Christine Jackson, DO'20, MPH'22**

Des Moines University, Des Moines, IA

Food security in the United States is an important issue, and it remains a pervasive problem both around the country and in Iowa. Current research evaluates the success of programs, but does not closely examine the variables contributing to food insecurity. The Mid-Iowa Food Insecurity Survey was designed to estimate the prevalence of food insecurity in zip codes within Dallas, Polk, and Warren counties. The survey data was then combined with census data, which contained 18 predictor variables for 50 out of 80 zip codes in the Iowa counties. Data was not provided for each zip code, so a statistical predicative modeling approach was performed using SAS modeling software. To create this model, linear regression estimates were performed on 70% of the data from the census variables, after which a simplified estimation model was created using backwards elimination of the census variables. The remaining 30% of the data was used to validate the predictive power of the regression model. Of the 18 predictor variables given in the census data, 4 were identified as significant predictors after the model was tested against the validation data. These 4 variables were then used to create estimates for zip codes from which data were not collected. This model can be used by policy makers and researchers, to better understand the variables that influence food insecurity, as well as develop programs and services. This predictive modeling approach to food insecurity can be replicated by other researchers throughout the United States.

♦ 12:45 pm G ♦

Mediterranean Diet Pattern in the Multi-Ethnic Study of Atherosclerosis

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Objective: Mediterranean Diet is believed to be cardioprotective. We aimed to describe this diet in a subsample of the Multi-Ethnic Study of Atherosclerosis (MESA) cohort that was studied for diet, microRNA, and coronary heart disease.

Methods: 180 participants older than 40 years and free of cardiovascular disease and diabetes at baseline were included from the MESA cohort. Data on usual diet at baseline was collected with a 120-item food-frequency questionnaire and a modified Mediterranean Diet Score (MDS) was created. A higher MDS represented a healthier diet that was moderate in alcohol consumption, low in meat and dairy, and rich in fruits, nuts, vegetables, whole grains, fish, legumes, and monounsaturated fatty acids. A Wilcoxon rank sum or Kruskal-Wallis test was used to examine group differences in the MDS.

Results: MDS ranged from 0-9 with a median value of 4.00 (interquartile range 3.00 - 6.00). MDS were statistically different among age groups [median (interquartile range): 4.00 (3.00-5.00) for ages 45-59 years, 5.00 (3.00-6.00) for ages 60-69 years, and 5.00 (4.00-6.00) for ages ≥70 years; $P<0.05$] and research sites [median (interquartile range): 4.00 (3.00-6.50) for North Carolina, 5.00 (4.00-5.50) for New York, 4.00 (3.50-6.00) for Maryland, 4.00 (3.00-5.00) for Minnesota, 4.00 (3.00-5.00) for Illinois, and 5.00 (4.00-6.00) for California; $P<0.05$]. MDS was not statistically different by gender or race (Caucasians, Chinese-Americans, African-Americans, and Hispanics) ($P>0.05$).

Conclusion: Older adults have healthier diets compared to younger individuals. Those living closest to the coast have healthier diets compared to those living farther from the coast.

Poster Abstracts

♦ 1 G ♦

Perceived Health and Pain Ratings in the Second and Third Trimester of Pregnancy

Britney Williams, DPT'20 and Catherine Stevermer, PhD

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Introduction: Pelvic pain reportedly affects 16-25% of pregnant women, and can interfere with physical functioning and overall health. Self-reported health ratings are recommended as a reliable measure of health in healthy adults. This descriptive project evaluated changes in perceived health and pain ratings of pregnant women with and without pelvic pain.

Methods: Participants were contacted based on involvement with a previous, on-site study that measured self-reported pain and health on a numeric scale of 0-10 and 1-4, respectively. One month following on-site participation, an electronic survey (Qualtrics, Provo, UT) emailed to each subject inquired about their health, physical activity, and any falls that occurred. Responses were categorized based on presence of pain and progression of pregnancy since laboratory participation (continuing 2nd trimester, continuing 3rd trimester, 2nd to 3rd trimester, or 3rd to delivery).

