

COLUMBIA PATHOLOGY AND CELL BIOLOGY REPORT

Summer 2016

From the Chair



Last fall, in my first newsletter as Chair of the Columbia University Department of Pathology and Cell Biology, I outlined several five-year departmental goals including increased

research funding, national recognition as a leader in precision medicine, expanded clinical subspecialty expertise, and enhanced faculty mentoring. Substantial progress has been made over the last year on all these goals but I'd like to update you on the rapid advances achieved in developing a new junior faculty mentoring program.

A large group of faculty members across all academic ranks and departmental divisions volunteered substantial time and effort over the last several months to work with me to define the goals of a junior faculty mentorship program and most importantly, to propose operational guidelines. Initially organized into two planning committees, basic science and clinically focused faculty members, the two committees were ultimately able to define both common and track-specific mentoring principles. Complete program details will be posted on the departmental website but highlights of the program are described below.

Common Mentoring Principles.

The mentor-mentee relationship is not evaluative in nature and details of discussions are not reported to the department chair, division director, or direct supervisor. Mentoring committees are not used for performance reviews but should provide the mentee with a realistic assessment of her or his career progress.

Assistant professors are strongly encouraged to actively participate in the mentoring process. Junior faculty who decline to participate have to opt-out in writing to the department chair.

Continued on page 2

After 473 years, Vesalius in English! A Wonderful Gift from the Gross Anatomy Students



Many people know that the 1543 edition of *De Humani Corporis Fabrica* by Andreas Vesalius was a seminal event in the development of modern medicine and science. What may be less known is that The Augustus C. Long Health Sciences Library has several original copies of this classical book—which was the first Anatomy text to be illustrated. The drawings, from woodcuts, are magnificent. It contradicted the reigning authority, Galen, whose ideas had been dogma for more than a millennium.

Until recently there was no English translation of the original Latin text.

Columbia's medical & dental students recently presented the Gross Anatomy faculty with a "small" token of appreciation; the 2 volume annotated translation of *De Humani Corporis Fabrica*. This translation took 20 years to complete and was published in 2014 to commemorate the 400th birthday of Vesalius. The Gross Anatomy faculty were touched and grateful for this recognition. The volumes will reside in Dr. Paulette Bernd's office, P&S room 14-426A; all are welcome to visit.



COLUMBIA UNIVERSITY
MEDICAL CENTER

In This Issue

Mentoring Principles.....	1
Pancreatic tumor suppressor gene	3
New Website Launched.....	4
Perzin and Spitalnik Receive Awards.....	5
New Residents.....	6
Retirements	7
Writing for the Public.....	8
First Women in Pathology.....	9
In Memoriam: Dr. Dorothy Warburton	10
Aptamers for PKU?.....	11
New Grants.....	12



From the Chair *(continued from page 1)*

Mentoring committees should be formed as soon as possible but not later than six months after the start date at CUMC.

Each committee includes two or more (basic science: three or more) faculty members. The composition and formation of the committees might differ between tracks.

Committees meet at least once a year; the department provides administrative support and keeps records of the meetings and their attendance.

Mentoring is expected to continue at least up to the first promotion.

Specific Policies for Clinical and Clinical-Science Faculty.

The goal of a faculty mentoring activity is to provide the opportunity of support and advocacy for the individual faculty member. Mentoring should help faculty to acquire key competences: scholarship, independence, educational skills and preparation for academic advancement, as well as the development of constructive professional relationships (professional networks). Mentee-mentor discussions may be wide-ranging to include personal issues such as managing professional and personal life balance.

The mentoring faculty/committee should have at least two faculty members, selected by the faculty mentee and must not include the faculty member's division director or direct supervisor. At least one member of the committee should be of a similar rank as the mentee and other(s) should be of senior academic rank. One faculty member of the committee may be from a different department. Faculty should initiate the process of identifying a mentoring committee and hold the first meeting early in the academic year, in order to establish a productive relationship with the committee. The composition of the mentoring committee may change at any time, as decided by either the mentee or the mentors.

