

# THE PATH WAY



December 2013

Volume 4, Issue 4

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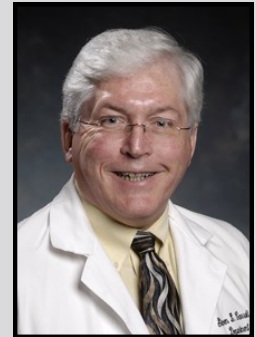


Mary S. Richardson, MD

## Steven L. Carroll, MD, PhD

Chair, Department of Pathology and Laboratory Medicine

Effective 3/1/2014

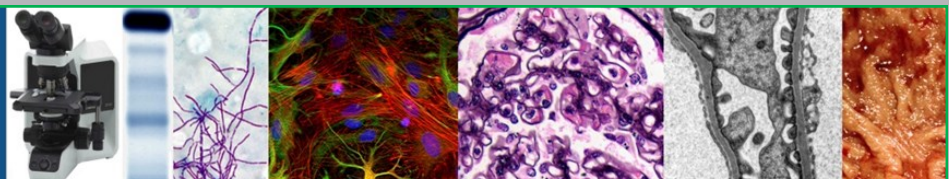


Dr. Carroll received his B.S. from Memphis State University and his PhD and MD from Baylor College of Medicine. He completed an Anatomic Pathology Residency, Neuropathology Fellowship, and Postdoctoral Research Fellowship in the Department of Pathology at the Washington University School of Medicine from 1988-1994. Following completion of his training, Dr. Carroll was appointed Assistant Professor of Pathology at the Washington University School of Medicine in 1994, and also served as a member of the Graduate Faculty in the Division of Biology and Biomedical Sciences.

In 1997, Dr. Carroll was recruited to the University of Alabama at Birmingham (UAB) as an Assistant Professor of Pathology and as Director of the UAB Brain Resource Program. He was promoted to Associate Professor with Tenure in 2001 and to Full Professor in 2008. Dr. Carroll served as Director of the Affymetrix Core Laboratory in the Department of Pathology from 2000-2002, and was appointed Director of the Division of Neuropathology in 2008. In addition to his appointment in the Department of Pathology, Dr. Carroll also has faculty appointments in the Departments of Neurobiology, Cell Biology, and Cell Developmental and Integrative Biology, and has served as a Scientist in the Department of Neurology/Alzheimer's Disease Center, the Intellectual and Developmental Disabilities Research Center, the Center for Neurodegeneration and Experimental Therapeutics, the Center for Aging, the Civitan International Research Center, the Center for Glial Biology in Medicine, and the Comprehensive Cancer Center. He served as Co-Director and Interim Director of the UAB Cancer Biology Graduate Program, and also served as Graduate Faculty for several training programs.

Dr. Carroll is involved with numerous professional organizations including the American Association for the Advancement of Science, the American Association for Cancer Research, the American Society for Investigative Pathology, the American Association of Neuropathologists, the International Society of Neuropathology, and the American Society for Neurochemistry. He has served on the editorial boards of journals including *The American Journal of Pathology*, the *Journal of Neuropathology and Experimental Neurology*, and *Neuro-Oncology*, and has served as an ad hoc reviewer for numerous journals. Dr. Carroll's primary research interests are in Neuregulin-1 growth and differentiation factors and their role in the pathogenesis of neurofibromatosis type-1 and -2 associated peripheral nerve sheath tumors, and he has received support from the NIH and DOD in support of his research endeavors. He has numerous peer-reviewed publications, and has presented at national and international meetings. In addition to his clinical and research endeavors, Dr. Carroll has been very active in educational activities to include training of graduate students, postdoctoral fellows, medical students, and clinical fellows.

Dr. Carroll brings an excellent combination of clinical, research, teaching, and administrative skills to lead the continued growth and development of the department.



DEPARTMENT of PATHOLOGY & LABORATORY MEDICINE

DEPARTMENT OF  
PATHOLOGY  
AND  
LABORATORY  
MEDICINE

NEWS FROM DEPARTMENT ADMINISTRATION & BUSINESS OFFICE

## ARRIVALS / DEPARTURES

### ARRIVALS:

**Hleb Fedarovich**, joined Dr. Turner's lab as a Research Specialist I on September 30, 2013.

**Yu Min**, joined Dr. Moussa's lab as a Visiting Volunteer on October 2, 2013.

**Christopher Attaway**, joined Dr. Smit's lab as a Research Specialist I on October 7, 2013.

**Robert Bowers**, joined Dr. Spyropoulos's lab as a Research Specialist II on October 28, 2013.

**Haishan Long**, joined Dr. Sha's lab as a Visiting Scholar on October 28, 2013.

### DEPARTURES:

**Debra Ellisor**, left Dr. Spyropoulos's lab as a Research Specialist II on October 11, 2013.



**Nomination:** She always works at 110% and recently found a genetic aberration that could have a potential clinical trial with a targeted therapy—now that is going above and beyond for patient care!

**Other Nominees:** Dolly Hope and Jarvis Jenkins

*Iya Znoyko*  
*Medical Technologist*

# CONGRATULATIONS!

*Dr. Russell Harley was granted  
Professor Emeritus  
Effective September 1, 2013*

## AACR CONFERENCE ABSTRACT

**Dr. David Turner**

*Advanced glycation end-products are increased in prostate cancer and may promote racial disparity*

My abstract entitled was assigned as one of two special Hot Topics Sessions at this year's AACR conference on the Science of Cancer Health Disparities in Atlanta. In the words of the conference organizers "the hot topics highlight some of the most innovative, high-impact research being conducted in the field". The abstracts represent the top 4% of abstracts submitted for this conference as reviewed by the conference Co-Chairs and Scientific Review Committee. The AACR also chose the abstract for enhanced media coverage, up to now three news articles are being put together by the ASCO post, Medical Research.com and malecare.org. The oral presentation was a great success and has led to several new collaborations across the country with regard to translational research and community outreach.

