72nd Annual
Senior Scientific Session
Wednesday, May 16, 2018
Oral Presentations
1:00 PM – 4:00 PM | Biological Sciences Learning Center – Room 115

Poster Presentations
4:15 PM - 6:30 PM | Gordon Center for Integrative Science – 3rd Floor Atrium

2018 Session Chair
Dr. Julian Solway, MD
Walter L. Palmer Distinguished Service Professor of Medicine and Pediatrics
Dean for Translational Medicine
Vice Chair for Research, Department of Medicine
Chair, Committee on Molecular Medicine

2018 Presentation Judges

<table>
<thead>
<tr>
<th>Name</th>
<th>Department</th>
</tr>
</thead>
<tbody>
<tr>
<td>Francis Alenghat, MD, PhD</td>
<td>Department of Medicine</td>
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<tr>
<td>Bree Andrews, MD, MPH</td>
<td>Department of Pediatrics</td>
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<tr>
<td>Matthew Brady, PhD</td>
<td>Department of Medicine</td>
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<tr>
<td>Paul Bottone, MD</td>
<td>Department of Pediatrics</td>
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<tr>
<td>Marshall Chin, MD, MPH</td>
<td>Department of Medicine</td>
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<tr>
<td>Andrew Davis, MD, MPH</td>
<td>Department of Medicine</td>
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<tr>
<td>Harriet deWit, PhD</td>
<td>Department of Psychiatry and Behavioral Neuroscience</td>
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<tr>
<td>Daniel Golden, MD, MHPE</td>
<td>Department of Radiation and Cellular Oncology</td>
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<tr>
<td>Elbert Huang, MD, MPH</td>
<td>Department of Medicine</td>
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<td>Scott Hunter, PhD</td>
<td>Department of Psychiatry and Behavioral Neuroscience</td>
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<tr>
<td>Shannon Martin, MD, MS</td>
<td>Department of Medicine</td>
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<tr>
<td>Peggy Mason, PhD</td>
<td>Department of Neurobiology</td>
</tr>
<tr>
<td>Cathryn Nagler, PhD</td>
<td>Department of Pathology</td>
</tr>
<tr>
<td>Sola Olopade, MD, MPH</td>
<td>Department of Medicine</td>
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<tr>
<td>Amber Pincavage, MD</td>
<td>Department of Medicine</td>
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<tr>
<td>Micah Prochaska, MD</td>
<td>Department of Medicine</td>
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<td>Tipu Puri, MD, PhD</td>
<td>Department of Medicine</td>
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<td>Juan Rojas, MD</td>
<td>Department of Medicine</td>
</tr>
<tr>
<td>Greg Ruhnke, MD</td>
<td>Department of Medicine</td>
</tr>
<tr>
<td>Sangram Sisodia, PhD</td>
<td>Department of Neurobiology</td>
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<tr>
<td>Audrey Tanksley, MD</td>
<td>Department of Medicine</td>
</tr>
<tr>
<td>Olga Zaborina, PhD</td>
<td>Department of Surgery</td>
</tr>
</tbody>
</table>
Welcome & Opening Remarks
Biological Sciences Learning Center - Room 115

1:00 PM  Holly J. Humphrey, MD’83  
Ralph W. Gerard Professor in Medicine  
Dean for Medical Education

Julian Solway, MD  
Walter L. Palmer Distinguished Service Professor of Medicine and Pediatrics  
Dean for Translational Medicine  
Vice Chair for Research, Department of Medicine  
Chair, Committee on Molecular Medicine

Oral Presentations
Abstracts on Pages 14 – 23

1:15 PM  Austin Blum, JD; Mentor: Jon Grant, JD, MD, MPH  
Quality of Life of Young Adults with Problematic Sexual Behaviors

1:30 PM  Ava Ferguson Bryan, MA; Mentor: Kevin K. Roggin, MD  
What Do Patients Know? Evaluating Patient Perceptions of Surgical Trainee Involvement on a Resident Acute Care Service

1:45 PM  Curtis Ginder, Mentor: Gaurav Upadhyay, MD  
Predicting Appropriate ICD Therapy with Real-Time Home Monitoring Data Using Traditional Logistic Regression and Machine Learning Models

2:00 PM  Aaron Hecht, PhD; Mentor: Juliane Bubeck Wardenburg, MD, PhD  
Bacterial Warfare in the Gut Microbiota Determines Intestinal Inflammatory Disease Outcomes

2:15 PM  Iboro Umana, PhD; Mentor: Daniel McGebee, PhD  
Nicotinic Modulation of Descending Pain Control Circuitry

2:30 PM  BREAK

2:45 PM  Sonja Boatman; Mentor: Olufunmilayo I. Olapade, MD  
LncRNA BLAT1 is Upregulated in Basal-like Breast Cancer through Epigenetic Modifications

3:00 PM  Sean McGuire; Mentor: Ernst Lengyel, MD, PhD  
Targeted Inhibition of Fascin in Cancer and Stromal Cells Blocks Ovarian Cancer Migration and Metastasis

3:15 PM  Jonathan Oskvarek; Mentor: Daniel Golden, MD, MHPE  
Doctor on Board: Innovative Education for In-Flight Medical Emergencies

3:30 PM  Kathleen Wiest; Mentor: Vineet Arora, MD, MAPP  
Use of Simulation to Assess Incoming Interns’ Recognition of Opportunities to Choose Wisely

3:45 PM  Luai Zakaria; Mentor: Dana Suskind, MD  
Technological Innovations to Scale the Thirty Million Words Initiative
Poster Presentations
4:15 PM - 6:30 PM | Gordon Center for Integrative Science - 3rd Floor Atrium
Abstracts on Pages 26 – 73

4:15 PM
Gaurav Ajmani, MHS
Kurt Alberson
Adam Baim, MA
Miguel Barajas
Ivana Barouhas
Lawrence Belcher
Brandon Berger
Raj Bhanvadia
Diana Bouhassira
Christina Chen
Ellen Daily
Elijah Darnell
Hunter Eason
Farida Esaa
Samantha Espinosa
Nolan Faust
Mila Grossman
Brennan Hodgson
Chester Kao, MSE
Colleen Kelly
Sarah Kennedy, M.Ed
J. Erik Kulenkamp
Sooyoung Lim
Linda Liu
Danielle LoRe
J. Mark Lunderberg, PhD
Joseph Lykins
Michael McCartin
Ryan McKillip
Magdeline Montoya
William Moser
Eron Mowers, PhD
Amol Naik, MS
Julia Nath
Joshua Piche
Abhinav Reddy
Darin Rosen
Connie Shao
Leslie Smebak
Claire Smith, MFA
Viktor Tollemar
Jeremy Treger, PhD
Margaret Wang
Stephen Winter, MS
Megan Zilla, PhD
Rebecca Zuckerman

Presentation Judging for the Following Awards

5:45 PM
ORAL PRESENTATIONS
Catherine Dobson Prize
For the best oral presentation given by a student in the area of Scientific Investigation in Clinical Research or Social Sciences

Leon O. Jacobson Basic Science Prize (MD/PhD students)
Granted to the MD/PhD student whose Basic Science Research is judged to be the most meritorious from among session participants

Leon O. Jacobson Prize (non-PhD students)
For the best oral presentation given by a non-PhD student in the area of the Basic Biological Sciences

Medical and Biological Sciences Alumni Association Prize
For the best presentation made by a student in the area of Applied Scholarship
(Global Health, Community Health, Medical Education, or Quality & Safety)

POSTER PRESENTATIONS
Award for Best Poster Describing Applied Scholarship
Award for Best Poster Describing Scientific Investigation in Basic Sciences
Award for Best Poster Describing Scientific Investigation in Clinical Research or Social Sciences

ORAL OR POSTER PRESENTATIONS
Franklin McLean Medical Student Research Award
Granted to the non-PhD student who has performed the most meritorious research in the medical field

Closing Remarks & Awards Presentation
6:15 PM Julian Solway, MD
Oral Presentations

In order of presentation

Page Number

Austin Blum, JD; Mentor: Jon Grant, JD, MD, MPH .................................................................14
Quality of Life of Young Adults with Problematic Sexual Behaviors

Ava Ferguson Bryan, MA; Mentor: Kevin K. Roggin, MD ..........................................................15
What Do Patients Know?: Evaluating Patient Perceptions of Surgical Trainee Involvement on a Resident Acute Care Service

Curtis Ginder; Mentor: Gaurav Upadhyay, MD ...........................................................................16
Predicting Appropriate ICD Therapy with Real-Time Home Monitoring Data Using Traditional Logistic Regression and Machine Learning Models

Aaron Hecht, PhD; Mentor: Juliane Bubeck Wardenburg, MD, PhD ...........................................17
Bacterial Warfare in the Gut Microbiota Determines Intestinal Inflammatory Disease Outcomes

Iboro Umana, PhD; Mentor: Daniel McGehee, PhD ....................................................................18
Nicotinic Modulation of Descending Pain Control Circuitry

Sonja Boatman; Mentor: Olofunmilayo I. Olopade, MD ..............................................................19
LncRNA BLAT1 is Upregulated in Basal-like Breast Cancer through Epigenetic Modifications

Sean McGuire; Mentor: Ernst Lengyel, MD, PhD ....................................................................20
Targeted Inhibition of Fascin in Cancer and Stromal Cells Blocks Ovarian Cancer Migration and Metastasis

Jonathan Oskvarek; Mentor: Daniel Golden, MD, MHPE ...........................................................21
Doctor On Board: Innovative Education for In-Flight Medical Emergencies

Kathleen Wiest; Mentor: Vineet Arora, MD, MAPP .................................................................22
Use of Simulation to Assess Incoming Interns’ Recognition of Opportunities to Choose Wisely

Luai Zakaria; Mentor: Dana Suskind, MD ..................................................................................23
Technological Innovations to Scale the Thirty Million Words Initiative
# Poster Presentations

*In poster order*

## APPLIED SCHOLARSHIP

<table>
<thead>
<tr>
<th>Poster Number</th>
<th>Poster Title</th>
<th>Mentor(s)</th>
<th>Page Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Ivana Barouhas; Mentor: Arshiya Baig, MD, MPH</td>
<td>Assessing the Effectiveness of a Training Intervention on Community Health Center Staff’s Ability to Implement Diabetes Group Visits</td>
<td>26</td>
</tr>
<tr>
<td>2.</td>
<td>Sarah Kennedy, M.Ed; Mentor: Anna Volerman Beaser, MD</td>
<td>Academic-Community Collaboration to Provide Reproductive Health Education in an Underserved Middle School Population</td>
<td>27</td>
</tr>
<tr>
<td>3.</td>
<td>Amol Naik, MS; Mentor: Liana K. Billings, MD</td>
<td>FIND MODY: Electronic Health Record Technology to Identify Patients at High-Risk of Having Monogenic Diabetes</td>
<td>28</td>
</tr>
<tr>
<td>4.</td>
<td>Joshua Piche; Mentor: Scott Hunter, PhD</td>
<td>The Relationship Between Self-Reported Executive Functioning and Risk-Taking Behavior in Urban Homeless Youth</td>
<td>29</td>
</tr>
<tr>
<td>5.</td>
<td>Brandon Berger; Mentor: Allison Bartlett, MD, MS</td>
<td>Cost-Effectiveness of Meglumine Antimoniate versus Miltefosine Caregiver DOT for the Treatment of Pediatric Cutaneous Leishmaniasis</td>
<td>30</td>
</tr>
<tr>
<td>6.</td>
<td>Margaret Wang; Mentor: Youlin Qiao, MD, PhD</td>
<td>Human Papillomavirus Viral Load: A Useful Triage Tool for Non-16/18 hrHPV Positive Women</td>
<td>31</td>
</tr>
<tr>
<td>7.</td>
<td>Samantha Espinosa; Mentor: Valerie Press, MD, MPH</td>
<td>COPD Readmissions Reduction Program: Barriers and Challenges Post-Discharge</td>
<td>32</td>
</tr>
<tr>
<td>8.</td>
<td>Mila Grossman; Mentor: Vineet Arora, MD, MAPP</td>
<td>Sleep for Inpatients: Empowering Staff To Act (SIESTA): Impact on Hospital Staff Knowledge &amp; Empowerment to Improve Patient Sleep</td>
<td>33</td>
</tr>
<tr>
<td>9.</td>
<td>Julia Nath; Mentor: Dana Edelson, MD</td>
<td>Identifying Local Interventions to Reduce Alarm Fatigue: Testing the Effectiveness of Simplifying the Telemetry Alarm Acknowledgement Process</td>
<td>34</td>
</tr>
<tr>
<td>10.</td>
<td>Kurt Alberson; Mentor: Rachel K. Wolfson, MD</td>
<td>Goals of Medical Students Participating in Scholarly Concentration Programs</td>
<td>35</td>
</tr>
<tr>
<td>11.</td>
<td>Adam Baim, MA; Mentor: Judith Farquhar, PhD</td>
<td>Getting the Picture: Visual Interpretation in Ophthalmology Residency Training</td>
<td>36</td>
</tr>
<tr>
<td>12.</td>
<td>Hunter Eason; Mentor: Jeanne Farnan, MD, MHPE</td>
<td>Students as Peer Educators: A Needs Analysis</td>
<td>37</td>
</tr>
</tbody>
</table>
13. **Farida Esaa; Mentor: Kamran Riaz, MD** ................................................................. 38
   Institution of a Surgical Curriculum for Trabecular Micro-Bypass Stent Placement

14. **Brennan Hodgson; Mentor: David Howes, MD** ...................................................... 39
    Assessment-Oriented Oral Case Presentations in the Academic Emergency Department: Objective Measurement of Presentation Content and Clinical Context

15. **Michael McCartin; Mentor: Lisa McQueen, MD** .................................................... 40
    The Effect of Checklist Characteristics on Measured Pediatric Trauma Team Performance

16. **Ryan McKillip; Mentor: Daniel Golden, MD, MHPE** ........................................... 41
    Toward a Resident Personal Finance Curriculum: Quantifying Resident Financial Circumstances, Needs, and Interests

17. **William Moser; Mentor: Christopher Straus, MD** ................................................ 42
    Medical Imaging Use by Pediatricians: Identifying Core Imaging Concepts and their Optimal Point of Introduction

18. **Leslie Smebak; Mentor: Jeanne Farnan, MD, MHPE** .......................................... 43
    Students as Peer Educators: Development and Implementation of a Teaching Skills Course for Medical Students

19. **Claire Smith, MFA; Mentor: Nancy Schindler, MD, MHPE** .................................. 44
    Resident Perspectives on Teaching during Awake Surgical Procedures

20. **Stephen Winter, MS; Mentor: Callum Ross, PhD** ............................................. 45
    A Proof of Principle for the Use of Automated, Graph-Based Curricular Tools in Anatomy Education

**SCIENTIFIC INVESTIGATION IN CLINICAL RESEARCH OR SOCIAL SCIENCES**

21. **Gaurav Ajmani, MHS; Mentor: Mibir Bhayani, MD** ............................................. 47
    Impact of a Proactive Swallowing Rehabilitation Program on Feeding Tube Placement in Patients Treated for Pharyngeal Cancer

22. **Lawrence Belcher; Mentor: Ney Alliey-Rodriguez, MD** .................................... 48
    Clinical and Anatomic Characteristics of Psychotic Patients Carrying a Common Variant Allele of NRXN1

23. **Ellen Daily; Mentor: Sangtae Park, MD, MPH** ................................................... 49
    Cost-Effectiveness Analysis of Adjuvant versus Salvage Radiotherapy after Radical Prostatectomy for High-Risk Disease

24. **Elijah Darnell; Mentor: Jayant Pinto, MD** ............................................................ 50
    Cytokine Correlates of Olfactory Dysfunction in Older U.S. Adults

25. **Nolan Faust; Mentor: Sonia Kapfer, MD** ............................................................ 51
    Low Rates of Genetic Counseling and Testing in Individuals at Risk for Lynch Syndrome Reported in the National Health Interview Survey
26. **J. Erik Kulenkamp; Mentor: Lewis Shi, MD** .................................................................52
    Characterization of Hip Fracture Risk Following an Upper Extremity Fracture: Review of 212,549 Patients

27. **Sooyoung Lim; Mentor: Jayant Pinto, MD** .................................................................53
    3D Image Analysis for Staging Chronic Rhinosinusitis

28. **Linda Liu; Mentor: Gaurav Upadhyay, MD** .................................................................54
    A Real-World Network Meta-Analysis of the Safety of Direct Oral Anticoagulants for Stroke Prevention in Non-valvular Atrial Fibrillation

29. **Danielle LoRe; Mentor: Dana Suskind, MD** .................................................................55
    TMW-Pediatrics: Strengthening the Pediatric Provider’s Role in Parent Education on Early Learning and Language Development

30. **Joseph D. Lykins V; Mentor: Michael Ward, MD** ...........................................................56
    Evaluation of Fluid Resuscitation in Patients with Severe Sepsis and Septic Shock

31. **Magdeline Montoya; Mentor: James Walter, MD** ...........................................................57
    A Descriptive Analysis of Patients Presenting to an Urban Academic Emergency Department with Ventricular Assist Device-Specific Complaints

32. **Abhinav Reddy; Mentor: Stanley Liauw, MD** .................................................................58
    Patterns of Failure after Radical Cystectomy for pT3-4 Bladder Cancer: Implications for Adjuvant Radiation Therapy

33. **Darin Rosen; Mentor: Susan Ksiazek, MD** .................................................................59
    Utilizing a Commercially Available Virtual Reality Device for Glaucoma Screening

34. **Rebecca Zuckerman; Mentor: Kevin Hellman, PhD** ......................................................60
    Somatic Symptoms in Women with Dysmenorrhea and Noncyclic Pelvic Pain

35. **Miguel Barajas; Mentor: Lainie Ross, MD, PhD** ..............................................................61
    Kidney Donors in ESRD Bypassing Priority Status: A Qualitative Interview-Based Study

36. **Diana Bouhassira; Mentor: Dana Suskind, MD** .............................................................62
    Assessment of Provider Knowledge in the Early Childhood Care Environment

37. **Christina Chen; Mentor: Valerie Press, MD, MPH** ..........................................................63
    Vision-Related Quality of Life and Visual Acuity as Measures for Fall Risk and Indicators for Follow Up Care in a Hospitalized Population

38. **Colleen Kelly; Mentor: Valerie Press, MD, MPH** ............................................................64
    Virtual Teach-to-Goal vs. In-Person Teach-to-Goal for Effective Respiratory Inhaler Technique Education: A Non-Inferiority Randomized Clinical Trial
39. Raj Bhanvadia; Mentor: Donald Vander Griend, PhD ................................................................. 66
MEIS1 and MEIS2 Expression and Prostate Cancer Progression: A Role for HOXB13 Binding Partners
in Metastatic Disease

40. Chester Kao, MSE; Mentor: R. Stephanie Huang, PhD ............................................................... 67
Identifying and Validating a Gene Network Responsive to Imatinib Treatment in a Chronic Myeloid
Leukemia Cell Line

41. J. Mark Lunderberg, PhD; Mentor: Olaf Schneewind, MD, PhD ..................................................... 68
Bacillus anthracis TagO is Required for Vegetative Growth and Secondary Cell Wall Polysaccharide
Synthesis

42. Erin Mowers, PhD; Mentor: Kay Macleod, PhD ........................................................................... 69
The SRC-Modulated Interaction of Paxillin and LC3B Promotes Autophagic Degradation of Paxillin and
Tumor Cell Motility

43. Connie Shao; Mentor: John Alverdy, MD ................................................................................... 70
The Role of the Western Diet on Altering the Microbiome

44. Viktor Tollemar; Mentor: Russell Reid, MD, PhD ........................................................................ 71
Repair of Critical Sized Cranial Defects with BMP9-transduced Calvarial Cells in a Thermoresponsive
Scaffold

45. Jeremy Treger, PhD; Mentor: Francisco Bezanilla, PhD ............................................................... 72
Optogenetics without Genetics

46. Megan Zilla, PhD; Mentor: Dominique Missiakas, PhD ............................................................... 73
LytR-CpsA-Psr Enzymes as Determinants of Bacillus anthracis Cell Cycle and Secondary Cell Wall
Polysaccharide/S-layer Assembly
The annual Senior Scientific Session was founded by Dr. Leon Jacobson in 1946 to highlight the caliber of Pritzker student scholarship and the quality of their medical education. Dr. Jacobson, a native of Sims, North Dakota, received a Bachelor of Science degree from North Dakota State University in 1935 and his Medical Doctorate from the University of Chicago in 1939. His professional career—invested entirely at the University of Chicago—included serving as Director of the Argonne Cancer Research Hospital, as well as Dean of the Division of Biological Sciences.

In 1942, during his residency at the University of Chicago Hospital, Dr. Jacobson was recognized for his scholarly promise. He was tasked with the responsibility of protecting the health of the staff of the Manhattan Project. Dr. Jacobson was chosen for this important position because of his research on the biological effects of radiation, as well as his reputation as one of the first doctors to treat blood disorders with radioactive phosphorus. By the conclusion of the Manhattan Project in 1945, Dr. Jacobson and his staff had pioneered several medical advances, including testing the first forms of chemotherapy used to fight cancer. He was later credited with creating the foundation for bone marrow transplantation and initiating the search for the erythropoietin, a hormone that regulates red blood cell production. Erythropoietin is now the basis for a drug that treats chemotherapy-induced anemia in many cancer patients, a revolutionary treatment in the field of oncology.

The Senior Scientific Session is upheld as an annual tradition. By providing graduating Pritzker students with the opportunity to disseminate their research and scholarship through oral and poster presentations, the legacy of Dr. Jacobson’s commitment to innovation through research continues.
Karnezis Research Scholarship

An orthopaedic surgeon at Advocate Health Care, Tom Karnezis, MD’88, is an active and generous alumnus. In 2017, Dr. Karnezis established the Karnezis Research Scholarship with two goals. The first is to recognize and reward achievement in research to promote scientific inquiry among all students in the Pritzker School of Medicine. The second is to reduce debt for the recipient by applying funds towards student loans in order to reduce overall debt as well as future interest payments.