Results: Respondents (N=47) reported an average pain rating of 0.8±0.4 (no pain) and 2.6±1.3 (pain). Perceived health ratings were recorded as 3.3±.02 (no pain) and 3.2±.01 (pain). Pain worsened for every pain category except the continuing 3rd trimester group, where pain decreased. Four 2nd to 3rd trimester women who reported pain had symptoms worsen. Perceived health ratings remained consistent among each group, with the continuing 2nd trimester control group reporting the lowest rating (2.9±0.7).

Conclusion: Pain appeared to increase for most participants, and perceived health ratings seemed to remain unchanged. Perceived health and pain ratings appear to be unrelated in this project.

♦ 2 UG ♦

Motorcycle Helmet Law Mandate: An Imperative for Iowa

Janelle Knight, PA-C[1], **Megan Bristow[2],** Pamela Duffy, PhD[3]

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Controversy surrounding motorcycle laws has led to inconsistencies in helmet use, more injuries and fatalities, and higher associated costs.

The **purpose** of this project was to investigate the history of helmet laws and propose policy solutions for the state of Iowa, one of only three states without helmet legislation. As a top public health cause of morbidity and mortality, motorcycle injuries result in severe economic consequences to individuals, states, and society. A comprehensive literature review using PubMed, ProQuest, as well as governmental reports, yielded state and national trend data, and summaries of state laws.

Our **results** concluded that mandatory helmet legislation is the most efficacious way to promote and enforce helmet use. Universal helmet legislation dramatically decreases head injuries, disabilities, and fatalities. Unhelmeted motorcyclists were more likely to be uninsured or rely on government assistance, increasing head injury incidence, and, subsequently, total expenses to the public. Nationally, it is estimated that $1.4 billion could be saved if all states implemented universal helmet laws. A policy paper was prepared for the Iowa Public Health Association to educate Iowa legislators.

This issue is extremely **significant** to Iowa because of the economic and the human toll in death and disability from failure to enact helmet legislation. A helmet mandate in Iowa is especially relevant due to recent budget shortfalls and deficits in Medicaid spending. This research project raises awareness of the need for a helmet law in Iowa, is supported by current data, and furthers advocacy work of public health and healthcare professionals.

♦ 3 G ♦

Investigation of Metabolic Responses in Macrophages Following C1q-Stimulation and AMPK Activation

Sumar Quint, DO'21 and Suzanne Bohlson, PhD

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C1q is the recognition component of the classical complement pathway, and is required for efficient clearance of apoptotic cells (efferocytosis). Deficiency in C1q results in autoimmunity and leads to the development of lupus. Our laboratory is investigating molecular mechanisms and enzymes involved in C1q-dependent immune responses. Macrophage stimulation with C1q has been previously shown to activate AMP-activated protein kinase α-1 (AMPK). AMPK plays an important role in cellular metabolism, but also has been shown to influence the immune response, including cytokine expression and phagocytosis. Here we tested the hypothesis that C1q modulates ATP levels in macrophages under conditions where AMPK is modulated. We utilized a bioluminescent assay to compare nucleotide levels in macrophages, and investigated these levels in relation to AMPK phosphorylation and activation. 5-aminoimidazole-4-carboxamide ribonucleotide (AICAR) stimulated mouse and human monocyte derived macrophages (HuMDM) showed increased AMPK activity, with no significant changes in ADP/ATP ratios measured after 18 hours. However, the assay failed to detect robust changes in ADP/ATP ratios in proliferating versus apoptotic Jurkat cells, conditions that should have served as a control in the assay. C1q stimulated HuMDM showed a lower ADP/ATP ratio than control macrophage, however there was no change in AMPK activation under these conditions. In conclusion, AMPK activation did not show a significant correlation to changes in ADP/ATP levels using the bioluminescence assay, and the data suggests a more sensitive assay for nucleotide detection will be required in future experiments.