## AABB POSTER 2013

◆ **Dr. Jerry Squires and Karen Garner**

**Squires JE, Garner KS, Riddle M, Moncada S, Clayton ME.** Department of Pathology and Laboratory Medicine; Medical University of South Carolina. Presented at the AABB 2013.



## POSTERS PRESENTED FROM FORENSIC PATHOLOGY

◆ **Dr. Nick Batalis and Dr. Jessie Forcucci**

**Forcucci JA, Damron A, and Batalis NI.** Examination of human remains encased in concrete: A case report and review of the literature. Presented at the 47th Annual Meeting of the National Association of Medical Examiners, Milwaukee, WI, October 2013.

◆ **Dr. Lee Marie Tormos**

1. Okun S, Behonick GS, **Tormos L.** Bismuth Sub salicylate Toxicity: Unexpected Death due to an Over-The-Counter Formulation. Presented at the 47th Annual Meeting of the National Association of Medical Examiners, Milwaukee, WI, October 2013.
2. Clayton M, Moncada S, **Tormos L.** Transfusion Medicine App Steps Up Healthcare Quality—The Use of Cellular and Tablet Devices as a Teaching and Information Resource Tool. Presented at the AABB Meeting, Denver, CO, October 2013.

**Dr. David Lewin**

elected as Vice-President  
of the ASCP

(American Society of Clinical Pathology)  
in September, 2013.



**Dr. Nick Batalis**

featured as one of the  
Top 20 Forensic Pathology Professors Online  
through Forensic Colleges at the link below:

<http://www.forensicscolleges.com/blog/profs/20-top-forensic-pathology-professors>



**Dr. Tom Soike**

selected as a CAP Committee member  
on the Commission on Laboratory Accreditation  
on December 24, 2013

# CONGRATULATIONS!

## LABORATORY ACCREDITATIONS

### **HLA laboratory:**

Successfully attained reaccreditation from the American Society for Histocompatibility and Immunogenetics (ASHI) inspection. The ASHI inspectors did not find any nonconformance's and were very complimentary of the department and staff. Of note, the inspectors found the staff to be open, friendly, and helpful. The inspectors shared during summation that it is evident the HLA staff truly care about the patients and provide quality services to transplant.

### **Transfusion Medicine Laboratory:**

Successful unannounced Food & Drug Administration (FDA) inspection. The FDA inspector did not find any nonconformance's and was very complimentary of the department and staff.

- ♦ **HTL(ASCP) (Histotechnologist Exam)**  
MUSC pass rate as of 11/14/13 is 86% .  
National Pass rate 2007-2012 is between 58.33% - 64.66%. Both figures include all examinees (1st time and repeats). The national percentage includes OJTs (On the Job Training). The program pass rate at the time of our site visit in 2010 was 75%.
- ♦ **SC POCT Meeting**  
Very successful meeting with 22 attendees representing statewide hospitals. The Histotech students who graduated in August, passed the registry.

## 2013 GOLDEN APPLE AWARDS

### NOMINATIONS & WINNERS

#### First Year Class Faculty Awards

**\*Dr. Michael Caplan**

Dr. Debra Hazen-Martin



#### Second Year Class Faculty Awards

Dr. Michael Caplan

Dr. Debra Hazen-Martin

Dr. Erin Presenell

#### Second Year Class Special Appreciation

Faculty

**\*Dr. Debra Hazen-Martin**

Administrator

**\*Sandy Nelson**

**\*Winners**



# RESEARCH DIVISION UPDATE

Statistics for the Division of Research from October through December.  
 Twenty Three grant proposals were submitted requesting \$ 3,766,540 in total first year costs. Also, during this period four grants were awarded totaling \$485,700.

Congratulations and many thanks to everyone involved in obtaining these awards.

Bradley Schulte, Ph.D., Vice Chair of Research

<b>GRANT APPLICATIONS 10/1/2013-12/31/2013</b>			
Principal Investigator	Proposed Start Date	Title	Total 1st YR Dollars
Cheung	7/1/2014	Elucidating the Role of Co-amplified GAB2 and IKBKB oncogenes in Ovarian Cancer	\$30,000
Cheung	7/1/2014	Role of GAB2 in PI3K Activation and Oncogene Interactions in ovarian cancer	\$233,361
Ethier	7/1/2014	Oncogene Interaction Networks in Breast Cancer Cells	\$373,750
Fan	7/1/2014	Fulvestrant Sensitizes ER-Breast Tumors to Chemotherapy and its Clinical Impact	\$299,000
Findlay	7/1/2014	MicroRNA 510 as a Biomarker of Response to Platinum-Based Chemotherapy	\$194,850
Guest	7/1/2014	The TRiC Chaperonin in Breast Cancer Cell Growth, Survival and Response to Taxane Therapy	\$30,000
LaRue (progress)	2/1/2014	Hemotopoietic Stem Cell-Derived Carcinoma Associated Fibroblasts in Tumor	\$261,449
LaRue (sub-award)	7/1/2014	Dissaccharide Cryopreservation Strategies for Hemotopoietic Stem Cells	\$50,000
Mehrotra	7/1/2014	Role of Hemotopoietic Stem Cells in Periodontal Ligament Homeostasis	\$112,125
Puligilla	12/1/2013	Role of SOX2 in Specification of Prosensory and Hair Cell Fate in Mouse Cochlea (Progress Report)	\$249,000
Puligilla	11/1/2013	CGM Pilot Program	\$30,000
Sha	7/1/2014	A Rapid Assay for Ribosome Binding Drugs	\$112,125
Smits	7/1/2014	Mechanistic studies on the human 8q24 non-protein coding prostate cancer susceptibility locus using a mouse gene desert megadeletion model	\$104,130
Spruill	7/1/2014	HPV Status and Outcomes in Oropharyngeal Cancer: A Study of 498 Patients	\$30,000
Spyropoulos	12/9/2013	The Utility of viable Patient Lung Tissues to Compare Tobacco Products	\$24,974
Spyropoulos	1/1/2014	GoMRI	\$377,964
Turner	7/1/2013	Defining the contribution of glycation associated reactive metabolites to periodontal disease in Gullah African Americans	\$29,000
Turner	1/1/2014	Increased Glycation Promotes ROS Production in the Tumor Micro-environment and Promotes Breast Cancer Disparity	\$30,000
Turner	7/1/2014	Project AGE: Linking Basic Science with Clinical Research Among Gullahs with Metabolic Syndrome	\$373,750