2018 Karnezis Research Scholarship Recipient

Ava Ferguson Bryan, MA

This year’s recipient, Ava Ferguson Bryan, grew up in Dallas and attended the University of Texas at Austin. She spent four years after college earning a graduate degree in the humanities, working as a fundraiser for Planned Parenthood, and completing pre-medical requirements before matriculating at the University of Chicago Pritzker School of Medicine. While at Pritzker, Ava took a year off to conduct research in obstetrics and gynecology under the guidance of Julie Chor, MD, MPH, for which she received funding from both the Institute for Translational Medicine and the Alpha Omega Alpha Carolyn L. Kuckein Student Research Fellowship. A committed institutional citizen, Ava has been integrally involved in the admissions process, serving as a student member of the Admissions Committee as well as Revisit Co-Chair in 2017. Ava was a peer educator for multiple classes and has been active in Physicians for a National Health Program and the Ultmann Fund. Next year, Ava will continue her medical education at the University of Chicago Medicine as a resident in general surgery.

2017-2018 Calvin Fentress Fellowship Recipients

Miguel Barajas
Mentor: Lainie Ross, MD, PhD

Brandon Berger
Mentor: Allison Bartlett, MD, MS

Austin Blum, JD
Mentor: Jon Grant, JD, MD, MPH

Ava Ferguson Bryan, MA
Mentor: Kevin Roggin, MD

Colleen Kelly
Mentor: Valerie Press, MD, MPH

Sarah Kennedy, M.Ed
Mentor: Anna Volerman Beaser, MD

Darin Rosen
Mentor: Susan Ksiazek, MD

Connie Shao
Mentor: John Alverdy, MD

Claire Smith, MFA
Mentor: Nancy Schindler, MD, MHPE

Margaret Wang
Mentor: Youlin Qiao, MD, PhD
JOHN D. ARNOLD, MD
SCIENTIFIC RESEARCH PRIZE

In 2012, a grateful alumnus, Dr. Charles Pak, established the John D. Arnold, MD, Scientific Research Prize. This prize was established in recognition of the impact that his mentor had on his education and future career in research. The Arnold Scientific Research Prize recognizes students whose research accomplishments as medical students are based on ongoing, sustained work with a single faculty mentor. The goal of the Arnold Scientific Research Prize is to provide support for the continuation of the mentoring relationship and collaborative research experience during the student’s fourth year of medical school. As part of the application, students are asked to comment on the contributions that their mentors have made towards their professional growth and development. Mentors of the selected students are honored with the 2017-2018 John D. Arnold, MD, Mentor Award for sustained excellence in mentoring medical students.

2017-2018 Scientific Research Prize Recipients

Raj Bhanvadia
Mentor: Donald Vander Griend, PhD

Sean McGuire
Mentor: Ernst Lengyel, MD, PhD

Luai Zakaria
Mentor: Dana Suskind, MD

2017-2018 Mentor Award Recipients

Donald Vander Griend, PhD

Dr. Donald Vander Griend’s research interests are aimed at understanding the function of prostate stem cells and their role in the development of prostate diseases such as prostate cancer and BPH. Dr. Vander Griend’s research focuses on understanding the normal function of the human prostate epithelial stem cell compartment as it relates to (1) stem cell maintenance and tissue turnover, (2) dependence upon androgen and the supporting stroma, and (3) molecular events driving prostate disease.

Dr. Vander Griend received the John D. Arnold, MD Mentor Award for his work with fourth year student Raj Bhanvadia. Dr. Vander Griend and Raj examined the role of MEIS expression in predicting progression from localized to clinically metastatic prostate cancer. This work led to a recently accepted paper in Clinical Cancer Research. Commenting on Dr. Vander Griend’s mentorship, Raj stated:

Donald Vander Griend has been an instrumental part of my research development since my first year at Pritzker when I joined his lab. He supports me on all of my research projects and has been extremely focused, balancing his basic science background with my clinical focus to provide me with a foundation to pursue clinically relevant translational research. He provides an environment where he actively promotes scientific reasoning and debate among colleagues.
Ernst Lengyel, MD, PhD

Dr. Ernst Lengyel is an expert in the diagnosis and treatment of gynecologic malignancies, specifically, ovarian, cervical and endometrial cancers. His primary clinical focus is on the treatment of ovarian cancer, including advanced surgical techniques designed to improve patient outcomes. Dr. Lengyel's research laboratory in the Center for Integrative Science focuses on the investigation of new therapies for the treatment of ovarian cancer. His research is funded by the National Institutes of Health (NIH).

Dr. Lengyel received the John D. Arnold, MD Mentor Award for his work with fourth year student Sean McGuire. Dr. Lengyel and Sean studied how the protein fascin, which regulates cytoskeleton structures in the cell, affects ovarian cancer metastasis and if it could be a novel therapeutic target. Commenting on Dr. Lengyel’s mentorship, Sean stated:

While searching for a lab during my first year of medical school, I actively sought an environment that was both academically and personally supportive. The scientific resources available in the Lengyel lab provide an ideal environment for making significant contributions to the field of ovarian cancer research. Dr. Lengyel is a model surgeon-scientist, with a busy clinical practice that fuels and complements the basic science research carried out in his laboratory. As a future surgeon with the goal of conducting basic science research, I can think of no better example to follow. The training I receive in the Lengyel lab is, I believe, perfect preparation for the next stage of my research career.

Dana Suskind, MD

Dr. Dana Suskind is Co-Director of the TMW Center for Early Learning + Public Health, Professor of Surgery at the University of Chicago, Director of the Pediatric Cochlear Implant Program, and Founder and Director of Thirty Million Words (TMW). Based on scientific research that shows the critical importance of early language exposure on the developing child, TMW helps parents, caregivers and practitioners harness the power of their language to build children’s brains and shape their futures. Since its inception, TMW has reached over 3,000 families in Chicago alone, with many more cities and municipalities requesting to launch TMW’s suite of interventions. This widespread interest led Dr. Suskind to partner with Dr. John List to establish the TMW Center for Early Learning + Public Health. The TMW Center aspires to create a population-level shift in knowledge and behavior of parents and caregivers to optimize the foundational brain development in children, particularly those born into poverty.

Dr. Suskind received the John D. Arnold, MD Mentor Award for her work with fourth year student Luai Zakaria. Dr. Suskind and Luai have worked together for three years to develop and analyze a cell phone application that can be used to scale the Thirty Million Words intervention to a larger population. Commenting on Dr. Suskind’s outstanding style of mentorship, Luai stated:

I chose to join the TMW organization because I had an interest in biomedical engineering prior to medical school. Together, Dr. Suskind and I came up with the idea to use my engineering background for disparities work. Dr. Suskind and the TMW organization have made a profound impact on my career interests and personal growth. Ultimately, I envision becoming an anesthesiologist with a combined passion for developing innovative medical technologies while serving a diverse patient population. Dr. Suskind has inspired me and been my role model of a physician-scientist dedicated to scholarship and excellent patient care. Through Dr. Suskind, I have seen the path I envision for my future career.
Oral Presentations
Quality of Life of Young Adults with Problematic Sexual Behaviors

Austin Blum, JD

Mentor: Jon Grant, JD, MD, MPH; Department of Psychiatry and Behavioral Neuroscience

Co-Authors: Samuel R. Chamberlain, MD, PhD; Jon Grant, JD, MD, MPH

Background: Appetitive urges related to sex are common and experienced by nearly all men and women. Some people, however, experience repetitive and intense preoccupations with sexual fantasies, urges, and behaviors that are perceived to be out of control or cause significant distress—a clinical phenomenon known as problematic sexual behavior (PSB). The goal of this study was to identify clinical characteristics linked with quality of life in a community sample of young adults affected by PSB. Because PSB has been conceptualized as a behavioral addiction or as a disorder with compulsive and impulsive features, we hypothesized that lower quality of life in PSB would be associated with poorer psychological well-being and deficits in self-control.

Methods: Participants were non-treatment-seeking young adults (ages 18–29 years) meeting proposed criteria for PSB. PSB was defined as the experience of sexual urges, fantasies, or behaviors that feel overwhelming or out of control. Participants were assessed using the Quality of Life Inventory (QOLI) and a variety of instruments examining aspects of mental health and psychological well-being. Participants also completed self-report impulsivity inventories and a computerized cognitive battery. Clinical measures associated with variation in quality of life were identified using the statistical technique of partial least squares (PLS). We used a two-step approach to identify the subset of predictor variables that explained significant variance in quality of life. First, we retained individual variables within the model that demonstrated threshold importance by conventional criteria (variable importance for the projection (VIP) statistic > 0.8). Second, in a more conservative approach, we computed 95% bootstrap confidence intervals for the standardized model coefficients of the remaining variables and excluded those that crossed zero (N = 2000 bootstraps).

Results: 54 participants with PSB (mean age = 23.6 ± SD 3.5 years; 67.3% male) were recruited. Most participants (70.4%) reported being excessively preoccupied with their sexuality or being overly sexually active; 31.5% reported out-of-control sexual fantasies, 37.0% reported out-of-control sexual urges, and 22.2% reported out-of-control sexual behaviors. The mean QOLI T-score was in the low range. Most participants reported very low satisfaction in three specific domains of quality of life: money (or standard of living), work or career, and love (romantic relationships). PLS identified an optimal one-factor model that accounted for 31.7% of the variation in the explanatory variables and 40.1% of the variation in quality of life. Lower quality of life was associated with attentional impulsivity, lower age at first alcohol use, emotional dysregulation, problematic use of the internet, clinically significant suicidality, elevated state symptoms of anxiety and depression, and lower self-esteem.

Conclusion: To our knowledge, the present study is the only to examine quality of life in young adults affected by PSB. We found that low quality of life in PSB was strongly associated with selective deficits in self-control—specifically, in attention and emotional regulation—and affective problems. These associations may have implications for our understanding of sexual behaviors that affect quality of life.

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What Do Patients Know? Evaluating Patient Perceptions of Surgical Trainee Involvement on a Resident Acute Care Service

Ava Ferguson Bryan, MA

**Mentor:** Kevin K. Roggin, MD; Department of Surgery

**Co-Authors:** Darren S. Bryan, MD; Jeffrey B. Matthews, MD; Kevin K. Roggin, MD

**Background:** There is currently no standard method of disclosing trainee involvement to surgical patients, and no literature addressing effective strategies for increasing patient understanding of and comfort with resident involvement in operations. Here we propose a strategy for patient education on the role of surgical trainees via use of a standardized pre-operative script. We aim to prospectively evaluate such an educational system, hypothesizing that implementation will lead to increased patient approval and understanding of resident involvement in their operative care.

**Methods:** Patients cared for by the Resident Acute Care Surgery (RACS) service were approached and consented, beginning in October 2017 and anticipated to continue through May 2018. Patients who agreed to participate and who had an operation with the daytime RACS team were considered enrolled. During the first half of the month, roles were explained per usual practice. During the second half of the month, the chief resident read a short script explaining the roles of trainees and attending surgeons in their operation. Enrolled patients were contacted on post-operative day three and completed a survey assessing their understanding of and comfort with their surgical care. Basic demographic information, insurance status, pre-operative ASA score, and operation type were also collected.

**Results:** To date, 37 patients have been enrolled. 29 patients completed the post-operative survey. Nineteen of these were in the control arm; ten were in the intervention arm. Nine (47%) of those in the control arm stated they did not believe residents should be allowed to perform portions of operations; ten (53%) believed they should. All ten patients (100%) in the intervention arm stated they believed residents should be allowed to perform portions of operations, making enrollment in the intervention arm significantly associated with the belief that trainees should be allowed to participate in their operation ($p = 0.011$). There were no observable statistical differences in the self-reported comfort with the roles of the members of their care team generally, nor of the attending and resident surgeon roles specifically. Roughly equivalent proportions of each group named a resident or trainee as “their doctor” (10 of 19 in the control group and five of 10 in the intervention group).

**Conclusion:** Our data suggests knowledge of and comfort with resident involvement in operative care is imperfect, with roughly half of patients at baseline believing residents should not be allowed to perform portions of their operation. We found that the use of a short, semi-structured script meant to standardize the education of patients around the academic care model has the ability to improve patient buy-in to resident and trainee operative participation without improvement in self-reported comfort with or understanding of surgical care team roles. This suggests that the act of patient education around the academic care model, even if it doesn’t improve specific knowledge, improves patient comfort with and confidence in resident participation in their care.

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Predicting Appropriate ICD Therapy with Real-Time Home Monitoring Data Using Traditional Logistic Regression and Machine Learning Models

Curtis Ginder

Mentor: Gaurav Upadhyay, MD; Department of Medicine, Section of Cardiology

Co-Authors: Warren Mo; Stephanie Besser, MSAS; Roderick Tung, MD; Ishanu Chattopadhyay, PhD; Gaurav Updahyay, MD

Background: Although device diagnostic data have been used to predict mortality and heart failure hospitalization, assessing real-time risk for VT/VF remains challenging. Due to the availability of real-time home monitoring data, advanced modeling techniques may allow for identification and prediction of patients at increased risk of VT/VF. We sought to compare traditional logistic regression and advanced machine learning modeling methods in the prediction of appropriate device therapy for patients enrolled in IMPACT, a multicenter randomized control trial evaluating atrial tachyarrhythmias and anticoagulation for patients with implanted cardioverter-defibrillator and resynchronization devices.

Methods: Home monitoring data and device electrograms (EGMs) were obtained for all patients enrolled in the IMPACT study. Patients receiving appropriate ICD therapy (antitachycardia pacing or shocks for sustained VT or VF) were compared to patients not receiving device therapy. Device diagnostic data were stratified using cut-points determined by ROC analysis, and then included in separate logistic regression and random forest models developed with training and validation sets. Model performances were compared using out of sample sensitivity, specificity, and AUC values.

Results: Demographic and thirty day device diagnostic data were obtained for a total of 2,262 patients (147 patients receiving appropriate device therapy, 2,115 control patients). Using logistic regression, increased risk of appropriate therapy for VT/VF was associated with a history of myocardial infarction, a decrease in lead impedance, and increases in VxVx sensed events, detected VT1 episodes, and detected VF episodes. Multivariate logistic regression yielded an AUC of 0.78 with a correctly classified rate of 89% and negative predictive value of 97% in the validation data set. Random forest methodology resulted in improved performance in the prediction of patients receiving appropriate device therapy with AUC of 0.85.

Conclusion: A decrease in shock lead impedance and an increase ventricular ectopy are associated with an increased risk of appropriate ICD therapy. Device diagnostic data and machine learning models may have a role in dynamic risk stratification for VT/VF.

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Bacterial Warfare in the Gut Microbiota Determines Intestinal Inflammatory Disease Outcomes
Aaron Hecht, PhD

Mentor: Juliane Bubeck Wardenburg, MD, PhD; Department of Pediatrics, Division of Critical Care Medicine, Washington University School of Medicine in St. Louis

Co-Authors: Benjamin W. Casterline; Zachary M. Earley; Juliane Bubeck Wardenberg, MD, PhD

Background: The importance of the gut microbiota in inflammatory bowel disease (IBD) pathogenesis and colonic malignancy is increasingly recognized. Pathogen exclusion through competition with the microbiota is a well-established mechanism of disease prevention, indicating that these relationships may underpin individual susceptibility to disease. One organism associated with intestinal illness is Enterotoxigenic Bacteroides fragilis (ETBF), a subspecies of B. fragilis that causes injury to the intestinal epithelium. ETBF is associated with acute exacerbations of IBD, and infection of experimental animals with ETBF produces an IBD-like colitis. In contrast to ETBF, non-toxinogenic B. fragilis (NTBF) is an intestinal commensal that provides protection from inflammatory disease. Humans exhibit variable patterns of colonization with NTBF and ETBF, harboring one of these organisms to the exclusion of the other. One strategy to remove the risk of ETBF colonization is targeted probiotic therapy. However, the mechanisms that underlie human susceptibility or resistance to ETBF acquisition remain undefined. We hypothesized that colonization of NTBF would restrict ETBF acquisition, dependent upon modular genetic determinants of bacterial competition.

Methods: We developed a model for co-infection or sequential infection of mice with B. fragilis strains and monitored the outcome of competitive colonization in the intestine. To determine the bacterial loci underpinning these competitive interactions, we utilized a candidate approach via selective deletion of genomic elements and competed the resulting mutants both in vitro and in vivo. Finally, we tested the relevance of these competitive interactions in disease using a mouse model of IBD.

Results: We found that NTBF was capable of killing ETBF during co-infection of the gut, suppressing the bacterial load of this pathogen in the feces by ~100 fold. One mechanism of interbacterial competition is type VI secretion (T6S), whereby an attacking cell destroys a target organism by injecting effector proteins through the outer membrane. Deletion of the T6S locus in NTBF allowed ETBF outgrowth, causing increased pathogen burden in the intestine. We further found that an effector in the NTBF T6S locus accounted for the entirety of this killing phenotype, suggesting that a single gene determines the outcome of this bacterial competition in the microbiota. Initial colonization of mice with NTBF provided complete colonization resistance to subsequent ETBF exposure, also requiring T6S. Challenge of mice susceptible to IBD-like illness with competing B. fragilis strains demonstrated that T6S-dependent NTBF killing of ETBF protects the intestine from exposure to toxin and inflammatory disease.

Conclusion: Our studies demonstrate novel roles for bacterial competition and T6S in protection against intestinal disease. As the colonization phenotypes exhibited by NTBF and ETBF include both exclusion and durability in human studies, early acquisition and deliberate re-colonization with NTBF strains may afford protection against ETBF-mediated disease in a variety of clinical settings. These observations provide a necessary framework to advance molecular probiotic targeting toward rational, therapeutic manipulation of the pathogenic microbiota.

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Nicotinic Modulation of Descending Pain Control Circuitry

Iboro Umana, PhD

**Mentor:** Daniel McGehee, PhD; Department of Anesthesiology and Critical Care

**Co-Authors:** Claire Daniele, PhD; Brooke Miller; Chandrika Abburi, PhD; Keith Gallagher; Meghan Brown; Peggy Mason, PhD; Daniel McGehee, PhD

**Background:** Although opioids are the most commonly used treatments for chronic pain, their use is associated with adverse events, including abuse liability and tolerance or loss of efficacy. Thus, exploring other analgesic targets is an ongoing goal in pain research. Nicotinic agonists have shown promise as alternatives to opioid drugs. Along with the well-known rewarding effects, activation of nicotinic acetylcholine receptors (nAChRs) can also relieve pain, and some nicotinic agonists have analgesic efficacy similar to opioids. A major target of analgesic drugs is the descending pain modulatory pathway, including the ventrolateral periaqueductal gray (vlPAG) and the rostral ventromedial medulla (RVM). Although activating nAChRs within this circuitry can be analgesic, little is known about the subunit composition and cellular/behavioral effects of activating these receptors, particularly within the vlPAG.

**Methods:** Retrograde labeling of vlPAG-RVM projection neurons: Stereotaxic surgeries were performed to inject a fluorescent dye (rhodamine microspheres) into the RVM of adult rats. After three days of recovery, electrophysiology was performed. Electrophysiology: Coronal slices were prepared from midbrain that included the cerebral aqueduct. Whole cell voltage clamp recordings were conducted in fluorescently labeled neurons in the vlPAG. To assess nAChR expression, acetylcholine (Ach, 1 mM) was focally applied; all other drugs were bath applied. Behavior: vlPAG guide cannula implantation surgeries were performed on adult Sprague Dawley rats. After surgery, the rats were singly housed and allowed to recover for 6 days. During recovery from surgery, the animals were habituated to limit stress-induced increases in corticosterone. On test day, the rats received drug injections via intra-vlPAG and/or systemic administration. Formaldehyde (37%, Fisher Scientific) was diluted to formalin (1.5%, 50 mL) and then injected into the intraplantar surface of the left hindpaw. After formalin injection, the rats were placed in the formalin box and nocifensive responses were monitored for 60 minutes.

**Results:** We found that 63% of PAG-RVM projection neurons expressed functional nAChRs, which were exclusively of the alpha7-subtype. Interestingly, the neurons that express alpha7 nAChRs were largely nonoverlapping with those expressing mu-opioid receptors (MOR). As nAChRs are excitatory and MORs are inhibitory, these data suggest distinct roles for these neuronal classes in pain modulation. Along with direct excitation, we also found that presynaptic nAChRs enhanced GABAergic release preferentially onto neurons that lacked alpha7 nAChRs. In addition, presynaptic nAChRs enhanced glutamatergic inputs onto all PAG-RVM projection neuron classes to a similar extent. In behavioral testing, both systemic and intra-vlPAG administration of the alpha7 nAChR-selective agonist, PHA-543,613, was antinociceptive in the formalin assay. Furthermore, intra-vlPAG alpha7 antagonist pretreatment blocked PHA-543,613-induced antinociception via either administration method. Systemic administration of submaximal doses of the alpha7 agonist and morphine produced additive antinociceptive effects.

**Conclusion:** Our demonstration of alpha7 nAChR expression by a subset of PAG-RVM-projection neurons provides insights into the physiology of these neurons. Our behavioral findings support the idea that vlPAG alpha7 nAChRs are a key site for nicotinic analgesia, and they can be combined with opioids to achieve maximal antinociception at intermediate opioid doses.

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LncRNA BLAT1 is Upregulated in Basal-like Breast Cancer through Epigenetic Modifications

Sonja Boatman

**Mentor:** Olufunmilayo I. Olopade, MD; Department of Medicine, Section of Hematology/Oncology

**Co-Authors:** Yoo Jeong Han, PhD; Jing Zhang; Xinxin Du; Albert C. Yeh, MD; Yonglan Zheng, PhD; Olufunmilayo Olopade, MD

**Background:** Basal-like breast cancer (BLBC), the major molecular subtype of triple-negative breast cancer, is associated with aggressive phenotype and poor prognosis, disproportionately affecting younger women and African American women. BLBC is clinically challenging to treat due to its heterogeneity and lack of targeted therapies. Long-noncoding (lnc) RNAs are known to participate in oncogenesis across a variety of cancers. However, our understanding of the role of lncRNA in BLBC remains limited. The aim of our study was to determine if BLBC had an altered lncRNA expression pattern compared to non-BLBC, whether BLBC-specific lncRNA are biologically active in BLBC, and to elucidate the mechanism regulating differential expression of lncRNA in breast tumors.

