

PATHOLOGY & LABORATORY MEDICINE NEWSLETTER Volume 3, Issue 2 2012



 MUSC
 DEPARTMENT of PATHOLOGY & LABORATORY MEDICINE

MUSC DEPARTMENT of PATHOLOGY & LABORATORY MEDICINE RESIDENTS & FELLOWS ~ MAY, 2012



DEPARTMENT of PATHOLOGY & LABORATORY MEDICINE

Inside this issue:

Welcome Dr. Maize Sr.	2
Promotions	2
Arrivals/Departures	3
National Lab Week	4-5
IT Update	6
Quest Speakers	7
HR News	8
Faculty Excellence	
Awards	9
New Fellows	10-12
New Residents	13-14
Research Division	15
Clin <mark>ical Chemistry</mark>	
F ellowship	16
Blood Transfusion	17
HPV in Cervical	
Cytology Specimens	18-20



DEPARTMENT OF PATHOLOGY AND LABORATORY MEDICINE NEWS FROM DEPARTMENT ADMINISTRATION & BUSINESS OFFICE

WELCOME!

PROMOTIONS



John C. Maíze, Sr., M.D.

Dr. John C. Maize, Sr. will be returning to our Department on August 1, 2012. Dr. Maize will have a dual appointment in the Department of Dermatology and the Department of Pathology and Laboratory Medicine in the Division of Anatomic Pathology, Surgical Pathology Section. Dr. Maize, Sr., is a nationally and internationally recognized expert in Dermatopathology and Dermatology. We are delighted to be working with him again!

Congratulations!

- **Dr. Yusheng Zhu** passed the Molecular Board Examination.
- Mia Taylor, JKU Post-Sophomore Fellow, was awarded a scholarship and inducted into the Student Leadership Society on April 11, 2012
- Kate Eichel, 4th year medical student, was selected one of the ten finalists to receive this year's ASCP 2012 Award for Academic Excellence and Achievement in Pathology.

Jack Yang, M.D. was promoted on July 1, 2012 from Associate Professor to Professor. Dr. Yang is in the Anatomic Pathology Division and is the Director of the Cytopathology Fellowship Program.



Lee M. Tormos, M.D. was promoted on July 1, 2012 from Clinical Instructor to Assistant Professor. Dr. Tormos works in Forensic Pathology in the Anatomic Pathology Division and in Transfusion Medicine.



ARRIVALS / DEPARTURES

New Hires:

Christiana Kappler, Ph.D., joined Dr. Ethier's Lab as a Postdoc Scholar on April 16, 2012.

Atul Pandey, Ph.D., joined Dr. Puligilla's Lab as a Postdoc Scholar on June 1, 2012.

Xinping Hao, M.D., joined Dr. Lang's Lab as a Visiting Scholar on June 14, 2012.

Kevin Hildreth, **M.S.**, joined our Department on June 18, 2012 as the Department Grants Coordinator.

Stephen Guest, Ph.D., joined Dr. Ethier's Lab as a Postdoc Scholar on July 1, 2012.

Jonathan Irish, Ph.D., joined Dr. Ethier's Lab as a Postdoc Scholar on July 1, 2012.

Faisal Radwan, Ph.D., joined Dr. Moussa's Lab as a Postdoc Scholar on July 9, 2012.

New First Year Residents:

Nicole Dominiak, M.D., Jessica Forcucci, M.D., Natalie Mason, M.D., Tripp Tracy, M.D., Austin Turner, M.D.

Post-Sophomore JKU (Jane K. Upshur) Fellow:

Jacqueline Savage

New Fellows:

Cytopathology: Ben Coulter, M.D., Yasmin Elshenawy, M.D., Steven Frame, M.D. *Dermatopathology*: Ben Hayes, M.D., Ph.D., Julie Swick, M.D. *Forensic Pathology*: Meredith Burge Frame, M.D. *Hematopathology*: Nicole Miller, M.D. *Surgical Pathology*: Christopher Campo, M.D., Laura Spruill, M.D., Ph.D.

Departures & Transfers:

Alina Sofronescu, Ph.D., Post Doc Fellow left our department of May 16, 2012 to work in the Department of Pathology and Microbiology at the University of Nebraska Medical Center. She completed a 2-year Fellowship in Clinical Chemistry.

Myroslawa Soloshchenko, Research Specialist II, left our department on June 4, 2012.

Bridget Varughes, Ph.D., Post Doc Scholar, will leave our department on July 20, 2012.

Congratulations to our:

Graduating Residents, July 2011

Resident:	Fellows	hip Training Program
Ben Coulter, M.I).	MUSC (Cytopathology)
Teresa Goldin, N	/I.D.	University of Virginia (Hematopathology)
April Hendryx, N	M.D.	UT Southwestern (Surgical Pathology)
Laura Spruill, M	.D., Ph.D.	MUSC (Surgical Pathology)
Roger Stone, M.	D.	University of North Carolina (Surgical Pathology)

NATIONAL LABORATORY PROFESSIONALS WEEK



National Medical Laboratory Professionals Week provides our profession a unique opportunity to increase public understanding of our profession and to express appreciation for clinical laboratory personnel. We celebrated 2012 Lab Week April 22 - 28 and, as always, planned a number of events. This year's theme was "Laboratory Professionals Get Results".

