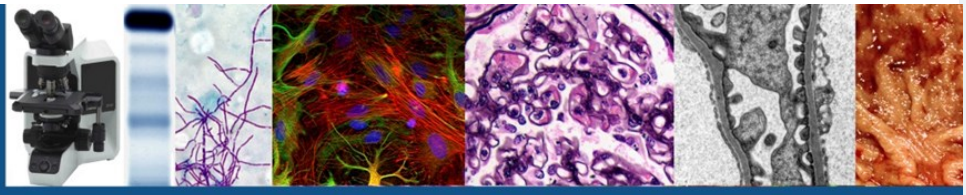
THE PATH WAY

September, 2014 **Volume 5, Issue 3**

MUSC
MEDICAL UNIVERSITY of SOUTH CAROLINA



DEPARTMENT of PATHOLOGY & LABORATORY MEDICINE

Steven L. Carroll, M.D., Ph.D.

Inside this issue:

DONOR NEEDED!

We in Pathology and Laboratory Medicine work on diagnosing patients daily that we do not know or have never met. We now have the opportunity to help one of our own.

Dr. Ellen Riemer is in need of a kidney transplant. She is a very private person but has realized that this is something that she needs to share with everyone around her, in hope that someone will have the opportunity to help her by donating a kidney to her.

Here are a few things to know if you are interested in being tested to find out if you are a match and if you are eligible to be a living kidney donor:

- Most people are born with two kidneys. After donating a kidney, a person can live a long and healthy life with just one. The remaining kidney simply grows bigger and takes over the work of both kidneys.
- The donor needs to be in good health, for example, without diabetes, high blood pressure or malignancy.
- The potential donor will incur no medical expenses from either being tested or from the donation itself. Dr. Riemer's insurance will pay this cost.
- If the donor's blood type isn't compatible with that of the recipient, a paired kidney exchange ("Paired Donation") can be done at MUSC. In paired donation, a kidney from such a donor is matched and transplanted into the recipient of a second donor-recipient pair (also whose blood type is incompatible), and vice-versa. The transplants are performed simultaneously.
- Most of the time, the kidney donation can be done by laparoscopic surgery, which is a less invasive procedure with shorter recovery time and smaller scars than an open procedure.
- Kidney donation is not a spontaneous decision, but a process. ***The purpose of the testing process is to make absolutely certain that the donor will not be harmed by donating, and that he or she is healthy and will remain healthy after donation.***
- While choosing to donate a kidney is not for everyone, it can be a rewarding experience in itself and a chance to be a real hero for another person.
- No one should ever feel pressured to donate a kidney. The potential donor has a right to say "no" and change his or her mind at any time during the testing process, no matter what the circumstances. The reasons can be kept a private matter between the potential donor and the transplant team.

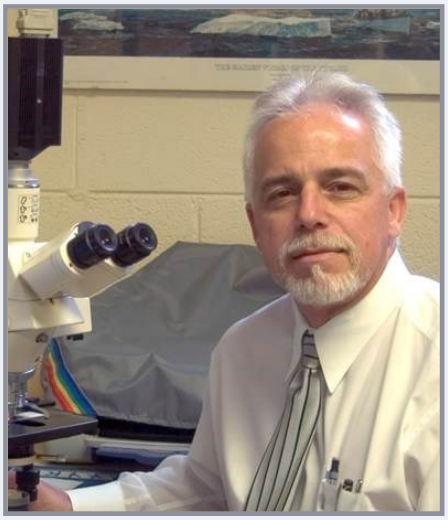
If you or someone you know are interested in exploring the possibility of kidney donation, have questions or want more information, please contact the MUSC Living Donor Transplant Coordinator at (843)792-4722. If preferred, you can also contact Dr. Riemer directly at 843-792-4032.

This newsletter is made possible from the generous contributions of MUSC's Pathology and Laboratory Medicine Faculty and Staff. The success of this publication is dependent upon this support. Thank you for your interest, time and information. For inquiries, suggestions or submission information please contact Lori Roten (roten@musc.edu).

NEWS FROM DEPARTMENT ADMINISTRATION & BUSINESS OFFICE

SERVICE AWARDS

EMPLOYEE NAME	POSITION	UNIVERSITY/HOSPITAL	YRS. OF SERVICE
RAYMOND D. EDWARDS	HEAD AUTOPSY TECHNICIAN	UNIVERSITY	30
AVTAR K. SINGH, M.D.	PROFESSOR / FACULTY	UNIVERSITY	20
DEMETRI D. SPYROPOULOS, PH.D.	ASSOCIATE PROFESSOR / FACULTY	UNIVERSITY	20
LISA L. STEED, PH.D.	PROFESSOR / FACULTY	UNIVERSITY	20
DENNIS K. WATSON, PH.D.	PROFESSOR / FACULTY	UNIVERSITY	20
HAINAN LANG, PH.D.	ASSOCIATE PROFESSOR / FACULTY	UNIVERSITY	10
CYNTHIA A. SCHANDL, M.D., PH.D.	ASSOCIATE PROFESSOR / FACULTY	UNIVERSITY	10
DARBY ANN BRASS	FAST FLOW & SATELLITE LABS	HOSPITAL	30
EMILY PALMER-GADSDEN	FAST FLOW & SATELLITE LABS	HOSPITAL	30
RONDA JEAN SANDERS	CYTOPATHOLOGY	HOSPITAL	30
PATRICIA A. COHEN	FAST FLOW & SATELLITE LABS	HOSPITAL	20
AILEEN SMALLS CROMWELL	VENIPUNCTURE	HOSPITAL	20
DEONNE NICOLE FRANCEWAR	HLA LABORATORY	HOSPITAL	20
PAULINE B. NELSON	FAST FLOW & SATELLITE LABS	HOSPITAL	20
MARILIA CASTELLO	TRANSFUSION MEDICINE	HOSPITAL	10
DAVID L. KERNS	FAST FLOW & SATELLITE LABS	HOSPITAL	10
JENNIFER L. MORSE	CYTOGENETICS	HOSPITAL	10
DONNA JEAN ODEN	DIAGNOSTIC MICROBIOLOGY	HOSPITAL	10
GLORIA PALMER-LONG	DIAGNOSTIC MICROBIOLOGY	HOSPITAL	10
CLAIRE CLARA SINGLETON	HISTOPATHOLOGY	HOSPITAL	10
LABERTHA E. WASHINGTON	VENIPUNCTURE	HOSPITAL	10



Vinnie Della Speranza

CONGRATULATIONS!!