**Methods:** Breast tumors and normal breast tissues were recruited from the University of Chicago Breast Cancer Tissue Bank. Microarray profiling was done using Human LncRNA Array v3 (Arraystar) and RNA-sequencing using Illumina TruSeq Stranded Total RNA with Ribo-Zero Human kit (Illumina HiSeq 4000). In vitro studies were performed by antisense oligonucleotide (ASO) knockdown of candidate lncRNAs in BLBC cell lines. Apoptosis was assayed using CaspaseGlo® 3/7 Reagent and flow cytometry. CpG methylation of lncRNA promoter regions was analyzed with TCGA HumanMethylation450 Array data. Bisulfite sequencing was performed on the CpG sites in breast cancer cell lines, which were then treated with 5-Aza-2'-Deoxycytidine and reanalyzed.

**Results:** BLBC has a unique lncRNA expression signature compared to non-BLBC through microarray profiling of thirty breast tissues consisting of non-malignant breast tissues (n=11) and breast tumors (n=19). These results were validated in an additional cohort of fifty breast tumors using RNA-sequencing. From the pool of lncRNAs specifically upregulated in BLBC, we further characterized the candidate lncRNA, Basal-Like breast cancer Associated Transcript 1 (BLAT1/RP11-19E11.1), which is highly upregulated in BLBC tumors compared to non-BLBC (p=0.004 and p<0.0001, microarray and RNA-seq, respectively). Knockdown studies using ASOs against BLAT1 in BLBC cell lines revealed that loss of BLAT1 led to significantly increased apoptosis (p<0.001). To assess the mechanism underlying the differential expression of BLAT1 in BLBC, we compared the methylation status of the BLAT1 promoter across molecular subtypes of breast cancer. TCGA data from 587 patient samples showed significantly lower methylation at three CpG islands of the BLAT1 promoter in BLBC tumors compared to normal breast tissues and other subtype breast tumors (p<0.001). Using bisulfite sequencing, we confirmed hypomethylation of the BLAT1 promoter in BLBC cell lines compared to non-BLBC cell lines. Inhibition of methylation resulted in a significant increase in BLAT1 expression in breast cancer cell lines (p<0.01). Lastly, using TCGA datasets we reported that patients with tumors harboring lower levels of BLAT1 promoter methylation, which is related to higher expression of BLAT1 transcript, showed poor overall survival (p=0.034) compared to patients with higher methylation levels.

**Conclusion:** BLAT1, a BLBC-specific lncRNA, is biologically active and may contribute to poor clinical outcomes in BLBC. In the future, BLAT1 could be used as a biomarker with prognostic implications for clinically aggressive BLBC and is a potentially attractive targeted therapy.

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Targeted Inhibition of Fascin in Cancer and Stromal Cells Blocks Ovarian Cancer Migration and Metastasis

Sean McGuire

**Mentor:** Ernst Lengyel, MD, PhD; Department of Obstetrics & Gynecology

**Co-Authors:** Betul Kara; Anthony Montag, MD; Kristen Wroblewski, MS; Sarah Fazal; Xin-Yun Huang, PhD; Hilary Kenny, PhD; Ernst Lengyel, MD, PhD

**Background:** Ovarian cancer (OvCa) remains the most lethal gynecologic malignancy with a 40% five-year survival rate. This poor survival rate is due to late stage diagnosis after the disease has metastasized throughout the peritoneal cavity. The main site of OvCa metastasis is the omentum, a fat pad that lays over the intestine. One of the key steps during metastasis into the three-dimensional microenvironment of the omentum is cellular migration, which requires actin cytoskeletal protrusions called filopodia. Fascin, a 55-kDa protein, is the main actin-bundling protein in filopodia and is essential for cell migration. Previous studies reveal contradictory data on the clinicopathologic role of fascin expression to predict patient survival, and studies testing the therapeutic effect of fascin inhibition on OvCa metastasis need to be conducted.

**Methods:** Here, we performed immunohistochemical analysis in human tissues to identify cells that express fascin and to correlate clinicopathologic data with fascin expression. In addition, we performed in-vitro, ex-vivo, and in-vivo experiments to determine if a small molecule fascin inhibitor, G2, could inhibit cellular migration and block OvCa metastasis.

**Results:** Mesothelial cells of the human omentum and cancer cells and cancer-associated fibroblasts (CAF) of OvCa tumors expressed fascin. Fascin expression was highest in the stromal cells when compared to cancer cell compartment of tumors. While fascin levels were highest in serous papillary OvCa, there was no correlation between fascin expression levels in tumors and patient survival in serous papillary OvCa. The only correlation discovered between fascin expression and survival was a negative correlation between survival and fascin expression in the cancer cells of non-serous OvCa primary tumors. Treatment with G2 blocked filopodia formation and decreased migration of cancer cell lines, primary human mesothelial cells, and primary human CAFs in vitro. A similar decrease in migration occurred with a knockdown of fascin expression in OvCa cells using a targeted siRNA. Treatment with G2, knockdown of fascin, or both inhibited cellular migration at the same rate, revealing that the inhibitory action of G2 in OvCa migration was fascin specific. Ex-vivo and in-vivo assays validated these results. G2 blocked OvCa colonization on ex-vivo human omentum cultures, while G2 prevented and blocked OvCa metastases in multiple in-vivo xenograft mouse models. Likewise, inhibition of fascin specifically in OvCa cells using a fascin-specific lentiviral-shRNA blocked in-vivo metastasis.

**Conclusion:** Our findings suggest that treatment with a fascin inhibitor targets both cancer cells and tumor stromal cells, and should be considered as a potential therapeutic to prevent OvCa metastasis.

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Doctor on Board: Innovative Education for In-Flight Medical Emergencies

Jonathan Oskvarek

**Mentor:** Daniel W. Golden, MD, MHPE; Department of Radiation and Cellular Oncology

**Co-Authors:** Marshall B. Segal, MD, JD; Daniel W. Golden, MD, MHPE

**Background:** In-flight medical emergencies are common. Estimates vary, but a study of British Airways found a rate of 1 in-flight emergency per 11,000 passengers. These emergencies are dangerous to the patient in the limited-resource environment of the airplane. Also, diversion of the aircraft off-course is costly to the airline and annoying to passengers. Thus, proper handling of the patient and the decision to divert the aircraft are crucial. Senior medical students fly on airlines frequently and they can offer medical assistance if they are aware of how to respond to medical emergencies. Prior research found senior medical students lacked confidence and competence with responding to in-flight emergencies.

**Description of innovation:** The goal of the educational intervention was to teach medical students and recent graduates about responding to in-flight medical emergencies. The principal piece of the intervention was a brief, engaging whiteboard video (https://youtu.be/5pDvyspxtKg). Information relayed in the video included resources commonly available on airliners, legal implications of responding to emergencies, when to recommend the pilot divert the airplane, and an overall approach to handling emergencies. The content was based on a needs assessment performed by other authors, discussion with a legal expert, and a thorough search of the literature on in-flight emergencies.

**Evaluation of innovation:** A survey with the educational video was sent to medical students and recent graduates of a medical school in the US. Although 36% of participants reported being on a flight with a medical emergency, 59% reported they were not at all comfortable or only slightly comfortable with responding to an emergency. Six participants had responded to a medical emergency. The most commonly cited concerns were not knowing how to help and not having resources to adequately diagnose the patient. Participants completed a five-question test before and after watching the video. Scores improved significantly on four of the five (26% vs. 74%, 36% vs. 86%, 3% vs. 36%, and 62% vs. 93%). After watching the video, 29% of participants reported they were not at all or slightly comfortable with responding to an emergency. Most participants reported they wanted additional information on common in-flight illnesses.

**Conclusion:** After watching a brief instructional video about in-flight medical emergencies, participants performed better on the post-test compared to the pre-test questions. Many participants have been on a flight with a medical emergency and many more reported wanting more information on common illnesses presentations on airplanes. A website will be built to accompany the video. The site will provide more information about common medical problems, medical kit contents for different airlines, and legal obligations in different countries. Further areas of innovation could include implementation of a reporting system on the website to gather data about in-flight emergencies and development of an app for reference on the fly. This free openly accessible educational intervention addresses an unmet need for knowledge and training for in-flight medical emergencies.

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Use of Simulation to Assess Incoming Interns’ Recognition of Opportunities to Choose Wisely
Kathleen Wiest

**Mentor:** Vineet Arora, MD, MAPP; Department of Medicine, Section of General Internal Medicine

**Co-Authors:** Jeanne M. Farnan, MD, MHPE; Ellen Byrne, MPP; Lukas Matern; Melissa Cappaert, MA; Kristen Hirsch; Vineet Arora, MD, MAPP

**Background:** Despite increasing healthcare costs, training on cost-consciousness is lacking in graduate medical education (GME). Medical centers must consider how best to incorporate value-based training into their GME curricula. At the University of Chicago, we previously implemented the “Room of Horrors,” a simulation for entering interns to promote the detection of patient safety hazards. In this abstract, we describe a modification to this simulation to embed low-value hazards in addition to traditional patient safety hazards. The aim of this study is to incorporate low-value principles into an existing GME simulation exercise and assess incoming interns’ recognition of low-value care.

**Methods:** Choosing Wisely™ lists were reviewed to identify four low-value hazards to be embedded into the simulation in addition to the eight patient safety hazards used previously. These low-value hazards included: 1) arbitrary blood transfusion despite stable hemoglobin (8.0 g/dL) and absence of cardiac symptoms 2) unnecessary stress ulcer prophylaxis 3) placement of a Foley catheter without indication and 4) unnecessary use of restraints. Each intern was given ten minutes to read the door chart, inspect the simulation room, and write down as many hazards as they could identify. Interns also completed a short survey on their prior training in medical school, and a follow-up survey one month into internship. T-tests were used to compare identification of low-value vs. safety hazards and to associate performance with prior training.

**Results:** One hundred twenty-five entering PGY1 interns participated in the simulation, representing sixty medical schools and thirteen specialties. The mean percentage of hazards correctly identified was 50.4% (SD 11.8%). Interns identified significantly fewer low-value hazards (mean 19.2%, SD 18.6%) than safety hazards (mean 66.0%, SD 16.0%) (P < .001). For example, while 96% of interns identified the hand hygiene hazard, only 6% identified the unnecessary blood transfusion and none identified the unnecessary stress ulcer prophylaxis. Interns who self-reported as confident in their ability to identify hazards were not any more likely to correctly identify hazards than those who were not confident. One month after the simulation, 68.9% (82/119) of interns reported being more aware of how to identify hospital hazards, and 52.1% (62/119) had taken action during internship to reduce a potential hazard that was included in the simulation.

**Conclusion:** While many GME orientations include simulation and safety training, this exercise is the first of its kind to incorporate low-value care from Choosing Wisely™ recommendations into simulated training. Given the simulation’s low-cost and minimal material requirements, it could be easily integrated into existing training programs with the support of a simulation center. Our results suggest that interns are on the lookout for errors of omission (e.g. absence of hand hygiene, absence of isolation precautions), but are often blinded to errors of commission, such that when patients are started on therapies there is an assumption that the therapies are correct and necessary. These findings suggest poor awareness of low-value care among interns, and highlight a need for the prioritization and inclusion of value-based training in GME.

**Acknowledgements/Disclosures:** The University of Chicago Pritzker School of Medicine Summer Research Program
Technological Innovations to Scale the Thirty Million Words Initiative

Luai Zakaria

**Mentor:** Dana Suskind, MD; Department of Surgery and Pediatrics

**Introduction:** Early childhood language exposure is directly correlated to academic school readiness, vocabulary growth, and IQ. Disparities in school preparedness fall heavily across socioeconomic lines and have been attributed to less overall language exposure in children from families of low socioeconomic status. Interventions to improve early childhood language environments have increased language exposure and academic readiness. The Thirty Million Words Initiative (TMW) is a parent-directed curriculum that sets to impact the achievement gap by implementing an early childhood intervention. Currently, part of the intervention uses an audio recording system called the Language ENvironment Analysis system (LENA) to measure and quantitatively assess how many words parents speak to their child. Previous studies revealed a significant increase in parent-child interactions after parents participated in this educational intervention. Yet, the LENA technology is expensive, hard-to-use, and is difficult to execute successfully on a large scale. We have developed an innovative, inexpensive, and easy-to-use mobile phone application to increase the scale and impact of the Thirty Million Words Initiative. We hypothesize that this mobile phone application will assess a child’s language environment comparable to the gold standard LENA audio recording system at a fraction of the cost.

**Methods:** We collected thirty-three audio recordings of a mother and child interacting. The subjects played with toys, read books, or talked. The complete thirty-minute session was recorded by the LENA recording device and our cell phone application simultaneously. We developed an algorithm to segment each audio recording into small audio fragments. Each audio fragment was then classified as adult speech, child vocalization, or noise by manual transcription. Thirty-eight audio signal features including signal strength, frequency content, and signal entropy were extracted from each audio fragment. With these features, we trained a machine learning algorithm to classify each audio fragment as adult speech, child vocalizations, or noise. We then assessed the sensitivity of the machine learning algorithm to correctly identify adult speech, child vocalizations, and noise.

**Results:** We have designed an iOS iPhone mobile application to assess a child’s language environment. With this application, the child wears a headset that records the audio environment and saves the recording to a Bluetooth-paired phone. We developed a machine learning algorithm to classify components of a child’s language environment including: adult speech, child vocalizations, and noise. The sensitivity for correctly identifying adult speech, child vocalizations, and noise was 70%, 66%, and 84% respectively.

**Conclusion:** Future investigation will focus on gathering more recordings to increase statistical power and to strengthen the machine learning classification model. Currently, this technology is only available for limited devices such as iOS iPhone and iPod Touch. The application will be published onto the Apple “App Store” completely free for any parent to use. Our vision is to bring a new tool to parents with young children to improve their child’s language environment and work to eliminate the achievement gap in early childhood education.

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Poster Presentations

Applied Scholarship ............................................26

Scientific Investigation in
Clinical Research or Social Sciences....47

Scientific Investigation in
Basic Sciences ..................................................66
Applied Scholarship
Assessing the Effectiveness of a Training Intervention on Community Health Center Staff's Ability to Implement Diabetes Group Visits

Ivana Barouhas

Mentor: Arshiya Baig, MD, MPH; Department of Medicine, Section of General Internal Medicine

Co-Authors: Sarah Perou-Hermans, BA; Erin Staab, MPH; Amanda Benitez, MPH; Amanda Campbell, BA; Cynthia Schaefer, RN, PhD; Michael Quinn, PhD; Arshiya Baig, MD, MPH

Background: Group visits, which supplement one-on-one medical care with shared education and social support, have been shown to improve health outcomes among adults with diabetes. We designed and evaluated the effectiveness of a training intervention to prepare community health center (CHC) staff to implement and sustain diabetes group visits. We also identified facilitators and barriers to the adoption of this care model, our aim being to help guide best practices in its widespread implementation.

Description of program/innovation: This 18-month pilot study included monthly webinars and two in-person learning sessions designed to guide the execution of six monthly group visits by twenty-six CHC staff at seven sites within the MidWest Clinicians’ Network (MWCN). We conducted surveys assessing staff preparedness to implement group visits before Learning Session 1 (LS1), after LS1, and after Learning Session 2 (LS2). Most questions were scored on a scale from 1=strongly disagree to 5=strongly agree. Questions asking the degree to which factors were barriers to group visits were scored from 1=major barrier to 4=not a barrier. We used paired t-tests to assess for change between pre- and post-LS1 values and between post-LS1 and post-LS2 values. P<0.05 was considered significant. We performed a qualitative analysis of audio-recorded team check-ins and telephone interviews to identify challenges and successes of the group visit programs.

Evaluation of program/innovation: The surveys showed increased staff awareness of: potential group visit barriers from 3.74 ± 0.76 (mean ± SD) pre-LS1 to 4.30 ± 0.47 post-LS1 (P=0.004), and to 4.83 ± 0.38 post-LS2 (P=0.0005); benefits of the group visit model from 3.96 ± 0.71 pre-LS1 to 4.48 ± 0.51 post-LS1 (P=0.0001); and key factors for group visit success from 3.00 ± 0.92 pre-LS1 to 4.26 ± 0.45 post-LS1 (P=0.0000). From post-LS1 to post-LS2, the degree to which transportation, concerns regarding lack of individual medical attention, and concerns regarding patient privacy impeded group visits improved from: 2.04 ± 0.76 to 2.50 ± 0.79 (P=0.0144), from 3.00 ± 0.68 to 3.67 ± 0.49 (P=0.0036), and from 3.00 ± 0.83 to 3.56 ± 0.51 (P=0.0014), respectively. Facilitators to group visits included having: thorough preparation and knowledge about the care model; a motivated team; experienced diabetes educators; CHC leadership support; and adequate space for the visits. Common barriers included patient barriers (recruitment, transportation, motivation), and staff barriers (time limitations). Participants also expressed that the training materials were key to preparing them for group visit implementation.

Conclusion: While CHC staff noted several barriers to implementation of diabetes group visits, our training intervention increased staff confidence, preparedness, and awareness of key group visit elements. Facilitators to sustaining group visits included preparation, team, and facility-related factors. Future research is needed to assess our training program in a larger sample of CHC sites and assess the impact of diabetes group visits on patient outcomes.

Acknowledgements/Disclosures: The University of Chicago Pritzker School of Medicine Summer Research Program
Academic-Community Collaboration to Provide Reproductive Health Education in an Underserved Middle School Population

Sarah Kennedy, M.Ed

Mentor: Anna Volerman Beaser, MD; Departments of Medicine and Pediatrics

Background: Teens from low-income communities have a higher burden of sexually transmitted infections (STIs) and unplanned pregnancies than their higher-income peers. This socioeconomic and racial disparity continues to grow despite improvements in nationwide trends. Chicago Public Schools (CPS) standards include 675 minutes per year of sexual health instruction for grades 5-12. The University of Chicago Charter School (UCCS) provides pre-kindergarten to 12th grade education across four campuses. Of 1900 students, 82% qualify for free and reduced lunch, and 97% are black or African American. Since August 2014, a cross-campus consortium with the University of Chicago Medicine (UCM) has implemented programs to improve student health and wellness. A needs assessment indicates that low resources limit provision of sexual health curriculum to the middle grades.

Description of the program/innovation: An innovative curriculum for 7th and 8th grade students was designed and implemented for all students at Carter G. Woodson Middle School. Four weekly one-hour sessions covered topics of puberty, reproductive anatomy, STI's, pregnancy, and healthy relationships. Volunteer mentors from the Pritzker School of Medicine were trained to lead small groups in objective-driven lessons with adequate time for question and answer. A survey to characterize reproductive health practices, probe attitudes about health education, measure knowledge, and elicit questions was administered to all students at the start of the course. At the end of the course, a modified survey measured growth in knowledge and assessed changes in practices and attitudes. Students were also asked to provide written feedback about their overall experience of the curriculum.

Evaluation of the program/innovation: In total, 184 students participated in the curriculum. The pre/post-evaluation was completed by 138 (75%): 53% female and 47% male. Following the course, students demonstrated increased knowledge in each of the five topic areas through multiple-choice questions; however, no increase was statistically significant. Skills and attitudes measured on a Likert scale changed to indicate improved comfort with skills for safe sex and increased interest in health education; none of the changes was statistically significant. Of open-ended subjective feedback about the curriculum, 49% was positive, with dominant themes of learning new material and enjoying interactions with mentors. 12% of feedback was negative, with dominant themes of missing PE and discomfort with the material. 39% of students gave no response.

Conclusion: This reproductive health curriculum built upon an existing collaboration between UCM and UCCS to meet a community need. Students’ subjective feedback with positive themes indicated successes of the curriculum not detectable by objective measures. In practice, lessons were often redirected by questions posed within the small group. Although this may have hampered gains in specific objective knowledge, mentors’ willingness to engage topics often perceived as taboo may improve students’ openness in thinking about and discussing these critical themes. Future iterations of the curriculum should involve an improved structure for answering questions to preserve focus on lesson objectives, and multiple modalities should be engaged in evaluation of program success.

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FIND MODY: Electronic Health Record Technology to Identify Patients at High-Risk of Having Monogenic Diabetes

Amol Naik, MS

Mentor: Liana K. Billings, MD; Department of Endocrinology, NorthShore University HealthSystem

Co-Authors: Yu-Chien Cheng, MD; Janet Yoo; Mohammad Imran Beig; David Carmody, MD; Rochelle Naylor, MD; Liana K. Billings, MD

Background: Despite the impact of knowing Maturity-Onset Diabetes of the Young (MODY) genetic mutations, MODY is currently grossly underdiagnosed. The Electronic Health Record (EHR) has been utilized to deliver more effective health care. We assessed whether current clinical risk assessment tools for identifying people at high-risk of having MODY could be applied using data extracted directly from an EHR without manual chart review.

Methods: The study took place at NorthShore University HealthSystem using Epic software. The sample included 2,193 subjects with confirmed young-onset (≤40 years old) diagnosis of Type 1 or Type 2 diabetes. We used the MODY Probability Calculator (≥25%, diabetesgenes.org) and Clinical Criteria (diagnosis age ≤25 years, parental diabetes diagnosis and BMI < 30 kg/m2). The performance of these risk-assessment tools using data extracted from the EHR was compared to the results of applying the tools using manual chart review.

Results: The accuracy of variables used in the tools extracted directly from the EHR ranged from 59.9%-95.3% when compared to chart review. When compared to chart review, the automated application of the MODY Calculator had a specificity of 92.1% and a sensitivity of 62.5% while the automated application of the Clinical Criteria had a specificity of 99.8% and a sensitivity of 55.1%. Furthermore, only 65 out of 422 subjects were identified as high risk by both tools. The subjects identified as high risk by each tool differed in current age, age of diagnosis, HbA1c, BMI, and HDL.

