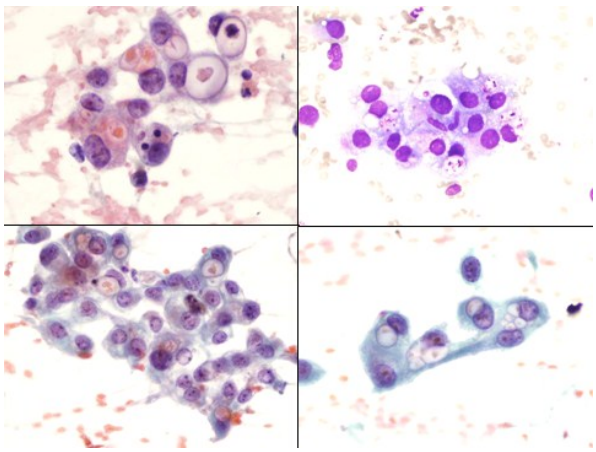
Fletcher Allen HEALTH CARE

The UNIVERSITY of VERMONT

Vermont's Academic Medical Center

Pathology & Laboratory Medicine Newsletter



TARGETOID VACUOLES IN METASTATIC UROTHELIAL CARCINOMA: A NEW FINDING IN FNA CYTOPATHOLOGY

Issue 5 - Spring 2013

A Note from the Chair

I want to express my sincere thanks for the very warm welcome I have received during these first few weeks on the job as the new Chair of Pathology and Physician Leader of Pathology and Laboratory Medicine. I have settled into my new administrative office in the Given Courtyard, Room S254, and am finding my way around both the UVM College of Medicine and Fletcher Allen. I would ask that you be patient and help me to learn your names by telling me your name again each time I see you until I greet you by name.

During my first weeks here, I am meeting with each of the faculty members individually to get to know the faculty, and to hear their perspectives on the department and the institutions. I have walked through the clinical laboratory areas several times in these first two weeks, spoken with some of the laboratory staff and faculty. I will begin signing out Molecular Pathology test results, which is my area of clinical expertise, in the next few weeks. The plans for development of molecular and genomic testing at Fletcher Allen are moving forward, with a more rapid phase focused on next generation sequencing for lung and pancreatic cancer, and a longer phase requiring a certificate of need and space renovations for a Clinical Genomic Medicine Program at Fletcher Allen. I am just beginning a strategic planning process for the department, and will be asking many of you for your thoughts and participation over the next 6 months.

On a personal note, my husband, Greg, and I are getting settled into our new house in South Burlington. We have sold our house in Brooklyn. And I am thoroughly enjoying my low stress, 10 minute commute to work on country roads, although my MINI Cooper (MINI 2) would likely prefer a longer drive on the open road. We are delighted to be in Vermont, I am delighted to be at Fletcher Allen and UVM College of Medicine, and I look forward to getting to know you and working with you over the coming years.

INSIDE THIS ISSUE

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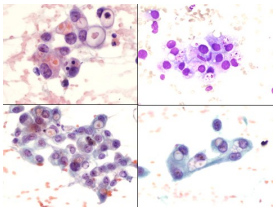


DO YOU SEE WHAT I SEE CONTEST

(photos from contest shown at bottom of page)

In November/December 2012, this contest was held by Pamela Gibson, M.D. Two photos received the most votes and were the designated winners of the contest.

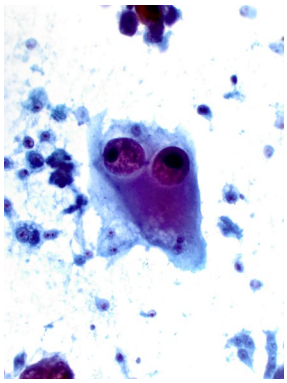
Congratulations to two residents, **Cherie Paquette for her "Scottie Dog"** and **Tricia Murdock for her "Basketball Player"** for winning the competition. They both received gift cards. The photos were displayed on the second floor for two weeks and then moved down to the first floor for viewing.

