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NF package on the News Center featuring Dr. Carroll’s work and the new national biobank. We also have a piece about our patient Tori and how NF has affected her life. Here are the links to the two stories and Emma’s nice infographic.

www.musc.edu/pr/newscenter/2015/neurofibromatosis-nf.html
www.musc.edu/pr/newscenter/2015/dr-steven-carroll-nf-biobank.html
2015 GOLDEN APPLE AWARDS

First Year Class Faculty Award
Debra Hazen-Martin, Ph.D. — Nominee

Second Year Class Faculty Award
Nick Batalis, M.D. — Nominee
Debra Hazen-Martin, Ph.D. — Nominee
Sally Self, M.D. — Nominee

CONGRATULATIONS!!

PROMOTIONS IN 2015

♦ Jonathan S. Ralston, M.D., promoted to Associate Professor, effective July 1, 2015
♦ Demetri Spyropoulos, Ph.D., promoted to Professor, effective July 1, 2015
♦ Shaoli Sun, M.D., promoted to Clinical Professor, effective July 1, 2015
♦ Julie Woolworth, Ph.D., promoted to Assistant Professor, effective July 1, 2015
♦ Yusheng Zhu, Ph.D., promoted to Professor, effective July 1, 2015

TENURE IN 2016

♦ Hainan Lang, Ph.D., granted Tenure, effective January 1, 2016
♦ Cynthia A. Schandl, M.D., Ph.D., granted Tenure, effective January 1, 2016

Great Job Dr. Stephen Ethier!

Click the link below to listen to the
SC Public Radio—Cancer Genomic Radio Interview with Dr. Stephen Ethier

http://etvradio.org/post/cancer-genomics
CONGRATULATIONS!! SERVICE AWARD RECEPTION

HOSPITAL
10 Years of Service!!
Nancy Alexis
Belinda Eloise Belisle
Samantha Shana Green
David T. Henderson
Najah M. Jones
Marketta P. Ladson
Rosemary Wright

HOSPITAL
20 Years of Service!!
Alvin J. Gadsden
Terry F. Heuer
Marla J. Lockhart

HOSPITAL
30 Years of Service!!
Gloria M. Barretto
Linda Wenger Hubbard

HOSPITAL
40 Years of Service!!
Juanita A. Epps
Nicholas Moussa Sarji
Elizabeth K. Welling

UNIVERSITY
10 Years of Service!!
Lisa Coulter
Brenton Grimball
Amy Haynes
Teresa Kennedy
Omar Moussa

UNIVERSITY
20 Years of Service!!
LaSonya Jordan
ARRIVALS AND DEPARTURES

ARRIVALS:
- Jason Flamm, Information Resource Consultant II, supervised by Dr. Jim Madory arrived on 12/14/15

DEPARTURES:
- Lixia Zhang, Post Doc Scholar in Dr. Cheung’s Lab left on 11/28/15
- Dayvia Russell, Research Specialist II in Dr. LaRue’s Lab left on 12/16/15

GRADUATE STUDIES UPDATE

Kayla Hill (Dr Sha) Successfully defended her PhD thesis November 2nd
Brooke King (Dr Findlay) Successfully defended her MS thesis December 10th

Student Research Day
- November 13th 2015
- 1 MSTP presentation (Poster)
  Jamie Mills (Ethier Lab) won 1st place Kinard-Gadsen Award
- 6 PhD presentations (6 poster, 3 oral)
- 1 MS presentation (Oral)
  Brooke King (Findlay Lab) won 2nd place oral
- 3 Post Doc presentations (2 poster, 1 oral)
- 5 Research Specialist presentations (poster)
  Lourdes Nogueira (Findlay Lab) won 1st place

Upcoming Dates
- Student Research Day Friday November 13th
- Alex Rutkovsky to propose January 18th
- First PhD Interview weekend January 21st

PhD Program Update
- Clarisse Panganiban (Lang Lab) passed the written qualifying exam

Council News
- Student Stipend increase to $27,500 starting September 2016
- New exposure format during PhD Interview weekends January 21st, February 18th, March 17th

Congratulations!

Su-Hua Sha, M.D., for successfully renewing her R01 for another 5 years.
This award provides total costs of $1.59 million to study molecular mechanisms associated with noise-induced hearing loss.

Congratulations!
Amanda Prechtl, Ph.D., a Postdoctoral Researcher, in Dr. Carroll’s Lab was awarded a $1,000 Histochemical Society Travel Award for the 2016 Experimental Biology Conference.
CONGRATULATIONS!
To: Dr. Kate Eichel and her husband Carl

{Image of balloons and baby}

Mira Lois Eichel Arrived on January 13, 2016
8 lbs. 1 oz. & 21 inches

PATHOLOGY AND LABORATORY MEDICINE MUSEUM – 2016
Below are the dates for the 2016 Glimpse in Medicine Tour Dates.