Conclusion: These findings indicate that (1) the automated application of existing risk assessment tools have reasonable specificity and moderate sensitivity compared to chart review and (2) the two risk assessment tools utilized in this study show limited agreement and appear to select for subjects with different clinical profiles. Clinical evaluation and genetic sequencing are underway for high-risk subjects to determine the overall utility of HER-based screening to identify patients with MODY.

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The Relationship between Self-Reported Executive Functioning and Risk-Taking Behavior in Urban Homeless Youth

Joshua Piche

Mentor: Scott Hunter, PhD; Department of Psychiatry and Behavioral Neuroscience

Co-Authors: Jason Kaylegian, MS; Dale Smith, PhD; Scott Hunter, PhD

Background: Almost 2 million U.S. youth are estimated to live on the streets, in shelters, or in other types of temporary housing at some point each year. Both their age and living situations make them more likely to engage in high-risk behaviors, particularly during adolescence, a time of increased risk taking. Much of self-control appears related to the development of the prefrontal cortex, which is at a particularly crucial period of elaboration and refinement during adolescence and emerging adulthood. Executive processes like decision-making, inhibition, planning, and reasoning may be vulnerable to adversity experienced as a result of homelessness and related impoverishment during childhood and adolescence. No study to date, to our knowledge, has directly investigated differences in risk-taking by homeless youth as it relates to their developing executive control.

Methods: One hundred and forty-nine youths between 18 and 22 years of age were recruited from homeless agencies in Chicago. Of this study sample, 53% were female and 76% African American. Measures: All participants completed, as part of a broader neuropsychological assessment, the Behavior Rating Inventory of Executive Functioning-Adult Version (BRIEF-A), the National Youth Risk Behavior Survey (YRBS), and the Mini-International Neuropsychiatric Interview (MINI). Analyses: Groups were separated based on level of self-reported EF, with two groups identified: High self-reported EF fell >1 SD above the normative average, and low self-reported EF fell >1 SD below the normative average. All analyses utilized Chi-square and Mann-Whitney tests.

Results: Analyses revealed a relationship between the level of self-reported EF and risk taking behaviors in this group of sheltered homeless urban youths. Those with lower self-reported executive functioning had higher rates of engagement in multiple substance-related risk taking behaviors.

Conclusion: These findings are important because they are a first step towards identifying contributions to risk-taking behavior in urban homeless youths. Identifying potential factors like low self-reported EF better allows us to potentially intervene, thereby providing focused support to youths who are at higher risk for engaging in problematic behaviors.

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Cost-Effectiveness of Meglumine Antimoniate versus Miltefosine Caregiver DOT for the Treatment of Pediatric Cutaneous Leishmaniasis

Brandon Berger

Mentor: Allison Bartlett, MD, MS; Department of Pediatrics

Co-Authors: Alexandra Cossio, MS; Nancy Gore Saravia, PhD; Maria del Mar Castro, MD, MS; Sergio Prada, PhD; Mai T. Pho, MD, MPH; Allison Bartlett, MD, MS

Background: Oral miltefosine has been shown to be non-inferior to first-line, injectable meglumine antimoniate (MA) for the treatment of cutaneous leishmaniasis (CL) in children. Miltefosine may be administered via in-home caregiver Directly Observed Therapy (cDOT), while patients must travel to clinics to receive MA. We performed a cost-effectiveness analysis comparing miltefosine by cDOT versus MA for pediatric CL in southwest Colombia.

Methods: We developed a Monte Carlo model comparing the cost-per-cure of miltefosine by cDOT compared to MA from patient, government payer, and societal perspectives (societal = sum of patient and government payer perspective costs). Drug effectiveness and adverse events were estimated from clinical trials. Healthcare utilization and costs of travel were obtained from surveys of providers and published sources. The primary outcome was cost-per-cure reported in 2015 USD. Treatment efficacy, costs, and adherence were varied in sensitivity analysis to assess robustness of results.

Results: Treatment with miltefosine resulted in substantially lower cost-per-cure from a societal and patient perspective, and slightly higher cost-per-cure from a government payer perspective compared to MA. Mean societal cost-per-cure were $531 (SD±$239) for MA and $188 (SD±$100) for miltefosine, a mean cost-per-cure difference of +$343. Mean cost-per-cure from a patient perspective were $442 (SD±$233) for MA and $30 (SD±$16) for miltefosine, a mean difference of +$412. Mean cost-per-cure from a government perspective were $89 (SD±$55) for MA and $158 (SD±$98) for miltefosine, with a mean difference of $69. Results were robust across a variety of assumptions in univariate and multi-way analysis.

Conclusion: Treatment of pediatric cutaneous leishmaniasis with miltefosine via cDOT is cost saving from patient and societal perspectives, and moderately more costly from the government payer perspective compared to treatment with MA. Results were robust over a range of sensitivity analyses. Lower drug price for miltefosine could result in cost saving from a government perspective.

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Human Papillomavirus Viral Load: A Useful Triage Tool for Non-16/18 hrHPV Positive Women

Margaret Wang

Mentor: Youlin Qiao, MD, PhD; Department of Epidemiology, National Cancer Center, Cancer Hospital & Peking Union Medical Center, Beijing, China

Co-Authors: Li Dong, MS, PhD; Xuelian Zhao, MS; Ruimei Feng, MS, PhD; Shangying Hu, MS, PhD; Li Zhang, MS; Youlin Qiao, MD, PhD; Jennifer S. Smith, MPH, PhD; Fanghui Zhao, MS, PhD

Background: ASCCP cervical-cancer screening guidelines recommend triaging high-risk human papillomavirus (hrHPV) positive women with cytology and genotyping, but cytology is often unavailable in resource-limited areas. We compared triaging type-specific hrHPV-positive women by viral load to cytology and visual inspection with acetic acid (VIA).

Methods: 1,742 Chinese women were screened by cytology, VIA, and HPV testing using Hybrid Capture 2 (HC2) and followed for ten years. All HC2-positive samples were genotyped. Viral load was measured by HC2 relative light units/cutoff (RLU/CO). The ten-year cumulative incidence rate (CIR) of cervical intraepithelial neoplasia grade 2 or worse (CIN2+) for type-specific hrHPV viral load was estimated using the Kaplan-Meier method.

Results: Type-specific hrHPV viral load positively correlated with concurrent cytological lesions (ptrend<0.001). The ten-year CIR of CIN2+ was associated with cytological grade and viral load for HPV16/18 and non-16/18 hrHPV positive women. The CIN2+ CIR for HPV 16/18-positive women with normal cytology was 15.3%, with abnormal VIA was 32.4%, with RLU/CO<10 was 23.6%, and with RLU/CO<100 was 33.8%. The CIN2+ CIR for non-16/18 hrHPV positive women with normal cytology was 2.0%, with abnormal cytology was 34.6%, with RLU/CO<10 was 5.1%, with RLU/CO≥10 was 27.2%, with RLU/CO<100 was 11%, and with RLU/CO≥100 was 35.5%. The CIN2+ CIR for normal and abnormal VIA were not significantly different among non-16/18 hrHPV women.

Conclusion: Our results support ASCCP guidelines to refer all HPV16/18 positive women to colposcopy and suggest triaging non-16/18 hrHPV positive women using viral loads in resource-limited areas where cytology is unavailable.

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COPD Readmissions Reduction Program: Barriers and Challenges Post-Discharge

Samantha Espinosa

Mentor: Valerie Press, MD, MPH; Department of Medicine, Section of Hospital Medicine

Co-Authors: Tina Shah, MD, MPH; Edward Kim; Steven White, MD; Valerie Press, MD, MPH

Background: Chronic Obstructive Pulmonary Disease (COPD) is the 3rd leading cause of hospital readmissions and cause of death in the US. The Center for Medicare and Medicaid Services instituted financial penalties for excess readmissions within 30 days after acute exacerbations of COPD (AECOPD). Interventions to reduce readmissions are needed and there is currently a dearth of evidence on effective methods. As part of the University of Chicago Medicine’s (UCM) inter-professional readmissions reduction program (RRP), 48 hour post-discharge nurse phone calls are made to identify barriers to ongoing health care needs. This study's objective was to quantify key responses from the phone call survey to identify barriers to care after discharge which contribute to readmission rates.

Methods: This is a quantitative sub-study of the observational survey from a RRP intervention at UCM of AECOPD patients admitted between January 1, 2015 and May 11, 2016. Patients who received care from the RRP’s inter-professional teams during admission had a nurse call them 48-hours after discharge to identify potential barriers to care including issues with discharge communication, medications, transportation to the follow-up pulmonary appointment, and ongoing symptoms. The percentages reported for survey responses are relative to the number of responses obtained for each specific question.

Results: Among 334 48-hr post-discharge phone call attempts to unique patients with their first RRP encounter, 63% (n=211) led to completion of the phone survey by the patient (58%, n=195) or a proxy (5%, n=16). Discharge communication was not reported to be a significant barrier as the vast majority (96%, n=201) of patients reported understanding their discharge summary and instructions. The majority of patients (78%, n=162) reported filling their prescriptions or were not prescribed new medications, with the most commonly unfilled medication being the rescue inhaler. Most patients also reported taking all of their medications doses (86%, n=177). With regard to transportation to the one week follow-up appointment, over half of the patients (61.2%, n=120) were relying on someone else, such as PACE medivan, friend, or family member. Lastly, some patients were suffering from COPD-related symptoms at least 48 hours post-discharge. 12% (n=25) of patients reported having more breathlessness than at discharge. Less than a quarter of the patients (21.2%, n=44) felt their activity level was either back to normal or they were more active than at discharge.

Conclusion: This study quantified survey responses from a COPD RRP, delineating four categories of challenges to patients utilizing healthcare resources and maintaining their health. The least significant barrier for patients was discharge communication, while transportation to the follow-up appointment, missing medication doses, and suffering from COPD-related symptoms were more commonly faced challenges. The presence of these challenges provides areas where UCM’s COPD RRP may consider focusing its efforts on subsequent Plan-Do-Study-Act cycles. There is ongoing data collection and analysis to determine if any of these identified factors are correlated to patient attendance for the follow-up appointment in the pulmonary clinic, and ultimately readmission rates. This further study will provide insight into specific interventions to reduce COPD-related readmissions which may be replicated in other hospitals.

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Sleep for Inpatients: Empowering Staff To Act (SIESTA): Impact on Hospital Staff Knowledge & Empowerment to Improve Patient Sleep

Mila Grossman

Mentor: Vineet Arora, MD, MAPP; Department of Medicine, Section of General Internal Medicine

Co-Authors: William Marsack, MS; Nimit Desai, MD; Babak Mokhlesi, MD, MSc; Vineet Arora, MD, MAPP

Background: Although sleep is critical to recovery from acute illness, hospitalization is far from restful. Poor sleep while hospitalized can lead to cardiometabolic derangements and delirium, while also undermining patient satisfaction. In addition, 2 out of every 5 inpatients are at risk for undiagnosed obstructive sleep apnea (OSA), which can impact their overall health and recovery. SIESTA (Sleep for Inpatients: Empowering Staff to Act) is an NHLBI-funded educational program to empower hospital staff to assist patients in obtaining better sleep and improve their knowledge of sleep disorders. In previous work, we have shown patients reported fewer sleep disruptions and greater satisfaction with SIESTA. The aim is to assess the impact of SIESTA’s targeted education on hospital staff’s knowledge and perception of empowerment to improve inpatient sleep and screen for sleep disorders.

Methods: Before the intervention, staff nurses, hospitalists and internal medicine residents completed surveys that contained multiple-choice questions to assess knowledge of inpatient sleep disturbances and OSA screening tools (i.e. STOP-BANG) and Likert items to determine providers’ perception of empowerment about improving the hospital sleep environment. All hospitalists and residents received targeted education via in-person seminars. Nurses in one general medicine unit that was designated as an intervention (SIESTA) unit received education, while nurses in another unit served as the control. Following the educational intervention, hospital staff, including nurses on the control unit, completed a post-survey with the same questions as the pre-survey. Percent correct for the multiple-choice style questions were calculated for each survey item pre and post-intervention. Results were compared by provider group via two-sample t-tests. To analyze the Likert items, data were dichotomized at a three-four cut-point. Percent agreeing was calculated for each statement, and pre- and post-intervention results were compared via Wilcoxon rank sum tests by provider group.

Results: Pre-intervention, 77 residents (82%) and 28 hospitalists (74%), 19 intervention unit nurses (83%) and 16 control unit nurses (84%) completed the survey. Post-intervention, 77 residents (82%), 25 hospitalists (60%), 22 intervention unit nurses (96%) and 15 control unit nurses (79%) completed the survey. Compared to residents, nurses on the intervention unit and hospitalists, were more likely to identify the correct OSA screening tool (STOP-BANG) post-education (33% vs. 91% intervention nurses, 26% vs. 65% hospitalists, 56% vs. 70% residents). In addition, nurses on the intervention unit were more likely to correctly identify the most common patient-reported noise source as staff conversation post-intervention (44 vs. 77%, p=0.02), while the other groups remained largely unchanged. When examining staff empowerment to improve patient sleep, residents and hospitalists were more likely to report higher agreement post intervention (44% vs. 69% residents, p=0.01, and 25% vs. 60% hospitalists, p=0.02). Likewise, physicians were also more likely than nurses to report increases in doing what they can to improve sleep.

Conclusion: A targeted education program aimed for hospital staff can result in improved staff knowledge and empowerment for improving inpatient sleep. The differences in what nurses and physicians gained may highlight differences in baseline education and empowerment among the groups and a need for tailoring the intervention to different provider groups.

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Identifying Local Interventions to Reduce Alarm Fatigue: Testing the Effectiveness of Simplifying the Telemetry Alarm Acknowledgement Process

Julia Nath

Mentor: Dana Edelson, MD; Department of Medicine, Section of Hospital Medicine

Co-Authors: Frank J. Zadravecz, MPH; Nicole Twu, MS; Matthew Churpek, MD, PhD; Dana Edelson, MD

Background: While telemetry was designed to improve patient safety, the volume and low positive predictive value of telemetry alarms can endanger patients by desensitizing healthcare providers to those alerts. Delayed or inadequate responses to alarms due to alarm fatigue can lead to preventable patient harm when the decompensation the alarm captures is, in fact, real. Though the Joint Commission has set a national patient safety goal requiring hospitals to manage their alarm systems to reduce alarm fatigue, the ideal approach to safely reduce the telemetry alarm burden is unknown. The University of Chicago Medicine (UCM) assembled an alarm safety committee and associated quality improvement projects to address alarm fatigue locally.

Methods: As part a quality improvement project, we first conducted a retrospective analysis of telemetry alarms at UCM from December 2014 – March 2015. We also completed a prospective 32-hour direct observation study, in which a trained observer followed telemetry alarms to the patient room to determine the cause, caregiver response, and if it reflected a true physiologic instability. After this initial assessment, an intervention was initiated to decrease the number of non-acknowledged telemetry alarms that were then escalated from the patient’s assigned nurse to his buddy nurse and then her charge nurse. To reduce this multiplicative burden, the nurse acknowledgement system was simplified in August – September 2015 from a seven to two-step process in some areas of the hospital. We tested the intervention’s effectiveness by comparing the proportion of escalated alarms on intervention versus control wards before (December 2014 – March 2015) and after (December 2015 – March 2016) the system change.

Results: In our initial analysis, over 1700 unique telemetry alarms sounded daily on adult units, with 95% escalated to the charge nurse. On the wards, 64% of alarms were technical in nature (e.g. “leads off”), and those technical alarms cyclically spiked every four hours. Of the directly observed alarms (n=390), 4% represented true physiologic instability, and these alarms were responded to more frequently than false alarms (86% vs. 38%, p<0.01). In addition, 16% of alarms were from patients without current telemetry orders. After implementation of the shorter acknowledgement system, the percent of alarms escalated to the charge nurse decreased from 95.7% to 94.3% in the intervention units, but also decreased from 93.6% to 92.9% on the control units. The difference between the proportion of fully escalated alarms on intervention units and control units was statistically significant (p<0.01). Over the same time period, the average number of alarms per bed per shift increased from 4.68 to 4.97 (p<0.01).

Conclusion: Our quality improvement project showed that an intervention to reduce the telemetry alarm burden by decreasing alarm escalation achieved a statistically significant decrease in the proportion of alarms escalated fully through the nurse acknowledgement system. However, the absolute magnitude of the attributable decrease was small (0.7%). Future interventions may be targeted at areas with excess non-actionable alarms identified in our initial descriptive analysis, such as reducing alarms from un-monitored patients by changing system defaults, or downgrading the prevalent “leads off” alarm.

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Goals of Medical Students Participating in Scholarly Concentration Programs

Kurt Alberson

Mentor: Rachel K. Wolfson, MD; Department of Pediatrics

Co-Authors: Vineet Arora, MD, MAPP; Karen Zier, PhD; Rachel K. Wolfson, MD

Background: Scholarly concentration (SC) programs are increasingly common in medical school curricula, fostering student participation in mentored research. Endpoints including publication rates and impact on career path have been reported, but student goals have not been described. We describe how career plans and gender impact the importance of students’ SC-related goals. Understanding student goals may enhance mentorship of professional development and self-directed learning skills.

Methods: First year students at two US medical schools were surveyed. Students reported intention for career-long research and specialty interests. Using a 5-point scale, students assigned importance to 13 goals (8 skill-related goals, 4 accomplishment-related goals, and mentorship); Composite scores for skills-related and accomplishment-related goals were used for analysis. Regression analyses, controlling for school, were used to determine whether intention for career-long research, interest in highly competitive residency, or gender were associated with increased importance of different goals.

Results: We surveyed 288 first-year medical students and received 186 responses (64.6% response rate). Compared to their peers, students interested in career-long research placed more importance on both skill-related goals (beta coefficient 1.87, 95% CI 1.03-2.71, p<0.001) and accomplishment-related goals (OR 1.71, 95% CI 1.09-2.69, p = 0.02). In contrast, compared to their peers, students interested in highly competitive specialties placed more importance only on accomplishment-related goals (OR 2.18, 95% CI 1.15-4.11, p = 0.02). Compared to men, women placed more importance on mentorship (OR 2.47, 95% CI 1.23-4.97, p = 0.01) and were less likely to be interested in highly competitive residencies (39.4% vs 54.9%, p = 0.04).

Conclusion: Gender and career plans are associated with importance of SC-related goals in the first year of medical school. This knowledge enables faculty to promote students’ appreciation of important learning goals in the setting of student research, which may help students engage in self-directed learning across their medical education.

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Getting the Picture: Visual Interpretation in Ophthalmology Residency Training

Adam Baim, MA

Mentor: Judith Farquhar, PhD; Department of Anthropology

Background: Visual interpretation is essential in many fields of health care. Although techniques have been developed to measure diagnostic competency as an educational outcome, few accounts have addressed tacit aspects of visual interpretation in clinical training: these include the disciplining of the trainee’s attentions and the trainee’s acculturation into expected styles of communicating visual interpretations to others. This paper describes the values and dispositions that are taught to ophthalmology trainees as they learn to reason through visual information, and explores how these qualities are evaluated during residency training.

Methods: The project was based on six months of ethnographic participant-observation and interviews in an ophthalmology residency program. Observational notes and interview transcripts pertaining to visual interpretation were isolated for qualitative analysis in the tradition of sociocultural anthropology, guided by literature on communication in medical education and the socialization of health professionals.

Results: Residents and faculty members identified visual interpretation as one of the most challenging skills expected of ophthalmology trainees. They expressed a belief that ‘systematic’ approaches, where visual information is parsed in a stepwise fashion, reduce the chance of trainees overlooking or misinterpreting key diagnostic features. This sensory discipline was represented in narrative form when faculty members asked residents to interpret images aloud, as residents were expected to follow prescribed sequences for describing the content of images before commenting on possible diagnoses.

Conclusion: Sensory processing is ordinarily opaque to outside observers, but the ritual of describing images in highly regimented narratives allows residents to demonstrate how they have gathered and reasoned through visual information. The structure of these narratives reflects values that residents are expected to embody during their training, such as being methodical and not leaping to premature diagnostic conclusions; it may also serve an important pedagogical function as a means for modeling and entrenching those values. Further research is needed to characterize how the verbalization of clinical reasoning shapes the interpretive skills of medical trainees.

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Students as Peer Educators: A Needs Analysis

Hunter Eason

Mentor: Jeanne Farnan, MD, MHPE; Department of Medicine, Section of Hospital Medicine

Co-Authors: Leslie Smebak, BA; Michael McGinty; H. Barrett Fromme, MD, MHPE; Jeanne Farnan, MD, MHPE

Background: Nearly all medical schools across the United States employ peer educator (PE) programs within their preclinical curriculum. The presence of PEs has been demonstrated to improve understanding of course material for both peer educators and learners alike. However, fewer than half of medical schools provide teaching skills or other types of training to PEs. At the University of Chicago Pritzker School of Medicine, peer educators are an integral part of the majority of preclinical courses, with eighty-nine unique peer educator positions each year. However, PEs do not currently undergo formal teaching skills training before assuming their roles. The objective of this project was to conduct a needs analysis of peer educators and preclinical basic science course directors to understand the benefits of and priorities for a PE teaching skills curriculum.

Methods: A focus group of eight fourth year peer educators was conducted utilizing an interview script developed with expert input. An anonymous survey of Pritzker medical students with peer educating experience and course directors from the scientific foundations of medicine curriculum was also conducted. Qualitative analysis using the constant comparative method and descriptive statistics were performed on the focus group transcript and survey results.

Results: Focus group data revealed that peer educators do not feel confident assessing learners, engaging struggling students, or prioritizing course material. Focus group participants agreed that teaching skills training would improve the PE experience and preferred a curriculum that focused on actionable skills, like teaching in unstructured environments and learner assessment. The peer educator survey (RR=40.4%) demonstrated that only 22% ofPes received any form of teaching skills training; however, 72% said they would benefit from training. Peer educators identified creating reviews and lectures, teaching in unstructured environments, providing feedback, and assessing learners as skills important to success as a PE. The course director survey revealed that only one in twelve course directors provide any training to their peer educators, but all course directors agreed that a curriculum would be beneficial to peer educator performance. Course directors identified teaching in an unstructured environment, assessing learning needs, and utilizing educational technology as essential skills for PEs.