## *RESEARCH DIVISION UPDATE, continued*

Wang	7/1/2014	Twist 1 Signaling in Cancer Stem Cells and Cancer Treatment	\$373,750
Wang	7/1/2014	Role of Twist1-Mediated Cancer Stem Cell Expansion in Cancer	\$224,250
Watson	7/1/2014	Defining Ets Target Gene Signatures and Their Utility Query Tumor Databases	\$193,062
Watson	1/1/2014	Defining ETS target gene signatures using next-generation sequencing and their utility to query patient tumor databases	\$30,000
<b>Total Proposals</b>	<b>23</b>		<b>\$3,766,540</b>

### GRANTS AWARDED 10/1/2013-12/31/2013

Spyropoulos	1/1/2014	Cryopreserved Whale iPSCs for Rapid, Highly Sensitive Screening for Obesogens	\$89,985
Cheung	2/1/2014	Functional Genomics Approaches to Identify Ovarian Cancer Genes	\$149,999
Spyropoulos	3/1/2013	Developmental Transcription Factors in Prostate Cancer	\$21,615
Puligilla	12/1/2013	role of SOX2 in specification of prosensory and Hair cell fate in mouse cochlea	\$224,101
<b>Totals</b>	<b>4</b>		<b>\$485,700</b>



## MUSC RESEARCH STUDENT DAY 2013 WINNERS!

### PhD Poster I

1st place: Lashardai Conaway

### Undergraduate Oral

1st place: Luke Hevens

### Postdocs/Residents/Fellows Oral

1st place: Dr. Shawn Stevens

**Dr. Hainan Lang's Lab**



## 2013 RALPH H. JOHNSON VAMC STUDENT RESEARCH AWARD WINNER!

1st place: Dayvia Laws

**Mentored by Dr. Mandy LaRue**

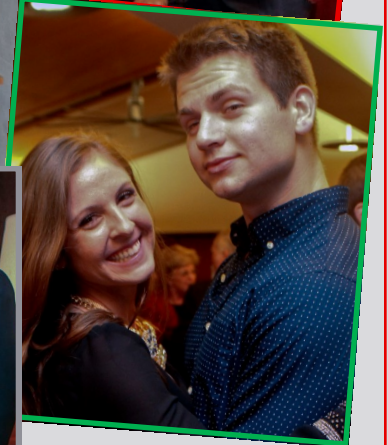
# HOLIDAY PARTY



2013



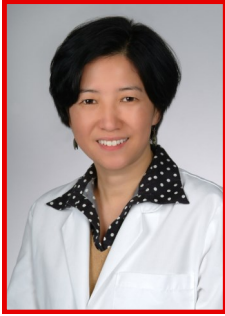
# HOLIDAY PARTY



2013







## *Noise induces permanent hearing loss and cochlear hair cell death*

**By Su-Hua Sha, M.D.**

The cochlea is the sensory organ responsible for hearing and verbal communication. The sensory cells (“hair cells”) of the organ of Corti transduce acoustic input into nerve impulses, which are then transmitted to the brain. It may be surprising that the auditory system, designed to process acoustic information, is sensitive to and can be damaged by intense sound. Exposure to loud sounds specifically causes damage or death to cochlear hair cells, leading to noise-induced hearing loss (NIHL). Unfortunately, NIHL is a major problem and is increasing in industrialized countries, stemming both from the workplace and from leisure activities. Many people are exposed to hazardous levels of sound on an everyday basis, whether it is from their work environment, such as factory workers, construction workers, or airport personnel, or from their own recreational activities, such as exposure to loud music on personal listening devices.

Above a certain level, the greater the intensity (perceived as loudness) of a sound stimulus, the greater the amount of damage to cochlear sensory hair cells can appear. Typically, normal moderate human conversation occurs around 60 dB sound pressure levels (SPL). Hearing protection is required at 85 dB SPL and above according to the National Institute of Occupational Safety and Health Administration (OSHA) standards. This includes protection of some everyday sounds that many people may not consider harmful, for instance, noise from a lawnmower can reach up to 90 dB SPL. At 120 dB SPL and above rapid hearing injury can occur. Noises such as chain saws and other power tools have intensities of 110-120 dB SPL. Around sixty million Americans own firearms, exposing themselves to potentially 140-170 dB SPL of noise. Worldwide, 250 million people suffer from NIHL. An estimated 30 million workers are exposed to potentially hazardous noise in the U.S. alone according to OSHA. As of 2010, NIHL was the predominant disability in war veterans, with an economic impact of \$660 million in compensation payments annually.

NIHL can be divided into two subtypes, temporary hearing loss and permanent hearing loss, based on duration and severity of hearing loss and the

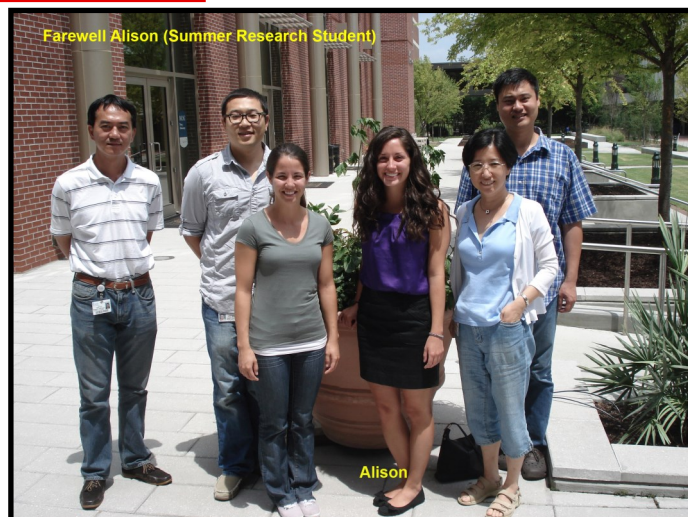
characteristic pathological feature of hair cells. Because mammals lack the ability to regenerate their cochlear hair cells, hair cell losses along the organ of Corti in the cochlea lead to a permanent hearing loss. Lower levels or transient high intensity noise can cause a temporary hearing loss for minutes, hours, or days, depending on the parameters of the sound stimulus. Hair cell loss is not observed with temporary hearing loss.