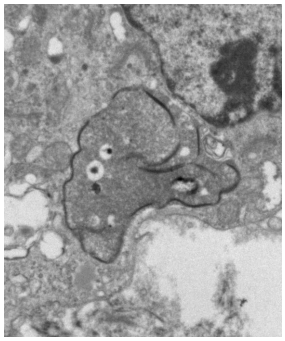
Slide Submissions (bottom of page - left to right):
Cherie Paquette - Scottie Dog
Tricia Murdock - Basketball Player
Joanna Conant - Duck
Jessica Wood - Monster
Pamela Gibson - Dove & Face in Kidney
Alexa Buskey - Heart

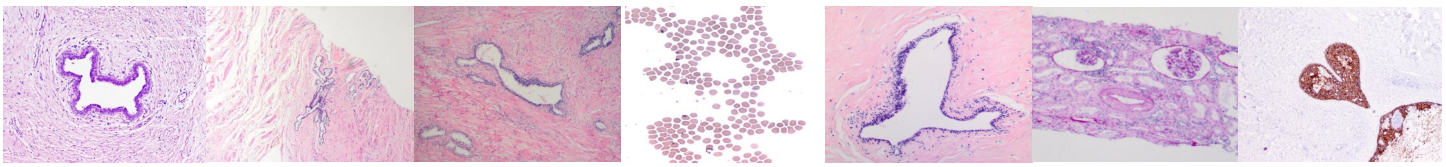
Thanks to all the people who submitted entries. We will do this again in the future and hope to have even more entries so keep your eyes out for cool images in the things you see every day!
Pam

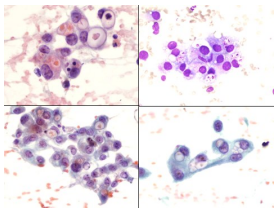
Pamela C. Gibson, MD
Director of Anatomic Pathology, Department of Pathology
Associate Professor of Pathology
Fletcher Allen Health Care/ University of Vermont

Two other slides submitted by Dr. Gibson were a Ghost in blue/purple photo below and an Elephant in black and white photo below:









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RESEARCH FOCUS

Nicholas H. Heintz, Ph.D.

What is your scientific background?

I can clearly remember when I first got interested in science. In the fifth grade, we repeated an experiment first done many centuries ago. We vacuum dried some soil, weighed it and a bean seed, and then planted the seed in the soil. After weeks of watering the growing plant, we carefully removed all the soil from the plant, dried the soil and the plant, and then weighed them both. We were asked to guess where the extra weight in the plant came from – there was not enough difference in the weight of the soil to account for the increased mass. Of course, we all guessed the water we had used to nurture the plant. I can distinctly remember my amazement when we were told the extra mass came from carbon dioxide in the air – my introduction to photosynthesis. Those giant maple trees on our front lawn were 99% air! From then on biology and chemistry captured my attention, and my father (an oral surgeon) tagged me for medical school. This remained the plan until I spent some time in a hospital during the summer in college and found that clinical medicine was just not my cup of tea. The love of science persisted, leading me to graduate school and academic medicine. I entered the research arena at the advent of molecular biology. What an exciting time! Cloning genes might seem trivial now, but in the late 70's isolating specific DNA clones and sequencing genes were major technical challenges.

What are your main areas of research? What might be one possible translational result from your research?

My initial endeavor in the growing world of molecular biology came when I was a postdoctoral fellow at the University of Virginia. It took me two years to clone the first mammalian origin of DNA replication from a cultured cell line, and to this day we still don't understand how it works. Focusing on the control of entry into the S phase eventually led us to signaling pathways that regulate cell proliferation, and for several years we studied how growth factors cause up-regulation of cyclin D1, phosphorylation of RB, and activation of E2F. During these studies, we came to appreciate mitogenic signaling pathways were modulated by reactive oxygen species (ROS), and that enhanced production of ROS that supported signaling in tumor cells was a consequence of altered energy metabolism. At first, we concentrated on suppressing ROS production in tumor cells, with modest results, but then we, and others, realized many tumor cells operate on the upper threshold of oxidative stress, and have little reserve capacity to deal with increased levels of ROS. Therapeutic drugs like arsenic trioxide operate on this principle – they induce profound oxidative stress and drive cells past the "redline" for survival. Our approach has been to concentrate on disabling the adaptive antioxidant response in tumor cell mitochondria. At this point, we have identified several small molecules that kill the activity of different enzymes in the major mitochondrial antioxidant network. Curiously, two of these compounds are antibiotics that have been in the pharmacopeia for 50 years. This approach kills malignant mesothelioma cells in culture, and markedly impairs tumor progression in mice, so our eventual aim is to test this strategy in the clinic. Fortunately, mesothelioma tumor cells are about 10 times more sensitive to these compounds than normal mesothelial cells. I expect that alone this strategy may not be successful, but I do think it may have promise if used in combination with drugs like arsenic trioxide that rely on a redox-dependent mechanism. If only grants from the NCI were easier to obtain!