2016 Glimpse in Medicine Tour Dates

Wednesday, January 6 – The Governor’s School (14 students)
Tuesday, January 19
Wednesday, January 27 – Ashley Hall (30 students)
Thursday, February 4 – Wando High School
(Tentative) Wednesday, February 17
Monday, February 22 – Stall High School
Tuesday, February 23 – Stratford High School
Tuesday, March 1 – Wando High School
Tuesday, March 8 – Ashley Hall (9th graders)
Monday, March 14
Tuesday, March 15
Thursday, April 14
Monday, April 25
Tuesday, April 26
Monday, May 2
Statistics for the Division of Research from October through December.

Eighteen grant proposals were submitted requesting $2,552,434 in total first year costs.

Also, during this period three grants were awarded totaling $296,626.

SUBMITTED 10/1/2015 – 12/31/2015:

Lashardai Brown  
Title: The Role of Alternative Complement in Macrophage-Mediated Auditory Nerve Replacement  
$47,584 – Proposed Start Date 7/01/16

Hui Cheung, Ph.D.  
Title: Role of Amplified GAB2 Gene in Ovarian Cancer Growth  
$373,750 – Proposed Start Date 8/01/16

Victoria Findlay, Ph.D.  
Title: miR-204 Regulation of Cav-1 as a Mechanism Driving Breast Cancer Disparity  
$224,250 – Proposed Start Date 7/01/16

Ryan Kelly  
Title: Modulating Hematopoietic Osteoprogenitors to Enhance Atrophic Non-union Repair  
$56,922 – Proposed Start Date 4/01/16

Hainan Lang, M.D., Ph.D.  
Title: Auditory Nerve Degeneration and Repair: Administrative Supplement  
$49,572 – Proposed Start Date 12/1/15

Meenal Mehrotra, Ph.D.  
Title: Role of HSCs in Establishing the Osteosarcoma Microenvironment  
$198,000 – Proposed Start Date 7/1/16

Jamie Mills  
Title: The oncogenic role of WHSC1L1 in 8p11-p12 amplicon-bearing breast cancer  
$57,683 – Proposed Start Date 7/1/16

Rick Nolte, Ph.D., D(ABMM), F(AAM)  
Title: A Web-Based Epidemiological Database to Track Respiratory and Gastrointestinal Pathogens in Real-Time  
$4,485 – Proposed Start Date 10/1/16

Rick Nolte, Ph.D., D(ABMM), F(AAM)  
Title: Film Array Trend Research Project & Epidemiology Grant  
$5,000 – Proposed Start Date 11/13/15

Suhua Sha, M.D.  
Title: Novel Aminoglycosides with Reduced Ototoxicity  
$74,750 – Proposed Start Date 9/1/16

Bartholomeus Smits, Ph.D.  
Title: The role of candidate susceptibility genes Myc and Fam84b in modulation of breast cancer risk by the 8q24 gene desert locus  
$30,000 – Proposed Start Date 1/1/16

AWARDED 10/1/2015 – 12/31/2015:

Demetri Spyropoulos, Ph.D.  
Title: The Obesogenic Potential of DOSS: a Novel Approach to Managing Maternal-Fetal Obesity  
$369,206 – Proposed Start Date 7/1/16

Demetri Spyropoulos, Ph.D.  
Title: Universal Tissue Cryopreservation for Biobanking  
$68,712 – Proposed Start Date 7/1/16

David Turner Ph.D.  
Title: Defining the Mechanistic Implications of Sugar Devived Metabolites (A.G.E.s) to Tamoxifen Resistance: Is it a Question of Lifestyle?  
$179,917 – Proposed Start Date 8/1/16

Gavin Wang, M.D., Ph.D.  
Title: Targeting Myc for Breast Cancer Treatment  
$373,750 – Proposed Start Date 7/1/16

Gavin Wang, M.D., Ph.D.  
Title: Role of Myc Signaling in Lung Cancer Radiotherapy  
$221,978 – Proposed Start Date 7/1/16

Qi Wang, Ph.D.  
Title: Transcriptome sequencing of recurrent tumors from a novel mouse model of HER2+ breast cancer  
$30,000 – Proposed Start Date 1/1/16

Je-seong Won, Ph.D.  
Title: Study on advanced enzyme replacement approach in Krabbe disease  
$186,875 – Proposed Start Date 7/1/16