Lab Week is always a time of good eating and one of the highlights was the very popular Ice Cream Social sponsored by Dr. Lage and the Department. This event was well attended and gave everyone the opportunity to gather and socialize with their coworkers.

In addition to our social events, there were two special "Connect to Purpose" presentations. "Morgan's Heart" featured the high profile pediatric heart transplant that took place at MUSC last January. Our laboratory medical directors showed what went on behind the scenes in the laboratory and how we helped contribute to the success of little Morgan's heart transplant. Our second "Connect to Purpose" presentation was, "The Everett German Story". Mr. German is a local Cougars radio commentator and television talk show host who underwent a living donor kidney transplant at MUSC last year. He helped celebrate Lab Week by telling us his engaging story. We also told our story of what went on behind the scenes in the laboratory and the vital role laboratory medicine plays in organ transplantation. Both events were well attended and generated many positive comments.

Three *Snack and Learn* educational opportunities were also offered: "Westgard Rules and Quality Management", "Autoimmune Hemolytic Anemia", and "Lab Education Programs and Opportunities". Each presentation was recorded along with the PowerPoint presentation to allow everyone the opportunity to see the presentation and to earn continuing education credits.

There was something for everyone this year during Lab Week. Our goal was to Connect to Purpose, provide continuing education, and to present opportunities to discover new things about the laboratory we work in every day. The planned activities helped generate new excitement and fostered renewed pride in our profession. Lab Week 2012 was a great success and we look forward next year's celebration.



Connect to Purpose: Morgan's Heart The Role of Pathology and Laboratory Medicine in Heart Transplantation



April 22-28, 2012



Exciting Snack & Learns were scheduled all week.

The Laboratory Faculty, Staff, and Student Appreciation was held on April 24th!

Connect to Purpose Everett German's Story









As we all begin to rely more and more on our beloved mobile devices, iPhone, Droids, and Blackberry's, to manage our professional and personal lives a certain level of security compliance needs to be met when connecting your mobile device to the MUSC enterprise.

In that effort the MUSC/MUHA/MUSC Physicians leadership teams, in conjunction with OCIO-IS, will soon be requiring all mobile devices connected to MUSC's Exchange email system to have the Zenprise mobile device management (MDM) client installed and configured. Currently this security model is in the testing phase however as MUSC moves closer to "go live" date, more information will become available. It is critical that everyone understands what information the MDM administrators can access and what information they cannot access.

What cannot be accessed: Email (Exchange or personal), Text Messages, Pictures, Camera, Speaker, Microphone, Contacts, Calendar, Voice recordings, and Passcodes/passwords

What can be accessed: Installed applications, Device location (if user enables location services. This will not be required) Battery life, Voice minutes used, Cellular Data usage (Amount of data consumed in megabytes) Free space, Detect if device is jail broken/rooted (hacked)

Please note that just because an item can be accessed doesn't mean that it will. Yes, technically, the MDM administrators will be able to see remaining battery life and that Angry Birds is installed, but they don't care, and really don't have the time to check these sorts of things. Operating system and security update compliance is what the MDM administrators are after.

More information on the Zenprise client can be found here: <u>http://www.zenprise.com/only-zenprise</u>

ALL HANDS MEETING (DEPARTMENT WIDE) October 17th, 2012 - 9:30 am - 10:30 am.

The meeting will be held in the Hollings Cancer Center, room HO120.

Please be sure to mark your calendars!

This will be in lieu of the regular scheduled faculty meeting.

PATHOLOGY AND LABORATORY MEDICINE QUEST SPEAKERS



Dr. Andrew Churg

On April 13, 2012, Dr. Andrew Churg visited the Department of Pathology and Laboratory Medicine at the Medical University of South Carolina and delivered a dynamic lecture on interstitial lung disease, in which he focused on the best approach of the pathologist to the diagnosis of various chronic interstitial pneumonias. As fibrosis and chronic inflammation may be nonspecific localized findings in the lung, Dr. Churg emphasized the importance of correlating the pattern, appearance and distribution of the fibrosis and inflammation in the lung biopsy with clinical and radiographic findings.

Dr. Andrew Churg is widely recognized as a national and international leader in pulmonary pathology. He has been on the faculty of the University of British Columbia for more than 30 years. He received his B.A. from Columbia University and M.D. and Ph.D. from the University of Chicago. He is currently Professor of Pathology at the University of British Columbia. He is the author of almost 400 journal articles, chapters, and books, including the AFIP Fascicle: Tumors of the Serosal Membranes. His research interests include the diagnosis of occupational lung diseases, malignant mesothelioma, interstitial lung disease, and COPD.