Research into NIHL using animal models has borne out two leading theories for the cause of hearing loss. One is mechanical damage from vibration of the organ of Corti beyond the tolerance of its physical structure. Another is a so called ‘metabolic damage’, wherein stress and metabolic overstimulation trigger cell death pathways. A variety of biochemical and molecular responses to noise trauma have been identified. For example, noise exposure elevates intracellular calcium levels in hair cells, likely through influx via calcium channels, and also activates calcineurin, a calcium-dependent phosphatase.

Another well-documented response to noise trauma is the generation of reactive oxygen species (ROS). It appears that excessive noise decreases cochlear blood flow, which leads to vasoactive lipid peroxidation and the generation of ROS. In addition, release of the neurotransmitter glutamate at inner hair cell synapses in response to traumatic noise has been implicated in excitotoxicity (neuronal damage and cell death from overstimulation by neurotransmitters) at this synapse. The traditional method for prevention of NIHL by the use of ear plugs to reduce noise levels reaching the ear has proven insufficient, primarily due to non-compliance. Based on animal experimentation, pharmacological prevention using a ‘hearing pill’ is a promising and appealing route. Antioxidants such as glutathione, D-methionine, ascorbic acid, and water soluble coenzyme Q10 have been reported to attenuate NIHL to some extent, while other antioxidants have failed to prevent NIHL. These conflicting results underscore the challenge still faced by the field in elucidating the detailed molecular mechanism causing NIHL and designing effective intervention strategies.

## *Noise induces permanent hearing loss and cochlear hair cell death — cont'd*

Currently, we are pursuing novel hypotheses based on our recent finding of energy depletion-induced changes in the activity of small GTPases in sensory hair cells and resultant actin cytoskeleton rearrangements. Our studies revealing that traumatic noise activates Rho-family GTPases through transient energy depletion were published in the *Journal of Neuroscience* in 2012 (*doi: 10.1523/JNEUROSCI.6381-11.2012*, PMID: 22956833), and were also highlighted in *Nature Reviews Neuroscience* (*doi:10.1038/nrn3359*). While our research projects provide valuable insights into the molecular events responsible for causing inner ear damage, we are also addressing translational questions with the goal of designing novel, rational pharmacological or molecular/genetic therapeutic interventions to ameliorate NIHL. I am fortunate to be able to lead an excellent and productive research team of postdoctoral research fellows and graduate students. For the upcoming 2014 Association for Research in Otolaryngology (ARO) annual meeting, my laboratory has submitted five abstracts for presentation. I am sincerely grateful for the collaborative research environment provided by the Department of Pathology and Laboratory Medicine. I am also indebted to the support of Drs. **Bradley Schulte, Hainan Lang, Chandrakala Puligilla, Kevin Wang, Omar Moussa**, and Drs. **Richard Schmiedt and Judy Dubno** from the Department of Otolaryngology.