Steven L. Carroll, M.D., Ph.D., FASCP, FCAP  
Title: Combinatorial Therapies for Neurofibroma and MPNST Treatment Prevention (NF140082)  
$261,626 – Start Date 8/1/15

Rick Nolte, Ph.D., D(ABMM), F(AAM)  
Title: Film Array Trend Research Project & Epidemiology Grant  
$5,000 – Start Date 11/13/15

Qi Wang, Ph.D.  
Title: Transcriptome sequencing of recurrent tumors from a novel mouse model of HER2+ breast cancer  
$30,000 – Start Date 1/1/16
The Gleason grading system for prostate cancer was first described by Donald Gleason in 1966 and was adopted as the method for histologic grading of prostate cancer in 1979 through consensus workshops. The grading system provided clinicians with a primary and secondary pattern grade based on volume, with a score from 1-5 for each based on the gland formation present within the tissue sample. The earliest descriptions of Gleason patterns 1-5 are roughly similar to those currently in use with the largest deviation being a greater emphasis on “well differentiated” patterns 1 and 2, and greater inclusion of complex patterns in pattern 3. Further refinements by Gleason and the Veterans Cooperative Urological Research Group in 1974 and 1977 tightened the definition of Gleason pattern 3 by expanding the description of pattern 4. Gleason pattern 5 was recognized as the most poorly differentiated, lacking gland formation and consisting of single cells or sheets. At the time of its adoption, acceptance centered on the Gleason Grading system’s ability to predict tumor behavior and patient survival. While the Gleason system’s limitations were recognized, other similar systems were equally flawed and often more complicated to apply.

Forty years after the initial development of the Gleason Grade, the clinical landscape had changed significantly. Development of the PSA test in 1979 and its widespread implementation as a screening method in 1994 led to earlier cancer detection, boosted by the implementation of prostate core needle biopsies in the 1980’s. Surgical technique changed and radical prostatectomies became prevalent. These advancements altered both clinical course and the material with which diagnoses were made. At the time of the Gleason Grading system’s development, Gleason had the advantage of large portions of prostate with which to evaluate architecture. By 2005, most diagnoses of prostate carcinoma were made on 18 gauge needle biopsies. With continued focus on the ability for the Gleason grading system to predict tumor behavior, disease progression and mortality, and recognition that this could be achieved only with consistent application of the system, the International Society of Urological Pathology (ISUP) convened a meeting in 2005 to address variabilities in diagnosis. More than 70 national and international urologic pathologists were involved in producing the parameters for histologic grading still largely in use today. The most important changes to the original Gleason system involved a stricter definition of what constituted Gleason grade 3 carcinoma, which was now predominantly limited to well-formed individual glands. Nearly all cribriform growth and poorly formed glands were relegated to Gleason grade 4. Individual cells were also no longer allowed to be a component of Gleason grade 3. Other changes included the consensus the Gleason Grade 1 or 2 be used rarely if ever as diagnosis based on architecture and circumscribed edges was exceedingly difficult on needle core biopsies and reproducibility among experts was poor. Gleason Grade 5 was modified to include any carcinoma with comedonecrosis.

Most recently, in 2014, the ISUP gathered 65 expert urologic pathologists and 17 other clinicians involved in the treatment of prostate carcinoma for another consensus conference. The purpose was to refine the definitions of the grade patterns, but to also discuss the implementation of a new grading system. Minor changes were made to the pattern definitions, the more important of which are the complete relegation of all cribriform and glomeruloid patterns to grade 4, the decision that mucinous carcinoma should be graded based on morphology rather than automatically being designated as Gleason grade 4 and the concept that intraductal carcinoma of the prostate is, by definition, not invasive carcinoma and should therefore not be given a Gleason grade.

The most dramatic change to prostate cancer reporting came with the discussion of how current grade combinations are inaccurately applied to clinically stratify prognosis and treatment, in part due to the complexity of the terminology, and the proposal of a simpler system. The new grading system, developed by Jonathan Epstein and colleagues, was formulated using prognostic data compiled at 5 different institutions and comprising over 20,000 patients having undergone radical prostatectomy with grading using the 2005 histologic pattern definitions. Similar prognostic data was obtained using needle core biopsies. The new Group designations were proposed to simplify terminology and clinician-patient conversations.
Continued: Histologic Grading of Prostate Carcinoma: A Historical Review with Summary of the New Grade Group System