SAVE THE DATE

September 24, 2012 RESIDENTS Breakfast with Dr. South-Paul CH204 – 8:30 am – 10:30 am September 24, 2012 FACULTY Lunch with Dr. South-Paul

HCC120 - 1:00 pm - 3:00 p.m.



University of Pittsburg, Department of Family Medicine

Jeannette E. South-Paul, MD Andrew W. Mathieson Professor Department Chair

Department of Family Medicine 3518 Fifth Avenue Pittsburgh, PA 15261-0001





BENEFITS UPDATE

These are <u>proposed</u> changes to the SC Retirement Systems.

- Creation of Class III Employees hired on or after July 1, 2012
- Class III employees required to have 30 years of service for full benefits (at any age)
- Close the TERI program to Class III employees

- Increase SCRS employee contributions to 7.5%
- Increase PORS employee contributions to 7%
- Increase SCRS employer contribution to 10/6% (total contribution would be 15.05%)
- Increase PORS employer contribution to 12/3% (total contribution would be 17%)

- Eliminate the additions of unused sick leave in the calculation of service credit after June 30, 2012
- Eliminate the retiree COLA based on the CPI
- The cost of service purchase would be the greater of an actuarially neutral payment or a set percentage of salary
- Inactive accounts will not earn interest

SUCCESS FACTORS

ANNUAL / ANNUAL CATCH UP REVIEW PERIOD

- Annual/Annual Catch Up reviews have been pushed to supervisors beginning June 15, 2012
- Annual/Annual Catch Up reviews are due August 1, 2012
- Planning Stages will push to supervisors beginning August 1, 2012
- Planning Stages to be completed by October 2012

MUSC EMPLOYEE

ASSISTANCE PROGRAM

Using EAP as an Effective Resource

Jeni Bowers-Palmer, M.Ed.

792-2848

CONGRATULATIONS DR. CAPLAN!

FACULTY EXCELLENCE AWARDS (SPRING 2012)

First Year Class

Winner: Dr. Michael Caplan

Runners Up: Dr. Paul McDermott Dr. Theirry Bacro

Second Year Class

Winner: Dr. LW Preston Church

Runners Up: Dr. Laura Kasman Dr. John Hildrebrandt

Clinical Years

Winner: Dr. Christopher Pelic Dr. David Mills

Runners Up: Dr. Stephanie Montgomery Dr. Rachel Stacey

Nominees for Basic Science and Clinical Years

First Year

Dr. Thierry Bacro Dr. David Bernanke Dr. Michael Caplan Dr. Wanda Gonsalves Dr. Debra Hazen-Martin Dr. Yi-Te Hsu Inda Johnson Dr. Donna Kern Dr. Sergey Krupenko Dr. Paul McDermott Dr. Matthew McEvov **Dr. Christopher Pelic** Dr. Jerome Ondo Dr. Daniel Smith Dr. Edward Soltis Dr. Francis Spinale Dr. John Woodwards

Dr. Nicholas Batalis Dr. Melanie Bienvenu Dr. Joseph Blumer Dr. Evelyn Bruner Dr. Gene Burges Dr. Kenneth Chavin Dr. Preston Church Dr. Jeffry Cluver Dr. Donald Courtney Dr. Albert Finn Dr. Perry Halushka Dr. Heidi Hamilton Dr. Debra Hazen-Martin Dr. John Hildebrandt Dr. Keri Holmes-Maybank Dr. Laura Kasman Dr. Donna Kern Dr. Vibhor Krishna Dr. David Kurtz

Second Year **Dr. Janice Lage** Dr. Lee Lewis Ms, Amy Mendez Dr. Sarah Mennito Dr. Matthew McEvoy Dr. Stephanie Montgomery Dr. Carola Neumann Dr. Shashidhar Pai Dr. Maggie Pierson Dr. Erin Presnell Dr. Andrew Savage Dr. Sally Self **Dr. Jerry Squires** Dr. Antine Stenbit Dr. Michael Ullian Dr. Gabriel Virella Dr. Daynna Wolff Dr. Ray Worthy

Dr. Dannah Wray

Clinical Years Dr. Kelly Barth Dr. Eugene Chang Dr. David Countryman Dr. Joshua Farrar Dr. Valerian Fernandes Dr. Patricia McBurney Dr. David Mills Dr. Stephanie Montgomery Dr. Baron Short **Dr. Christopher Pelic** Dr. Rachel Stacey Dr. Erin Swanson Dr. Sheven Swift Dr. Nancey Tsai Dr. Leigh Vaughan

2012-2013 FELLOWS

Dr. Chrístopher Campo Surgícal Pathology

Dr. Laura Spruíll Surgícal Pathology



I am originally from New Orleans. In my previous life, I was a salesman for Otis Elevator Company and a high school Biology teacher. I graduated from the University of Saint Eustatius School of Medicine in the Caribbean. I completed my pathology residency from St. Joseph's Hospital in Phoenix, Arizona. I have been married for 7 months to Sara, a microbiologist at St. Joseph's Hospital. We have 2 dogs, Ozzy and Harriett.