Conclusion: Overall, both course directors and peer educators believe that PEs would benefit from a training curriculum. Our continued work involves building a PE teaching skills curriculum with the advice of experienced medical educators. We plan to implement a pilot curriculum in Fall 2017 to assess the feasibility and effectiveness of a teaching skills training course for peer educators.

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Institution of a Surgical Curriculum for Trabecular Micro-Bypass Stent Placement
Farida Esaa

Mentor: Kamran Riaz, MD; Department of Ophthalmology and Visual Sciences

Co-Authors: Varun Malhotra, MD; Kamran Riaz, MD

Background: Ophthalmic surgical teaching has traditionally occurred by an apprenticeship model. However, simulation and step-based procedural learning can allow for a more efficient, uniform and comprehensive learning experience. Successful curricula for procedures such as cataract and strabismus surgery incorporate structured wet labs and simulations to improve resident preparedness as primary surgeons. Micro-invasive glaucoma surgery (MIGS) has recently gained prominence within ophthalmology, with many MIGS procedures designed for and intended to be performed concurrently with cataract surgery. The iStent (Glaukos Corporation, Laguna Hills, CA, USA) is a trabecular micro-bypass stent for the reduction of intraocular pressure in patients with mild to moderate open-angle glaucoma that is intended for placement at the time of cataract surgery. Given the increasing popularity and efficacy of MIGS procedures, and specifically the iStent trabecular micro-bypass stent, residency programs may be interested in incorporating curricula to train residents to correctly perform these procedures. A surgical curriculum for micro-bypass stent placement has not previously been described. The objective of this study is to determine whether a targeted, step-wise curriculum for micro-bypass stent placement leads to successful insertion of the iStent by resident surgeons.

Methods: Senior (PGY-4) ophthalmology residents (6 residents) participated in a 3-stage curriculum. First, a wet lab was held for residents to gain familiarity with the device and develop bimanual surgical proficiency. Next, residents practiced bimanual intraoperative gonioscopy after routine phacoemulsification procedures. Finally, residents performed combined phacoemulsification and iStent insertion under the supervision of an experienced attending surgeon. Primary success was determined by correct anatomical placement of the device, confirmed via subsequent intraoperative gonioscopy by the supervising surgeon. Secondary success was measured by change in IOP and number of topical hypotensive medications used after surgery.

Results: There were no significant intraoperative complications. The iStent location was confirmed during postoperative gonioscopy and was noted to be in appropriate position for the duration of the follow up period for all patients. Average preoperative IOP in our subjects was 16.5 ± 4.4 mmHg. At 6 months post-op, average IOP was 13.5 ± 2.0 mmHg (18% reduction from baseline (± 22%)). At twelve-months post-op, average IOP was 13.2 ± 3.9 mmHg, with a reduction of 20% (± 19%). When comparing post-operative IOP to baseline IOP, a statistically significant difference in the mean was found between 6 months post-op and baseline (p=0.01) and 12 months post-op and baseline (p=0.007). There was no statistically significant change in medication requirement

Conclusion: This stepwise targeted surgical curriculum for trabecular micro-bypass stent placement lead to successful procedures by resident surgeons. This curriculum may be a useful model for other residency programs.

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Assessment-Oriented Oral Case Presentations in the Academic Emergency Department: Objective Measurement of Presentation Content and Clinical Context

Brennan Hodgson

Mentor: David Howes, MD; Department of Medicine, Section of Emergency Medicine

Background: The assessment-oriented oral case presentation (AO-OCP) has been presented as an effective alternative to the traditional oral case presentation (T-OCP). AO-OCPs have been demonstrated to take less time with similarly reported attending satisfaction. However, objective measures of content, including physical exam (PE) and review of system (ROS) findings, have not previously been measured. Resident perceptions of the styles and the clinical contexts in which they are used have also not been addressed.

Methods: Researchers observed OCPs presented by emergency medicine (EM) residents to EM attendings. The researcher tracked the number of review of systems and physical exam features presented, along with time, number and time of interruptions, number of clarification questions, and the type of presentation style. After each OCP, both the resident and attending were asked to complete a paper-based survey to evaluate the OCP for content, organization, confidence in diagnosis, and predicted diagnosis. Results were analyzed using T-tests.

Results: 161 OCPs were observed - 104 T-OCPs and 57 AO-OCPs. AO-OCPs were shown to take about half the time of T-OCPs, 1.77 min vs 3.25 min (p<0.01). This decrease in time was paralleled by a decrease in both the number of PE and ROS findings in the AO-OCP (p<0.01 for both). The AO-OCPs experienced fewer external interruptions (p<0.01) with an equivalent number of teaching moments (p=0.85). There was no significant difference found between the number of clarification questions total (p=0.12) or between the questions that had already been answered earlier in the presentation (0.14) or not (0.35). Residents on average used the T-OCP 48% more often than the AO-OCP, this was not significantly different across PGY year. Residents reported higher confidence in preliminary diagnosis when using the AO-OCP (p<0.01). In subjective ratings post-OCP, residents rated their organization and overall satisfaction with the presentation higher for AO-OCP (p<0.01 for both). Conversely, they rated both perceived content (p=0.81) and desired additional data (p=0.76) similarly for both presentation styles. Attendings reported a higher overall satisfaction and organization rating with the AO-OCP (p<0.01 and p=0.02, respectively), while rating content, and desired additional data similarly (p=0.06, p=0.83, p=0.26 respectively).

Conclusion: The AO style represents a trade-off between a decrease in time with a loss of quantified content. Despite this quantified decrease, the AO-style shows higher reported rates of satisfaction and organization with no perceived loss of content among both residents and attendings. The decreased time is also associated with fewer external interruptions to allow for more streamlined presentations. Residents were more likely to use the T-OCP overall and used the AO-OCP most when they were confident in the final diagnosis. These comparisons help to illustrate the utility of the AO-OCP. In the fast-paced, high acuity setting of an ED, where delivering pertinent information rapidly is necessary for patient care, the AO-OCP presents a viable alternative to the more T-OCP currently taught at the medical school level.

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The Effect of Checklist Characteristics on Measured Pediatric Trauma Team Performance

Michael McCartin

Mentor: Lisa McQueen, MD; Department of Pediatrics

Background: The resuscitation of a critically injured child is a rare event, making Simulation an increasingly popular strategy for training physicians and nurses in pediatric trauma. The value of simulation-based medical education is subject to little debate. However, the most effective way to proctor simulated scenarios and provide constructive feedback to participants is still an area of active research. This lack of consensus has resulted in the independent development of several pediatric trauma simulation assessment checklists across the US. The purpose of this study was to identify the checklist or checklist qualities that most reliably distinguish high-performing trauma teams from low-performing trauma teams. We aimed to accomplish this by comparing them in a head to head fashion against a single item global rating scale. Global rating scales (GRS) outperform binary checklists in interstation reliability and ability to capture nuance of performance. However, GRS require experts to interpret performance, while checklists allow novices to observe performance and guide constructive feedback. Thus, identifying the pediatric trauma checklist with characteristics that best approximates the interpretation of an expert using a GRS would be valuable.

Methods: We selected 10 trauma team scenarios from archived simulation footage of University of Chicago Comer Children’s Hospital trauma teams participating in simulated pediatric trauma scenarios. Trauma teams consisted of one emergency medicine resident, one surgery resident, and two emergency medicine nurses. Each scenario lasted approximately ten minutes. The scenarios were graded using four previously published pediatric trauma simulation assessment checklists (Checklists A, B, C, and D). These checklists vary in emphasis on crisis resource management skills (CRM), procedural competency and timeliness. Each trauma scenario was also given single item GRS (scale 1-10), based on how well the evaluator believed the team performed independent of the checklist score results. We examined the range of scores given to a trauma scenario depending on the checklist used and determined which checklists were most strongly correlated with GRS.

Results: Checklist A was a binary checklist that placed emphasis on primary and secondary survey task completion. Checklist A had the weakest correlation (r = 0.38, p = 0.275) with GRS. Checklist B was the most detailed checklist used and included measurements of timeliness, CRM skills, and procedural competency. Checklist B had the strongest correlation (r = 0.802, p = 0.005), but was the only checklist too complex for real-time evaluation. Checklist C included measurements of timeliness, CRM skills, procedural competency and task completion, but less measurements of timeliness than Checklist B; Checklist C had the second strongest correlation (r = 0.779, p = 0.008) with the GRS. Checklist D measured timeliness and procedural competency, but had no measurements of CRM skills included. Checklist D had the third strongest correlation (r = 0.756, p = 0.011) with GRS.

Conclusion: We demonstrate that measurements of CRM skills, procedural competency, and timeliness on pediatric trauma simulation checklists improved strength of correlation with GRS. These findings suggest that the inclusion of these measures in checklist scoring is needed to accurately measure pediatric trauma team performance.

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Toward a Resident Personal Finance Curriculum: 
Quantifying Resident Financial Circumstances, 
Needs, and Interests 

Ryan McKillip

Mentor: Daniel Golden, MD, MHPE; Department of Radiation and Cellular Oncology

Co-Authors: Michael Ernst, MD; James Ahn, MD, MHPE; Ara Tekian, PhD, MHPE; Eric Shappell, MD; Daniel Golden, MD, MHPE

Background: Resident financial health has been linked to wellness and resiliency, yet financial literacy among residents is highly variable. While some medical school curricula include budgeting and student loan education, content on managing finances as a resident is usually lacking. We sought to quantitatively assess residents’ financial circumstances, needs, and interests to inform the design of a resident personal finance curriculum.

Methods: Surveys were sent to residents in eight specialties at an academic medical center. Likert-type responses allowed respondents to rate their level of comfort (1=Very Uncomfortable-7=Very Comfortable) and interest (1=Very Uninterested-7=Very Interested) in various personal finance topics including budgeting, loan repayment, disability insurance, life insurance, home buying, and retirement planning. Details regarding financial circumstances, including assets, liabilities, and insurance, were also collected. Results are reported as median (interquartile range).

Results: Of 346 residents surveyed, 144 (41.6%) responded. Residents were from Internal Medicine (56, 38.9%), Pediatrics (34, 23.6%), Emergency Medicine (18, 12.5%), and other specialties (36, 25.0%). Ninety-one (63.2%) reported educational loans, with an average balance of $191,730. Credit card balances exceeding $3,000 were reported by 11 (7.6%) respondents. One-hundred-two (70.1%) reported emergency savings, but only 65 (45.1%) reported having a retirement account (average balance $27,608). Respondents rated highest comfort levels with budgeting (5[4-6]), and lowest level of comfort with disability insurance (2[2-4]) and home buying (2[2-5]). Interest in learning each topic was high (6[5-7]), with retirement planning (6[5-7]), investing (6[5-7]), and home buying (6[5-7]) the topics of highest interest.

Conclusion: These results highlight the deficits in personal finance literacy among residents. Future work should focus on development of a nationally scalable personal finance curriculum for residents.

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Medical Imaging Use by Pediatricians: Identifying Core Imaging Concepts and their Optimal Point of Introduction

William Moser

Mentor: Christopher Straus, MD; Department of Radiology

Background: Results from a national survey of medical school and radiology departments indicate that 75% of medical schools have no imaging requirements and greater than 90% of student imaging education are taught by non-radiologists. These results indicate that training is non-standardized leading to a potential variability in intern skills, adding to both the cost of training and variability of these future practicing physicians. Pediatric trainees, in particular, have a higher responsibility given the potential risks and deleterious effects resulting from radiation exposure. A pediatric topic-specific module was developed targeting core imaging principles relevant to referring pediatricians for medical students in their last year, to provide a more uniform imaging experience for those embarking into pediatrics. In this study we examined when trainees and students would prefer to learn the information included in the module.

Methods: The pediatric medical imaging module was compiled by known educational experts in radiology and pediatrics, each identifying key vocabulary, concepts, and cases pertinent to pediatric care. To focus evaluation on the global concepts, key examples were selected for survey purposes to test the level of content. A Likert item questionnaire was validated and distributed to clinical medical students and pediatric house staff via email or a paper survey.

Results: We received an overall 21% response rate without evidence of nonresponse bias. All of the respondents agreed that the content presented in the module was pertinent and of the appropriate level. All but one respondent thought it would be helpful prior to a pediatric internship. The clear majority (37/56) of respondents thought the material should be presented during clinical medical school. Students preferred to be exposed to the material during medical school significantly more than post graduate trainees (Fisher’s = 0.002), which demonstrates an anticipated self-selection bias.

Conclusion: A topic-specific imaging module with content targeting future non-radiologists prior to graduating medical school was identified as relevant and of high value to both students and post graduate trainees specializing in pediatrics.

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Students as Peer Educators: Development and Implementation of a Teaching Skills Course for Medical Students

Leslie Smebak

**Mentor:** Jeanne Farnan, MD, MHPE; Department of Medicine, Section of Hospital Medicine

**Co-Authors:** Hunter Eason; H. Barrett Fromme, MD, MHPE; Jeanne Farnan, MD, MHPE

**Background:** Nearly all medical schools across the United States employ peer educator (PE) programs within their preclinical curriculum. Peer educators improve understanding of course material for both peer educators and learners alike. Despite the widespread use of PEs, fewer than half of medical schools provide them with teaching skills or other types of training. At the University of Chicago Pritzker School of Medicine (PSOM), peer educators are an integral part of most preclinical courses, with eighty-nine unique peer educator positions each year. However, PEs do not currently undergo formal teaching skills training before assuming their roles. Previous research has demonstrated that PSOM faculty members and peer educators believe that a teaching skills course for PEs would improve the peer educator experience.

**Methods:** The study was conducted at the University of Chicago Pritzker School of Medicine during December 2017. Twelve fourth year medical student peer educators participated in a 3.5-hour teaching skills curriculum pilot. The pilot included interactive sessions on learner assessment, engaging struggling learners, teaching in an unstructured learning environment, creating effective review PowerPoints, and creating review questions. The students reported their comfort with various aspects of the peer educator role before and after the course via anonymous survey. Open ended feedback was elicited from participants during the post-course survey. Descriptive statistics were performed comparing students’ comfort with the peer educator role before and after the teaching curriculum. Open ended feedback was evaluated for trends and common themes among participants.

**Results:** Twelve fourth year medical students participated in the teaching skills pilot. Eight of the twelve (75%) completed both the pre-course and post-course surveys. Seven out of eight (87.5%) of participants agreed that participating in the course improved their confidence with the peer educator role. Students rated their confidence with aspects of the peer educator role on a scale from 1 to 5, 1 being very unconfident and 5 being very confident, both before and after the teaching skills course. Participants identified the greatest improvements in their confidence with engaging struggling learners (mean confidence score 3.22 pre-course and 4.25 post-course) and teaching in an unstructured learning environment (mean confidence score 3.44 pre-course and 4.25 post-course). Students requested more information on adult learning theory and additional didactic sessions on writing and editing test questions.

**Conclusion:** Our study found that peer educators currently do not feel prepared for their teaching roles. Their confidence improves after teaching experience, but ideally peer educators would begin their teaching roles with greater confidence and experience. A pilot of a peer educator training course successfully improved PEs’ confidence with the peer educator role.

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Resident Perspectives on Teaching during Awake Surgical Procedures
Claire Smith, MFA

**Mentor:** Nancy Schindler, MD, MHPE; Vascular Surgery, NorthShore University HealthSystem

**Co-Authors:** Robert Nolan; Kristina Guyton, MD; Mark Siegler, MD; Alexander Langerman, MD, SM; Nancy Schindler, MD, MHPE

**Background:** Residents learn technical and communication skills during training, and practice both concurrently during awake surgical procedures. However, patients express mixed views on resident involvement in their surgical care, making this context challenging for residents to navigate. We sought to explore resident perspectives on teaching during awake surgical procedures.

**Methods:** Residents in Urology, OB/Gyn, and General Surgery who had been exposed to 10 or more awake surgical procedures were recruited for recorded focus groups at the University of Chicago. Recordings were transcribed, coded and reviewed by three researchers using the constant comparative method until thematic saturation was reached.

**Results:** Twenty-five residents participated. Residents identified positive educational techniques during awake surgery including pre-procedural communication, explaining teaching and the resident role, whispering/non-verbal signaling, involving the patient in education, and comfort of the educator. Residents described challenges and failures in education, including hesitance toward asking questions, hesitance toward correcting a learner, whispering/non-verbal signaling, and taking over. Residents also discussed informed consent during awake procedures; while some residents indicated that the consent process was modified for awake procedures to include more details regarding the resident role, others reported that preoperative discussions with patients did not address the unique aspects of awake procedures.

**Conclusion:** Residents participating in awake surgical procedures offer new insights on successful techniques for teaching during awake surgery, emphasizing that good communication in the procedure room starts beforehand. They also identify challenges with teaching in this context, often related to a lack of inclusive and clear communication between the educator, the trainee, and the patient. Residents identify some strategies, such as whispering/non-verbal signaling, as both positive and as presenting challenges, which suggests that context and patient personality can make a difference in the success of some tactics. Different residents view informed consent differently; some disclose more information regarding their involvement with an awake patient. This discrepancy emphasizes the extent to which awake surgery highlights ethical tensions inherent in all surgical and procedural training. Moving forward, we plan to administer a patient survey to quantitatively explore patient's responses to different teaching and communication strategies.

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A Proof of Principle for the Use of Automated, Graph-Based Curricular Tools in Anatomy Education

Stephen Winter, MS

Mentor: Callum Ross, PhD; Department of Organismal Biology and Anatomy

Background: Recent efforts to update the University of Chicago anatomy course have focused on validating existing multiple-choice and short-answer questions to determine student competency across multiple different subcategories of material. To test these subcategories in a statistically valid way, the number of validated questions has needed to increase. Considerable resources are currently required to identify concepts for new questions, write questions to test those concepts, and validate the new questions. Our group has previously produced the GALEN system to validate questions. However, the process for and ability to generate new test questions has largely remained unchanged, manual, and time-consuming. Here, we describe the theory, design, and proof of concept for a system to automatically generate multiple choice questions from a large anatomy dataset.

Methods: We evaluated data structures for their ability to store and expose large sets of relational data that could be extracted to form questions with clinical question stems. We chose a graph database for these qualities and the ability generate complex queries more efficiently than standard tabular (SQL) data. Python was used to generate extraction, transformation, and load (ETL) protocols to import the Web Ontology Language (OWL) format Foundational Model of Anatomy (FMA) into a Neo4J graph database. The graph was then queried with Python, a Neo4J driver, and CYPHER to generate multiple choice questions in a way that can be generalized to a template query that can generate many such questions automatically.

Results: We initially believed that we would need to generate our own anatomy dataset, but we were relieved to find the FMA, an OWL representing an immense amount of curated structural and functional data. We were able to import 104,523 elements of the dataset and over 600,000 properties and relationships representing ~97% of the FMA data. From the graph representing these data, we were able to create complex multiple choice questions that tested structural and functional anatomy.

Conclusion: This work demonstrates a model for creating graph-based curricula from web ontologies to generate questions for both conceptual evaluation and study of anatomy or the topic of any web ontology. We hope that this concept and the proliferation of web ontology languages will provide the foundation of new, innovative, and inexpensive means to study and evaluate knowledge for anatomy and other subjects.

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Scientific Investigation in Clinical Research or Social Sciences
Impact of a Proactive Swallowing Rehabilitation Program on Feeding Tube Placement in Patients Treated for Pharyngeal Cancer

Gaurav Ajmani, MHS

Mentor: Mihir Bhayani, MD; Department of Surgery, NorthShore University HealthSystem

Co-Authors: Cheryl C. Nocon, MD; Bruce E. Brockstein, MD; Nicholas P. Campbell, MD; Amy B. Kelly, MA; Jamie Allison, MA; Mihir Bhayani, MD

Background: A proactive Speech and Language Pathology (SLP) program is an important component of the multidisciplinary care of head and neck squamous cell carcinoma (HNSCC) patients. Swallowing rehabilitation can reduce the rate of feeding tube placement, thereby significantly improving quality of life. We evaluated the impact of a proactive SLP rehabilitation program at a single institution on feeding tube placement and dietary intake in HNSCC patients.

Methods: This is a retrospective evaluation of patients treated for squamous cell carcinomas of the hypopharynx, oropharynx, and nasopharynx from 2004 to 2015 with radiation or chemoradiation in the definitive or adjuvant setting. Patients who received <5000 cGy radiation or underwent re-irradiation were excluded. A proactive SLP program for HNSCC patients was initiated in 2011. Study cohorts were divided into two groups: 2004-2010 and 2011-2015. Outcomes assessed were SLP referral placement, timing of referral, feeding tube placement, and ability to tolerate oral intake at completion of treatment.

Results: 254 patients met inclusion criteria (135 pre- and 119 post-SLP program). With the initiation of a proactive SLP program, pre-treatment evaluations increased from 21.5% to 58.8% (RR 2.74; 1.92-3.91), and rate of referral overall at any time increased from 60.0% to 79.8% (RR 1.33; 1.13-1.57). G-tube placement rates decreased from 45.9% to 29.4% (RR 0.64; 0.46-0.89). Among patients receiving a swallow evaluation, feeding tube requirements were lower for those receiving a pre-treatment evaluation (31.3%) than for those referred during (61.1%) or after (64.4%) treatment. The rate of tolerating any oral intake at the end of treatment improved from 71.1% in the pre-implementation period to 82.4% (RR 1.16; 1.01-1.33).

Conclusion: A proactive SLP program can be successfully established as part of the multidisciplinary care of HNSCC patients and significantly impact the quality of life of HNSCC patients.