♦ 4 UG ♦

FcγR-Mediated Signaling is Regulated by C1q

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A deficiency in C1q, the recognition component in the classical complement pathway, is the strongest genetic link to development of Systemic Lupus Erythematosus (SLE). SLE is an autoimmune disease that results from the build-up of immune complexes (IC), and subsequent IC-mediated propagation of the inflammatory response through *Fcγ receptors (FcγR) on myeloid cells.* It has been previously demonstrated that C1q regulates *FcγR-mediated phagocytosis, and here we tested the hypothesis that C1q regulates signal transduction downstream of FcγRs.* Incubation of both human monocyte-like THP-1 cells and primary mouse bone marrow derived macrophages (BMDM) on C1q triggered an enhancement of *FcγR-mediated* phagocytosis compared to the control. To better understand this regulation, an attempt was made to look at two known downstream kinases of the *FcγR*, ERK1/2 and Syk, in both BMDMs and THP-1 cells. Stimulation with IC enhanced ERK1/2 phosphorylation in THP-1 and BMDM, however no increase in Syk phosphorylation was detected under these conditions. C1q treatment reduced ERK1/2 phosphorylation in both THP-1 cells and BMDMs, suggesting that ERK1/2 activity is regulated by C1q. Future studies will require optimizing conditions to detect Syk, as well as identifying the functional consequence of C1q-dependent ERK1/2 regulation.

♦ 5 G ♦

Conditional T-Cell Knockout of the Cytosolic Branched Chain Aminotransferase 1 (BCAT1) in Mice: Breeding Strategy

Sean McNitt, DO'20, Michael Boyer, BS, Elitsa Ananieva, PhD

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T cell activation, during the development of an immune response, is nutrient demanding. The amino acid, leucine, is indispensable for T cell function and survival. To explore the role of leucine metabolism in T cells, we developed a breeding strategy to create a T-cell specific deletion of the branched chain aminotransferase 1 (BCAT1), an enzyme that catalyzes the first step in leucine degradation. We used the Cre-LoxP strategy, where a gene of interest (BCAT1) is flanked between 2 LoxP sites in a BCAT1 floxed mouse. Another mouse, called CD4-Cre, contains a Cre recombinase, that catalyzes recombination between the 2 LoxP sites, under the control of T cell specific CD4 promoter, so that the BCAT1-LoxP gene is deleted from T cells. A series of three breedings were undertaken to achieve a total deletion of BCAT1 from T cells (T-BCAT1$^{-/-}$ mice). The first breeding, between heterozygous BCAT1 floxed mice, resulted in 26.3% of the offspring being homozygous BCAT1 floxed mice. The second breeding between homozygous BCAT1 floxed and CD4-Cre mice, created an offspring that was heterozygous BCAT1 floxed and hemizygous CD4-Cre mice with a 57.1% distribution. In our third breeding, heterozygous BCAT1 floxed, hemizygous CD4-Cre mice will be bred with homozygous BCAT1 floxed mice to achieve deletion of BCAT1 from T cells of around 25% of the offspring. We will use this mouse model to explore the role of BCAT1 in T cell immunity which will ultimately lead to the development of new metabolic approaches for immunotherapy and cancer.

♦ 6 G ♦

Lactate, mTORC1, and AMPK are Differentially Impacted by Modulations in Leucine Uptake and Catabolism in Bone Sarcomas

William Reiche, DO'20, Shailer Martin, DPM'19, MBS'20, Michael Boyer, BS, Elitsa Ananieva, PhD

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Osteosarcoma and chondrosarcoma are rare, devastating bone sarcomas with low survival rates. Currently, the prognosis for individuals with bone sarcomas depends upon the patient's response to chemotherapy and surgical intervention. A novel approach to treat bone sarcomas is to target leucine, an indispensable amino acid for tumor growth. Our objective was to elucidate how modulations in leucine uptake and catabolism impact metabolic (glycolysis) and signaling (mammalian target of rapamycin complex1, mTORC1, and AMP-activated protein kinase, AMPK) pathways in osteosarcoma (143B) and chondrosarcoma (SW1353) cells. To achieve this objective, we treated 143B and SW1353 cells with a leucine antagonist, N-acetyl-leucine-amide (NALA), and an inhibitor of leucine degradation, gabapentin, for 24hrs and measured: lactate release and activity of mTORC1 and AMPK in the presence of 0 and 5mM glucose. Next, we compared the effects of NALA and gabapentin to rapamycin (inhibitor of mTORC1) and 2-Deoxy-D-glucose (2-DG, inhibitor of glycolysis). Our results showed that NALA and gabapentin inhibited lactate release from 143B cells in the presence of 5mM glucose, which strongly correlated with decreased mTORC1 but increased AMPK activity. In contrast, there was either no effect (gabapentin) or an increase (NALA) in lactate secretion from SW1353 that correlated with increased mTORC1 activity under 0 and 5mM glucose. Compared to 2-DG, NALA, and gabapentin showed milder inhibitory effect on lactate release from 143B cells, which could result in less side effects in cancer patients. Thus, inhibiting lactate secretion by targeting leucine could be a promising anticancer treatment in patients with osteosarcoma but not chondrosarcoma.