I am Laura Simmons Spruill, born in Rochester NY. I completed my bachelor's degree in Biochemistry at SUNY Genese and came to South Carolina after meeting my late husband, Joshua Spruill during a summer research program at MUSC. I obtained my MD and PhD degrees after completing the Medical Scientist Training Program at MUSC and stayed on for my Pathology AP/CP residency. I have two children, Samantha (7) and Luke (4) from my first marriage and I am very excited to be gaining two additional children, Kinga (13) and Benett (10) in my impending marriage on July 21, to Pal Suranyi, who works as a Radiology attending at MUSC. We will live in West Ashley with my dog, Myrtle. I am very excited to be one of this year's Surgical Pathology fellows.

Ben Coulter, M.D.



I am a North Carolina native and graduated from NC State University and the Wake Forest University School of Medicine. My wife, Rebecca, and I have enjoyed raising our children, Rubygail and Grayson, here in Charleston during my residency at MUSC. We also have a rescue dog named Honey, who is sure to let us know of any approaching thunderstorms. In my spare moments, I enjoy the art and science of amateur vinification.

Yasmín Elshenawy, M.D.



I was born in Alexandria, Egypt, where I received my M.D degree. Relocated to Atlanta, Georgia and joined the Centers of Diseases Control (CDC) for one year fellowship in the infectious pathology branch. Afterward, I finished my residency in Anatomic & Clinical Pathology at East Tennessee State University in Johnson City, TN. Now, I am about to start my cytopathology fellowship at MUSC. My husband and I have two boys Yasin and Yusuf. All of us are excited about our move to Charleston, especially that we have a lot of beach, shopping and dining out activities awaiting us.

2012-2013 FELLOWS

CYTOPATHOLOGY

Steven Frame, M.D.



I grew up in Central Illinois and attended medical school at Southern Illinois University. I moved to Lexington, KY for residency at the University of Kentucky in 2008. While there, I met my husband, Steven Frame. We were just married on April 28, 2012. Steven is from Western Kentucky. He attended the University of Kentucky for medical school. We are looking forward to our time in Charleston. In our free time, Steven is teaching me how to golf, which should be a lot of fun in Charleston! Steven loves fishing and cooking. I enjoy baking, so I promise to bring treats to the department!

FORENSIC PATHOLOGY

Meredíth Burge Frame, M.D.



Ben Hayes, M.D., Ph.D.

DERMATOPATHOLOGY

Julie Swick, M.D.



Ben Hayes comes to us from Nashville, TN where he has practiced dermatology for five years before deciding to come back to school. He did his dermatology residency at Vanderbilt University. His wife, Laura, four children, and Charlie the chocolate lab are excited about being in Charleston and a part of the MUSC family.



My name is Julie Swick and I will be one of the dermpath fellows starting in July. I am from Florence, South Carolina and attended Clemson for my undergraduate degree. My husband, Brian, is from Texas. We met during college and were married after my first year of med school here in Charleston. We now have a 9 month old boy named Colt, who is basically awesome. We also have a Cavalier Spaniel named Alfie who spends most of his time begging for attention now that there is a baby around. I have spent the last three years with the Dermatology Department here at MUSC. I am excited about the year to come and glad to be a part of this department.

2012-2013 FELLOWS

HEMATOPATHOLOGY

Nícole Míller, D.O.



I have lived most of my life in Arizona. I grew up in Phoenix and went to the University of Arizona for undergrad. Between undergrad and med school, I worked at a blood bank and I spent a year teaching English in Japan with the JET program in Usa-shi on Kyushu. I then attended the Arizona College of Osteopathic Medicine in Glendale, AZ, and had my first son, Keegan, just before graduation. I did AP/CP residency at the University of Kentucky where my second son, Grant, was born in 2009. I stayed in Lexington, KY, for one more year, where I completed a Cytology fellowship. I am married and my boys are now 5 and 2. I am expecting my third child in December 2012. I am excited to start my year of Hemepath here at MUSC. Jane K. Upshur Fellowship Jacqueline Savage



I am a current 3rd year medical student here at MUSC. I am a Cuban-American and I moved to South Carolina from Miami, FL, in 2002. I went to Wofford College and majored in Biology and Spanish. I spent 6 months in Santiago, Chile learning about their healthcare system and getting immersed in the culture. Following graduation, I came to MUSC for medical school. I am a member of the Student National Medical Association and I am involved in the Dermatology Interest Group. My hobbies include cooking foreign cuisine, salsa dancing, playing tennis and watching House Hunters-International. My lifetime goal is to be able to treat patients not only here in the United States, but also make a difference abroad and travel the world, one country at a time.

WELCOME FELLOWS!

2012-2013 1st Year Residents



Jessíca Forcuccí, M.D.

Jessie is from Fort Mill, South Carolina. She is a graduate of USC and attended MUSC for medical school. She lives with her husband, Aaron, who is a family medicine resident at Trident Medical Center, and their two dogs, Pinna and Hashimoto. They are both excited to continue their medical education in Charleston, but also enjoy cooking, baking, and spending time with their dogs, friends, and family.