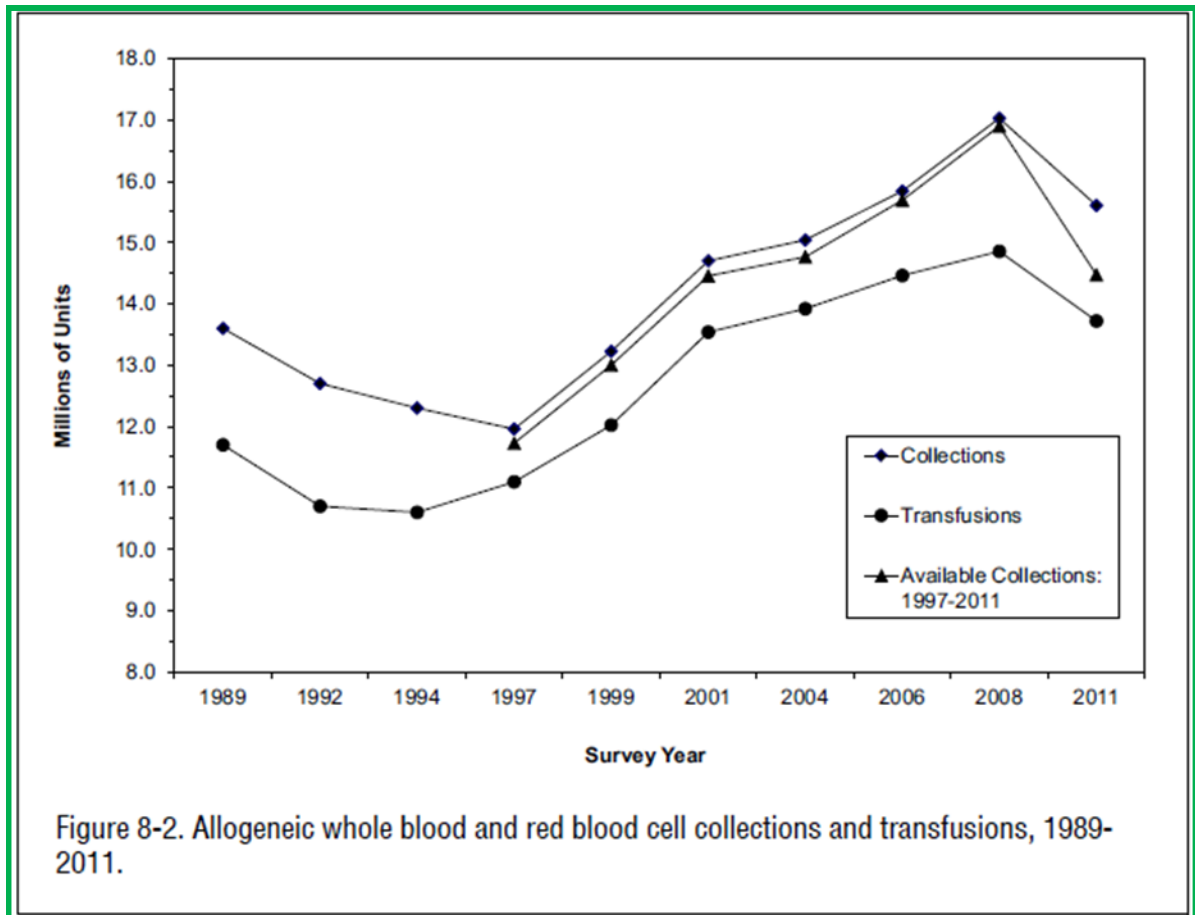




# Blood: Who Needs It?

By Jerry E. Squires MD, PhD

Blood transfusion has been an integral part of medical therapy for at least the last 70 years. However, over that period of time there have been significant changes in the use of blood in the United States. This is particularly true of the past four decades as demonstrated in data from the 2011 National Blood Collection and Utilization Survey (NBCUS), below.

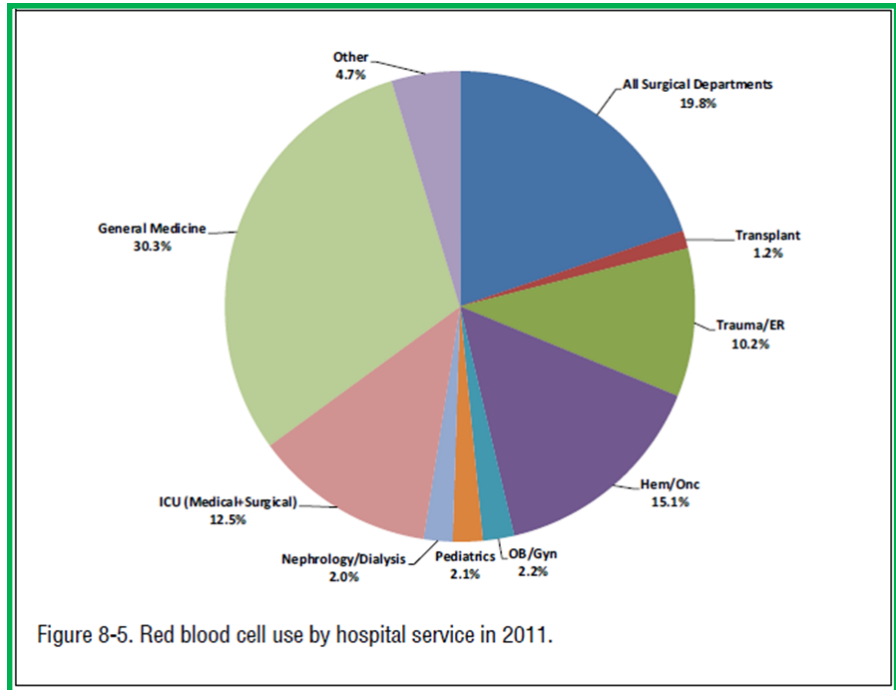


The decrease in blood usage in the late 1980's and early 1990's is typically ascribed to concerns about the risk of HIV transmission during that time. However, the significant decrease in red cell transfusions between 2008 and 2011 is more difficult to explain simply. In all probability this marked change in blood transfusion has been caused by several factors. One of these may be heightened awareness of the risks of blood transfusion (even though blood components are safer now than ever before, particularly with respect to infectious disease transmission). But in addition there has been increasing concern that "unnecessary" blood transfusions are actually associated with poorer patient outcomes such as increased hospital length of stay, increased ICU length of stay, and even increased 30 to 60-day mortality. This concern has, in all probability, led to more cautious use of transfusion in patient therapy.

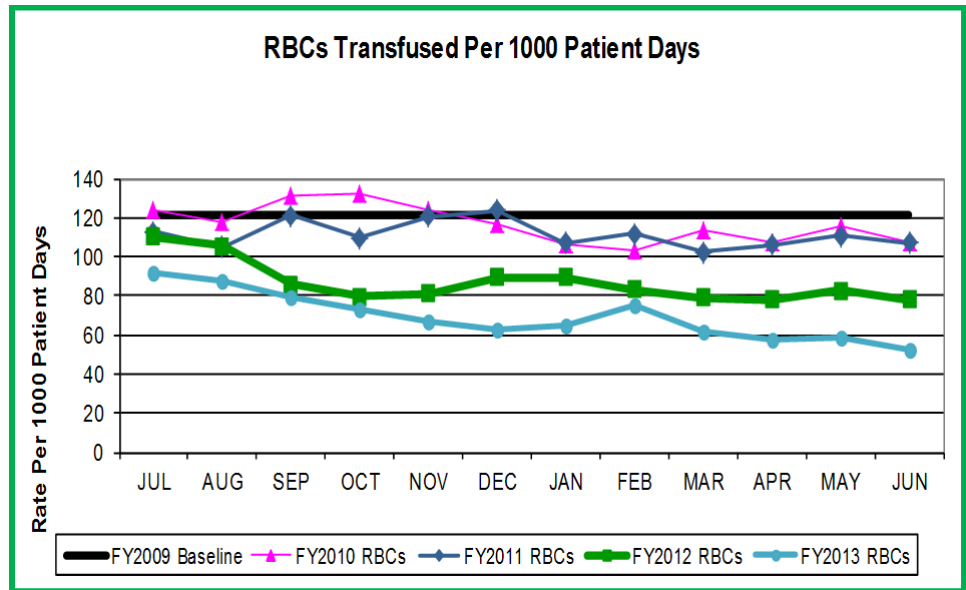
## *Blood: Who Needs It? - cont'd*

In this regard, it is probably important to emphasize that in those patients who clinically require a blood transfusion it is, in fact, a life-saving therapy. Finally, another factor that probably contributes to the decline in the overall transfusion rate is the fact that transfusion represents a significant cost to both patient and hospital that is difficult to justify in those patients whose prognosis is not definitively improved by transfusion.