♦ 7 UG ♦

A New Function of *Candida albicans* EFG1 in Starvation Survival

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EFG1 is a critical gene involved with inducing the pathogenic filamentous form of the dimorphic fungus, *Candida albicans.* Although the functions of EFG1 are generally well understood, its role in carbohydrate metabolism has yet to be explored thoroughly. In our lab, we set out to examine the role of EFG1 on starvation survival, and how low viability of an Efg1p-deficient mutant may be due to ineffective storage of the carbohydrate glycogen. To test this correlation in *Candida albicans*, glycogen content and survival rates of the efg1 mutant and the wildtype were tracked during starvation over the course of 5 weeks. At both 4°C and 30°C, our data showed a decrease in viability for the efg1 mutant before a decrease in viability for the wildtype occurred, suggesting that EFG1 plays a critical role in starvation. The cells starved at 30°C showed reduced viability in both the mutant and the wildtype prior to the reduction in viability at 4°C. Results also showcase a decrease in glycogen content just before survival rates decrease, indicating a negative effect of low glycogen stores on viability. Unexpectedly, the cells present at 4°C averaged a lower glycogen content at the start of the experiment than at 30°C. Our preliminary data in this area of research indicates that low glycogen in efg1 is correlated to a low survivability in the cells present after starvation.

♦ 8 G ♦

Characterization of Enzymes Involved in Maltose Utilization by the Sexually Transmitted Pathogen *Trichomonas vaginalis*

Seth Mommsen, DO'21, MSA'17, Prajakta Pradhan, MS, Wayne Wilson, PhD, Andrew Brittingham, PhD

Des Moines University, Des Moines, IA

Trichomonas vaginalis is the causative agent of the sexually transmitted disease trichomoniasis, which is the most prevalent non-viral sexually transmitted infection in the world. *T. vaginalis* is an obligate parasite and depends upon its host for the provision of nutrients required for growth. The vaginal epithelium contains rich glycogen reserves, which are thought to provide the required carbohydrate. Previous studies have shown that *T. vaginalis* secretes multiple glucosidases which degrade vaginal glycogen, supplying simple carbohydrates that support growth. Our current work focuses on the localization of an α-glucosidase that acts on maltose. Other investigators have reported that this α-glucosidase is not secreted, but rather is associated with the surface of the trichomonads. However, the activity has neither been well-characterized nor purified. Here, we have used a simple, colorimetric assay to investigate the localization of α-glucosidase activity in *T. vaginalis*. Analysis of total cellular lysates demonstrate that *T. vaginalis* possess a robust α-glucosidase activity, which does not vary significantly during its growth cycle. While we are unable to detect any α-glucosidase activity released into the growth media during in vitro cultivation of T. vaginalis, analysis of live intact cells suggest that a percentage of activity may be associated with the cell surface of the parasite. Additionally, the amount of total cellular, and cell associated activity is dependent on pH. Future studies will seek to characterize the cell associated α-glucosidase activity further, since inhibition of this enzyme should block growth of the parasite, providing a novel therapeutic avenue.