Specific Policies for Tenure-Track Basic Science Faculty.

An appointment to the tenure track represents a significant investment in the future of a junior faculty member. At the time the offer letter is signed, the department (together with the hiring scientific unit) will iden-

tify a tenured faculty member to act as the initial mentor. In this one-on-one mentoring relationship, practical questions related to setting up a lab and starting an independent research program will be discussed. By the time the junior faculty member is ready to submit a first major federal grant, the mentee together with the department (and the scientific unit) will choose two or three additional tenured faculty members to join the committee.

The committee will meet at least once a year to provide feedback on the junior faculty member's research and productivity, and to be available for review of major grant submissions and key manuscripts. To facilitate competitive grant submissions, especially for R01 applications, the committee will review the grant proposal in depth; ideally, the mentee will provide the committee with a full draft of the research proposal at least two months prior to the submission deadline and the committee will meet with the mentee at least six weeks before submission to provide critical feedback in a group setting. Additionally, the committee will assess other tenure criteria, including service to the university, and teaching. The committee will discuss exposure in the form of presentations at national and international meetings and offer sponsorship if appropriate. Throughout the mentorship period, the mentee will maintain a current CV in Columbia format to document her/his career development. A continuation of the mentoring relationships beyond the tenure decision is optional.

Specific Policies for Basic Science Faculty on the 'at CUMC'-Track.

Faculty members who are designated 'at CUMC' represent a diverse group of researchers who are typically recruited and supported by a Senior Faculty Mentor within the Department as part of larger programs that are critical to Columbia University and research advancement. The primary goal of all mentorship committees is to promote professional development and facilitate scientific growth as a contributing member within the CUMC community and in their scientific field. This can include promotional opportunities both internally and externally (e.g., to gain a tenure-track/tenured position at another academic institution). Membership of the committee should be tailored to the needs of the mentee, including their

scientific discipline, aspirations and career goals. Each mentoring committee will be expected to prepare the mentee for promotion "at CUMC" or to be competitive for a tenure-track position at another institution.

The mentoring committee will not include the mentee's immediate supervisor to avoid any real or perceived conflict of interest toward retaining the mentee in the current position. If the junior faculty member is applying for independent funding, by the time they are ready to submit their first major federal grant (i.e., R01), the mentee should form a committee of three senior faculty members who can review this grant prior to submission (see above under tenure-track). The committee will provide a thorough review of the grant proposal six weeks before the submission deadline and work with the mentee in developing a competitive proposal. Mentees should select members of the mentoring committee carefully and with forethought for the previous experiences of the mentors and as to which mentors would represent an appropriate "fit" with corresponding career goals. Mentorship committee membership can be amended at any time as deemed fit by mentee or mentors.

Conclusion

The rapid development of a junior faculty mentorship program is a substantial accomplishment and reflects the collaborative and supportive environment existing in the Department of Pathology and Cell Biology. However, the program will only be effective if we make a sustained commitment to its implementation. Thus, I encourage junior faculty members to enthusiastically embrace the program and to rapidly establish mentoring committees and senior faculty members to volunteer your time and effort as mentors to ensure the success and career development of all faculty members.