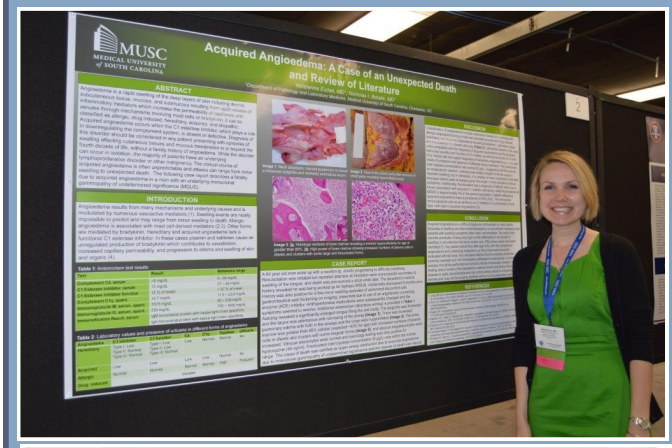
Vinnie Della Speranza was honored with the NSH Histotechnologist of the Year award.

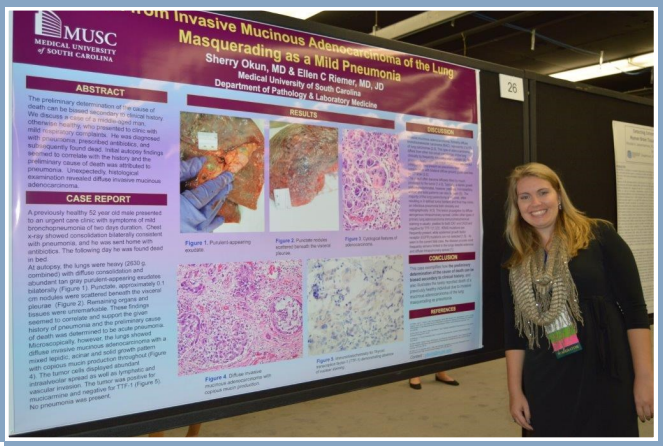
The National Society of Histotechnology (NSH) is a national organization that includes histotechnologists from the U.S. and Canada. Vinnie received the award last Saturday night in Austin, Texas with a standing ovation from 800 in attendance at the ceremony. Vinnie has been active in the field for over 35 years and is nationally recognized for his expertise and experience.

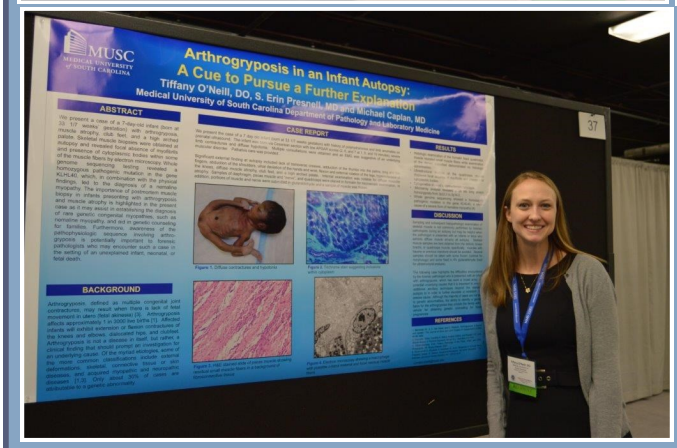
Please join me in congratulating Vinnie on receiving this prestigious award!

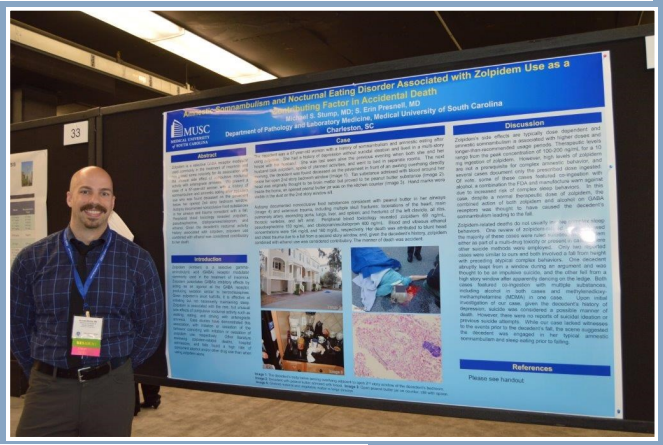
PATHOLOGY AND LABORATORY MEDICINE "WINS"

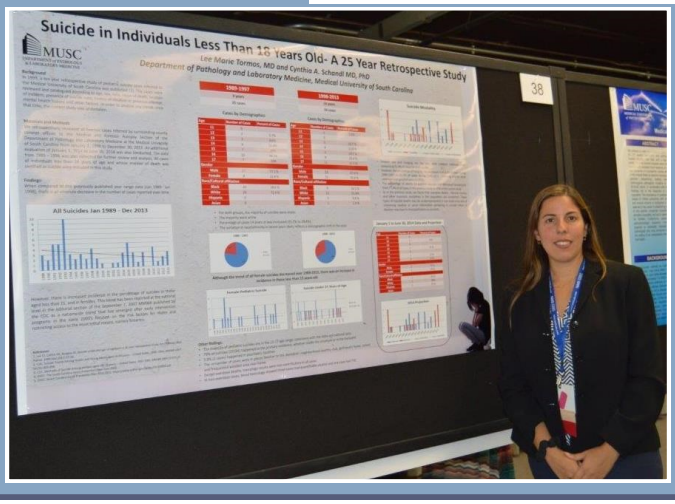
Our Department had the most poster/platform presentations of any department/office represented at the National Association of Medical Examiners' Annual Meeting that was held September 19-23, 2014, in Portland, Oregon. Special congratulations goes to Kate Eichel who won the Best Resident Award for her poster. Thanks to all for continuing to submit abstracts for presentation and publication.