♦ 9 G ♦

The Effects of T1R3 Deletion on Lipid Metabolism and Atherosclerosis in Apolipoprotein E-Deficient Mice

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Previous data from the Wauson laboratory suggest that inhibition of the T1R3 receptor reduces mTORC1 activation, thereby increasing autophagy. In addition, we observed that T1R3 inhibition decreased gene expression of proteins necessary for cholesterol synthesis in cell lines. It was rationalized that less lipid will accumulate in the livers of T1R3 knockout mice. Previous studies suggest that elevated autophagy and mTORC1 inhibition in vascular smooth muscle cells reduce the progression of atherosclerosis in mice. Thus, our central hypothesis was that the inhibition of the T1R3 receptor will reduce atherosclerotic plaque formation and hepatic steatosis in mice. To test this hypothesis, we generated T1R3 $^{-/-}$ and T1R3 $^{+/+}$ mice bred into the ApoE $^{-/-}$ background. Mice were fed a high fat diet for seven weeks before being euthanized. Blood was collected via cardiac puncture and aortas were harvested. Aortic roots and aortas were stained for neutral lipids with Oil Red O. Livers were collected, sectioned, and stained with both Oil Red O and hematoxylin. Additionally, a cholesterol assay was performed on the mouse serum. While we do not have data from enough mice to run statistical analysis, our preliminary results suggest that the T1R3 deletion may cause a decrease in LDL/VLDL levels in male mice and less hepatic macrosteatosis in both males and females. T1R3 deletion does not appear to strongly affect the percentage of aortic plaque area. Current results imply that therapeutic benefits may be achieved through inhibition of the T1R3 receptor.

♦ 10 G ♦

Very High Concentrations of Various Sugars Do Not Generate Reactive Oxygen Species in THP-1 Cell

Hannah Glanz, DO'21, MSA'21, Vesna Pandurovic, Kevin Carnevale, MD

Department of Microbiology and Immunology, Des Moines University, Des Moines, IA

Sugar and Fructose consumption has dramatically increased in the last 30 years. The principal form is consumption of high-fructose corn syrup (HFCS) found in soft drinks and processed food. The effect of excessive fructose consumption on human health is only beginning to be understood. Fructose has been confirmed to induce several obesity related complications leading to the development of metabolic syndrome, production of fatty liver, and hyperuricemia. These elevated risks drive atherosclerosis and cardiovascular disease which are major causes of morbidity/mortality in patients with metabolic syndrome and have been associated with activation macrophages and formation of the atherosclerotic plaque. This study evaluates the role high concentrations of sugars and HFCS on the reactive oxygen species (ROS) generation in THP-1 cells. THP-1 cells were grown in the presence of in very high concentrations of pure glucose, pure fructose, 42 HFCS, 55 HFCS and 90 HFCS for 24 hours. There was no activation of ROS in THP-1 cells after 24 hours exposure of very high concentrations of various sugars in microplate assays confirmed by microscopy to using CellROX® Deep Red Reagent. The same results were found when growing THP-1 cells in very high concentrations of fructose for 28 days and measuring ROS generation on days 7, 14, 21, and 28. This was compared to the generation of ROS THP-1 cells exposed to Zymosan A. Finally, there was no further generation of ROS in THP-1 cells exposed to oxLDL in combination with very high concentrations of these various sugars.

♦ 11 G ♦

IL-31 Exerts a Powerful Anti-Tumor Effect Against Bladder Cancer

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Background: Bladder cancer (BC) is the second leading cancer of the genitourinary system. IL-31 is a new member of the IL-6 family, mainly produced by Th2 cells. Its role in immunity is very complicated and little is known about its role in cancer. This study was performed to investigate the effect of IL-31 on the growth of bladder cancer.

Methods: Clonogenic survival assay, cell proliferation and caspase-3 activity kits were used to evaluate the effects of IL-31 on cell survival, proliferation and apoptosis of the J82 bladder cancer cell line. We further investigated the possible molecular mechanisms by using RT-PCR.

Results: We found the percentage of colonies of J82 cells decreased after treatment with IL-31. This paralleled the decrease in the OD value of cancer cells after treatment with IL-31. The relative caspase-3 activity in cancer cells also decreased in the presence of IL-31. The anti-proliferative effect of IL-31 on cancer cells correlated with downregulation of the pro-proliferative molecule cyclin D. The pro-apoptotic effect of IL-31 correlated with upregulation of the pro-apoptotic molecule Fas.