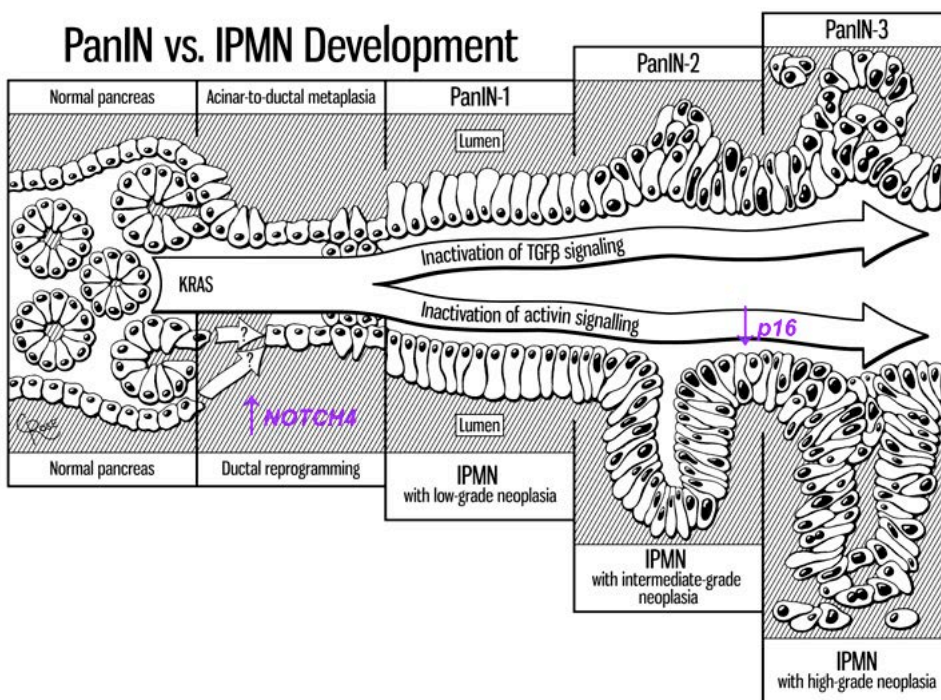
Activin receptor 1B is a pancreatic tumor suppressor in vivo

By Gloria Su

The Transforming Growth Factor- β (TGF- β) signaling pathway drives human tumorigenesis, including pancreatic cancer. However, little is known about activin signaling, one of three major TGF- β family members, in pancreatic tumorigenesis. We found sporadic mutations of the Activin receptor type 1B (ACVR1B) gene in human pancreatic ductal adenocarcinoma (PDA); therefore we investigated the potential tumor-suppressive role of ACVR1B. In our recent publication (Qiu et al, *Gastroenterology* 2016; 150(1):218-28), we reported that loss of ACVR1B from the pancreata of mice increased proliferation of pancreatic epithelial cells, formation of acinar to ductal metaplasia, and focal inflammatory changes, compared with control mice. Disruption of the *Acvr1b* in the context of oncogenic *Kras* in the pancreas

accelerated growth of intraductal papillary mucinous neoplasms (IPMNs) but did not alter growth of pancreatic intraepithelial neoplasias in mice. This process also involves NOTCH4 activation and the loss of p16. We also observed progressive loss of p16 in human IPMNs of increasing grades.

Our data provide the first evidence that *Acvr1b* acts as a tumor-suppressor gene in vivo. Notably, the IPMN to invasive cancer progression sequence observed here is distinct from the PanIN (pancreatic intraepithelial neoplasia) to PDA phenotype previously reported in the context of TGF- β inactivation and *Kras* activation, suggesting dichotomic roles for TGF- β and activin signaling pathways in early pancreatic tumorigenesis (PanIN vs. IPMN).



A model depicts the differential roles of Activin and TGF- β signaling pathways in regulating pancreatic tumorigenesis. Our data have demonstrated that activin signaling preferentially represses the development of pancreatic intraductal papillary mucinous neoplasms (IPMN) in a SMAD4-dependent manner, and the engineered deletion of *Acvr1b* in the context of oncogenic *Kras* can lead to the expansion of IPMNs and their progression to invasive pancreatic ductal adenocarcinoma (PDA), which also requires additional sporadic activation of NOTCH4 and inactivation of tumor-suppressor gene p16. In contrast, TGF- β signaling deficiency cooperates with *Kras* activation in the rapid development of invasive PDA through a fast progression from (pancreatic intraepithelial neoplasia (PanINs) to invasive carcinoma that is not solely dependent on SMAD4 activity.