PATHOLOGY AND LABORATORY MEDICINE "WINS"

The Pathology and Laboratory Medicine Residency Program has been selected along with a select few programs as an Pier Alpha Test Site.
PIER (Pathology Informatics Essentials for Residents) is a new curriculum developed jointly by APC, API, and CAP.
This curriculum is to supplement the Resident's experience & Informatics Testing.

The Medical Student Interest Group has been awarded the ICPI MSIG Grant for $500 from The Intersociety Council for Pathology Information

Two students in Dr. Hainan Lang's Lab, Conaway Lashardai and Dr. Yazhi Xing, won travel awards from Gordon Conference meeting on Auditory System this month.
The GRC on Auditory system is considered one of the field's most prestigious conferences, bringing together world-leading researchers from academia and national labs to discuss the latest, most exciting research in auditory system and to speculate on future directions for the hearing research field.
It is a GREAT HONOR for our students to won this award!

US News and World Report (Doximity) Residency Rankings for Pathology

Doximity (which is what US News and World report is using for ranking of medical centers) has a ranking of residency programs.
Based on their ranking, our Pathology Residency Program is # 16 in the US and #3 in the south (behind Vanderbilt and Emory).
This is a GREAT ACCOMPLISHMENT!

Nomination: For her knowledge and expertise. She always goes the extra mile.

Other Nominees: Tony Eisenhart, Dolly Hope, Jarvis Jenkins, Teresa Kennedy, Linda McCarson, Susan Morgan, Joe Rozier, and Nancy Smythe

Margaret Romano

Research Specialist I

ARRIVALS / DEPARTURES

ARRIVALS:

- **Collin Homer-Bouthiette arrived in Dr. Smits lab as a Research Specialist II on 7/7/14**
- **Mary Bridges arrived in Dr. Lang's lab as a Research Specialist II on 8/4/14**
- **Amanda Prechtl arrived in Dr. Carroll's lab as a Postdoc on 9/8/14**
- **Van Phan arrived in Dr. Turner's lab as a Research Specialist I on 9/22/14**
- **Sean Courtney arrived in Dr. Hardiman's lab as a Postdoc on 9/22/14**
- **Anandakumar Shunmugavel will arrive in Dr. Cheung's lab as a Postdoc on 10/1/14**

DEPARTURES:

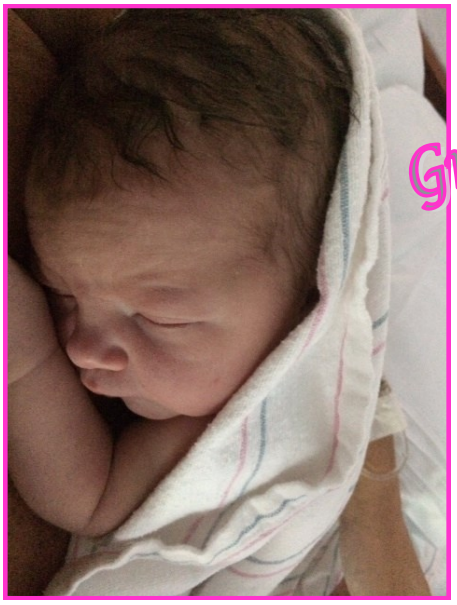
- **Anne Bartlett, M.D., left on 6/30/14**
- **Michael Caplan, M.D., left on 6/30/14**
- **Hleb Federovich, a Research Specialist I in Dr. Turner's lab left on 8/1/14**

CONGRATULATIONS!

To: Dr. Julie Robinson and her husband, Chad

Camille Jane Robinson Arrived on August 8, 2014
7 lbs. 12 oz.

To: Dr. Debra Hazen-Martin



Granddaughter

Emma Lawrence Martin (Wrenny)
Arrived on July 7, 2014 7 lbs. 8 oz.

RESEARCH DIVISION UPDATE

Statistics for the Division of Research from July through September.
Thirteen grant proposals were submitted requesting $2,183,883
in total first year costs.
Also, during this period three grants were awarded totaling $422,529.

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

SUBMITTED 7/1/2014 – 9/30/2014:

Tiffany Baker, M.D., Ph.D.
Title: Heat Shock Protein-Induced Protection Against Cisplatin-Induced Hair Cell Death $46,466 – Proposed Start Date 9/28/14

Steven L. Carroll, M.D., Ph.D.
Title: NF-140082-Combinational Therapies for Neurofibroma and MPNST Treatment and Prevention $261,625 – Proposed Start Date 3/1/15

Hui (Tony) Cheung, Ph.D.
Title: Role of ID4 in Ovarian Cancer Development and Metastasis $100,000 – Proposed Start Date 12/1/14

Meenal Mehrotra, M.D., Ph.D.
Title: Role of Hemototopoietic Stem Cells in Periodontal Ligament Homeostasis $112,125– Proposed Start Date 4/1/15

Suhua Sha, M.D.
Title: Molecular Mechanisms in Noise-Induced Hearing Loss $373,750 – Proposed Start Date 4/1/15

Demetri Spyropoulos, Ph.D.
Title: Unlimited Expansion of Cells with Parential Tumor Features by a Novel Approach that Utilizes Post-Thaw Viable and Intact Prostate Tissues and Adenocarcinomas $112,125 – Proposed Start Date 10/1/14

Demetri Spyropoulos, Ph.D.
Title: LC140642: Unlimited Expansion of Cells with Parental Tumor Features by a Novel Approach that Utilizes Post Thaw Viable and Intact Lung Tissues and Adenocarcinomas $149,500– Proposed Start Date 9/1/15

Demetri Spyropoulos, Ph.D.
Title: Personalized Decision to Treat and Expansion of Metastatic Prostate Tumor Cell Targets for Therapies Based on "Thawed Live" tissue Technology and 3-D Human ex Vivo and in vivo Models $334,000– Proposed Start Date 3/1/15

Demetri Spyropoulos, Ph.D.
Title: Using Embryonic Stem Cell Fate to Determine Potential Adverse Effects of Petroleum/Dispersant $380,157– Proposed Start Date 12/1/14