The NBCUS also tracks the use of blood by various service lines within the medical community. As demonstrated in the graph below, General Medicine, particularly when combined with Hematology/Oncology and Nephrology/Dialysis account for almost half of all red cell transfusions.



At MUSC blood Utilization has been a particular concern for several years. Beginning in 2010, the Transfusion Service began providing blood utilization reports to track the use of blood within the hospital. This has been accompanied by efforts within many Departments and Service Lines to utilize blood transfusion more conservatively. Clearly, as demonstrated in the graph below, MUSC has met with real success in controlling blood use:



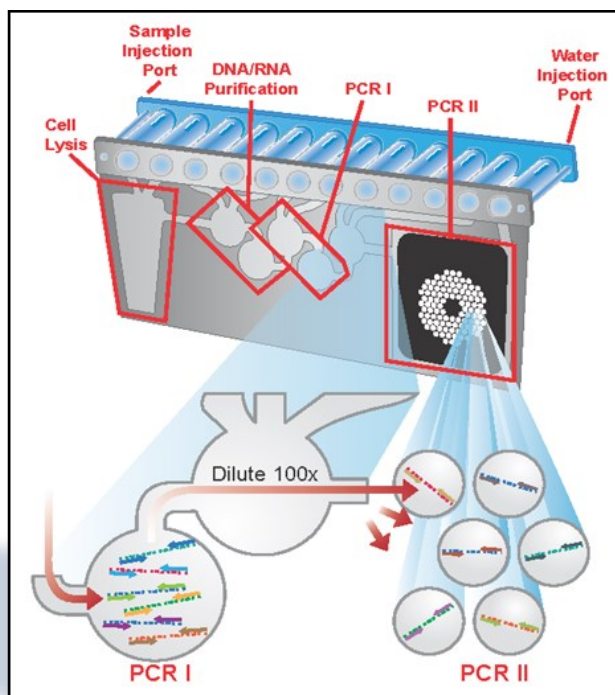
When red cell transfusions at MUSC are compared based on 1000 patient days (to account for monthly variations in hospital occupancy rates), it is apparent that at MUSC red cell transfusions have decreased from 121.2 red cell transfusions per 1000 patient days in 2009 to 69.3 transfusions per 1000 patient days in 2013—a 42.8% reduction. While I think that the entire hospital system should be pleased with this progress, it is now time to look more specifically at how these blood products are used. In other words, how effectively are we using these individual blood components on a patient by patient basis.



## Frequently Asked Questions about the Blood Culture Identification Panel (BCID) Multiplex PCR assay

**By Lisa L Steed, PhD, D(ABMM), John M. Hurst, PharmD, BCPS,  
and Frederick S. Nolte PhD, D(ABMM), F(AAM)**

The BioFire Diagnostics FilmArray Blood Culture Identification (BCID) Panel is a completely automated, massively multiplex, nested PCR assay that is capable of simultaneous detection and identification of 27 different gene targets including 19 bacteria, 5 *Candida* spp., and 3 antimicrobial resistance genes. Approximately 90% of all positive blood culture isolates can be identified with the BCID multiplex PCR panel. This assay is performed directly on positive blood cultures and the results are available in 1.5-2 hours after the blood culture is positive.



**The FilmArray pouch**

This short article will describe fine points of this BCID multiplex PCR assay in a series of FAQs, two interesting cases that occurred in the first two weeks of use of the assay, and how use of this assay has affected patient care.

The following organisms can be detected:

Gram-positive organisms:	Gram-negative organisms:	Yeasts:
<i>Staphylococcus aureus</i>	<i>Acinetobacter baumannii</i>	<i>Candida albicans</i>
Coagulase negative Staph	<i>Enterobacter cloacae</i> complex	<i>Candida glabrata</i>
<i>Enterococcus</i>	<i>Enterobacteriaceae</i>	<i>Candida krusei</i>
<i>Listeria monocytogenes</i>	<i>Escherichia coli</i>	<i>Candida parapsilosis</i>
<i>Streptococcus</i> sp.	<i>Haemophilus influenzae</i>	<i>Candida tropicalis</i>
<i>Streptococcus agalactiae</i>	<i>Klebsiella pneumoniae</i>	
<i>Streptococcus pneumoniae</i>	<i>Klebsiella oxytoca</i>	
<i>Streptococcus pyogenes</i>	<i>Neisseria meningitidis</i>	
	<i>Pseudomonas aeruginosa</i>	
	<i>Proteus</i> sp.	
	<i>Serratia marcescens</i>	

## Frequently Asked Questions about the Blood Culture Identification Panel (BCID) Multiplex PCR assay - *cont'd*

The following resistance mechanisms can be detected:

- *mecA*-mediated methicillin resistance in staphylococci
- *vanA* and *vanB*-mediated vancomycin resistance in enterococci
- *bla*<sub>KPC</sub> carbapenemase resistance in enteric gram-negative bacilli

Positive blood cultures are still subcultured to solid media for conventional identification and complete susceptibility testing. In addition, conventional techniques are required to identify organisms not detected by the BCID panel such as *Cryptococcus* sp., to provide species identification for vancomycin-resistant enterococci (i.e., *E. faecium* vs *E. faecalis*), and to identify streptococci and *Enterobacteriaceae* such as *Enterobacter aerogenes* and *Salmonella* sp. not specifically identified by the multiplex PCR.

**Q1.** My patient's blood culture isolate is reported as "*Staphylococcus aureus* NOT methicillin resistant by multiplex PCR". What is the likelihood that this isolate will be methicillin resistant by the standard susceptibility test?

**A:** Possible but very unlikely. Methicillin resistance in staphylococci is primarily but not exclusively due to the *mecA* encoded altered penicillin binding protein PBP2a.

**Q2.** My patient's blood culture isolate is reported as "*Enterobacteriaceae* by multiplex PCR". What is the likelihood that this isolate will be carbapenem resistant by the standard susceptibility test?