Link: (<http://www.ncbi.nlm.nih.gov/pubmed/26408346>)



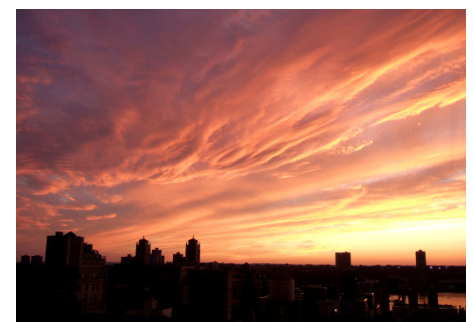
Molecular Pathologists at Columbia help guide therapy for a young patient with chemotherapy-resistant cancer

The case involves a highly collaborative effort from many physicians and scientists at the medical center including molecular pathologists Dr. Susan Hsiao and Mahesh Mansukhani from the Laboratory of Personalized Genomic Medicine. Careful review of whole exome sequencing and transcriptome data performed on the patient's chemotherapy-resistant acute lymphoblastic leukemia revealed a rare fusion between NUP214 and ABL1 which guided the development of a successful treatment strategy. The gratifying story of the young patient, her family, and her physicians appeared in this summer's Columbia Magazine, written by David J. Craig and can be found here at:

<http://magazine.columbia.edu/features/summer-2016/meet-girl-gene-nup214-abl1>.

Anthony N. Sireci, MD, MSc
Assistant Professor of
Pathology and Cell Biology at CUMC

Our Far-Flung Photographers



Sunset Across the Hudson
Photograph by Richard V. Miller

Department of Pathology & Cell Biology Kicks Off a New Website Project

By Tevra Francis

On Monday, April 25th, 2016 close to 50 faculty, staff, and students gathered in the Taub Conference Room to learn about the Chairman's vision for a new Pathology and Cell Biology website. This project is one of Dr. Roth's initiatives in bringing a new look and feel to the Department of Pathology and Cell Biology. "Our website is our face to the world... the initial impression is important," said Dr. Roth of this endeavor. The website kick-off meeting was met with excitement and participation by many committee members, "I'm really looking forward to seeing this project rolled out," said Tria Roddy of Research Administration, "We need a resource for internal and external parties alike." With an anticipated go-live date in early 2017, this monumental project will encompass all areas of Pathology and Cell Biology at Columbia University.

One of the goals established for this project is to serve the needs of our patients and their physicians through a user-friendly,

informative, and comprehensive website. One intention of this project is to build a stronger sense of community within the department, create a modern and intuitive web presence, and to maintain dynamic content. Joann Li, Department Administrator, introduced the project's objectives to the meeting's attendees, detailing the need for inclusion and teamwork. The website committee consists of teams that are a multi-specialty blend of faculty, students, and administrative staff who bring diverse points of view to their groups. Each team, called Working Groups, will focus on specific areas of the proposed site, including Education, Research, Diagnostic Services, Customer Service, and Administration. One of the Working Groups is responsible for coordinating the updates of all faculty profiles in a University-wide directory system called the Columbia University Profile System (CUPS). There is also a Focus Group, a selection of faculty and staff that represent a cross-section of the department

to ensure that the website includes all the constituencies in our large department.

"It's been really inspiring to see the department work together on what is an extremely important project. I have had the opportunity to see my co-workers in a new light, and it has been truly gratifying," stated Milan Fredricks, who serves in the project's Core Planning Group. Several colleagues in the department have contributed suggestions that have become key components to the development of the new and improved website. The website committee hopes that the final result is an on-line presence that captures the innovation, history, diversity, and promising future of Columbia's Department of Pathology and Cell Biology at Columbia University.

Ideas and feedback are always encouraged, and can be sent to:

PathWebMaster@columbia.edu.

Anniversaries

The Department of Pathology and Cell Biology must be a good place to work because people stay for a long time. There are so many veterans that Pathology and Cell Biology Reports is listing anniversaries in increments of five years.