Designated the Grade Group System, this new terminology was accepted at the above described ISUP consensus conference in November 2014 and by the 2016 World Health Organization and is based on the following: Diagnosis of Gleason grade 1 or 2 pattern carcinoma has essentially vanished, thus leaving the lowest score prostate carcinoma a Gleason 3+3=6; Gleason grade 3+4 prostate carcinoma has a better prognosis with regard to recurrence-free progression than does Gleason 4+3 carcinoma; Gleason scores summing to 8 (4+4, 3+5, 5+3) all behave similarly and Gleason grades summing to 9 or 10 behave the worst (see figure) without distinction between the two. Therefore, Grade Group 1 is comprised of Gleason 3+3 pattern carcinoma. Grade Group 2 has Gleason grade 3+4 pattern. Grade Group 3 has Gleason grade 4+3 pattern. Grade Group 4 has any pattern summing to 8 and Grade Group 5 comprises all 4+5 or 5+4 pattern carcinoma, and each higher grade group has a poorer chance at recurrence free progression (see figure).

We have recently implemented reporting of the Grade Group in addition to the Gleason Grade at MUSC in accordance with the ISUP recommendations. Practical application of this new system was recently challenged with a case in which a tertiary Gleason pattern 5 was identified. Under the current CAP guidelines Gleason 4+3 with tertiary 5 on a core biopsy would sum to 9, using the directive to sum the most prevalent pattern and the worst pattern. However, a review of the literature demonstrates that in several series, while tertiary 5 in this case would relate a poorer prognosis than Gleason 4+3 (Grade Group 3), it would not carry as poor a prognosis as Gleason 9 (Grade Group 5). Indeed, the prognosis is closer to Gleason 4+3 than Gleason 4+5, leading one author to suggest that Gleason 4+3+5 = 7.5. Similar decrements in prognosis were identified in other scores with a tertiary 5 pattern. However, despite this information, the new Grade Group System does not address tertiary scores and how to report them. An attempt to directly clarify Epstein’s recommendation regarding Grade Group reporting when a tertiary pattern is present was unfruitful. Therefore, combining the consensus statement, literature published by Epstein regarding the prognostic information used to derive the Grade Groups and literature by other experts in the field regarding the impact of the tertiary grade on recurrence free survival and prognosis, our reports for prostate cores with carcinoma will have the Gleason Grade followed by the Grade Group in parentheses. If a tertiary pattern is present, the Grade Group is reported as that correlating to the first and second most common patterns “with tertiary pattern 5”, for example Gleason Grade 3+4+5 carcinoma will be reported as “Gleason Grade 3+4+5 (Grade Group 2 with tertiary pattern 5)”.

As with all newly implemented terminology, and especially with prostate cancer designations that have been refined over nearly 50 years, modifications are inevitable. We will continue to keep you updated as they occur.

References:
Tuberculosis, one of the oldest diseases known to mankind, made a dramatic reappearance in the 1990s. The resurgence of TB was fueled by many factors, including the HIV epidemic, increases in immigration from TB endemic countries, TB transmission in congregate settings such as prisons and the development of multi-drug resistant TB. Although the United States government has invested in many resources for controlling disease, only recently has a new assay been introduced to replace the 100-year-old TB skin test.

The Clinical Immunology laboratory will soon be bringing on board the Quantiferon-TB test, an interferon gamma release assay (IGRA) for the diagnosis of latent tuberculosis. Based on my experience in performing this assay since it was FDA approved in 2001, I have found it to provide useful diagnostic information for health care providers, employee health and public health agencies. What I find fascinating about this assay was that it was originally developed in Australia for the diagnosis of Mycobacterium bovis infection in cows. The testing for bovine tuberculosis in cows had been a difficult and expensive ordeal. Cows were actually skin tested in the same manner as people for the detection of TB, and if even one animal tested positive, they ended up killing the entire herd to prevent the spread of *M. bovis*. As you can probably imagine, cattle can have false positive reactions, just like people. In response, an enterprising biotech company started researching assays that would replace the skin test with a blood test that had fewer false positives. They came up with an innovative lymphoproliferative assay using TB as the antigen and interferon gamma as a way to measure the response of memory T cells that were previously exposed to TB. The researchers had devised an inexpensive way to perform a lymphoproliferative assay that would normally cost $1,000 in a specialized clinical immunology laboratory. The assay was approved for agricultural use in the 1990s and was hugely successful in preventing unneeded culling of herds. So, as the story goes, if it works in cows, maybe it will work in people too. And it does! The biotech company adapted the test for people and the first generation Quantiferon TB test was FDA approved in 2001.

The Quantiferon TB test is a blood test that uses three tubes of blood, a negative control tube (nil) that measures background interferon gamma, a TB antigen tube (contains the TB antigens) and the positive control tube (mitogen) that makes sure the patient has adequate T cells and that the test was performed properly.