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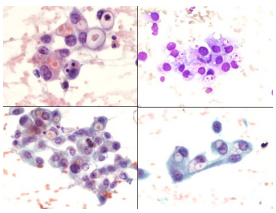


RESEARCH FOCUS

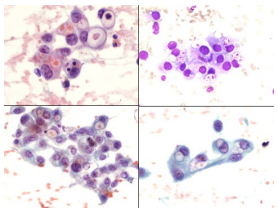
Nicholas H. Heintz, Ph.D.

Dr. Heintz at summer cottage on Prince Edward Island

On the personal side, what do you like to do to relax?

I grew up on a small dairy farm, and my wife Margot grew up with horses, so we live out in the country and spend most of our time outdoors. Margot has a Morgan mare – but I don't ride. We ski and snowshoe in the winter, and bike, hike, swim and canoe in the summer. I have played ice hockey all my life, and must confess have a soft spot for watching Hockey Night in Canada. Nobody adds more to a hockey telecast than Don Cherry! But most of all we enjoy our extended family, and we're fortunate our kids and grandkids live nearby. In July, you can find all of us (and a couple of dozen other members of our extended clan) on the eastern end of Prince Edward Island. We love traveling, but PEI remains a special place for us – it's quiet, calm, and just plain beautiful. Once there, we are completely disconnected from the electronic world – no TV, cell phones, or internet. Guess what? Even the grand-kids like it that way!

Dr. Heintz' s - three granddaughter's and one niece:
Left to Right: Jeannie, Ellie, Tatie (niece) and Gussie



Congratulations to Nels Olson, Ph.D. for achieving the Roger R. Williams Award for Genetic Epidemiology and the Prevention and Treatment of Atherosclerosis!

Submitted By - **Russell P. Tracy, Ph.D.**
Professor of Pathology and Biochemistry
Director, Laboratory for Clinical Biochemistry Research
Director, Translational Technologies - Center for Clinical and Translational Science
Emeritus, Senior Associate Dean for Research and Academic Affairs
University of Vermont

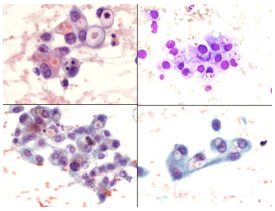
I'm happy to tell you that Nels Olson Ph.D., who is a Post-Doc in my lab, won the **Roger R. Williams Award for Genetic Epidemiology and the Prevention and Treatment of Atherosclerosis,** which was presented during the American Heart Association Epidemiology and Prevention/Nutrition, Physical Activity and Metabolism 2013 Scientific Sessions, which took place in March 19-22, 2013, in New Orleans, Louisiana. This prestigious award is not an early career or post-doc award, but the award for the abstract that achieved the highest average score of all applicants who submit abstracts to the category of genetic epidemiology. It is named for Dr. Roger R. Williams' pioneering work in the field of the genetics of inherited lipid disorders and the prevention of atherosclerosis. The winner of the Roger R. Williams Genetic
Epidemiology Award will have their name announced during the conference at the Council Dinner, usually attended by ~500 – 1000 people. Nels will receive a cash prize of $1,500 and a plaque.

The title of Nels' abstract is: Common Single Nucleotide Polymorphisms in the Coagulation Factor XII Gene (*F12*) are Associated With Endogenous Thrombin Potential via *In Situ* Activation of the Intrinsic System of Coagulation: the Cardiovascular Health Study

The authors are: Nels C. Olson[1], Saulius Butenas[3], Ethan Lange[4,5], Leslie A. Lange[4], Nancy Swords Jenny[1], Jeremy Walston[6], Mary Cushman[2], Russell P. Tracy[1, 3], and Alex P. Reiner[7] Departments of Pathology[1], Medicine[2], and Biochemistry[3], University of Vermont College of Medicine, Burlington, VT; Departments of Genetics[4] and Biostatistics[5], University of North Carolina School of Medicine, Chapel Hill, NC; [6]Division of Geriatric Medicine and Gerontology, Johns Hopkins University School of Medicine, Baltimore, MD; [7]Department of Epidemiology, University of Washington, Seattle, WA.