Lee Stecher (left) and her aunt, someplace in Florida

We are proud to note that Lee R. Stecher has served the Department for fifty years. In February of 1966, Lee was 22 years old and paid an agency to help her find a job. She applied to the Columbia Department of Pathology and heard nothing, so she was forced to take a job on the East Side, which was a terrible commute from her home in Rockland County. One day she got a call out of the blue saying she had the job at P&S if she wanted it. Lee remembers that as a great moment and has been here ever since, serving most recently as a Transcriptionist. She says that what she loves is learning new things and the kindness of her mentors, particularly Dr. Karl Perzin (see Honors and Awards), Dr. Hanina Hibshoosh, and Dr. Kathleen O'Toole. We don't know who made that call out of the blue in 1966, but it started a good run.

Elaine Silvia has been with us for 40 years and Elnora Johnson for 35. Eric Koonming Ho and Sindu Krishna have logged 30 years.

The 25-year club includes:

Robin Miller, Chih-Chao Chang, Anjali Saqi, Phyllis Faust, Istvan Boldogh, Alcmena Chalazonitis-Greene, and Sunilda Valladares-Silva. I conclude that 1991 was a good year for our department.

The 20-year cohort includes Ming Ming, Hong Holly Jiang, Zhimin Yu and Melvin Acevedo. There are ten people who have made the Department of Pathology and Cell Biology their home for 15 years, and 17 for ten years. We will recognize them in the next issue of Pathology and Cell Biology Reports (PCR).

Honors and Awards

Pathology and Cell Biology Reports (PCR) would like to salute its members who have received recognition from their colleagues and students.



Dr. Karl Perzin, MD (*right*) has been awarded the College of Physicians and Surgeons Distinguished Service Award in Basic Science, presented at the May 18 graduation ceremony. He is shown here with Dr. Kevin Roth. Dr. Perzin's long career of teaching and research can be found in a memoir he wrote for an earlier PCR issue: My (First) 56 years at Columbia. You will learn a lot about the Department and Pathology by reading it:

http://pathology.columbia.edu/newsletter/newsletter_anniversary_issue.pdf

Interesting Review of GI Lymphoproliferative Disorders

"Indolent T- and NK-cell lymphoproliferative disorders of the gastrointestinal tract: a review and update" by Rahul Matnani, MD, PhD a post-doctoral clinical fellow and colleagues, has been accepted for publication in Hematological Oncology. The review describes these indolent T-cell LPD of the GI tract that are now a provisional entity in the updated 2016 WHO classification for lymphoid neoplasms. It promises to be a useful update.



Dr. Ellen Ezratty, PhD has won the Dr. Ines Mandl Research Fellowship to support her research on the stem cells of the skin. Dr. Ezratty received her PhD from Columbia in 2008 for work with Dr. Gregg Gundersen, left for a post-doctoral fellowship with Elaine Fuchs at The Rockefeller University, and has now, happily, returned.



Dr. Patrice Spitalnik, MD has been awarded the Charles W. Balmfok Award, named after a member of the P&S class of 1884 to recognize her contributions to teaching in the pre-clinical years. Patrice has reorganized the teaching of histology and taken on other important teaching roles for medical students in their preclinical years.

The New Gross Anatomy Teaching Facility



Dr. Paulette Brandt in the New Gross Anatomy Teaching Facility of the Diana & Roy Vagelos Education Center. Opening soon.

Residents joining the department in July, 2016



Alex Lyashchenko CP

B.A.: Columbia University, Biochemistry; summa cum laude, Phi Beta Kappa, Golden Key International

Honour Society

M.D.: Columbia University College of Physicians and Surgeons

Ph.D.: Columbia University College of Physicians and Surgeons, Neuroscience; FUS mutations and amyotrophic lateral sclerosis with Neil Schneider, M.D., Ph.D.



Ijeuru Chikeka AP/CP

B.S.: University of Maryland Baltimore County, Biochemistry and Molecular Biology; summa cum laude

M.D.: University of Maryland

Post-doc research on Rickettsial infections with Stephen Dumler, MD, and on melanoma with Thomas Hornyak, M.D.