Lisa Steed, Ph.D.
Title: Invasive Aspergillosis and Rare Molds Virtual Advisory Network $3,250– Proposed Start Date 9/1/14

David Turner, Ph.D.
Title: Vitamin D3 Supplementation for Low-Risk Prostate Cancer: A Randomized Trial $19,260– Proposed Start Date 10/1/14

Dennis Watson, Ph.D.
Title: Differential Alternative Splicing and Gene Expression Stratifies Lung Cancer $261,625– Proposed Start Date 7/1/15

Je-Seong Won, Ph.D.
Title: S-Nitrosoglutathione Reductase in Regulation of chronic Cerebral Hypoperfusoin-Induced Vascular Dementia $30,000– Proposed Start Date 12/1/15

AWARDED 7/1/2014 – 9/30/2014:

Tiffany Baker, M.D., Ph.D.
Title: Heat Shock Protein-Induced Protection Against Cisplatin-Induced Hair Cell Death $23,983 – Awarded Date 8/11/14

Hainan Lang, Ph.D.
Title: Auditory Nerve degeneration and Repair $368,750– Proposed Start Date 7/1/2014

Ying Xiong, Ph.D.
Title: Targeting HSC-derived circulating fibroblast presucrsos in primary fibrosis $29,796– Proposed Start Date 7/1/14

FACULTY FOCUS

Help!

I've fallen into an alveolus and I can't get out!

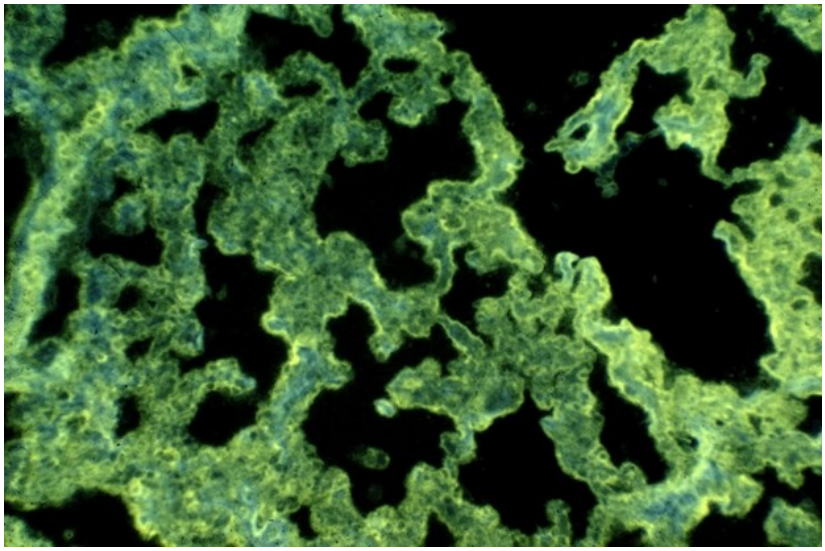
RUSSELL A. HARLEY, JR., M.D.
PROFESSOR

Longstanding members of our department know me; some of the younger don't since I've been in Washington much of the last five years. I first came in contact with the Department of Pathology in 1961 as a sophomore medical student. I have been on the faculty since returning from Vietnam in 1969, but it was my earlier associations that got me into pathology and my particular specialty, pathology of the lung. I'm amazed at how much of this happened by chance.

I was born dead in 1937 in my grandmother's hospital in Walterboro. My maternal grandfather was a doctor and his Norwegian-American wife a nurse. They met at St. Francis and later set up practice in Walterboro including a clinic. Since there were no available nurses, my grandmother established a nursing school. The Tumbleston sisters were among the first nurses, and when the doctor who had delivered me pronounced me dead and left the room, one of the Tumblestons said, "We can't let Mrs. Es'Dorn's first grandchild die!" and picked me up by my feet and injected adrenalin into my heart. Seems to have worked. I grew up and went to med school. In 1961 when I was a rising sophomore, a plaque was dedicated to my grandmother at the new hospital in Walterboro. Afterward my sister and I ate hamburgers with lettuce and tomatoes, and 21 days later both came down with hepatitis A. Not sure Walterboro is lucky for me. Med school started without me, but I got two books: Robbins Pathology, a big book, and Zinsser's Microbiology. I tried to keep up with the class, but I found Robbins, a single author book, more readable. Six weeks later when I started classes, I was far ahead of the rest of the class in pathology and about as far behind in micro. Forde McIver was on the Pathology faculty, a wonderful man who had been a chest surgeon before contracting TB. I needed a part-time job, and he gave me one injecting emphysematous lungs with colored latex and embedding representative slices in plastic. The pathologic classification of emphysema was new at the time and these specimens were useful in demonstrating the types. I became interested in trying to determine the site of expiratory airway obstruction that led to grossly obvious air trapping and hyperinflation in emphysema. On my 24th birthday while I was dissecting down airways with a tiny pair of scissors I tumbled into an alveolus and haven't been able to find my way out since. The following summer, still trapped in my alveolus, I started a year of post-sophomore fellowship and for the next year participated in departmental activities. That year I presented the pathologic findings in my first clinicopathologic conference (CPC), a case of fatal dermatomyositis in a man younger than I was. The clinical discussant was Dr. Vince Mosely, the most respected internist and "diagnostician" in the state, and when I dared to correct his comments on the prevalence of foot drop in such cases, aside from his glare I remember noticing that the older faculty present had tears in their eyes as they tried to smother their laughter. I had a thing back then for fixing lungs in the inflated state. Horse lungs are most like human ones regarding secondary lobular septation and they sometimes get a mild degree of centrilobular emphysema. I went to a dog food factory and talked them out of some horse lungs.