There are a number of distinct advantages of using the Quantiferon TB test rather than the PPD TB skin test. First of all, there is one blood draw requiring only one patient visit. There is no need for a second visit as there is for a PPD TB skin test, which requires that the test site be observed for induration within 48-72 hours. This has obvious advantages in populations where follow up visits are difficult.
Continued: **Of Cows and Men: A strange path to a new TB test**

Since the Quantiferon TB test uses a positive control, the test is especially useful for patients infected with HIV. Many of these patients can have a false negative PPD TB skin test simply because they do not have enough T cells to mount an adequate reaction even if they were exposed to TB. The Quantiferon TB test positive control allows the detection of patients that do not have an adequate cell mediated immune response. With the PPD TB skin test, there is no control and false negatives can be a real concern.

Most important of all, the Quantiferon TB test is a very highly sensitive and specific test that uses recombinant TB antigens that are not contained in the BCG vaccine. These antigens are also not found in most environmental non-tuberculous mycobacteria. This specificity greatly reduces the number of false positive tests in BCG vaccinated people (a practice in many countries outside the USA), and low risk individuals. Although more expensive than the PPD TB skin test, the Quantiferon test is a cost effective TB screening tool since it greatly reduces the number of patients that will undergo unnecessary chest X-rays and TB prophylactic therapy from false positive PPD results. We can thank the cows for this important advance in controlling the TB epidemic.

**References:**


When I first arrived in Charleston to interview for the Medical Scientist Training Program in 1991, I stayed at the Motel 6 off the I-26 at the Ashley Phosphate exit. Since then, I have learned many things including the fact that there are better hotels in town. The town itself has changed slowly, marked it would seem by a march of chain stores further up King Street; fortunately the beauty of the surrounding wild spaces has remained largely intact.

MUSC has changed as well. I did my graduate work in what was called the Quadrangle building; it was demolished to install the new Hollings Oncology Center (now Hollings Cancer Center). I studied BCL2, a newly identified protein found to be overexpressed in the cytoplasm of follicular lymphoma cells that somehow prevented apoptosis, which no one knew exactly how to say. With my mentor, Dr. Mark C. Willingham, I found using immunofluorescence that BCL2 was in many cell types, expressed on the chromosomes during metaphase. We postulated that it may provide a protective function during mitosis when the nuclear membrane is gone. Another graduate student in the lab was working with another newly described protein – BRCA1. Dr. Kristy Johnson is now an Associate Professor of Biology, Bioterrorism, and Descriptive Histology at the Citadel.

It was during medical school that I had the opportunity to work with the Autopsy section. There was no other elective that I wanted to take more than the 2-month autopsy rotation. I had the opportunity to work with Drs. Kim Collins and Erin McConnell (now Presnell) who contributed a great deal to my professional growth and development; not to mention that they invited me to join their professional team here at MUSC. Forensic autopsy was a lasting passion and I performed over 200 autopsies during my residency and more than 2000 more since.

Encouraged and supported by another mentor, Dr. Janice Lage, I developed other subspecialty expertise along the way, working with placental pathology, molecular pathology, and cytogenetics. Dr. Sally Self instructed me in medical renal pathology, another favorite of mine, before Dr. Evelyn Bruner joined the group. At one point, I served as Interim Director for the Tissue Biorepository and through necessity and interest, became well versed in medical and research ethics including completion of a one year Fellowship in Clinical Research Ethics Certificate Program. In the realm of research sample acquisition and distribution, ethical considerations must take a front seat to all others in our cultural climate.

Most recently, I have had the support of our inspired leader, Dr. Steven Carroll in the expansion of my work with the Clinical Molecular Genomics and Genetics laboratory. Drs. Dayna Wolff, Julie Woolworth-Hirshhorn, and I in consultation with Drs. Rick Nolte, Steve Ethier and Bob Wilson, are devising a 5-year strategic plan to expand the clinical services in that area to include expanded mutational analysis for solid and myeloid malignancies. I am especially interested in the translation of cell-free circulating tumor DNA analysis into the clinical space. To these ends, we plan to leverage digital droplet PCR technology and possibly MALDI-TOF mass spectrometry to validate extremely high sensitivity mutational analysis for cancer patients. The application of this to clinical practice may be transformative in diagnostic, prognostic, treatment, and particularly disease surveillance efforts. To be successful, we will need a cooperative effort between the clinical and research labs and significant long-term administrative commitment.

MUSC and our pathology department will continue to grow, expand, and improve. I hope to continue to do the same. The excellence of the people I work with assures this and I am lucky to be a part of the family.
2015 HOLIDAY PARTY
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