The major support for this work is a grant on which I am a co-investigator and Alex Reiner, Ph.D. at the University of Washington is the PI; the title is THROMBOSIS GENETICS, MI AND STROKE IN OLDER ADULTS. Nels received his Ph.D. with Albert van der Vliet, and is currently supported by our NIH-funded Hemostasis and Thrombosis Training Grant, directed by Ken Mann Ph.D..

- Russell P. Tracy, Ph.D.



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Listed below are the Award Winners and Nominees from Pathology

Listed below are winners and people from Pathology who were also nominated as related to Pathology.
Note: (non-related Pathology nominees or Awards without Pathology people named for said awards are listed).

Outstanding Foundations Course

CRR

A&D

Convergence

Foundations Teaching Award

Rebecca Wilcox

Abiy Ambaye
Kelly Butnor
Pamela Gibson
Andrew Goodwin
Nicholas Hardin
John Lunde
Thomas Trainer

The Dean Warshaw Integration Award

This is for the faculty member whose teaching best captured the spirit of the VIC.

Robert Low

Kelly Butnor
Nicholas Hardin
Rebecca Wilcox

The Silver Stethoscope

A.K.A

"**Inspirational Cameo of the Year**"

This is for the faculty member who had few lecture hours, but made a substantial contribution to your education.

Ellen Black

Pamela Gibson
John Lunde
Sharon Mount
Rebecca Wilcox

Above and Beyond

This is for the faculty member (not necessarily a lecturer) who went above and beyond the call of duty to help the students in their learning objectives.

William Hopkins

Kelly Butnor
Pamela Gibson
Nicholas Hardin
Rebecca Wilcox

The AMSA Golden Apple Award

This is for Teaching Excellence recognizes the contributions of a medical school professor who has made a significant impact on medical students' education.

William Raszka

Nicholas Hardin

The AMWA Gender Equity Award

A faculty member who:

- Promotes a gender-fair environment in education
- Assures equal opportunities for women and men to study medicine
- Encourages gender equity amongst current and future physicians

The candidate should also:

- Use gender neutral language
- Discourage harassment & inappropriate comments on rounds or in classrooms
- Respect patients' privacy with regard to physical exams and language

Pamela Gibson

Kelly Butnor
Rebecca Wilcox

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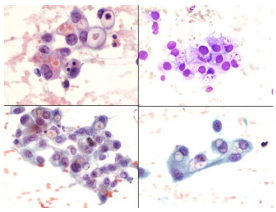

Posters Presented by our Pathologists and House Staff at United States Canadian Academy of Pathologists (USCAP) in Baltimore, MD

Monday - March 4th

Maryam Zenali - Poster Presentation:
"Cmet Mutations Comutations and Survival Outcome"

Javier De Luca-Johnson, Taka Ashikaga, Edward Krawitt, Rebecca Wilcox - Platform Presentation:

"The Prevalence of True Non-Alcoholic Steatohepatitis (NASH) in Patients Presenting with Autoimmune Hepatitis (AIH) and Pericellular Trichrome Staining, a Potential Mimicker of NASH in Active AIH"

Tuesday - March 5th

Gladwyn Leiman - Invited Presentation:
"Liver Cytopathology" cytology course

Kirsten Threlkeld, Thomas Trainer, Christine Adamson, Mark Evans, Rebecca Wilcox - Poster Presentation:

"Molecular, Histologic and Clinical Features of Persistent Intestinal Spirochetosis"

Kirsten Threlkeld was awarded runner up for the Binford Dammin Society of Infectious Disease Pathology Award for best infectious disease presentation by a resident at USCAP for this Poster.

Wednesday - March 6th

Kelly Butnor with James L. Burchette - Poster Presentation:
"p40 (ΔNp63) and Keratin 34ßE12 Provide Greater Diagnostic Accuracy than p63 in the Evaluation of Small Cell Lung Carcinoma in Small Biopsy Samples"

Donald Weaver, with: Onega T, Allison KH, Oster N, Elmore J - Poster Presentation:

"Digitized Whole Slides for Breast Pathology Interpretation: Pathologists Use and Perceptions."

Donald Weaver - Invited Presentation:

"Epithelial and spindle cell lesion of the breast: a case presentation."