Natalie Mason, M.D.

I moved here from Upstate New York with my boyfriend in spring of 2010. After completing an intern year in pediatric medicine and a year in the pathology department as a Post Sophomore Fellow, I am so excited to be beginning my residency in pathology at MUSC! My boyfriend, Steve, and I love Charleston and spend as much time as possible enjoying its gorgeous outdoors and delicious food. Our rather eccentric puppy, Audrey, takes up an inordinate amount of our free time, but we love her anyway!

Nícole Domíníak, M.D.



My name is Nicole Dominiak and I am an incoming PGY-1. I am from Toledo, Ohio where I studied at the University of Toledo for both my undergraduate degree as well as for medical school. I am recently married as of May 26th to a wonderful man, Sean Powers. We are so excited to be moving to Charleston! We absolutely fell in love with the area and the people while we were here visiting last year. I look forward to working with everyone in the department, and ultimately hope to pursue a career in dermatopathology. I cannot wait to get started!

2012-2013 1st Year Residents



Trípp Tracy, M.D.

I was born and raised in Charleston and received a BS in Electrical Engineering from Clemson in 2002. After completing medical school prerequisites, I attended MUSC from 2003-2007.

After graduation, I completed a 5-year active duty service obligation with the US Navy, including a transitional internship in San Diego, CA and 3 ½ years as a Diving and Undersea Medical Officer with a submarine support unit in Kings Bay, GA. I met my amazing wife in 2003 and we were married in 2005. During our time with the Navy, we welcomed our 2 wonderful daughters: Izzie, 3, and Elin, 9 months. Austín Tuner M.D.

I'm originally from Nashville, TN, and have spent the last few years finishing up medical school rotations in Chattanooga, TN. When I'm not looking through the microscope, I love running, hiking, and basketball. And though I miss the hills back home, the palm trees and beaches here more than make up for it. I'm excited about starting at MUSC and look forward to meeting everyone.

WELCOME RESIDENTS!



Statistics for the Division of Research from April through June. Nine grant proposals were submitted requesting \$1,383,541 in total first year costs. Also, during this period seven grants were awarded totaling \$2,359,822 (see table below). Congratulations and many thanks to everyone involved in obtaining these awards.

GRANTS SUBMITTED 4/1/12 - 6-30-12					
Faculty	Current Year Start Date	Title	Total 1st YR Dollars		
Annamalai		Development of S-Nitrosothiol-based Therapy for Late-onset Alzheimer's Disease	\$59,262		
Baker		Heat Shock Protein-Induced Protection Against Cisplatin-Induced Hair Cell Death	\$35,099		
Ethier		Breast Cancer Oncogenes on the 8pll Amplicon			
Ethier	Ethier Amphiregulin Signaling in Human Breast Cancer		\$292,718		
Lang		Human Hematopoietic Stem Cells and the Aging Inner Ear	\$395,865		
Steed		Prospective study into the performance of the KeyPath			
Wang	MicroRNS's and Cancer Therapy-Induced Bone Marrow Toxicity		\$330,862		
Wolff	Wolff Evaluation of the Infinium HD Cytogenetic Abnormality Test Reproducibility Study		\$29,626		
Won		Development of S-Nitrosothiol-based Therapy for Late-onset Alzheimer's Disease	\$39,734		
Total Submissions = 9			\$1,383,541		
		AWARDS RECEIVED 4/1/12-6-30-12			
Annamalai	6/1/2012	Development of S-Nitrosothiol-based Therapy for Late-onset Alzheimer's Disease	\$59,262		
Ethier, S	5/7/2012	Breast Cancer Oncogenes on the 8pll Amplicon	\$163,461		
Ethier, S	5/1/2012	Amphiregulin Signaling in Human Breast Cancer	\$292,718		
Lang	6/1/2012	Rescuing a Congenital Form of Progressive Hearing Loss in Mice Using Viral Gene Transfer of MicroRNA	\$50,000		
Lazarchick, J	12/16/2011	Safety and Efficacy of NNC 0155-0000-0004 in Prevention and Treatment of Bleeds in Pediatric Previously Untreated Patients with Hemophilia A	\$3,953		
Mehrotra, M	4/1/2012	Hematopoietic Stem Cell Transplantation in Osteogenesis Imperfecta	\$69,027		
Moussa, O	4/1/2012	The Role of Thromboxane A2 (TP) Receptor Beta in Bladder Cancer	\$296,881		
Sha, S	4/1/2012	/2012 Molecular Mechanisms in Noise-Induced Hearing Loss			
Singh	4/1/2012 Development of S-Nitrosothiol-based Therapy for Late-onset Alzheimer's Disease		\$150,000		
Singh	5/1/2012	2 Nitrosylation Mechanisms for Protection Against Neurovascular Inflammatory Injury			
Singh, A	4/1/2012	4/1/2012 Mechanisms of Krabbe Disease Pathobiology and Therapy			
Spyropoulos	4/1/2012	Mammary Gland Laterality in Normal and Neoplastic Development	\$167,103		
Steed, L	5/11/2012	Prospective Study into the Performance of the KeyPath	\$36,914		
Wolff	6/20/2012	Evaluation of the Infinium HD Cytogenetic Abnormality Test Reproducibility Study	\$29,626		
Won	5/1/2012	5/1/2012 Development of S-Nitrosothiol-based Therapy for Late-onset Alzheimer's Disease \$39,734			
Total Awards = 15			\$2,359,822		