(Yes, Black Beauty, it's worse than you thought.) I brought the lungs back to Charleston where I used pumps to inflate them at a constant pressure until one malfunctioned and filled an entire room with formalin. My nose still burns. The next year the new Research Building opened thanks to the efforts of Dr. Bob Walton. I was given the lab where EM now is and used the hood to fix lungs by inflating them with acrolein (tear gas). You can imagine. A couple of years later at Yale I had a baby swimming pool filled with glutaraldehyde solution for inflating lungs. Smelled like flowers. Early in my senior year in Med School, after Gordon Hennigar was recruited to be the new Chairman of Pathology I visited his department at Downstate in Brooklyn and I learned techniques of preserving and mounting specimens for the museum he wanted to build in Charleston. While I was at Downstate, I gave a presentation on the role of surfactant in the pathology of infant lungs with hyaline membrane disease. Hennigar liked it and asked what I was going to do after med school. I told him I wanted to go into pulmonary medicine, but thought doing another year of lung pathology would help me solidify my knowledge of pulmonary disease. I thought I'd probably go to Duke. Hennigar said no, I should go to Yale to work under Dr. Averill Liebow and shortly thereafter I found myself on the train to New Haven. I was interviewed by Dr. Liebow as well as Bill Glenn, a South Carolinian thoracic surgeon who had developed a well-known procedure (Glenn shunt) and with whom Liebow had written a book. I did not know at the time that what Liebow really wanted was to hear a Newberry accent. He read stories to his children about a mythical Paul Bunyan-like African American man from Newberry, my home town. Liebow offered me a traineeship in pulmonary pathology that opened a great many doors for me in subsequent years.

I think advances in medicine and science come partly from inductive reasoning and more often from following up unexpected observations; however, you don't catch a fish unless your hook is in the water. In the mid 1950's,Drs. Pattle in England and Clements in the US were examining the effects of war gases. Those that damaged the lungs often caused pulmonary edema which led to froth filling the tracheobronchial tree and suffocation. They tried substances to reduce surface tension and break up the bubbles but nothing worked. They realized that the surface tension in the bubbles was lower than anything they could find. They calculated that the surface tension in alveolar-sized bubbles had to be close to zero; otherwise the alveoli would collapse, as they did in premature babies. They hypothesized the existence of a surface film in alveoli that lowered surface tension. During my post-sophomore fellowship I was intrigued with the nature of pulmonary surfactant and in the summer following my junior year of med school, I enlisted the help of the surgery department in providing me lobectomy specimens from animals which I lavaged to get surfactant. I injected this into rabbits, then later drew blood from the rabbits, dialyzed the serum, and tagged the globulins with fluorescein then applied the fluorescent antibody to frozen sections of lung which demonstrated a layer lining the alveolar walls. I had no technical help. I learned how to cut frozens from the pathology staff and how to do the rest by asking questions and reading. With the help of Forde McIver, Kelly McKee, and Dean Cheves Smythe, I was able to present my findings at a national meeting for clinical research in New Orleans and at the American Academy of Allergy in Miami. I was one of the few med students in either crowd. I was starting to run with the big dogs and liked it. I don't know what particular antigen in the alveolar lining layer

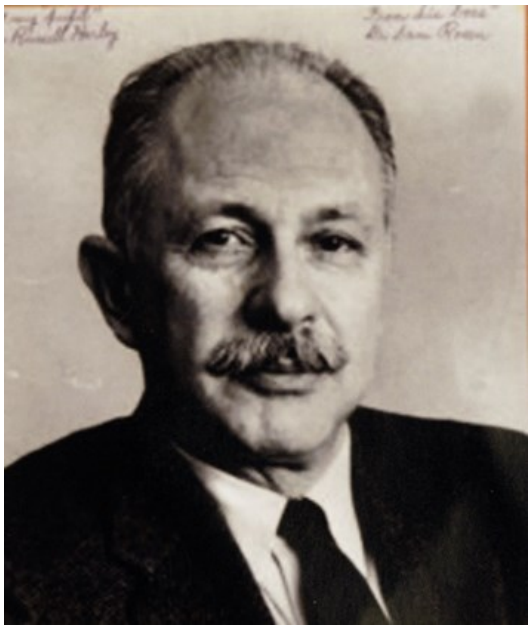


I had found, but probably surfactant related proteins which were unknown at the time. My presentations may have provided the first visual demonstrations.

In 1963, Laurell and Ericsson surveyed serum electrophoretic patterns in 1500 people and noticed that five of them lacked the alpha-1 globulin band. Some of the patients were at a TB sanitarium and they thought they had found something that contributed to TB, but after investigation discovered these patients had emphysema. In the same year, Paul Gross in Pittsburgh tried to lessen the fibrosis caused by silica dust in rats by injecting papain ("Adolph's Meat Tenderizer") into the rat lungs and was surprised to find that this caused emphysema in the rats. Eventually the significance of these two findings taken together led to an understanding of the basic mechanism of emphysema – proteolysis, especially elastolysis. I worked with Dr. Gross and watched the blossoming of science and medicine that arose from those two serendipitous observations. In 1972 colleagues and I published a CPC regarding a man with drowsiness and liver dysfunction that may have been the first case of alpha-1 antitrypsin deficiency recognized in South Carolina. I saw PAS positive globules in the cytoplasm of hepatocytes but didn't figure out what they meant so I left them out of the paper. They were, of course, alpha-1 antitrypsin that couldn't get out of the liver into the circulation. Could kick myself.

My years at Yale involved a lot of work and enjoyment, but ended when I was drafted into the Army. I found myself assigned to Pulmonary and Mediastinal Pathology at the AFIP with Drs. Sam Rosen and Lisa Hochholzer. Dr. Rosen had been first author on the paper describing alveolar proteinosis along with Liebow and Castleman. I learned more pulmonary surgical pathology in a year at the AFIP than I had in two and a half at Yale, but there was no time for research. My next year was in Vietnam with the 9th Med Lab in Saigon and later at Long Binh Post. For a while, my title was "Surgical Pathologist for Southeast Asia". I arrived back in San Francisco in August 1969, picked up some hitch-hiking hippies and drove down California 1 to La Jolla to visit Averill Liebow who had become the first Chairman of Pathology at the new UC San Diego medical school. Here's a picture of him at his house on top of a hill looking out to the adjacent hill where his neighbor Dr. Seuss lived. I then hitch-hiked from Lake Tahoe across the country to Newberry where I got my old Triumph TR3 working and ended up in Charleston hanging out with my brother and his friends until we went fishing and I got my picture in the News and Courier behind a huge tiger shark we had caught. Hennigar tracked me down that day and told me that I was a month late and I should come to work. He didn't use those words. I did as The Chief said and took over the autopsy service and did surgical and pulmonary path. I loved working with the residents, medical, dental, tech, and graduate students. One of my early lung biopsies at MUSC was a case of desquamative interstitial pneumonia (DIP). Our excellent chief resident at the time was Gist Farr who enjoyed electron microscopy. He examined tissue from the DIP case and