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Clinical and Anatomic Characteristics of Psychotic Patients Carrying a Common Variant Allele of NRXN1

Lawrence Belcher

**Mentor:** Ney Alliey-Rodriguez, MD; Department of Psychiatry and Behavioral Neuroscience

**Co-Authors:** Elliot S. Gershon, MD; Ney Alliey-Rodriguez, MD

**Background:** Numerous studies have identified neuroanatomic abnormalities in patients with the major psychotic disorders, schizophrenia (SZ) and bipolar disorder (BD). Well-established findings in these patients include enlargement of several areas within the brain's ventricular system. A recent GWAS from our group found a new significant relationship between the volume of the temporal horn of the left lateral ventricle and a common variant intronic SNP in NRXN1 (rs80262609, chr. 2p16.3). NRXN1 codes for neurexin, a transmembrane protein in the CNS involved in the formation of synaptic relationships between adjacent neurons. Several mutations in this gene have been previously associated with schizophrenia. In our study population of 740 patients with psychotic disorders (SZ, BD, and schizoaffective disorder), the NRXN1 minor allele of interest was identified in 79 participants. We set out to better characterize this subset of patients, looking for unique imaging and clinical features that may distinguish them from patients carrying only the major NRXN1 allele.

**Methods:** As part of the multisite Bipolar and Schizophrenia Network for Intermediate Phenotypes (B-SNIP) study, “deep phenotyping” data were collected from more than 2,400 psychotic patients, relatives, and healthy controls. Participants gave a genetic sample and participated in the measurement of several phenotypes, including MRI and DTI imaging, EEG, ERP, oculomotor testing, cognitive testing, and numerous validated clinical scales. This analysis focuses on MRI data, which was processed into voxels using FreeSurfer v5.1, and clinical scales. Numerical data were analyzed using Stata 14 (College Station, TX).

**Results:** 75 minor allele carriers (Aa) did not significantly differ from 665 major allele homozygotes (AA) in age, sex, specific psychotic diagnosis, presence of a first degree relative with psychosis, or age at symptom onset. Minor allele homozygotes (aa) were excluded from analysis due to small sample size (n=4). Minor allele heterozygotes were significantly less likely to be African-American (25.33% vs. 39.40%, p<.05) compared to major allele homozygotes. They were also less likely to have attempted suicide (28.77% vs. 42.22%, p<.05). Imaging analyses were performed on a subset of 491 patients who participated in an MRI. 13 brain volumes were found to be significantly different between minor allele carriers and major allele homozygotes. Areas identified were the left lateral ventricle, left interior lateral ventricle, third ventricle, left choroid plexus, right lateral ventricle, right inferior lateral ventricle, right amygdala, right choroid plexus, right caudal anterior cingulate thickness, left CA1 (of hippocampus), right CA1, right entorhinal cortex, and right insula. All varying volumes were found to be larger in the minor allele carriers. Despite these notable structural differences, the two groups did not differ in aggregate or itemized symptom severity on the Positive and Negative Symptom Severity Scale (PANSS), social impairment (SFS), or global assessment of functioning (GAF) scores. They also did not differ in performance on cognitive exams (BACS, WRAT).

**Conclusion:** Psychotic patients with one copy of a common variant in NRXN1 (rs80262609) have distinctive neuroanatomy, notably enlargements at several locations within the ventricular system, compared to major allele homozygotes with equivalent psychiatric diagnoses. These structural differences do not appear to translate to differences in clinical presentation.

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Cost-Effectiveness Analysis of Adjuvant versus Salvage Radiotherapy after Radical Prostatectomy for High-Risk Disease

Ellen Daily

Mentor: Sangtae Park, MD, MPH; Department of Urology, NorthShore University HealthSystem

Background: There is continued debate on adjuvant radiotherapy (ART) compared to observation plus salvage radiotherapy (SRT) after radical prostatectomy (RP) in men with adverse pathology (seminal vesicle invasion, positive surgical margins, extra-prostatic extension). While three randomized clinical trials (SWOG 8794, EORTC 22911 and ARO 9602) have consistently demonstrated improved PSA-free survival with ART, metastases and overall survival rates are inconsistent. Furthermore, if ART were given to ALL high risk post-RP patients, those who would have never had PSA recurrence would be overtreated, with its attendant costs and impact on post-RP bowel, urinary and sexual function. Thus, this cost-effectiveness analysis was conducted to integrate overall survival, need for adjuvant therapies, quality of life, and healthcare costs in comparing ART versus SRT in these patients.

Methods: A Markov model was created using TreeAge (Williamstown, MA), to compare ART versus SRT for a hypothetical cohort of 65-year-old men with adverse RP pathology. PSA survival, radiotherapy success, progression to androgen deprivation and castrate resistance requiring chemotherapy, overall survival, and treatment-related toxicities were obtained from the published literature. Quality of life utilities were collected using a time tradeoff survey of prostate cancer specialists, and 2015 Medicare healthcare costs were used.

Results: Our model showed that in men with adverse pathology after RP, PSA surveillance with SRT as needed results in more quality-adjusted life years (QALYs) than ART (4.38 versus 3.67, respectively). ART is also the more expensive strategy, with an incremental cost of $17,206 over SRT in the patient’s lifetime, for an incremental cost effectiveness ratio of $24,233 per QALY. One way and two way sensitivity analyses by varying patient age, radiation costs, urinary/bowel/sexual QOL, utility values confirmed the robustness of our model, and SRT remained the more cost effective strategy.

Conclusion: In men with adverse pathological features after RP, our study suggests that the strategy of PSA surveillance plus selective SRT is less costly, and preserves more QALYs than universal ART. Future randomized trials should aim to gather more detailed quality of life data on radiotherapy after RP, and future analyses should integrate private and public healthcare costs in order to refine the appropriateness of ART and SRT in high-risk prostate cancer patients.

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Cytokine Correlates of Olfactory Dysfunction in Older U.S. Adults

Elijah Darnell

**Mentor:** Jayant Pinto, MD; Department of Surgery, Section of Otolaryngology-Head & Neck Surgery

**Co-Authors:** Kristen E. Wroblewski, MS; Kristina L. Pagel, PhD; David W. Kern, PhD; Martha K. McClintock, PhD; Jayant Pinto, MD

**Background:** Peripheral blood cytokines serve as biomarkers of physical frailty. Whether cytokine profiles can serve as markers of sensory impairment remains an open question. Given that olfactory impairment predicts increased odds of 5-year mortality and is closely associated with neurodegenerative disease, a plasma cytokine correlate of olfactory dysfunction would be clinically useful as a biomarker for identifying high-risk patients for poor health outcomes.

**Methods:** We analyzed data from the National Social Life, Health and Aging Project, a representative sample of home-dwelling older US adults (age 62-90, N=2,089, age eligible without acute inflammation N=1684). Plasma cytokine levels (n=18) were measured with Luminex xMAP multiplex assay using standard protocols. Olfactory function was measured with validated tests (n-butanol sensitivity and odor identification, each via Sniffin’ Sticks). We tested the association between cytokine profiles associated with frailty and immunologic function and olfactory function using multivariate ordinal logistic regression, adjusting for age, gender, race/ethnicity, education level, cognition, and comorbidity.

**Results:** The (IL-1Ra)high-(IL-4 and IL-13)low cytokine profile was associated with worse n-butanol odor sensitivity (OR 1.63, 95% CI 1.21-2.20) and worse odor identification (OR=1.42, 95% CI 1.11-1.82). Profiles of proinflammatory, Th1, or Th2 cytokines showed no associated with olfaction, although some individual cytokines (IL-5 and IL-10) also showed associations with olfactory dysfunction.

**Conclusion:** We have identified a plasma cytokine signature, (IL-1Ra)high-(IL-4 and IL-13)low, as a candidate biomarker of olfactory dysfunction in older US adults. These data implicate systemic inflammation in olfactory dysfunction in older adults and support the concept of a complex immune mechanism connecting sensory impairment and dysregulated immunologic control, a relationship that warrants additional scrutiny.

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Low Rates of Genetic Counseling and Testing in Individuals at Risk for Lynch Syndrome Reported in the National Health Interview Survey

Nolan Faust

Mentor: Sonia Kupfer, MD; Department of Medicine, Section of Gastroenterology, Hepatology, & Nutrition

Co-Authors: Sang Mee Lee, MS, PhD; Sonia Kupfer, MD

Background: Lynch syndrome (LS) is the most common inherited cancer syndrome, with a prevalence of approximately 1 in 279. Affected individuals are at greater risk for a variety of cancers, most commonly colorectal and endometrial. Yet while the identification of patients with hereditary cancer syndromes impacts future screening and management practices, evidence suggests that genetic counseling and testing rates remain low even in individuals at high risk. The number of individuals at high risk for LS, and the association of LS risk factors with genetic testing, remains unknown.

Methods: This study used data from the National Health Interview Survey (NHIS) Cancer Control Supplement to explore and quantify whether risk factors for LS are associated with patient report of receiving genetic counseling and testing. Cross-sectional data from the NHIS was pooled from three years (2005, 2010, 2015). Eligible patients were those who responded to all questions regarding (1) discussion of genetic testing with a healthcare provider, (2) whether the provider advised genetic testing, and (3) whether the patient received genetic testing. The number of LS risk factors for each patient was calculated based on National Comprehensive Cancer Network screening criteria. Outcomes included the proportion of individuals with risk factors who reported discussion of, recommendation for, and receipt of genetic testing. Trends in each outcome over time were also examined by calculating the change in outcome percent with the presence of one or more risk factors for each survey year.

Results: Of 89746 respondents, 2172 (2.4%) met one risk factor criteria and 292 (0.3%) met two or more. The most common risk factor met was “>=1 first-degree relative with colorectal or endometrial cancer age <50” (n=1764). Highest frequencies of genetic testing were seen in those who met criteria of “personal history of colorectal or endometrial cancer and >=1 first-degree relative with LS-related cancer diagnosis at age <50” (10.14%). For individuals who met no criteria, 2.53% discussed, 1.11% were advised to undergo, and 0.77% received genetic testing. For those with one criteria met, 5.62% discussed, 3.04% were advised, and 1.89% tested. If two or greater criteria were met, 10.27% discussed, 6.85% were advised, and 5.14% were tested. The change in each outcome percent for patients who met one or more criteria, compared to patients who met none, grew in each survey year. From 2005 to 2015, the delta increased from 1.87% to 4.71% for discussed, 1.03% to 3.25% for advised, and 0.15% to 2.55% for tested.

Conclusion: Overall, reported rates of discussing, being advised to have, and undergoing genetic testing are low for patients at risk for LS. One contributing factor may be that only a fraction of patients who discuss genetic testing with a healthcare provider eventually receive it. Trends over time show that genetic counseling and testing rates are increasing but remain low. Further research is warranted to determine predictors and reasons for low rates of genetic testing, and to improve rates of early diagnosis, surveillance, and treatment of patients at high risk for LS associated cancers.

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Characterization of Hip Fracture Risk Following an Upper Extremity Fracture: Review of 212,549 Patients

J. Erik Kulenkamp

Mentor: Lewis Shi, MD; Department of Orthopaedic Surgery and Rehabilitation Medicine

Co-Authors: Mark C. Dougherty; Haroutioun Boyadjian, MD; Douglas R. Dirschl, MD; Michael J. Lee, MD; Lewis Shi, MD

Background: Recent studies have demonstrated increased hip fracture frequency among patients who have experienced prior upper extremity fractures, particularly those involving the distal radius. The purpose of this study is to compare the risk of hip fracture in patients with initial shoulder, elbow, or wrist fractures, as well as the impact of chronic comorbidities on hip fracture risk.

Methods: This was a retrospective cohort study using MarketScan, a database containing the private insurance claims of approximately 55 million Americans between 2003-2013. International Classification of Diseases-Ninth Revision, Clinical Modification (ICD-9) codes were used to identify patients over the age of 20 with non-pathologic fractures of the proximal or distal humerus, radius, or ulna. The follow-up requirement was a minimum of 3 years of continuous enrollment after the initial fracture. Similarly, controls were identified, without upper extremity fracture, with the same age and follow-up requirements. Multinomial logistic regression was employed to calculate relative risk of hip fracture within 3 years of an index upper extremity fracture. The final model adjusted for age, gender, and comorbidities including osteoporosis, osteopenia, rheumatoid arthritis, diabetes mellitus, and dementia.

Results: A total of 212,549 patients with an index upper extremity fracture were identified, and 3.29% (6,995) suffered a hip fracture within 3 years. A total of 897,365 control patients were identified, and 0.50% (4,530) suffered a hip fracture within 3 years of enrollment within the database. After controlling for age, gender, and comorbidities, the relative risk of hip fracture following a shoulder fracture (proximal humerus) was 4.31 (±0.19, p<0.001). The relative risk following an elbow fracture (distal humerus, proximal radius or ulna) was 2.11 (±0.12, p<0.001). The relative risk following a wrist fracture (distal radius or ulna) was 2.71 (±0.12, p<0.001). As expected, age was associated with increased hip fracture risk (p<0.001), with each additional year beyond 20 representing a 7.3% increase. Likewise, female sex represented a relative risk of 1.11 (±0.05, p<0.001) in the adjusted model. Among patients with osteoporosis, treatment with bisphosphonates reduced the relative risk of hip fracture by 15.22% (p= 0.004). The presence of comorbidities including osteoporosis, osteopenia, rheumatoid arthritis, diabetes mellitus, and most notably, dementia, were associated with increased hip fracture risk (p<0.001 each).

Conclusion: Upper extremity fractures were associated with increased frequency of hip fractures during the subsequent 3-year period. Proximal humerus fracture, rather than distal radius fracture, represented the greatest risk. Age, female sex, and other comorbidities all increased rate of hip fracture. This information can improve counseling and guide treatment of patients with index upper extremity fractures.

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Mentor: Jayant Pinto, MD; Department of Surgery, Section of Otolaryngology-Head & Neck Surgery

Co-Authors: Michael Ramirez, MD; Jonathan C. Garneau, MD; Megan K. Ford, MD; Katherine McKeough, BS; Daniel T. Ginat, MD; Fuad M. Baroody, MD; Samuel G. Armato III, PhD; Jayant Pinto, MD

Background: Traditional methods of staging chronic rhinosinusitis (CRS) through imaging do not differentiate between degrees of partial mucosal sinus inflammation, thus limiting their utility as imaging biomarkers. We hypothesized that software-aided, quantitative measurement of sinus inflammation would generate a metric of disease burden that would correlate with clinical parameters in patients with suspected sinus disease.

Methods: Adults with rhinologic complaints undergoing CT imaging were recruited at an urban, academic, tertiary care center (n=45 with Lund-Mackay [LM] scores ≥ 4). 3D volumetric image analysis was performed using a semi-automated method to obtain a “Chicago-modified Lund-Mackay” (Chicago MLM) score, which provides a continuous scale to quantify extent of opacification. Linear regression was used to test the association of the Chicago MLM score with concurrent symptoms (total nasal symptom scores [TNSS]) and disease-specific quality of life (Sinonasal Outcome Test-22 [SNOT22]).

Results: Chicago MLM scores were significantly associated with both symptoms (p=0.037) and disease-specific quality of life (p=0.007). Inflammation in the ethmoid and sphenoid sinuses appeared to influence these associations. These findings were even more robust when analysis was limited to patients with more severe disease (LM>6).

Conclusion: The quantitative measurement of sinus inflammation by computer-aided 3D analysis correlates modestly with both symptoms and disease-specific quality of life. Posterior sinuses appear to have the greatest impact on these findings, potentially providing an anatomic target for clinicians to base therapy. The Chicago MLM score is a promising imaging biomarker for clinical and research use.

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A Real-world Network Meta-analysis of the Safety of Direct Oral Anticoagulants for Stroke Prevention in Non-valvular Atrial Fibrillation

Linda Liu

Mentor: Gaurav Updahyay, MD; Department of Medicine, Section of Cardiology

Co-Authors: Benjamin Weber, MD; Stephanie Besser; Adam Oesterle, MD; Roderick Tun, MD; Gaurav Updahyay, MD

Background: Direct oral anticoagulant (DOAC) use in atrial fibrillation (AF) has been demonstrated to have favorable bleeding outcomes in randomized controlled trials (RCTs) compared to vitamin K antagonists (VKAs), however the scope of their “real-world” use has broadened since the original landmark trials that led to their approval. The aim of this study is to systematically analyze observational data from cohort and registry studies to compare the patient characteristics and safety outcomes of DOACs in real-world use with that from their original trials.

Methods: A network meta-analysis of cohort and registry studies of apixaban, dabigatran, edoxaban, and rivaroxaban compared to landmark RCT trial data was performed. The primary safety endpoints were incidence of major bleeding, gastrointestinal bleeding, and intracranial bleeding. Secondary endpoints include all-cause mortality and fatal bleeding. Study quality was assessed using the Cochrane risk of bias tool for RCTs and the Downs and Black Instrument for observational studies.

Results: Of 5,802 reviewed studies, 68 observational articles and 5 RCTs representing a total of 383,378 unique patients treated with DOACs were included in this study. Pooled baseline patient characteristics from observational studies versus RCTs were: weighted mean age 73 years vs 71 years; 40% vs 37% women, 46% vs 22% paroxysmal AF, average CHADS2-VASc score 3.2 vs 2.6, CHF 18% vs 47%, HTN 74% vs 88%, Age >75 47% vs 38%, DM 26% vs 31%, history of stroke/TIA 13% vs 31%. Safety analysis represented 202,653 person-years of follow up. Pooled DOAC bleeding rates from observational data expressed as a weighted mean per 100 person-years are as follows: major bleeding 3.26, ICH 0.48, and GI bleeding 2.52. Major bleeding rates for Dabigatran, Rivaroxaban, and Apixaban alone were 2.95, 3.65, and 2.46 respectively.

Conclusion: Patients receiving DOACs in real-world use differ from the patients studied in the original RCTs. In pooled safety analysis, bleeding rates associated with DOAC use are comparable to that of VKAs.

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TMW-Pediatrics: Strengthening the Pediatric Provider’s Role in Parent Education on Early Learning and Language Development

Danielle LoRe

Mentor: Dana Suskind, MD; Department of Surgery and Pediatrics

Co-Authors: Peter Ladner; Logan Galansky; Dana Suskind, MD

Background: Infants born into poverty show disparities in cognitive development as early as nine months of age, when compared with peers born into higher socioeconomic (SES) families. These disparities broaden over time, doubling by the age of two and impacting school readiness. This discrepancy stems from a ‘word gap’ first elucidated in a landmark study by Hart & Risley (1995), where children from low SES backgrounds were found to hear 30 million fewer words from birth through age three than children from high-SES backgrounds. Educating and empowering parents to use their words to stimulate their child’s early brain and language development is critical in order to prevent this disparity. Pediatricians’ longitudinal relationship with parents and children starting from birth makes them well suited to provide this early education.

Description of program/innovation: The Thirty Million Words® Initiative (TMW) seeks to impact doctor-patient communication on early learning through the development of the TMW-Pediatrics curriculum. TMW-Pediatrics targets pediatric health care providers and strengthens their knowledge and skills in giving anticipatory guidance to parents about the role of early learning and language environments in cognitive development. As a scalable, technology-based program, TMW-Pediatrics will consist of self-guided modules administered online. These modules will first focus on educating providers on this language and cognitive development disparity and its underlying neurodevelopmental science. Secondly, they will teach providers how to educate parents using the 3T’s, our easy-to-understand behavioral strategies, which encourage parents to Talk More with their children using descriptive words, Tune In to what their child is communicating, and Take Turns to foster conversation with their child. To inform development of the curriculum, we administered an adaptation of TMW’s existing Survey of Parent Expectations and Knowledge (SPEAK) assessment to identify current practices and areas of weakness regarding early language development. These topics include child-directed speech, intellectual malleability, parent responsiveness and attachment, and electronic media use.

Evaluation of program/innovation: The adapted SPEAK surveys were completed by 322 trainees, including medical students, residents, and fellows. Among the trainees, 75% reported that early childhood learning and language development were addressed in their curriculum. When asked how often they discuss early learning and language development with parents, 23% reported 0-25% of the time, 26% reported 25-50%, 24% reported 50-75%, and 28% reported 75-100%. The average age at which they started discussing early learning and language development with parents was 3.43 months. On the adapted SPEAK surveys, trainees scored lowest on items testing parent attachment and responsiveness and intellectual malleability.

Conclusion: Although the majority of trainees are receiving education on early childhood learning and language development, only 28% are consistently addressing these topics with parents. These discussions are taking place around 3 months of age, missing critical months of brain development. The TMW-Pediatrics curriculum will address the importance of discussing these behaviors early with parents in the newborn period, as well as strategies for parents to best promote early learning environments.

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Evaluation of Fluid Resuscitation in Patients with Severe Sepsis and Septic Shock

Joseph D. Lykins V

**Mentor:** Michael Ward, MD; Department of Emergency Medicine, University of Wisconsin

**Co-Authors:** Hani Kuttab, MD; Michelle Ho, MD; Eric Keast, MD; Mobola Kukoyi, MD; Jason Kopec, MD; Stephen Hall, MS; Kristen Wroblewski, MS; Michael Ward, MD

**Background:** The Surviving Sepsis Campaign recommends patients with sepsis-induced hypoperfusion receive 30 mL/kg of crystalloid fluid within three hours. CMS measures are within six hours. However, data on this weight-based fluid resuscitation is conflicting and often does not take into consideration a patient’s medical comorbidities. This study aims to determine predictors of fluid resuscitation and determine how fluids may affect outcomes for patients with severe sepsis and septic shock.

**Methods:** This was a single-center retrospective cohort study. Using ICD 9 and 10 codes in combination with Sepsis-2 criteria, 1,144 patients were included between January 1, 2014-May 30, 2017. Patients were placed into four groups - 30 mL/kg crystalloid bolus within three hours, 3-6 hours, between 6-24 hours, or did not reach by 24 hours of sepsis onset. Outcome parameters included rates of in-hospital mortality, need for ventilator or vasopressor support, ICU admission, and delayed hypotension. Statistical analyses included multivariate Cox regression analyses using variable factors as dependent variables.