The Two Years' Experience of the Postdoctoral Clinical Chemistry Fellowship Program

Yusheng Zhu, PhD, DABCC, FACB Associate Professor Director of Clinical Chemistry & Toxicology Director of Postdoctoral Clinical Chemistry Fellowship Program

The Postdoctoral Clinical Chemistry Fellowship Program in the Department of Pathology and Laboratory Medicine at MUSC is now over two years old. The Program has made great achievements because of strong support from the Department and the hard work of other faculty members. Some of these members include Drs. Frederick S. Nolte, Maria Lopes-Virella, David Lewin, John Lazarchick, Sally Self, and James E. Madory. The help from Ms. Molli N. Diaz, lab managers and staff is also essential for the success of the Program.

Since 2010, two fellows have entered the Program and the third one will be joining us soon. Our fellows are actively involved in clinical service, teaching, and research. In clinical service, they take numerous clinical calls, interpret protein electrophoresis and immunofixation results, review hemoglobinopathy analysis, develop and validate new tests and participate in quality improvement projects. Our fellows also assist faculty in teaching residents and medical students who are on the clinical chemistry rotation. In terms of research, the fellows have participated in several clinical and translational research projects. These projects include discovery of SNPs related to radiotherapeutic effects, stability of serum bilirubin, using serum HE4 and CA125 levels to monitor disease progress in ovarian cancer, evaluation of a new homogeneous immunoassay for measuring methotrexate, and comparison of a new binding protein based 25-hydroxy vitamin D assay with a liquid chromatography -tandem mass spectrometric method.

Dr. Alina Sofronescu, the first fellow of the Program, has published three abstracts, three papers, and an additional two papers are in preparation. The paper published in Clinical Chemistry, "Unexpected Hemoglobin A1c Results" was selected by the Society for Young Clinical Laboratorians (SYCL) of the American Association for Clinical Chemistry (AACC) to make a podcast on the AACC website for the education of Laboratory Medicine students, residents, and fellows. Due to excellence in research, Alina received Student Travel Award from AACC and Christopher Frings Travel Award from the AACC Southeast Section. Her abstract "TGFB1 -509 C>T and XRCC1 399 Arg>Gln (28152G>A) Correlate with Increased Side Effects Induced by Radiotherapy in Prostate Cancer Patients," was selected from more than 900 abstracts for an oral presentation at the 2012 AACC annual meeting. Alina has successfully completed her fellowship and she is now a faculty member in the Department of Pathology and Microbiology at the University of Nebraska Medical Center.

As a first-year fellow, Dr. Zengliu (Leo) Su presented his abstract, "A Preliminary Evaluation of Using Serum HE4 and CA125 Levels to Monitor the Disease Progress in Ovarian Cancer Patients" at the Hollings Cancer Center Research Retreat Conference. He will be presenting another abstract, "Comparison of a New Binding Protein Based 25-Hydroxy Vitamin D Assay with a Liquid Chromatography -Tandem Mass Spectrometric Method," at the 2012 AACC annual meeting. Through intense competition, Leo won the AACC SYCL Domestic Travel Grant award. His abstract was selected for the Student Poster Contest at the 2012 AACC annual meeting. He has been invited by the AACC Southeast Section to give a webinar on, "Early Detection of Ovarian Cancer," in August, 2012. In just one year, Dr. Su has completed the drafts of three manuscripts.

Although our program is very young, the program has earned a very good reputation and has attracted many applicants. In 2012, there were over fifty applications for just one position. We are confident that with the strong support from the Department of Pathology and Laboratory Medicine and the dedicated work of our faculty, staff, and fellows, our Program will contribute more and more to the Department, MUSC, and the field of Laboratory Medicine.



Blood Transfusion; Can We Have Too Much of a Good Thing?

Jerry E. Squires MD, PhD Medical Director, Transfusion Service

Blood transfusion has been a common hospital procedure since the 1940's. In 2008, the most recent year for which national statistics are available, 23.6 million blood components were transfused in the United States to 5 million patients. This included a 5.8% increase in red cell transfusions and a 16% increase in platelet transfusions. Another way of looking at these statistics is to consider that in the US we are transfusing over 64,000 blood components per day.

So clearly, we must think we are doing some "good" for patients. Undoubtedly, the risks of transfusion transmitted disease have decreased dramatically over the past 2 decades with the current risk of transfusion acquired HIV and Hepatitis C being less than 1 in 2,000,000 transfusions. With respect to those "other" transfusion risks, the ongoing implementation of a positive patient identification system, an upcoming revision of CPOE, and the use of a bar coded dispense order all contribute to improved patient safety. So with improved—and improving—safety, why are there both local and national interest in reducing unnecessary blood transfusion?