showed that the cells filling the alveoli were macrophages, not desquamated type 2 cells. We prepared a manuscript and I called Dr. Liebow to tell him we were going to publish a paper indicating his newly described entity DIP was a misnomer. He said that other people had suggested the same and it was fine with him. The paper was published in the American Journal of Pathology in 1970. As it turns out, one of the main functions of the alveolar macrophage is removal of surfactant. We knew that the foamy macrophages often associated with airway obstruction included phospholipid from surfactant, but the role of ordinary macrophages in surfactant removal is even now a new field of study. It is the failure of that system that leads to most cases of alveolar proteinosis, a disease that was described by Rosen, Castleman and Liebow in the New England Journal in 1958. Here's a picture of Dr. Rosen, another of my teachers, an elegant man who sometimes wore a cape. Only after studying lungs of rats exposed to certain fine dusts (e.g. silica, metallic aluminum) did it occur to me that the process of alveolar proteinosis could protect the lung from severe interstitial damage. If deadly particles of dust can be caught and taken in by macrophages, even though the macrophage dies the dust is trapped in a paste that eventually turns to a hard resin which finally cracks apart and is cleared leaving the alveolar wall intact and relatively unscathed. If the dust is only moderately cytotoxic, more particles get through and into the alveolar wall and may produce severe fibrosis. I have presented the concept at a few meetings, but have not pushed it to the point that it is recognized. You may have all sorts of arcane knowledge, but until it's in a peer reviewed journal, it doesn't mean a thing. On the other hand, publish something that's totally wrong and it never goes away.



In 2009 I accepted a position as Chairman of Pulmonary and Mediastinal Pathology at the AFIP. This was to be a limited position since the AFIP, perhaps the world's greatest institute of pathology, was scheduled to close along with the rest of the Walter Reed campus. It did close, but portions of the old AFIP were kept alive including the National Museum of Health and Medicine, the Armed Forces Medical Examiner System, and the second opinion consultative service which is now the Joint Pathology Center (JPC). The Medical Examiner's office is presently in Dover, DE and the Museum and JPC are now in what was the Walter Reed Annex, now simply "The Annex" located in Maryland just north of the DC line. The old AFIP building stands empty and the old Walter Reed is now a giant piece of beautiful real estate in northwest Washington emptied of its wounded warriors and the thousands of people who took care of them. In 2011, the tri-service Walter Reed National Military Medical Center was opened in Bethesda across from the NIH and includes large new hospitals, the National Naval Medical Center and USUHS. The variety of the cases I see at the JPC is remarkable, most of them challenging, predominantly surgicals, all ages, both sexes, and occasional consults from the large Veterinary Pathology group. In addition to the consultative work, I've been able to present papers and posters in the last few years at IAP meetings in Brazil and South Africa and the European Society of Pathology in Helsinki. It has been a great experience, but I'm backing off from my work at the JPC and looking forward to spending more time back home on Sullivan's and at MUSC where I'd like to try to find out more about a mysterious arachnoid-like cell in the lung that nobody knows anything about. If I look for it I might find it, but chances are I'll find something else instead. If I don't look for it, I won't find anything. But I might be able to climb back out of my alveolus and find more time for family, friends, and pluff mud. That would be OK too.

Identifying E-Mail from External Sources and other Phishing Tips

By: Tony Eisenhart

We've all seen them. We've all gotten them. Phishing emails, asking you to follow a link to verify your account credentials or your account will be turned off. Or perhaps something as bold as asking you to reply directly with your account user name and password. Some of these Phishing attempts are easy to detect others however are extremely well crafted and very difficult for an untrained, or less vigilant, user to recognize as fraudulent.

To help mitigate this risk and as part of MUSC's ever expanding and through approach to Information Security a new notification mechanism will soon be seen in your MUSC Exchange email. A large Yellow banner stating "CAUTION: This email was sent from outside MUSC" will be inserted into every message originating from outside of our organization. At this time OCIO-IS has not released a firm "Go Live" date for this additional notification mechanism but rest assured, it's coming soon.

How to Identify a Phishing Email

Currently there are two very simple but sure fire ways to identify a phishing email.