**A:** While KPC carbapenemases are currently the most common cause of carbapenemase-mediated resistance, they are not the only carbapenemases present in the USA. In addition, decreased cell membrane permeability can result in carbapenem resistance in some enteric Gram negative rods.

**Q3.** Why can't yellow pediatric or orange and green adult blood culture bottles be tested by this multiplex PCR assay?

**A:** These bottles contain charcoal which will interfere with the assay because they may contain non-viable organisms and/or nucleic acid at a detectable level, giving false positive results.

**Q4.** The multiplex PCR can identify coagulase-negative staphylococci and *mecA*-mediated methicillin resistance. Why doesn't the report say "Coagulase negative *Staphylococcus*, NOT methicillin resistant by multiplex PCR" or "Coagulase negative *Staphylococcus*, methicillin resistant by multiplex PCR"?

**A:** Since coagulase-negative staphylococci are common skin contaminants in blood cultures, susceptibility testing may not be warranted. If susceptibility testing is warranted, the report will be updated with the methicillin result.

**Q5.** The blood culture result was reported as coagulase-negative *Staphylococcus* but the multiplex PCR assay had no result and I know routine, non-charcoal bottles were used. What happened?

**A:** The BCID panel has 3 assays for the detection of staphylococci. The *S. aureus* assay detects only *S. aureus* without cross reactivity with other staphylococci. The other 2 assays detect 13 species of coagulase-negative staphylococci, including *S. lugdunensis*, but not all coagulase-negative staphylococci.

## Frequently Asked Questions about the Blood Culture Identification Panel (BCID) Multiplex PCR assay - *cont'd*

**Q6.** The multiplex PCR reports “*Streptococcus*” but doesn’t tell the species. Why not?

**A:** The BCID panel has 4 assays for the detection of streptococci. Assays for *S. pyogenes* (Grp A), *S. agalactiae* (Grp B), and *S. pneumoniae* are specific for the organism and do not cross react with each other or with the Streptococcus assay. The *Streptococcus* assay will detect *S. anginosus/constellatus/intermedius*, *S. bovis*, *S. mitis* group, *S. mutans* group, *S. salivarius* group.

**Q7:** The blood culture result was reported as *Morganella morganii* but the multiplex PCR assay had no result for *Enterobacteriaceae*. What happened?

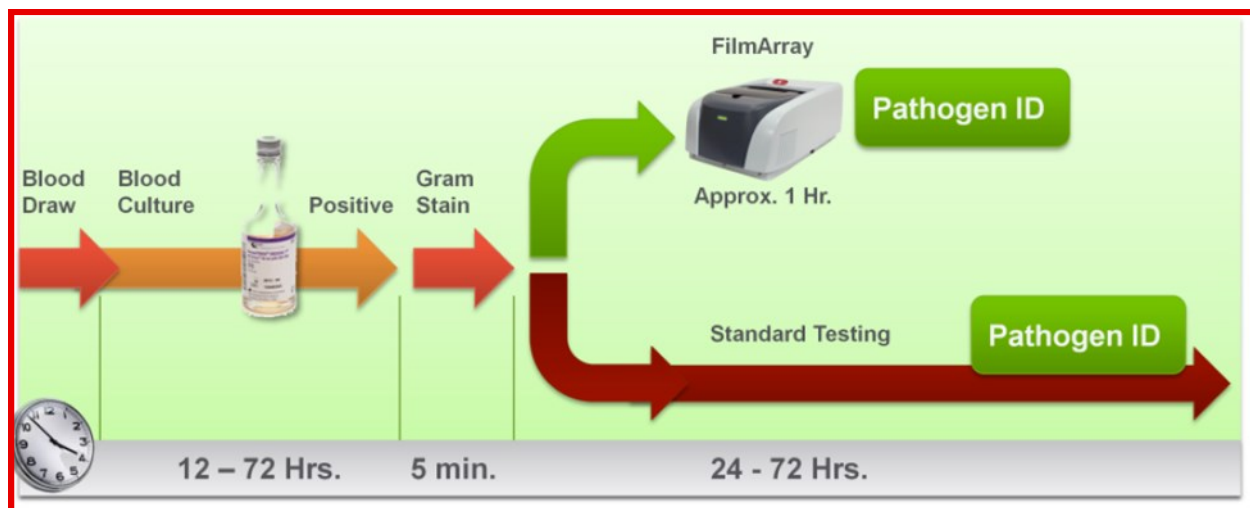
**A:** The *Enterobacteriaceae* assay detects many members of this family, including *Citrobacter* spp., *Enterobacter* spp., and *Salmonella* spp. However, *Enterobacteriaceae* assay will not detect *Morganella* spp., *Providencia* spp., or most *Yersinia* spp.

**Q8:** The blood culture result was reported as coagulase-negative *Staphylococcus* and *Staphylococcus aureus*, methicillin resistance detected in one or both organisms”. What does that mean??

**A:** Both organisms are present in the blood culture. The *mecA* gene, which confers methicillin resistance, is also present. However, the BCID panel cannot determine which organism or if both organisms contain the *mecA* gene. That requires testing isolated colonies after subculture to solid media. It would be wise to assume MRSA is present until further results based on the subculture are available.

**Q9:** With the multiplex PCR assay, the organism is known but it takes 2 days to get the susceptibility back. Why so long?

**A:** Susceptibility testing beyond the capabilities of the BCID panel requires isolated colonies grown on solid media. The blood must be subcultured to obtain isolated colonies. In addition, susceptibility testing requires 18-24 hours. Timelines for pathogen identification by standard conventional methods and the BCID multiplex PCR are shown below:



## Frequently Asked Questions about the Blood Culture Identification Panel (BCID) Multiplex PCR assay - *cont'd*

In the 2 weeks since the launch of the BCID panel its clinical utility has been demonstrated in the following scenarios.