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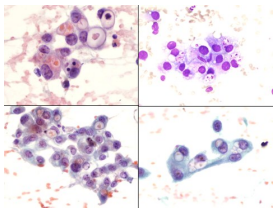
Vermont Visiting Program - Pathology International Education Program

In our international educational effort, UVM/FAHC Pathology Department receives medical students and residents from foreign countries (Vermont Visiting Program). This is a part of Pathology International Education (PIE), the goal of which is to produce global citizens in medicine by promoting and providing a variety of international experiences for current and future health care professionals, under the umbrella of Affiliated Programs in Pathology Learning and Education (APPLE). Each year, in the spring and/or summer, groups of medical students visit Vermont for a short period of time (usually 2 weeks to 1 month). The Vermont Summer Visiting Program started in 2001, and the Spring Visiting Program in 2005. Since then, 102 medical students and 3 residents have visited Vermont.

The Vermont Visiting Program hosts medical students and residents from other countries. The participants visit hospitals and clinics, attend conferences, and interact with their U.S. counterparts. Their experiences in the United States also include visiting cultural and historical events/sites.

The mission of the program is:

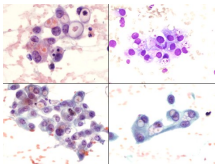
- To develop a long-term partnership between medical schools, students, and faculty members in both the United States and the other countries.
- To provide students and faculty members a first-hand opportunity to experience medical practice within each country.
- To prepare students to enter the world of working in the 21st century through enhanced global understanding.



Vermont Visiting Program - Pathology International Education Program

The most recent visit took place this March and April 2013, and it was a busy period for Brenda Shinosky, Dawn Richardson, and Reiko Kida, who took responsibility for more than a dozen visiting Japanese medical students and pathology residents. The students came from Kanazawa Medical University (Kenshiro Fujimoto, Mari Nakajima, and Yoko Yamazaki) , Kawasaki Medical University (Anri Hattori, Mai Koeda, Nanao Nakamura, and Takuro Sugiyama), Tottori University (Hiroaki Ehara, Yoshiki Fujikawa, Hiroko Hayakawa, and Megumi Okamoto) and a resident from National Cancer Center Hospital, Tokyo (Dr. Takashi Yorozu), arrived just as Dr. Kida landed unexpectedly in the hospital. With amazing organizational skills, these women guided the students smoothly to rotations in the ER, FACT, OR, and various clinics throughout the hospital. Cultural events included a tour of Burton Snow Board Factory, Trapp Family Lodge in Stowe, and the UVM COM Talent Show.
Dr. Sharon Mount hosted the visitors at her home, with Dr. Rebecca Wilcox and her husband Bruce Cohen who cooked a delicious venison chili. Sharon's dogs and Rebecca's darling daughters vied for the most popular attractions as the visiting students and resident relaxed with a glass of wine and Ben and Jerry's ice cream for dessert.

Dr. Kida is very pleased with the visit and the people involving PIE are very grateful for all the support offered by the Pathology Department, especially our faculty members, residents, and pathology assistants who helped to make this international program a successful one!



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Please don't miss the Articles posted in Vermont Medicine - University of Vermont, College of Medicine Special Edition 12, Year In Review, which features several of the UVM Pathology and Pathology Research faculty located at this website address:

http://www.uvm.edu/medicine/vtmedicine/documents/VM_2012_YIR.pdf

Debra G. B. Leonard, M.D., Ph.D. - **New Chair of Pathology** - Page 3

Vikas Anathy, Ph.D. - **Received Grant** from the American Thoracic Society Foundation/Pulmonary Fibrosis Foundation - Page 7

Russell Tracy, Ph.D. **- Appointed to the 11-member The UVM President's Advisory Council** - Page 5

Albert van der Vliet, Ph.D. **- Co-Authored Online Article** in the journal ***Nature Chemical Biology*** in July 2012 - Page 7

CMB Students Garner Awards - Kheng Newick (above left) and Brian Cunnif (above right) - Two doctoral students in the Cell, Molecular and Biomedical Sciences (CMB) Program have received prestigious awards related to their research on mesothelioma. Both students are mentored by Nicholas Heintz, Ph.D., Professor of Pathology (above center) - Page 6

Dr. Roy Korson, M.D. (center) established a Green and Gold Professorship in the Department of Pathology during 2012. Department of Pathology and Laboratory Medicine - Page 37. The image above was originally taken at an occasion to honor Dr. Roy Korson, the first to receive the Buttles Chair in Pathology for excellence in teaching. He is shown surrounded by colleagues who also are or have been recipients of this honor. Shown left to right are: Drs. William Pendlebury, John Lunde, Sharon Mount, Roy Korson, Bruce MacPherson, and Nicholas Hardin.