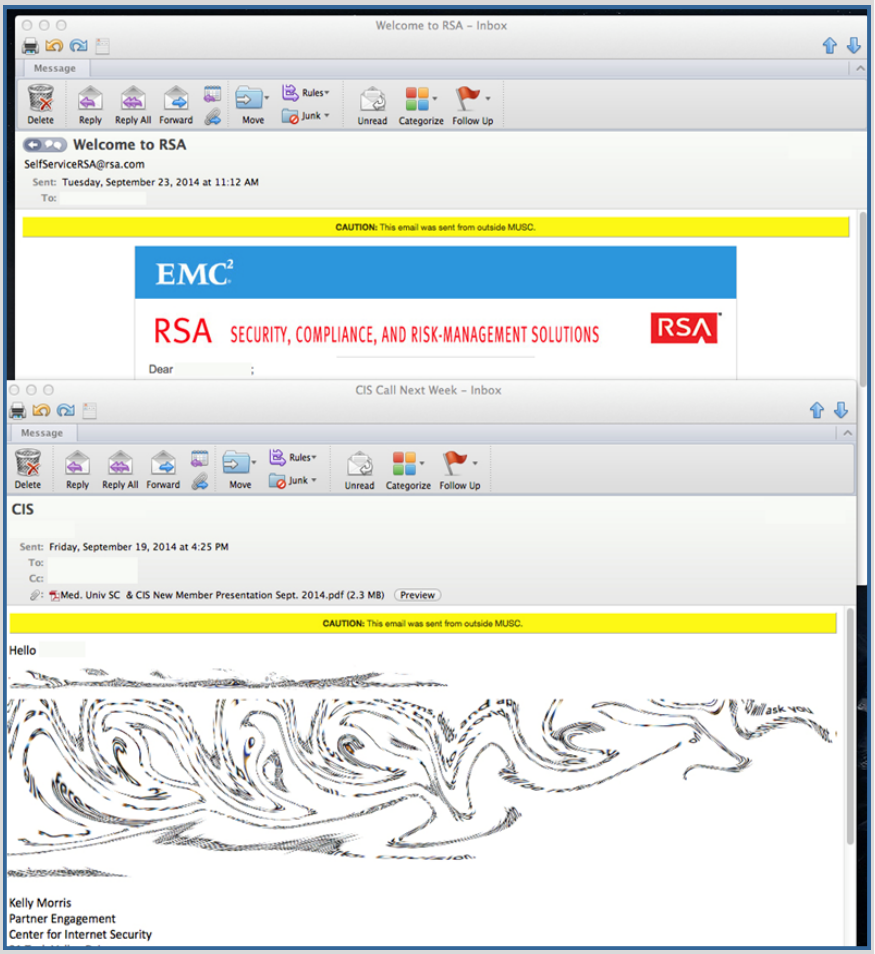
1. The email asks you to verify, confirm or otherwise authenticate your NetID and NetID password, or asks you to click on a link that takes you to a website where you have to enter, verify, or otherwise confirm your NetID and/or NetID password.

You will NEVER get an email from OCIO asking you to confirm, authenticate, or otherwise verify your NetID password for any reason.

2. The email asks you to verify, confirm, or take some other kind of action in order to increase your email quota.

You will NEVER get an email from OCIO asking you to take action of some sort in order to increase your email quota. Email quotas increases are NEVER handled by email.

If you receive an email you suspect is a phishing email, please forward it to phishing@musc.edu.

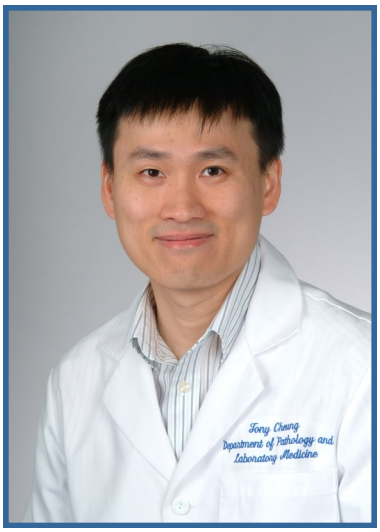


How to Compose Emails so they Don't look like Phishes

Sometimes legitimate emails look suspicious because of the way they are formatted or the information they contain.
Here are some helpful tips on how to send emails so they don't appear to be a phish.

1. Include verifiable information -
   Provide your full name, job titles,-phone numbers, and/or specific department names. If you can, provide the names of specific applications the email is in regards to, ex. Oasis, Epic, and include specific dates and times if applicable.
2. Personalize your greeting –
   Address the email to someone by using their first and last name.
3. Include a detailed signature on all of your emails. Here's an example of a good signature. It includes information that would be difficult for a hacker to obtain but easy for you to verify.

John Doe
System Analyst
Medical University of South Carolina
261 Calhoun St., Suite 305
Charleston, SC 29425
Ph: 843-876-6789
Fax: 843-876-1234



Targeting Amplified Oncogenes in Ovarian Cancer

By: Hiu Wing (Tony) Cheung, Ph.D.

Ovarian cancer is the deadliest gynecological malignancy among American women. Nearly 22,000 new cases are diagnosed each year, causing more than 14,000 deaths annually in the United States alone[1]. Approximately 200,000 new cases are diagnosed every year worldwide, and more than 50% of patients die of this disease[2]. Serous ovarian carcinoma is the most common histologic subtype, accounting for greater than 50% of ovarian epithelial carcinomas[3]. The majority of ovarian cancer patients (>80%) are diagnosed at an advanced stage [International Federation of Gynecology and Obstetrics (FIGO) stages III-IV] with widely disseminated disease in the peritoneal cavity[4]. Despite advances in surgery and chemotherapy[5], the 5-year survival rate ranges from 9-34%[4]. Most ovarian cancer patients relapse with progressively chemotherapy-resistant and lethal disease. Therefore, great hope has been placed on personalized therapy with targeted agents.

Cancer arises from progressive acquisition of genetic alterations in cells, resulting in activation of oncogenes and inactivation of tumor suppressor genes[6,7]. Knowledge of these genetic alterations has led to groundbreaking discoveries in targeted therapies for cancer. Among these are imatinib which targets BCR-ABL fusion oncoprotein in chronic myeloid leukemia[8], erlotinib which targets mutated *EGFR* in lung cancer[9-11], vemurafenib which targets mutated *BRAF* in melanoma[12] and trastuzumab which targets HER2 in HER2-positive breast cancer[13]. However, identifying targeted therapeutic approaches for treating ovarian cancer remains in its infancy. One challenge is that not many driver oncogenes are known in ovarian cancer.

Most of the advanced ovarian cancers are classified as 'high-grade' because of marked nuclear atypia with high mitotic index[3]. High-grade serous ovarian carcinoma (HGSOC) is distinct from other subtypes for its unique genetic alterations[14,15]. The Cancer Genome Atlas (TCGA) project has characterized 489 primary HGSOC genomes to enumerate all recurrent genetic alterations[16]. HGSOC exhibits marked genomic instability and contains *TP53* mutations in all cases and germline/somatic mutations of *BRCA1/2* in approximately 20% of cases[16]. This highly aggressive disease is characterized by widespread recurrent regions of copy-number alterations. Statistical analysis has identified 1825 genes as targeted by 63 recurrent regions of genomic amplification events[16,17]. A small number of these recurrent genomic events harbor known oncogenes such as *MYC*, *CCNE1*[14,18]. However, as in other cancers, the majority of genes targeted by recurrent amplification events remain undefined. Therefore, strategies are required to further dissect the hierarchies among oncogenes to identify promising therapeutic targets.