Conclusions: IL-31 exerts a powerful anti-tumor effect against bladder cancer by downregulation of cyclin D and upregulation of Fas. Further studies might be helpful to develop a promising immunotherapeutic strategy to treat bladder cancer.

♦ 12 UG ♦

Pumpkin: A Potentially Beneficial Vegetable for Patients with Lung Cancer

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Background: Despite advances in medicine which improve lung cancer survival with targeted therapies and screening, lung cancer is still the leading cause of death in cancer. The beneficial effects of pumpkins for urinary disorders have been known for centuries and recent studies have indicated that it might inhibit growth of some cancers. However, the role of pumpkin in lung cancer has not been investigated. This study was performed to investigate if pumpkin extract (PE) could be beneficial for patients with lung cancer and its possible molecular mechanisms.

Methods: Clonogenic survival assay, cell proliferation and caspase-3 activity kits were used to evaluate the effects of PE on cell survival, proliferation and apoptosis of a widely used lung cancer cell line, A549. We further investigated the possible molecular mechanisms by using RT-PCR.

Results: We found that the percentage of colonies and the OD value of A549 cells decreased in PE group compared to those in medium alone group. The relative caspase-3 activity in cancer cells increased in PE group compared to those in medium alone group. The anti-proliferative effect of PE on cancer cells correlated with downregulation of pro-proliferative molecule cyclin B. The pro-apoptotic effect of PE correlated with downregulation of anti-apoptotic molecule survivin.

Conclusions: PE has an anti-tumor effect on A549 cells by inhibition of proliferation and promotion of apoptosis, suggesting that pumpkin might be a beneficial vegetable for patients with lung cancer.

♦ 13 G ♦

Contribution of Tonic Peripheral Chemoreflex Activation to HIF1α/miR-155 Dependent Renal Fibrosis in Chronic Heart Failure

Michael S. Weinfeld, DO'20[1]*, Shaohan Deng, DO'20[1]*, Jennifer Giles, MA[1], Harold D. Schultz[2], Rodrigo Del Rio[3], Noah J. Marcus, PhD[1]

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Cardiorenal syndrome is a condition characterized by a complex bi-directional relationship between cardiac and renal function in which dysfunction in one organ precipitates dysfunction in the other. Current theories suggest this is due to increased renal sympathetic nerve activity (RSNA) and decreased renal blood flow (RBF), an effect which is mediated in part by tonic hyperactivation of the carotid body chemoreceptors (CBC). These changes in RSNA and RBF are associated with renal fibrosis and decline in kidney function. CBC-mediated increases in RSNA and decreases in RBF may contribute to renal tissue hypoxia, thus causing accumulation of Hypoxia-inducible factor 1-α (HIF1α). Recent studies indicate that HIF1α can activate the pro-fibrotic cytokine Transforming growth factor beta (TGF-β) via microRNA 155 (MiR-155), suggesting a link between renal hypoxia and renal fibrosis in CHF. We propose that enhanced CBC signaling in CHF contributes to renal fibrosis by increasing expression of HIF1α /MiR-155 in renal tissue and that denervation of the CBC (CBD) in CHF will attenuate these changes. CHF was induced in sprague-dawley rats through ligation of the left anterior descending coronary artery (CAL), and CBD was performed (4 weeks post-CAL) by cryogenic ablation of the CBC. RSNA and RBF were measured 8 weeks post-CAL after which the rats were humanely euthanized and renal tissue was collected. Renal cortical and medullary tissue from sham, CHF, and CHF-CBD rats was probed via western blot for expression of HIF1α, phospho-SMAD3, and α-Smooth Muscle Actin. MiR-155 expression will be measured using RT-qPCR.