For a number of years, hospitals have been vitally interested in reducing unnecessary blood use which has been largely focused on financial considerations. A national estimate of the true cost of blood transfusion suggests that every red cell transfusion costs the hospital over \$1,000. Since MUSC transfuses over 23,000 red cells every year, you can see that this is not an insignificant concern. However, this cost is "well-spent" for every unit of blood that saves a patient life or improves an outcome. The question really is: are there transfusions that are unnecessary and simply contribute to patient risk (small, though that might be)? The answer is unquestionably, YES. This derives from a growing number of studies that demonstrate rather conclusively that patients transfused conservatively do just as well (and often *better*) than patients transfused more liberally. It derives from studies that show on a "per patient" basis, we use 1 ½ to 2 times as many red cell transfusions as other countries with advanced medical care systems. And, it derives from studies that show drastic variations in blood use among surgeons and among hospitals performing the same procedures on the same patient populations. But perhaps most troubling are the increasing number of reports suggesting that blood transfusions—particularly when unnecessary—are actually independently associated with poorer patient outcomes including increased 30 and 60 day mortality. So, now we have not only a financial issue, we also have a patient safety and outcomes issue. These are certainly sufficient—really excellent—reasons for us to carefully manage patient transfusion, not only nationally, but here at MUSC.

So, what has happened here at MUSC? In 2009 we transfused 209.1 blood products per 1000 patient days. Year-to-date in 2012, our usage is down to 146.1 units per 1000 patient days or a 30% reduction in blood use over an approximate 3 year period. How has this happened? While the Transfusion Service provides information and reports, and the Blood Utilization Review Committee reviews blood use, I think the real credit should go to the clinicians in this hospital who are coming to realize more and more acutely that while blood can save the lives of our patients, it can also contribute to poorer outcomes when it isn't necessary.

I was once told that blood transfusion was somewhat like a marriage since neither marriage nor transfusion should be entered upon thoughtlessly or irresponsibly, but with due and serious understanding and appreciation of the ends for which they are undertaken. We seem to be taking this rather seriously at MUSC— and our patients are better off for it.



Testing for High-risk Human Papillomavirus (HPV) in Cervical Cytology Specimens

Frederick S. Nolte, PhD Vice-Chair, Laboratory Medicine Professor, Pathology and Laboratory Medicine Director, Clinical Laboratories



Electronphotomicrograph of HPV

It is now firmly established that persistent cervical infection with any of the 14 high-risk (HR) HPV genotypes (types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) is necessary for the development of cervical cancer and its immediate precursor lesion, cervical intraepithelial neoplasia grade 3 (CIN 3). HR HPV can be detected in almost 100% of cervical cancer cases. HPV type 16 is the most carcinogenic genotype and accounts for up to 60% of all cervical cancers. Type 18 is the next most carcinogenic type and accounts for up to 15% of cervical cancers. The other HR types cause the remaining 25% of cervical cancer. HR HPV causes all common and most rare histological types of cervical cancer. The current model for cervical carcinogenesis is HR HPV acquisition with onset of sexual activity, persistent infection (vs. clearance), progression to pre-cancer and invasion.

Cytology (Pap test and liquid-based) screening has been very successful in reducing cervical cancer incidence however its limitations include suboptimal sensitivity, limited reproducibility, and large numbers of equivocal results (atypical squamous cells of undetermined significance or ASC-US). HR HPV tests performed in conjunction with cytology better forecast which women will develop CIN3+ over the next 5 to 15 years than cytology alone. Incorporation of HR HPV testing into cervical cancer screening strategies allow both increased disease detection and increased length of screening intervals. A summary of the recent joint recommendations for the prevention and early detection of cervical cancer of the American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology is shown in the Table (1).

Currently there are four FDA-approved tests for HR HPV, Hybrid Capture 2 (Qiagen), Cerivista (Hologic), Cobas (Roche) and Aptima (Gen-Probe). The first three tests detect the presence of HR HPV genomic DNA and Aptima test detects the presence of messenger RNA of the viral oncoproteins E6 and E7.

The HPV genome is a double-stranded circular DNA approximately 7900 bases in length. It has eight overlapping open reading frames. There are six early (E) genes and two late (L) genes and one untranslated long control region. The L1 and L2 genes encode the major and minor capsid proteins. Early genes regulate HPV viral replication. The E6 and E7 genes of HR HPV genotypes are known oncogenes. Proteins expressed from E6/E7 polycistronic mRNA alter cellular p53 and retinoblastoma protein functions, leading to disruption of the cell-cycle check and cell genome instability.

HPV infections are very common and most women will clear infections within 6 to 12 months. The presence of HPV nucleic acid does not mean that cervical dysplasia is present. A more effective approach to detection of cervical disease is to target those oncogenic elements of HPV that foster persistent viral infection and cellular transformation. The E6 and E7 mRNA of HR HPV genotypes are such targets.