First, Gram stain of a positive blood culture bottle showed gram-positive cocci in clusters and gram-positive cocci in chains. The BCID panel of that same positive bottle detected MRSA, VRE, *P. aeruginosa*, *Streptococcus* sp., *Candida tropicalis*, and *Candida glabrata*. Re-examination of the Gram stain eventually showed budding yeast but not gram-negative bacilli. Subculturing the bottle to additional selective agars allowed detection of all 6 organisms. Had the multiplex PCR not been performed, the only organisms that would have been recognized on the subculture plates were MRSA and one of the yeasts. The BCID panel also allowed the Antimicrobial Stewardship Team to work with the primary team to order appropriate therapy for all six pathogens within two hours of culture positivity (in addition to the antibiotics for cystic fibrosis). Without the BCID panel, antifungal therapy would have been delayed 24-48 hours, *P. aeruginosa* therapy would have been delayed 48-72 hours, and the VRE would not have been found or treated. An Infectious Diseases Consult was recommended and obtained to assist with management for this patient.

Second, Gram stain of a positive blood culture bottle showed gram-negative rods. The multiplex PCR detected *K. pneumoniae* and *P. aeruginosa*. *K. pneumoniae* grew on subculture, however, no *P. aeruginosa* could be recovered using several different techniques. The BCID panel may occasionally detect organisms not grown in culture but whose presence can be confirmed by alternative PCR methods (1, 2). The patient was switched from amoxicillin-clavulanic acid to anti-Pseudomonal therapy with meropenem within 2 hours of the multiplex PCR result of *K. pneumoniae* and *P. aeruginosa*. After discussion with the Antimicrobial Stewardship Team the patient was transitioned to cefepime per the MUSC Bacteremia Pathways. The patient was seen by Infectious Diseases consult and was transitioned to oral ciprofloxacin and discharged to complete a 14-day course.

In addition, 5 patients with coagulase-negative staphylococci were not been given any antibiotics following culture positivity. Often these patients would have been admitted or started on antibiotics until the culture was identified as coagulase negative staphylococci.

The FilmArray Blood Culture Identification (BCID) Panel is a reliable, rapid, direct identification method for bacteria and yeast in blood culture bottles with high sensitivity and specificity. This multiplex PCR in combination with more organism-appropriate antimicrobial usage should improve patient care and reduce hospital costs. Studies to document the clinical impact of rapid identification of blood culture isolates with the multiplex PCR BCID panel are in development.

### References:

1. Blaschke AJ, Heyrend C, Byington CL, Fisher MA, Barker E, Garrone NF, Thatcher SA, Pavia AT, Barney T, Alger GD, Daly JA, Ririe KM, Ota I, Poritz MA. 2012. Rapid identification of pathogens from positive blood cultures by multiplex polymerase chain reaction using the FilmArray system. *Diagn. Microbiol. Infect. Dis.* 74: 349-355.
2. Altun O, Almuhayawi M, Ullberg M, Ozenci V. 2013. Clinical evaluation of the FilmArray blood culture identification panel in identification of bacteria and yeasts from positive blood culture bottles. *J. Clin. Microbiol.* 51:4130-4136.



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2014 ASCP

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**ASCP ANNUAL MEETING**

**OCTOBER 8-11, 2014**

103<sup>rd</sup>

**USCAP**

**ANNUAL MEETING**

**MARCH 1-7, 2014**

**ADASP**

2014

**ANNUAL MEETING**

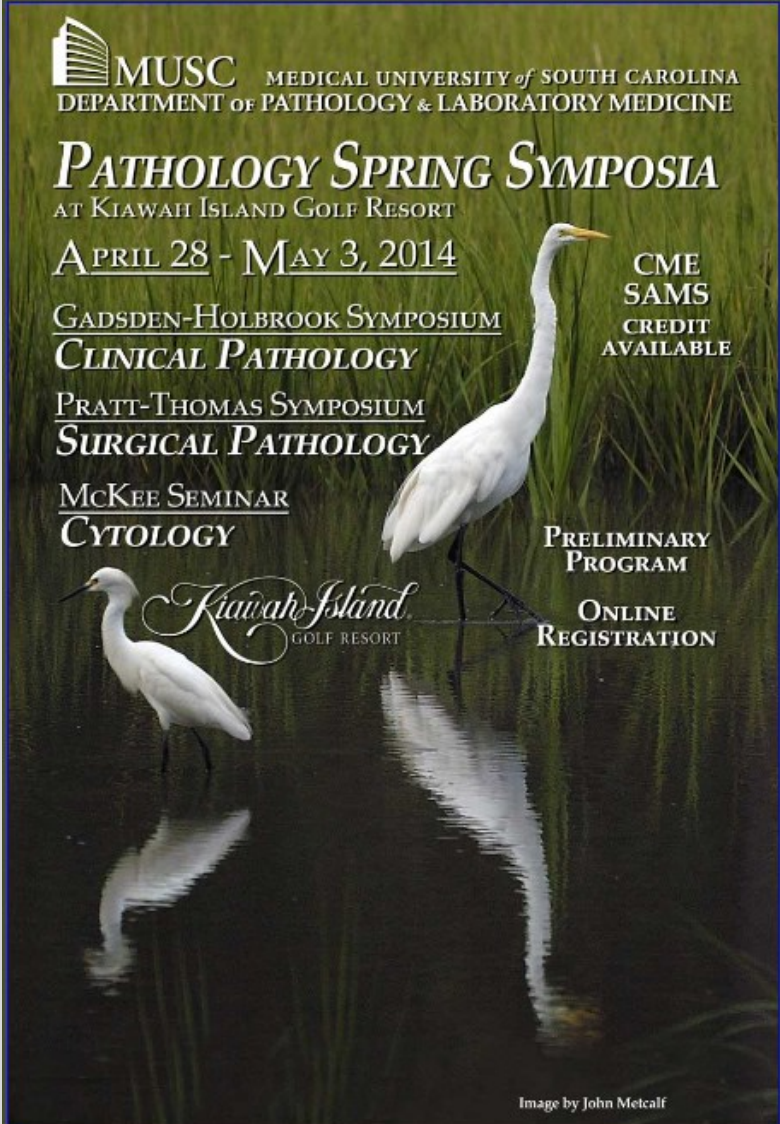
**MARCH 1, 2014**

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Image by John Metcalf

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