**Results:** Patients received a 30 mL/kg bolus within 3, 6, and 24 hours 49.7%, 65.1%, and 80.0%, respectively. At 3 hours, age >65 (OR 0.80, 95% CI 0.70-0.92), body mass index (BMI) >30 (OR 0.36, CI 0.31-0.43), men (OR 0.83, CI 0.73-0.94), ESRD (OR 0.33, CI 0.25-0.44), and CHF (OR 0.49, CI 0.41-0.59) were less likely to reach fluid goals while patients with shock were more likely to achieve fluid goals (OR 1.54, CI 1.34-1.77). Conclusions were the same when looking at time to achieve fluid goals using survival analysis. Patients who did not receive 30 mL/kg within the first three hours of sepsis onset were at increased odds for in-hospital mortality (OR 1.6, 95% CI 1.1-2.3) and delayed hypotension (OR 1.39, CI 1.02-1.91), adjusting for age, MEDS, septic shock, BMI >30, gender, ESRD, and CHF.

**Conclusion:** Advanced age, obesity, history of ESRD or CHF, and men were less likely to receive the recommended 30 mL/kg. Additionally, patients with severe sepsis and septic shock who did not receive the recommended fluid bolus had increased odds of in-hospital mortality when controlling for MEDS, age, BMI, history of CHF or ESRD, sex, and septic shock. Therefore, the 30 mL/kg in three-hour fluid goal recommended by the Surviving Sepsis Campaign appears to be appropriate for mortality reduction in severe sepsis and septic shock.

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A Descriptive Analysis of Patients Presenting to an Urban Academic Emergency Department with Ventricular Assist Device-Specific Complaints

Magdeline Montoya

**Mentor:** James Walter, MD; Department of Medicine, Section of Emergency Medicine

**Co-Authors:** Anand Gopalsami, MD, MBA; Gene Kim, MD; Eric Shappell, MD; James Walter, MD

**Background:** The number of patients with a ventricular assist device (VAD) continues to increase, with over 13,000 implants to date. However, research examining how these patients present to the emergency department (ED) is lacking. Characterizing ED presentations is the first step toward understanding what ED physicians need to know to treat this medically complex patient population.

**Methods:** Focused retrospective chart review of data collected from 143 unique VAD patients followed by the University of Chicago Medical Center from 7/1/2009 to 6/30/2014. Data collected included chief complaint, diagnostic testing, interventions required, final ED diagnosis, and disposition. Specific focus on patients who presented to the ED with VAD-specific complaints defined as (1) abnormal device reading/alarm, (2) grossly damaged equipment, and (3) non-specific complaints (dyspnea, hematuria, abnormal lab values) not attributed to other organ dysfunction.

**Results:** In total, 143 VAD patients presented to the ED 682 separate times. 7.6% of these ED visits were for VAD-specific complaints, and 59.6% of these patients were diagnosed with VAD thrombosis or suspected VAD thrombosis. 51.9% required VAD-specific interventions including device setting adjustment, hardware repair/replacement/adjustment, pump exchange, heart transplantation, and catheter directed thrombolysis.

**Conclusion:** >90% of VAD patients presenting to the ED did not have VAD-specific complaints. Patients who did present with VAD-specific complaints were most often diagnosed with and treated for VAD thrombosis. Emergency physicians should be familiar with the diagnosis, presentation, and treatment of VAD thrombosis, as it is a potentially fatal complication.

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Patterns of Failure after Radical Cystectomy for pT3-4 Bladder Cancer: Implications for Adjuvant Radiation Therapy

Abhinav Reddy

Mentor: Stanley Liauw, MD; Department of Radiation and Cellular Oncology

Co-Authors: Joseph J. Pariser, MD; Shane M. Pearce, MD; Ralph R. Weichselbaum, MD; Norm D. Smith, MD; Gary D. Steinberg, MD; Stanley Liauw, MD

Background: In patients with muscle-invasive bladder cancer, local-regional failure (LF) has been reported to occur in up to 20% of patients following radical cystectomy. The goals of this study were to describe patterns of LF, as well as assess factors associated with LF in a cohort of patients with pT3-4 bladder cancer. This information may have implications towards the use of adjuvant radiation therapy.

Methods: Patients with pathologic T3-4 N0-1 bladder cancer were examined from an institutional radical cystectomy database. Preoperative demographics and pathologic characteristics were examined. Outcomes included overall survival and LF. Local-regional failures were defined using follow-up imaging reports and scans, and the locations of LF were characterized. Variables were tested by univariate and multivariate analysis for association with LF and overall survival.

Results: A total of 334 patients had pT3-4 and N0-1 disease after radical cystectomy and bilateral pelvic lymph node dissection. Of these, 46% received perioperative chemotherapy. The median age was 71 years old, and median follow-up was 11 months. On univariate analysis, margin status, pT stage, and pN stage, were all associated with LF (P<.05), however, on multivariate analysis, only pT and pN stages were significantly associated with LF (P<.05). Three strata of risk were defined, including low-risk patients with pT3N0 disease, intermediate-risk patients with pT3N1 or pT4N0 disease, and high-risk patients with pT4N1 disease, who had a 2-year incidence of LF of 12%, 33%, and 72%, respectively. The most common sites of pelvic relapse included the external and internal iliac lymph nodes (LNs) and obturator LN regions. Notably, 34% of patients with LF had local-regional only disease at the time of recurrence.

Conclusion: This study of 334 patients with locally advanced bladder cancer provides useful information regarding patterns of failure after radical cystectomy. To our knowledge, this is the first study to assess LF and patterns of LF in a cohort of pT3-4 patients. Patients at the highest risk of LF were those with pT4 stage or LN involvement with a 2-year risk of LF that exceeds 30%. Therefore, this group of patients may be appropriate candidates for adjuvant radiation therapy. The hypothesis that adjuvant radiation therapy can improve pelvic relapse free survival in men with pT3-4N0-2 bladder cancer after radical cystectomy is currently being tested in randomized clinical trials.

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Utilizing a Commercially Available Virtual Reality Device for Glaucoma Screening

Darin Rosen

Mentor: Susan Ksiazek, MD; Department of Ophthalmology and Visual Sciences

Background: Glaucoma is the most common cause of irreversible blindness worldwide, with the majority of cases representing primary open angle glaucoma (POAG). It also poses as a serious national health problem in the United States, as at least 2.2 million Americans have the disease and over half of these patients remain undiagnosed. The initial manifestation of POAG is frequently peripheral visual field loss, which may remain undetected by patients until they have already suffered significant irreversible field loss. Early diagnosis and treatment are crucial for preventing further vision loss. Modern visual field testing provides an accurate and frequently utilized diagnostic tool, however, current devices are not ideal for screening due to cost, portability, and accessibility. Recent advances and commercialization of virtual reality (VR) technology have allowed for a more affordable solution which has been demonstrated to have comparable results to conventional perimetry technology. Given the design benefits and the encouraging results, we aimed to design and test the efficacy of a visual field test using a VR headset as a screening tool for glaucoma.

Methods: A total of 26 eyes of 21 patients being evaluated for glaucoma or a suspected glaucoma diagnosis were recruited. Patients with reliable 24-2 SITA Humphrey Visual Field Analyzer (HFA) exam results were eligible for inclusion, with the most recent exam taken during the previous 6 months. The Oculus Rift Development Kit 2 (DK2) headset was used to display the visual field test and an office laptop was used for data collection. The program applies standard perimetry techniques to the same 54 stimuli as the 24-2 SITA software in the HFA. The program determines the lowest threshold intensity that can be seen by the patient at a given location. Fixation loss is determined by randomly presenting stimuli in the blind spot that was confirmed prior to initiating the test. The algorithm used to generate a positive or negative screening result is based on the interpretation of results by two glaucoma specialists and one general ophthalmologist. The results of the visual field test were compared to the gold-standard for perimetry, the Humphrey Visual Field Analyzer (HFA) to determine sensitivity and specificity.

Results: The test was successfully performed in 26/28 eyes on 21/22 patients. As compared to the gold standard, the program achieved a sensitivity of 94.7% and a specificity of 85.7%. The eye that had a positive HFA exam but negative screening test had a HFA result with a mean deviation of 0.93, indicating very mild disease. Overall mean fixation loss was 37.8%, however refinement in blind spot mapping on the last 12 eyes reduced fixation loss to 20.1%.

Conclusion: This device can reliably achieve screening results similar to the gold standard. This suggests that glaucoma screening with VR technology may be achievable in the primary care setting. Subsequent studies should assess reliability with a larger sample size and whether this tool may be more efficacious for select patient populations. Studies should also evaluate whether careful blind spot calibration can reduce fixation loss.

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Somatic Symptoms in Women with Dysmenorrhea and Noncyclic Pelvic Pain
Rebecca Zuckerman

Mentor: Kevin Hellman, PhD; Department of Obstetrics and Gynecology
Co-Authors: Rebecca L. Silton, PhD; Frank F. Tu, MD, MPH; Joshua S. Eng, PhD; Kevin M. Hellman, PhD

Background: Somatic symptoms are a robust, transdiagnostic risk factor for pain conditions. However, the extent to which somatic symptoms contribute to the manifestation of women’s pain syndromes, such as dysmenorrhea and noncyclic pelvic pain (NCPP), is unclear due to high rates of co-occurrence. Therefore, the present study investigated the primary hypothesis that somatic symptoms would be elevated in NCPP and distinctly influence the relationship between dysmenorrhea and co-occurring NCPP.

Methods: A secondary analysis was performed on cross-sectional questionnaire data from 1012 nonpregnant reproductive-aged women. Eligible analyzed participants (n = 834) were categorized into four groups: healthy, dysmenorrhea, NCPP, and NCCP with co-occurring dysmenorrhea (NCPP+dysmenorrhea). A parallel mediation analysis was run to evaluate the primary hypothesis that somatic symptoms are the primary factor associated with increased NCPP accounting for dysmenorrhea.

Results: The NCPP+dysmenorrhea group had higher somatic, anxiety, and depression symptom T-scores (respectively: 61, 61, 60) compared to the health controls (46, 51, 51; p’s <.001) and the dysmenorrhea group (50, 53, 54; p’s <.001). The pain and psychological symptoms were significantly correlated across the entire sample (r’s = .29, -.64, p’s <.01). Results from parallel mediation analysis showed that somatic symptoms were distinctly associated with NCPP+dysmenorrhea.

Conclusion: Women with NCPP+dysmenorrhea have increased psychological and somatic symptoms compared to women with dysmenorrhea alone. Given that NCPP often co-occurs with dysmenorrhea, failure to account for comorbidity in previous studies has likely led to an overestimation of psychological symptoms in dysmenorrhea. Future studies should evaluate whether somatic sensitivity is a modifiable risk factor for NCPP.

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Kidney Donors in ESRD Bypassing Priority Status: A Qualitative Interview-Based Study

Miguel Barajas

Mentor: Lainie F. Ross, MD, PhD; Department of Pediatrics

Co-Authors: Colin M.E. Halverson, PhD, Center for Biomedical Ethics and Society. Vanderbilt University

Background: Approximately 6,000 living kidney donations (LKD) and 10,000 deceased kidney donations occur annually in the United States. However, demand greatly outpaces supply with nearly 100,000 people waiting for a kidney transplant. Although most living donors do well after nephrectomy, Dr. Lainie F. Ross has compiled a database of kidney donors who have gone into end stage renal disease (ESRD). Since September 1996, the United Network for Organ Sharing (UNOS), the institution that allocates deceased donor organs, gives some priority to former living donors who develop ESRD, allowing these former donors to get a deceased donor kidney quickly. It is unknown why some former living donors do not take advantage of this priority status.

Methods: This project is part of a larger ongoing study, which seeks to build a database of prior living kidney donors who have gone into ESRD. From this pool, we contacted individuals who had not taken advantage of their priority status and either obtained a living kidney donor or elected long-term dialysis. We developed 2 different scripts, one for those on dialysis and one for those who had received LKD. Former living donors in ESRD were interviewed over the telephone using a semi-structured interview wherein patients were asked about their experiences as donors, experiences as recipients, dialysis experiences, and current health status. An 18-category coding tree was then developed iteratively by the three researchers (MB, CMEH, LFR), making modifications until there was unanimous agreement about the definitions of each code. For the five interviews with LKD recipients, all three investigators triple-coded 2 interviews to ensure inter-coder reliability. The remaining 3 were double-coded by two investigators (CMEH and MB), achieving 88.5% inter-coder reliability. Two interviews with the dialysis patients were double-coded by 2 investigators (LFR and MB).

Results: Seven individuals who had not taken advantage of their priority status were interviewed: 5 received LKD grafts and 2 remained on dialysis. Among this group, 4 were women, 5 were White, one was Black, and one identified as “Other.” The average age at donation for our participants was 29.7 years and the average age at diagnosis of ESRD was 54 years. Five of 7 initial donations were between siblings and two between parents and their children. Of the 5 participants who received living donor kidneys, 2 received the kidney from a sibling, 2 from a non-biological family member, and one from her daughter’s friend. The one who had a friend as the source of the living donor did not receive this kidney directly but participated in a living donor chain. Emerging interview themes included a sense of “duty to family” in making the decision to donate, relatively sophisticated “strategizing” within an allocation system that affords them priority on the deceased donor kidney wait list, the importance of kinship, fairness, and participation in electronic and off-line social networks and support groups.

Conclusions: We have gathered and analyzed insights from a group of uniquely situated kidney transplant patients. For participants living with an LKD graft, they have chosen to bypass expedited access to cadaveric grafts in favor of universally perceived higher quality LKD. In addition, it was revealed that one participant had been inappropriately excluded from LKD by a transplant program. Contact with the patient and his dialysis physician is ongoing, and he has recently been referred for transplantation at another center.

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Assessment of Provider Knowledge in the Early Childhood Care Environment

Diana Bouhassira

Mentor: Dana Suskind, MD; Department of Surgery and Pediatrics

Background: In the United States, approximately 76% of children under age four spend time in non-parental care, often in early education centers or childcare programs. The quality of these programs is assessed by state-level organizations that provide training and funding to programs based on their determined quality. In Illinois, this program is called ExceleRate. The primary aim of our study was to determine if ExceleRate ratings correlate with childcare provider knowledge about the importance of language in child cognitive development as assessed by a previously developed and validated assessment tool, the Survey of Parental/Provider Expectations and Knowledge about Language Learning (SPEAK). Our secondary aim was to better characterize the factors that influence scores on the SPEAK.

Methods: The SPEAK was administered online in collaboration with the Illinois Network of Childcare Resource & Referral Agencies (INCCRRA) to childcare providers throughout Illinois over two 10-week periods. Survey participation was incentivized by optional enrollment in a raffle following survey completion. Data were collected through RedCap and analysis was performed using Microsoft Excel and StatPlus.

Results: For the primary outcome, no significant differences were found in mean performance on the SPEAK when comparing providers at programs with different ExceleRate ratings (one-way ANOVA, p = 0.983). Mean SPEAK score did, however, correlate significantly with provider education level (Pearson correlation, p = 0.0072) and provider income (Pearson correlation, p = 0.0028). Participants with a history of prior coursework in cognitive development performed significantly better on the SPEAK than those without coursework (p = 0.050). Mean scores did not differ whether the course work was at the undergraduate level, graduate level, or in a professional development course. Mean scores did not significantly differ between providers who primarily served different age groups (0-2 year olds, 2-3 year olds, or 3-5 year olds) (p = 0.44), nor were there differences correlating with length of time the provider had been working (p = 0.58). No differences were found in mean scores in providers located in high population density areas (Chicago, Springfield, or Bloomington zip codes) compared to those in less urban areas (p = 0.39).

Conclusion: No differences in knowledge about early childhood language development were found in providers at programs differentiated by ExceleRate. This suggests that quality assessment and ExceleRate training may not adequately address the importance of language in child cognitive development. SPEAK scores did correlate with provider education and income, suggesting that better education for childcare providers as well as further assessment of factors causing low-income providers to perform less well are potential areas to target for improvement.

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Vision-Related Quality of Life and Visual Acuity as Measures for Fall Risk and Indicators for Follow Up Care in a Hospitalized Population

Christina Chen

**Mentor:** Valerie Press, MD, MPH; Department of Medicine, Section of Hospital Medicine

**Co-Authors:** Elizabeth Donnelly, MD; Vineet Arora, MD, MAPP; David Meltzer, MD, PhD; Valerie Press, MD, MPH

**Background:** With an aging population, visual impairment and associated health risks with poor vision are becoming an increasingly common problem in the United States. Blindness or insufficient vision as defined by worse than 20/40 vision in the better eye affects 1 in 28 Americans older than 40 years with a projection that the population of visually impaired would increase by 70% by 2020. Impaired vision has been shown to be associated with many negative health outcomes such as delirium, falls, decreased health literacy, and decreased quality of life. There have been limited data on the vision-related quality of life (VRQOL) of hospitalized patients with insufficient vision or the impact interventions could have on improving their vision and associated health outcomes in the hospital setting.

**Methods:** Hospitalized general medicine patients at the University of Chicago were consented and completed a visual acuity test by Snellen Eye Chart and a National Eye Institute Visual Function Questionnaire (VFQ-25) as part of the VISION study (Vision in Senior Inpatients: Outcomes and Needs). A subgroup of participants was contacted 30 days post-discharge to assess if they had any new falls or hospitalizations during the 30 day interval. Another subgroup who had initially failed vision screening or had a history of diabetes received information on getting outpatient vision care during their hospitalization and was contacted 30 days post-discharge to repeat the NEI VFQ-1 and assess vision care follow up.

**Results:** One thousand three hundred eighty four patients completed the vision screening and VFQ-25 during hospitalization. Only 977 (70.1%) were found to have sufficient vision with 20/40 vision or better in at least one eye. Age greater than 65 years, African American ethnicity, less than high school education completion, or a history of diabetes was associated with higher rates of insufficient vision and worse vision functioning as measured by VFQ-25. In the 346 patient subset assessed on fall history, a recent fall in the year prior to hospitalization was associated with a lower VFQ-25 score (p=0.002). However, a lower VFQ-25 score was not predictive of a new fall in the 30 days post-discharge after controlling for race, gender, race, and education. Only 54 of 132 participants (41%) completed a post-discharge survey on vision care follow-up. There was no significant improvement in VFQ-25 score regardless of whether or not the patient received a pair of reading glasses in the hospital (p=0.11) or sought vision care (p=0.40). Only 11 of 54 patients (20%) actually saw an eye doctor or made an eye care appointment during the 30 day period post-discharge.

**Conclusion:** A significant percentage of hospitalized patients have insufficient vision and lower VRQOL that can be addressed during their hospital stay. The NEI VFQ-25 may be underutilized as a quality of life metric to assess potential risk for poor vision-related outcomes like falls in the elderly population. Further studies with larger sample size and longer term follow up would be necessary to elucidate the utility of making outpatient vision care referrals during hospitalization.

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Virtual Teach-to-Goal vs. In-Person Teach-to-Goal for Effective Respiratory Inhaler Technique Education: A Non-Inferiority Randomized Clinical Trial

Colleen Kelly

Mentor: Valerie Press, MD, MPH; Department of Medicine, Section of Hospital Medicine

Co-Authors: Steven R. White, MD; Vineet M. Arora, MD, MAPP; Wan Wen, PhD; Valerie Press, MD, MPH

Background: Using an inhaler correctly is difficult, requiring both conceptual understanding and ability to coordinate multiple steps to ensure that medication is effectively delivered to the lungs. Despite current education efforts, previous research revealed that a majority of hospitalized patients incorrectly use their respiratory inhalers. This puts patients at higher risk for exacerbations and other disease complications while also increasing healthcare use and expenditures. Misuse can be corrected utilizing a patient-centered educational strategy called Teach-to-Goal (TTG), which consists of rounds of education and assessment until skills attainment. In-person TTG has been proved to be effective in teaching inhaler technique, but is costly and does not have a lasting effect. To improve upon these deficiencies, we developed Virtual Teach-to-Goal (V-TTG), an adaptive learning technology that provides narrated video instruction of correct inhaler technique with rounds of tailored questions. In this study, we compared and evaluated the effectiveness of V-TTG vs. in-person TTG for teaching correct inhaler technique to determine if V-TTG is non-inferior to in-person TTG.

Methods: A total of 118 hospitalized adult patients (age>18) with a diagnosis of asthma or COPD were enrolled. Participants were randomized into two intervention groups: V-TTG to TTG. Inhaler technique was evaluated pre- and post-intervention on a 12-step validated checklist by a trained assessor. In-person TTG involved a trained educator demonstrating correct inhaler use and then assessing and correcting patient technique for up to three rounds. V-TTG is an interactive iPad-based platform that combines up to three rounds of narrated demonstrations of correct inhaler technique with tailored self-assessment questions. Patients answered the questions before and after watching the demonstration; if any questions were answered incorrectly, patients were prompted to re-watch the demonstration. Chi-square and Fisher’s exact tests were used to evaluate pre vs. post-education within each arm. Generalized Estimating Equation Regression was used to assess whether V-TTG is non-inferior to in-person TTG.

Results: 118 participants had complete pre/post data (V-TTG n=59; TTG n=59). The majority of participants were Black (114/118) and female (75/118), with a mean age of 55 years. The proportion of inhaler misuse significantly decreased for both V-TTG (98% to 31%, p<0.001) and TTG (83% to 17%, p<0.001). After adjusting for baseline misuse, V-TTG was non-inferior to TTG (non-inferiority margin: -0.1, group mean diff = 0.0273, 90% CI: -0.071, 0.126).

Conclusion: Inhaler misuse among COPD and asthma patients is widespread and problematic, contributing to increased hospital readmissions, exacerbations, and healthcare expenditures. Current educational interventions to teach correct inhaler technique are not adequate. Therefore, it is essential that feasible, effective, durable, and low-cost self-management strategies are developed and implemented. This RCT demonstrates that V-TTG is non-inferior to in-person TTG intervention. While future work is needed to determine if V-TTG will be effective for improving long-term inhaler technique skills and patient health outcomes, V-TTG is a viable, lower cost method of providing both in-hospital and at-home patient self-management education.