HPV genomic DNA is present in transient infections but very little E6/E7 mRNA is expressed. When the infection persists and the HPV genome integrates into the cervical cell chromosomal DNA, the expression of E6/E7 mRNA greatly increases. As a consequence, detection of E6/E7 mRNA is as sensitive as detection of HR HPV DNA but more specific for identifying women with progression of cervical disease.

We recently compared the Aptima HPV test for HR HPV E6/E7 mRNA to our test of record, the Cervista HPV test, which detects HR HPV genomic DNA. We tested a total of 208 cervical specimens in parallel which included 106 HR HPV DNA positive and 102 HR HPV DNA negative specimens. All discordant specimen results were resolved with second FDA-cleared test for HPV DNA (Cobas HR HPV test). We found that the Aptima test was as sensitive as the Cervista test for detecting women with cytology of low-grade squamous intraepithelial lesion or more severe and for detection of women with significant cervical lesions on biopsy (≥CIN2). However, the Aptima test had fewer false-positive results on specimens from women with normal or ASC-US cytology, and in women with normal cervical biopsies. Our results are consistent the results of several published evaluations of the Aptima HPV test (3, 4, 5). An Aptima HPV genotyping test to specifically identify types 16 and 18 has been developed and FDA-approval is pending.

Based on our own experience and that reported in the literature, we will change our test for HR HPV from the Cervista to the Aptima test effective July 2, 2012. Consequently, fewer women may be referred to colposcopy unnecessarily when the Aptima HPV assay is used either in ASC-US reflexive testing or PAP co-testing algorithms. The Aptima HPV assay has the added advantages that it will be run on the same automated platform (Tigris) as our well-established nucleic acid amplification tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* (Aptima Combo2 assay) and that it is less labor intensive than the Cervista test. Specimen requirements, reports, and turn-round-time for results will remain the same.

Population	Screening Method	Management of Screen Results	Comments	
Aged < 21 years	No screening		HPV testing should not be used for screening of management of ASC-US	
Aged 21-29 years	Cytology alone every 3 years	HPV positive ASC-US or cytology \ge LSIL, refer to ASCCP guidelines	HPV testing should not be used for screening	
		Cytology negative or HPV-negative ASC- US, rescreen with cytology in 3 years		
Aged 30-65 years	HPV and cytology co- testing every 5 years (preferred)	HPV positive ASC-US or cytology \ge LSIL, refer to ASCCP guidelines ²	Screening by HPV testing alone is not recommended for most clinical settings	
		HPV positive, cytology negative: Option 1. 12 m follow-up with co- testing Option 2. Test for HPV 16/18 genotypes. 16/18 positive refer to colposcopy. 16/18 negative 12 m follow-up with co-testing		
		Co-test negative or HPV negative ASC- US, rescreen with co-testing in 5 years		
(Cytology alone every 3 years (acceptable)	HPV positive ASC-US or cytology \ge LSIL, refer to ASCCP guidelines		
		Co-test negative or HPV negative ASC- US, rescreen with co-testing in 3 years		
Aged > 65 years	No screening following adequate negative prior screening		Women with history of ≥ CIN2 should continue screening ≥ 20 years	
After hysterectomy	No screening		Applies to women w/o a cervix and w/o history of ≥ CIN2 in past 20 years or cervical cancer ever	
HPV vaccinated	Follow age-specific recommendations above (same as unvaccinated women)			



Cervical cytology (Pap test) showing evidence of a high-grade intraepithelial lesion

References

- 1. Saslow, D. et al. 2012. American Cancer Society, American Society for Colposcopy and Cervical Pathology and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. CA Cancer J. Clin. 62: 147-172.
- Wright, T.C. 2007. American Society for Colposcopy and Cervical Pathology-Sponsored Consensus Conference. 2006 consensus guidelines for the management of women with abnormal cervical screening tests. J. Low. Genit. Tract. Dis. 11:201-222.
- 3. Wu, R. et al. 2010. Human papillomavirus messenger RNA assay for cervical cancer screening. The Shenzhen cervical cancer screening trial 1. Int. J. Gynecol. Cancer 20:1411-1414.
- 4. Ratnam, S. et al. 2011. Aptima HPV E6/E7 mRNA test is as sensitive as Hybrid Capture 2 assay but more specific at detecting cervical precancer and cancer. J. Clin. Microbiol. 49:557-564.
- 5. Szarewski, A. et al. 2012. Comparison of seven tests for high-grade cervical intraepithelial neoplasia in women with abnormal smears: the Predictors 2 Study. J. Clin. Microbiol. 50:1867-1873.

MUSC Department *of* Pathology & Laboratory Medicine Mission Statement:

To serve patients, health care providers, research scientists, scholars, and society by providing excellence and innovation in diagnostic services and educational resources in a respectful, professional and culturally diverse atmosphere.

Vision:

To become a preeminent leader in academic anatomic and clinical pathology while translating basic science discovery to improved clinical care.

www.musc.edu/pathology