♦ 14 G ♦

Effect of Peripheral Chemoreflex Denervation on Factors Affecting Renal Sodium Transport in Chronic Heart Failure

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Fluid retention and cardiac congestion resulting from alterations in renal sodium reabsorption exacerbates cardiac dysfunction and is associated with poor prognosis in chronic heart failure (CHF). Under normal circumstances Na(+)-H(+) exchanger isoform 3 (NHE3) plays a major role in controlling sodium reabsorption in the proximal tubule of the kidney, and thus fluid balance. Sodium reabsorption is increased in CHF by renal oxidative stress and inflammation an effect which may be mediated by alterations in NHE3 expression or activity. Increased renal sympathetic nerve activity (RSNA) and decreased renal blood flow (RBF) are known to cause oxidative stress and inflammation, and previous work suggests that increased carotid body chemoreceptor (CBC) activity contributes to increased RSNA and decreased RBF in CHF. Based on this previous work, we hypothesize that denervation of CBC will reduce renal oxidative stress and inflammation as well as expression of NHE3 and sodium reabsorption in the proximal tubule. To address this hypothesis, CHF was induced in Sprague-dawley rats through ligation of the left anterior descending coronary artery (CAL), and CBD was performed (4 weeks post-CAL) by cryogenic ablation of the CBC. RSNA and RBF were measured 8 weeks post-CAL after which the rats were humanely euthanized and renal tissue was collected. Superoxide levels (electron paramagnetic resonance), and expression of IL-8 and NHE3 (western blot) was measured in renal cortical tissue from sham, CHF, and CHF-CBD animals.

♦ 15 G ♦

The Role of Estrogen in Regulating Microglia's Ability to Augment Sympathetic Nerve Activity

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Women have an increased incidence of hypertension shortly after menopause, which is believed to be related to changes in estrogen levels. Estrogen signals through two nuclear receptors, estrogen receptor (ER) alpha and ER beta, as well as membrane-bound G-protein coupled (GP) ER. These receptors have all been localized to various areas of the brain, including the rostral ventrolateral medulla (RVLM) and paraventricular nucleus (PVN) of the hypothalamus which are known to be involved in the regulation of arterial pressure. Previous studies have shown that activation of microglia in the hypothalamus and brainstem may have a role in the development of hypertension by augmenting activity of pre-sympathetic neurons. Our overarching hypothesis is that estrogen inhibits the action of microglia to increase sympathetic activity and this protection would be disinhibited during menopause and lead to elevated blood pressure. The first step in testing this hypothesis was to characterize the expression of estrogen receptors on microglial cells. We used an immortalized microglia cell culture (EOC; ATCC) derived from 10 day old female mice to determine if and what type of estrogen receptors are present. We used Western blot and RT-PCR to characterize the expression of estrogen receptors in these cells. This study is ongoing at this time.

♦ 16 UG ♦

Trichomonas vaginalis UDP-Glucose Pyrophosphorylase: An Important Enzyme During Glycogenesis

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Trichomonas vaginalis is a protozoan parasite responsible for the widespread sexually transmitted disease trichomoniasis. Like many other organisms, *T. vaginalis* uses the branched polysaccharide glycogen as a storage form of carbon and energy, possessing a suite of enzymes that polymerize glucose into glycogen. One such enzyme, UDP-glucose pyrophosphorylase (UDPGase), is responsible for converting glucose-1-phosphate into UDP-glucose, which serves as the glucose donor in glycogenesis. To examine the activity of this protein in *T. vaginalis* during different growth periods, we compared UDPGase activity in cell extracts prepared from 24 hour and 42 hour culture samples. We found no significant difference in activity between the logarithmic (24 hour) and stationary (42 hour) phase of growth, hinting that constant expression of this enzyme might occur during growth. This is of interest since we have previously shown that glycogen synthesis is maximal during logarithmic growth. The *T. vaginalis* open reading frame TVAG_102390 encodes a putative UDPGase. To purify this protein using recombinant expression, we transformed *E. coli* with an expression vector containing previously amplified TVAG_102390. The expressed protein was then purified by column chromatography and found to have activity towards the substrate UDP-glucose. We therefore conclude that the TVAG_102390 open reading frame does indeed encode UDPGase in *T. vaginalis*. We have previously identified, cloned, and expressed recombinantly both glycogen phosphorylase and glycogen synthase from *T. vaginalis.* As we continue to identify and purify these metabolic enzymes, we add to our toolkit of possible targets for growth inhibition and disease prevention.