The recent development of genome-scale tools, such as the short hairpin RNA (shRNA) library[19] and the open reading frame (ORF) expression library[20], enable systematic approaches to study the functional

consequences of the somatic genetic alterations found in such genome characterization efforts. We recently used an shRNA-based approach to identify genes that are both amplified in human primary tumors and essential for the proliferation of ovarian cancer cells[21,22] (Figure 1).

We identified *PAX8* as a lineage-specific survival factor in ovarian cancers[21], and *ID4* as a target of genomic amplification at the chromosome 6p22 region[23]. More recently, we performed ORF-based expression approach to assess nearly 500 amplified genes for their ability to promote tumor formation in vivo (Figure 2). We identified the signaling adaptor GAB2 as a recurrently amplified gene that potently transforms immortalized ovarian and fallopian tube secretory epithelial cells. We are currently studying the mechanisms by which these amplified oncogenes contribute to the pathogenesis of ovarian cancer.

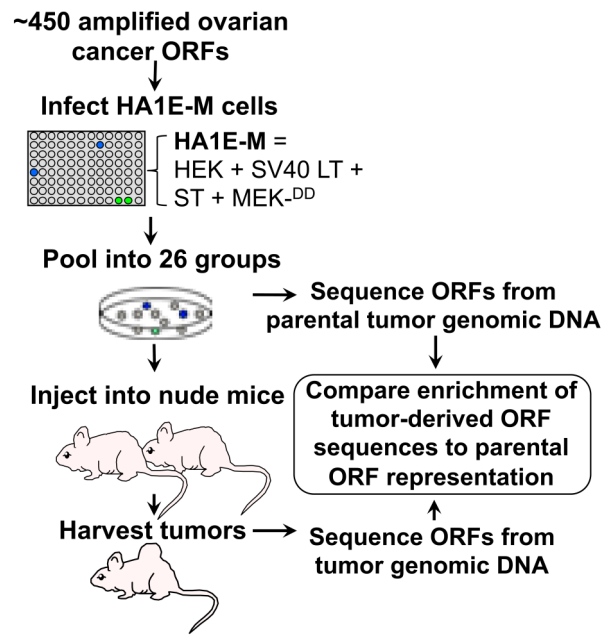


Figure 2. In vivo ORF-based expression screen to identify tumor-promoting gene. Individual ORFs were expressed in immortalized HA1E-M cells. Pools from these cells were implanted subcutaneously in im-

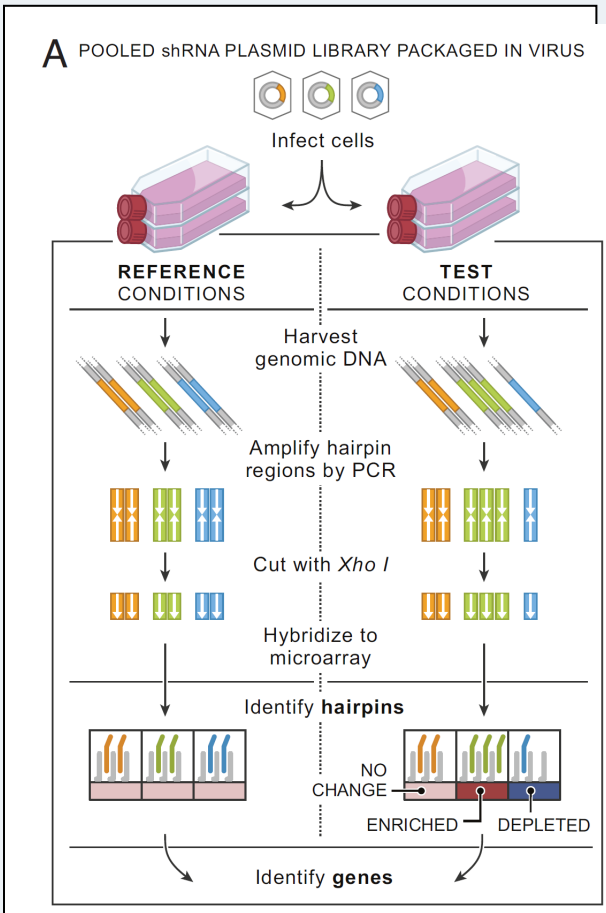


Figure 1. Pooled RNAi screening strategy to identify essential genes for cancer cell proliferation and survival. Cancer cells were transduced with pooled shRNAs and cultured for 16 population doublings. At the conclusion of the experiment, genomic DNA was extracted to measure the rela-

GAB2 gene is located at the chromosome 11q14.1 region that is highly amplified in 14% of HGSOCs. Our preliminary studies indicated that ovarian cancer cells harboring amplification of the chromosome 11q14.1 region required GAB2 for AKT-mTOR and MAPK activation, consistent with its role in regulating the p85 regulatory subunit of PI3K and SHP2[24-27]. We also observed that overexpression of GAB2 in ovarian cancer cells may induce expression of multiple chemokines, such as IL8, CXCL1 and CXCL2. IL8 and CXCL1/2 are potent pro-inflammatory and pro-angiogenic factors that are often upregulated in serum, ascites and tumors of ovarian cancer patients and associated with poor survival[28,29]. These cytokines exhibit co-regulated expression pattern in ovarian cancer and are known IKKb and NF-kB target genes[30]. The NF-kB pathway holds great promise for cancer therapy as NF-kB target genes are associated with many cancer hallmarks including proliferation, survival, angiogenesis, metastasis and inflammation[31]. We are currently investigating whether targeting IKKb would provide therapeutic benefits to ovarian cancer harboring *GAB2* amplification.

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UPCOMING MEETINGS

- **SNO - Society for NeuroOncology Meeting, November 13 - 16, 2014**

PATHOLOGY SPRING SYMPOSIA

FEBRUARY 24– 28, 2015

AT THE CHARLESTON PLACE HOTEL

ALL HANDS MEETING

Wednesday, December 17, 2014 - 9:30-10:30 AM - HCC120

DEPARTMENT HOLIDAY PARTY

Friday, December 19, 2014

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