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Scientific Investigation
in Basic Sciences
MEIS1 and MEIS2 Expression and Prostate Cancer Progression: A Role for HOXB13 Binding Partners in Metastatic Disease

Raj Bhanvadia

Mentor: Donald Vander Griend, PhD; Department of Surgery, Section of Urology

Co-Authors: Calvin Van Opstal; Hannah Brechka, PhD; Nimrod Barashi, MD; Erin McAuley, PhD; Wen-Ching Chan, PhD; Donald Vander Griend, PhD

Background: Prostate cancer remains the second leading cause of cancer related death among American men. Importantly, not all patients with biochemical recurrence have the same prognosis. While currently established predictors of prostate cancer recurrence rely on commonly used pathologic criteria, including Gleason grade, there remains a need to both identify improved molecular markers of metastatic progression in prostate cancer. Furthermore, there is a critical need for a more thorough understanding of the biologic processes that alter prostate cancer behavior in order to more successfully risk-stratify and effectively treat patients. MEIS1 and MEIS2 are transcription factors that regulate important functions in cell fate determination during development and cell proliferation. Importantly, many identified germline HOXB13 mutations, which confer increased incidence of prostate cancer, occur within the MEIS-interaction domains of HOXB13. However, the functional and predictive role of changes in MEIS expression within prostate tumor progression, however, remain largely unexplored.

Methods: RNA expression datasets, gene micro-array expression datasets, immuno-histochemical staining of annotated tissue microarrays, and cell-based functional assays were utilized to determine the role of MEIS1 and MEIS2 in prostate cancer and metastatic progression.

Results: The GEO GDS2545 microarray derived from 170 prostate specimens showed significant positive correlation between MEIS1 and MEIS2 expression within samples (R2 = 0.60; P <0.05). Comparative analyses demonstrate step-wise decreases in both MEIS1 and MEIS2 expression across normal prostate, localized prostate cancer and metastatic prostate cancer in the GEO data set (MEIS1; 140.3 v. 84.4 v. 11.1, P <0.05) (MEIS2; 434.7 v. 242.0 v. 57.6, P<0.05). The annotated RNA-seq dataset showed a supported a correlation in MEIS1 and MEIS2 expression (R2 = 0.47; P <0.05) and similar decline in MEIS mRNA expression from normal, to localized, and to metastatic prostate cancer (P <0.05). There was no significant difference in HOXB13 mRNA expression different between benign, tumor, and metastatic tissues across either data set. Immuno-histochemical staining of annotated tissue microarrays showed that retention of expression of MEIS proteins in primary tumors is associated with a lower hazard of biochemical recurrence (HR = 0.37), and lower hazard of clinical metastasis (HR = 0.28) after multivariable analysis. Pathway and gene set enrichment analyses identified MEIS-associated networks involved in cMYC signaling, cellular proliferation, motility, and local tumor environment. Depletion of MEIS1 and MEIS2 resulted in increased tumor growth over time in vivo, and decreased MEIS expression in both patient-derived tumors and MEIS-depleted cell lines was associated with increased expression of the pro-tumorigenic genes cMYC and CD142, and decreased expression of AXIN2, FN1, ROCK1, SERPINE2, SNAI2, and TGFβ2.

Conclusion: These data implicate a functional role for MEIS proteins in regulating cancer progression, and support a hypothesis whereby tumor expression of MEIS1 and MEIS2 expression confers a more indolent prostate cancer phenotype, with a decreased propensity for metastatic progression.

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Identifying and Validating a Gene Network Responsive to Imatinib Treatment in a Chronic Myeloid Leukemia Cell Line

Chester Kao, MSE

Mentor: R. Stephanie Huang, PhD; Department of Experimental and Clinical Pharmacology, College of Pharmacy, University of Minnesota

Co-Authors: Fan Wang, MS; R. Stephanie Huang, PhD

Background: The current treatment for chronic myeloid leukemia (CML) is imatinib, a tyrosine kinase inhibitor (TKI), which specifically semi-competitively binds the ATP-binding site of the BCR-ABL fusion protein interfering with downstream signal transduction, and treatment has shown strong success in the early-chronic phase of CML with 88% survival. Despite the success of TKIs, nearly 20-30% of patients will either be unresponsive to drug treatment or relapse after successful therapy. Thus, it is crucial to decipher the detailed mechanism of action for imatinib and how these dynamic molecular changes encourage resistance development.

Methods: We carefully analyzed several high-throughput datasets (both in vivo and in vitro) that contain information on transcriptome changes after TKI exposure and selected the key gene/pathway (AKT2) for subsequent functional experiments in the K562 cell line (a CML cell line). To explore imatinib’s effect on K562 cells, we treated cells with either 1 μM imatinib or control (DMSO) for 72 hours. To assess AKT2’s direct role in apoptosis and survival in K562 cells, we transfected cells with 10 nM AKT2 siRNA or Silencer Negative Control. We measured gene expression with qPCR, apoptosis with Caspase-Glo 3/7 Assay, and cell survival with CellTiter-Glo Assay for both experiments.

Results: A sequential analysis of transcriptome changes in response to TKI treatment from CML patients to cell lines followed by pathway analysis revealed the enrichment of the apoptotic pathway and genes within for imatinib response. Specifically, an AKT2 centered gene network which included BCL2L1 and PIK3CD was selected because of multiple levels of evidence for its role in CML patients/cell lines. After imatinib treatment, AKT2 expression was significantly upregulated from 6 to 48 hours (p<.001), BCL2L1 was down-regulated from 6 to 48 hours (p<.05), and PIK3CD was significantly upregulated from 6 to 24 hours (p<.01). Furthermore, after imatinib treatment, cell apoptosis was increased (p<.01) and cellular proliferation was decreased (p<.001). After transfection with AKT2 siRNA, AKT2 inhibition resulted in significant decrease in AKT2 mRNA expression (p<.001) and cell proliferation was decreased (two-way ANOVA p<.01).

Conclusion: Imatinib treatment upregulates AKT2 and alters the expression of associated genes BCL2L1 and PIK3CD, increases apoptosis, and decreases cellular proliferation. AKT2 knockdown shows a decrease in survival suggesting that AKT2 may be a marker for imatinib resistance.

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Bacillus anthracis TagO is Required for Vegetative Growth and Secondary Cell Wall Polysaccharide Synthesis

J. Mark Lunderberg, PhD

Mentor: Olaf Schneewind, MD; PhD Department of Microbiology

Co-Authors: Megan Liszewski Zilla, PhD; Dominique Missiakas, PhD; Olaf Schneewind, MD, PhD

Background: Bacillus anthracis is the causative agent of anthrax disease. It is a Gram-positive, spore-forming bacterium which propagates disease through the germination of spores in mammalian hosts. Following spore germination, the B. anthracis cell envelope functions in supporting vegetative cell growth as well as in facilitating infection of the host. Within the vegetative cell envelope is a linear secondary cell wall polysaccharide (SCWP) that retains surface (S)-layer and associated proteins via their S-layer homology (SLH) domains. The SCWP is comprised of trisaccharide repeats [\(\rightarrow 4\)-\(\beta\)-ManNAc-(\(1\rightarrow 4\)-\(\beta\)-GlcNAc-(\(1\rightarrow 6\)-\(\alpha\)-GlcNAc-(\(1\rightarrow\)]) and tethered via acid-labile phosphodiester bonds to peptidoglycan. Proteins in the S-layer perform specific functions during host infection, including heme-iron uptake, adherence to host cells and separation from elongating chains. Earlier work identified UDP-GlcNAc 2-epimerases GneY (BAS5048) and GneZ (BAS5117), which act as catalysts of ManNAc synthesis, as well as a polysaccharide deacetylase (BAS5051), as factors contributing to SCWP synthesis. The function of additional genes involved synthesis of the SCWP is uncharacterized. The B. anthracis genome contains tagO (BAS5050) a homologue of other Gram positive tagO genes, a UDP-N-acetylglucosamine:undecaprenyl-P N-acetylglicosaminyl 1-P transferase, the enzyme that initiates the synthesis of murein linkage units. Previous attempts to delete tagO in B. anthracis were unsuccessful, the basis for this work is to define the roles of genes involved in SCWP assembly, including BAS5051 and tagO (BAS5050).

Methods: B. anthracis Stern 34F2 and its variants were grown under standard conditions in brain heart infusion broth or agar. Escherichia coli was grown in Luria Bertani broth or agar. Allelic replacement was performed using the temperature-sensitive plasmid pLM4 and mutant allele transduction was performed with bacteriophage CP-51. Biochemical and microscopic methods were used to assess vegetative cell growth, SCWP production and S-layer protein assembly of wild-type and mutant strains.

Results: We used phage transduction to demonstrate that a marked deletion of tagO can only be obtained in B. anthracis strains merodiploid for tagO and we generated a B. anthracis variant with conditional expression of tagO. Depletion of tagO leads to a loss of SCWP synthesis and S-layer assembly, as well as cell rounding, impairment of cellular division, and death, indicating that tagO is indeed essential for B. anthracis growth. These data suggest that TagO-mediated murein linkage unit assembly supports SCWP synthesis and attachment to the peptidoglycan via acid-labile phosphodiester bonds. We also show that BAS5051 (polysaccharide deacetylase) is not required for SCWP synthesis and S-layer assembly.

Conclusion: Here, we show that some, but not all, SCWP synthesis is dependent on TagO-derived murein linkage units and subsequent attachment of SCWP to peptidoglycan. The data implicate secondary polymer modifications of peptidoglycan and sub-cellular distributions as a key feature of the cell cycle in Gram-positive bacteria and establish foundations for work on the molecular functions of the SCWP and on inhibitors with antibiotic attributes.

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The SRC-Modulated Interaction of Paxillin and LC3B Promotes Autophagic Degradation of Paxillin and Tumor Cell Motility

Erin Mowers, PhD

Mentor: Kay Macleod, PhD; Ben May Institute for Cancer Research

Co-Authors: Marina Sharifi, MD, PhD; Lauren Drake, PhD; Kay Macleod, PhD

Background: Autophagy is a conserved catabolic process critical for the degradation of damaged organelles and protein aggregates as well as the intracellular recycling of proteins and lipids. Autophagy occurs at a basal rate in all cells and may be upregulated under conditions of stress; in particular, some tumor cells utilize autophagy to survive nutrient stress, hypoxic conditions, and cytotoxic therapies. Research into the role of autophagy in primary tumor growth suggests that autophagy may be tumor suppressive through its promotion of genome stability, limitation of necrosis and inflammation, and induction of growth arrest. However, other studies indicate a tumor-promoting role for autophagy, highlighting the fact that the role of autophagy is highly context-dependent, varying with oncogenic status, state of progression, and environment. With respect to metastasis, clinical studies have correlated increased autophagic flux with tumor metastases. We sought to determine the mechanism by which autophagy modulates the metastatic cascade using the 4T1 breast cancer model.

Methods: The 4T1 orthotopic murine model of breast cancer was used for in vivo experiments. 4T1 breast cancer cells stably expressing scramble control, Atg5, or Atg7 shRNA grown under standard cell culture conditions were subject to complementary in vitro analyses, including immunofluorescence, western blotting, immunoprecipitation, in vitro binding assays, and transwell assays.

Results: Autophagy is not required for primary tumor growth in the 4T1 orthotopic murine model of breast cancer but is critical to the formation of metastases. In vitro, autophagy-deficient tumor cells exhibit a rounded morphology and impaired motility due to the impaired disassembly of focal adhesions and the accumulation of the focal adhesion protein paxillin. The levels of paxillin are dependent on autophagy, but the p62/Sqstm1 and Nbr1 cargo adaptors are dispensable for paxillin accumulation. Autophagic degradation of paxillin is mediated through direct binding of paxillin to LC3B, and a conserved LC3-interacting region (LIR) motif in paxillin is required for binding and subsequent cell motility. Finally, oncogenic Src can stimulate the binding of paxillin with LC3B, and the ability of Src to promote cell motility requires intact autophagy.

Conclusion: Our work demonstrates that autophagy is required for metastatic tumor cell migration and invasion. Paxillin binds directly to LC3 through in a conserved LIR motif in a Src-regulated manner, and that this binding targets paxillin for autophagic degradation and subsequent focal adhesion turnover. Together, our data establish a novel function for autophagy in tumor motility and metastasis.

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The Role of the Western Diet on Altering the Microbiome

Connie Shao

Mentor: John Alverdy, MD; Department of Surgery
Co-Authors: Sara Gaines, MD; John Alverdy, MD

Background: Anastomotic leak is a disheartening surgical outcome that continues to plague patients and general surgeons. Enterococcus faecalis has been shown to be associated with anastomotic leak due to its capacity to degrade collagen and activate tissue MMP9 in host intestinal tissues. It has been proposed that various peri-operative exposures can contribute to the induction of this pathologic phenotype. This project will focus on how a pre-operative PUFA diet, modeling the high fat, low fiber Western diet, can affect the microbiome after anastomotic surgery, complementing previous studies to understand the microbiotal mechanism by which risk factors for anastomotic leak can lead to post-operative complications. Specifically, the previously described collagenolytic strain of E. faecalis (col Ent) and collagenolytic Gram negative (col GN) species will be quantified and compared for mice receiving PUFA vs chow feeds. Understanding how the microbiome changes with certain exposures and how they result in postoperative complications (anastomotic leak, colorectal cancer recurrence, etc.) can help redefine bowel preparation and intraoperative technique.

Methods: Mice (Blab c) were fed chow feed or PUFA feed for four weeks, after which a subset underwent an operation under general anesthesia with pre-operative antibiotics (oral clindamycin, subcutaneous cefoxitin) and an anastomosis of the distal colon was created. A subset of those that underwent anastomosis creation also received an E. faecalis enema. On POD7, the mice were sacrificed. The anastomotic tissue/distal colon and stool were collected. Each were homogenized and plated on both Ent/TSB+skim milk plates and MacConkey milk plates to quantify collagenolytic E. faecalis and Gram (-) colonization, respectively.

Results: With 5-6 mice in every sample group, we were able to make the following observations. Collagenolytic Enterococcus bacteria in PUFA mice exceeded those in chow mice. Antibiotic treatment increase col Ent for chow mice, but not PUFA mice. There was an increase in col Ent for PUFA mice that also received an E. faecalis enema. Col GN in the colon lumen for chow and PUFA mice were similar at baseline. Antibiotic treatment was associated with a profound increase in col GN in anastomotic tissue compared to chow mice by several orders. There was also a profound increase in col GN in PUFA mice receiving an E. faecalis enema.

Conclusion: Compared to mice on the chow diet, mice on the PUFA diet have an increased collagenolytic population of E. faecalis but not of Gram (-). PUFA induces colonization of the anastomotic site with Gram (-) after anastomosis as well as enema. Collagenolytic E. faecalis is not increased after anastomosis in PUFA group, but is with enema. There are several considerations for future experimentation. It is unknown what the microbiome looks like at the time of surgery - intra-operative sample collection should be included to predict future bacterial growth. The observed increase in bacteria may not be specific to this location. Additional tissue samples at the time of surgery and at sacrifice should be taken from anastomosis, proximal colon, cecum, and ileum. Lastly, there are confounding factors for mice on the PUFA diet, as it leads to excessive grooming and potentially additional stress.

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Repair of Critical Sized Cranial Defects with BMP9-transduced Calvarial Cells in a Thermoresponsive Scaffold

Viktor Tollemar

Mentor: Russell Reid, MD, PhD; Department of Surgery

Co-Authors: Zari P Dumanian, BS; Jixing Ye, PhD; Guillermo A. Amee, ScD; TongChuan He, MD, PhD;

Background: Large skeletal defects caused by trauma, congenital malformations, and post-oncologic resections of the calvarium present major challenges to the reconstructive surgeon. We previously identified BMP9 as the most osteogenic BMP in vitro and in vivo. Here we sought to investigate the bone regenerative capacity of murine-derived calvarial mesenchymal progenitor cells (iCALs) transduced by BMP9 in the context of healing critical-sized calvarial defects.

Methods: BMP9-transduced iCALs were delivered to the defect site within a thermoresponsive biodegradable scaffold consisting of poly(polyethylene glycol citrate-co-N-isopropylacrylamide mixed with gelatin (PPCN-g). A total of three treatment arms were evaluated: PPCN-g alone, PPCN-g seeded with iCALs expressing GFP, and PPCN-g seeded with iCALs expressing BMP9. Each arm was followed for 12 weeks with serial computed tomography to track changes in defect volume. Subsequently, each mouse was euthanized and bone from the defect site was harvested for histological analysis.

Results: Defects treated only with PPCN-g scaffold did not statistically change in size when evaluated at eight weeks postoperatively (p = 0.72). Conversely, both animal groups treated with iCALs showed significant reductions in defect size after 12 weeks of follow-up (BMP9-treated: p = 0.0025; GFP-treated: p = 0.0042). However, H&E and trichrome staining revealed more complete osseointegration and mature bone formation only in the BMP9-treated group.

Conclusion: These results suggest that BMP9-transduced iCALs seeded in a PPCN-g thermoresponsive scaffold is capable of inducing bone formation in vivo and is an effective means of creating tissue engineered bone for critical sized defects.

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Optogenetics without Genetics
Jeremy Treger, PhD

Mentor: Francisco Bezanilla, PhD; Department of Biochemistry and Molecular Biology

Co-Authors: Joao Carvalho-de-Souza, PhD; Bobo Dang, PhD; Stephen Kent, PhD; David Pepperberg, PhD; Francisco Bezanilla, PhD

Background: Optogenetics is a powerful laboratory technique wherein light-sensitive ion channels are expressed only in a cell population of interest. This allows for stimulation of selected populations of excitable cells, a feat not achievable with traditional electrode stimulation. However, despite its utility, this technique requires genetic modification of the target organism which is often difficult and expensive in laboratory animals and currently infeasible in humans. Our aim was to design a new technique that could accomplish the same task but without requiring genetic modification.

Methods: We used either chemical ligands or antibodies to specifically bind gold nanoparticles to rat DRG neurons. We compared the performance of these particles to those of unbound gold nanoparticles when stimulating the neurons with millisecond pulses of light. In addition, we studied the feasibility of the technique in mouse hippocampal brain slices. Finally, we investigated the biophysical basis of the technique by applying the nanoparticles to a painted bilayer composed of pure phospholipids with no membrane proteins.

Results: We show that nanoparticles targeting three different cellular targets all render the attached cells sensitive to optical stimulation, while unbound neurons are unaffected by the light. The particles are resistant to washout, meaning that the cells remain sensitive to light for an extended period of time, and the technique allows for repeated stimulation at rapid rates. The technique works well in hippocampal slices, and we show that an all-optical investigation technique is possible by combining gold nanoparticle neuronal stimulation with a voltage-sensitive fluorescent dye to monitor electrical activity. Finally, we found that the mechanism of the optical stimulation relies on the particles transducing incident light into heat, leading to an increase in capacitance the cell's plasma membrane. This in turn causes cellular depolarization and thus an action potential.

Conclusion: By providing a novel method for optical stimulation of specific populations of excitable cells, our technique represents a promising alternative to optogenetics in situations where genetic modification is impractical. This may have implications for human therapeutics as genome modification must overcome significant technical and regulatory hurdles before it can be routinely used in human patients.

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LytR-CpsA-Psr Enzymes as Determinants of Bacillus anthracis
Cell Cycle and Secondary Cell Wall Polysaccharide/S-layer Assembly

Megan Liszewska Zilla, PhD

**Mentor:** Dominique Missiakas; PhD, Department of Microbiology

**Co-Authors:** Justin Mark Lunderberg, PhD; Yvonne G.Y. Chan, PhD; Ya-Ting Wang, PhD; Olaf Schneewind, MD, PhD; Dominique Missiakas, PhD

**Background:** *Bacillus anthracis* replicates as chains of vegetative cells via controlled separation of septal peptidoglycan. Surface (S)-layer proteins and associated proteins (BSLs) function as chain length determinants and are assembled in the envelope by binding to the secondary cell wall polysaccharide (SCWP). In *S. aureus*, LytR-CpsA- Psr (LCP) proteins attach wall teichoic acid (WTA) and polysaccharide capsule to peptidoglycan. *B. anthracis* does not synthesize such polymers yet its genome encodes six *lcp* genes. We considered whether these genes may be responsible for attaching the SCWP to peptidoglycan in *B. anthracis*.

**Methods:** The six *lcp* genes of *B. anthracis*, i.e. *lcpB1, lcpB2, lcpB3, lcpB4, lcpC, and lcpD*, were characterized by generating strain variants that lack any one or express only one *lcp* gene. These mutant strains were analyzed for their ability to undergo the normal *Bacillus anthracis* lifecycle. The genes were also expressed in an *lcp* null model of *Staphylococcus aureus* for their ability to anchor wall teichoic acid to the peptidoglycan.

**Results:** The expression of *lcpB2, lcpB3, lcpB4, lcpC* and *lcpD*, but not *lcpB1*, promoted WTA attachment in the envelope of Δ*lcp* *S. aureus*. A *B. anthracis* Δ*lcpD* variant displayed increased chain length, defective S-layer assembly and reduced SCWP attachment to peptidoglycan. In contrast, *B. anthracis* Δ*lcpB3* displayed reduced cell size and chain length, changes that were correlated with increased deposition of BSLs. Variants expressing *lcpB4, lcpC* or *lcpD* alone displayed severe defects in growth and cell shape. Variants expressing *lcpB2, lcpC* or *lcpD* alone were unable to support S-layer assembly. The deposition of S-layer proteins was drastically altered in all strains expressing a single *lcp* gene with one exception, *lcpB3*. Sporulation efficiency of bacilli also required LCP activity. *lcpB3* was the sole *lcp* gene supporting wild-type levels of *B. anthracis* spore formation, whereas strains expressing *lcpB2, lcpC* or *lcpD* alone altogether failed to generate spores.

**Conclusion:** The data presented here suggest that *B. anthracis* LCPs promote attachment of SCWP precursors to peptidoglycan. We propose a model whereby LcpB3 represents the housekeeping LCP, anchoring SCWP along the cell envelope of vegetative bacilli. LcpB2, LcpC and LcpD attach SCWP at the poles or septa, enabling BSL murein hydrolase separation of daughter cells. LcpB4 appears to anchor specialized SCWP along the cylindrical axis to guide asymmetric cell division during sporulation. LcpB1 is presumed to anchor SCWP polymer with discrete structure to support sub-cellular compartmentalization in *B. anthracis*.

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