♦ 17 UG ♦

Renal Inflammation in Sensitization-Induced Hypertension

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A better understanding of the link between inflammation and hypertension could contribute new therapeutic strategies for treating hypertension. Pro-inflammatory molecules, such as tumor necrosis factor (TNF)-α, transcription factors (NFκB), are found in higher abundance in hypertensive patients and animal models than in normotensive controls. Anti-inflammatory cytokines (AIC), such as interleukin (IL)-10, must counter the cellular effects of PIC to maintain homeostasis. We have shown previously that short sensitization periods can have sustained effects on blood pressure; the current study aimed to investigate the balance of PIC and AIC in the kidneys of animals exposed to a sensitization paradigm. In brief, animals were subjected to a one-week sensitization period with sub-pressor infusion of angiotensin (ANG) II, then rested one week followed by infusion of a pressor dose of ANGII. We evaluated the protein abundance of TNFα (a prototypical PIC), IL-10 (a prototypical AIC) and p65 (a subunit of the pro-inflammatory transcription factor, NF-κB) in renal cortex samples from the experimental animals. We found a decrease in renal cortical expression of TNFα and p65 and an increase in IL-10, as compared to control samples. We contend this may be a protective mechanism for the kidney to try to balance the detrimental effects of the sensitization paradigm on blood pressure, as these results counter those found in specific brain regions. Future studies are needed to explore the cross-talk between the central nervous system and peripheral sites in the sensitization of hypertension.

♦ 18 UG ♦

Herpes Simplex Virus 1 Inhibition by Co-Administration of EGCG and the Telomerase Inhibitor MST-312

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It has been estimated that over 80% of all individuals in their sixties show seroprevalence of herpes simplex virus (HSV-1). HSV-1 causes cold sores and blisters, which generally occur around the mouth. Under certain conditions, further complications may occur in an infected individual, including encephalitis or disseminated infections. At this time, antivirals exist for HSV-1, but there is no cure. Mutations in HSV-1 can result in resistance to multiple commonly used pro-drug treatments. Patients infected with drug resistant HSV-1 have limited treatment options. Thus, the need for a novel drug for treatment of HSV-1 is significant.

Two compounds recently studied in our laboratory for their antiviral properties are epigallocatechin gallate (EGCG) and MST-312. EGCG is a flavonoid found in green tea. MST-312 is a telomerase inhibitor with a chemical structure modeled after EGCG. Previous studies have shown that both EGCG and MST-312 can inhibit the HSV-1 life cycle when added alone to infected cultures. In this study, the antiviral properties of combination treatment with MST-312 and EGCG in Vero and HEp-2 cells were assessed using immunoblotting and plaque assays. Additionally, the cytotoxicity of the compounds was measured using trypan blue exclusion. Treatment with MST-312 and EGCG did not increase cytotoxicity compared to controls. The presence of EGCG did not hinder the antiviral effects of MST-312 on HSV-1 progeny virus production and viral protein accumulation in Vero cells. Together, these results support further study into the potential for combination treatment of HSV-1, using EGCG and its chemical analogue MST-312, is warranted.

♦ 19 G ♦

Effects of Stress on the Human Gut Microbiome

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The central nervous system (CNS) and gastrointestinal (GI) tract interact via bidirectional communication, and the microbiota of the gut play an important role in mediating this signaling. Our interest lies in the effect of stress on GI microbiota and the role the microbiome plays in coping with stress. We investigated the relationship between chronic stress and the gut microbiota in our own medical students, by comparing the taxonomic composition present in fecal samples before and after various amount of time in medical school. Incoming first-year medical students were recruited (n=31) for the study. Using stress/anxiety surveys and physiological measures such as plasma cortisol levels, we evaluated their levels of stress before their first year started and at two additional time points (October and December 2016) throughout their first semester. GI microbiome samples were taken to assess gut microbial populations at each time point. Our findings suggest that the reported level of depression increased gradually over the trial. This elevation was accompanied with an overall increase in the ratio of firmicutes: bacteroidetes (F:B), the largest phyla in human gut microbiome. Plasma cortisol levels remained constant between time point 1 and 2, but decreased at time point 3. Perceived stress in students followed a similar pattern. There were notable differences between males and females in reported level of depression. Results yield from this study may shed light on potential treatment to reduce stress/anxiety in general, as well as to promote wellbeing of our future health care providers and physicians.

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