Chun-Chieh (Paul) Lin AP/NP

M.D.: Fu Jen Catholic University School of Medicine, Taiwan; Outstanding Medical Graduate Award

Ph.D.: Johns Hopkins University, Neuroscience

Post-doc research on genetic mapping of olfactory neurons in *Drosophila* with Christopher Potter, PhD



Magdalena Jurkiewicz AP/CP

B.A.: University of Chicago, Biological Sciences; B.A. with Honors

M.P.H.: Yale University, Chronic Disease Epidemiology

M.D.: Stony Brook University

Ph.D.: Stony Brook University, Genetics; genomics of stress and anxiety with a focus on gene network regulation by micro RNA with Turhan Canli, Ph.D.



Osama Al Dalahmah AP/NP

M.D.: University of Jordan Faculty of Medicine; University Award for Academic Excellence and Distinction

D. Phil: University of Oxford, Department of Physiology, Anatomy, and Genetics. Stem cell biology,

Neurodevelopment and Molecular Neurobiology

Post-doc research fellow with Francis Szele, PhD



Elizabeth Stone AP/CP

B.A.: Barnard College, Biology major and Chemistry minor; cum laude

Post-baccalaureate research with Robert Darnell, M.D., Ph.D., at Rockefeller University, binding properties of RNA-binding protein FMRP.

M.D.: Columbia University College of Physicians and Surgeons

Ph.D.: Columbia University Graduate School of Arts and Sciences, Neurobiology and Behavior, *Drosophila* model of Fragile X syndrome with Mimi Shirasu-Hiza, Ph.D.

Promotions

Vaidehi Jobanputra Ph.D, Assistant Professor of Clinical Pathology has been promoted to Associate Professor

Michael Barry Stokes, MB, BCh, Associate Professor of Clinical Pathology has been promoted to Full Professor

Tilla Worgall, MD, PhD, Assistant Professor of Clinical Pathology, has been promoted to Associate Professor

Retirements



Mildred Rodriguez

Millie Rodriguez has worked in Pathology for 33 years. The following quote from Nicole Suci-Foca explains her enormous contributions:

Mildred Rodriguez joined our division some 30 years ago when she was in her early 20's. She was the most gracious, efficient and competent secretary I have ever known. Her thirst for knowledge expanded to learning a lot about book-keeping, administration, manuscripts, grants budgeting, editing and submission. In times of great stress related to deadlines, inspections and other stressful events, Millie brought calm to all of us and with her extraordinary efficiency helped us to finish our "paper work" on time. She witnessed the growth of the laboratory from a staff of about 10 to 37 members, reflecting the increased scope and workload in our division. Millie was a great colleague and enjoyed everybody's love and respect. Although my opinion of her qualities are objective, she was and will always be a very dear friend of mine.

Dr. Nicole Suci-Foca
*Professor Emeritus of
Pathology and Cell Biology*



Steve Russo

Steve Russo was our Deputy Departmental Administrator and Director of Sponsored Projects and the master of all of our incredibly complex NIH and other grants. He was the guru of overhead rates and accounting. This complexity rivaled that of medical billing or the tax code but Steve had it all in his head. Supplicants came to his door to find their account balances and whether they could afford to hire that most wonderful technician or graduate student. He would look at your accounts and then pronounce. Often this came with a bit of benevolent sarcasm or good cheer cut with a witticism—but you could rely on that data.

For a number of years Steve has been preparing a little retirement apartment in Italy, in a town called Sapri, which is on the Mediterranean about an hour south of the Amalfi coast. The apartment is being renovated and Steve does not plan an immediate move because he is caring for his elderly parents and also learning sausage making from them. Who knew that sausage casings can no longer be bought locally, but Amazon has them? He is also creating a family genealogy. Steve has been learning Italian for quite a while. He says he misses us, but rather enjoyed going back to sleep during the cold and rainy weather last spring. We wish him the best.



George Rosa

George Rosa was one of those people who just knew where everything was in the department and managed to get things done. He plans to travel, and coach his grandchildren's Little League teams. George is very proud that one of his sons is a police officer and the other a fireman. The editor, Rich Kessin will especially miss him because he was always a reliable guy to talk about baseball. Never mind that he was a Mets fan, George has an excellent knowledge of baseball and chatting with him for a few minutes every day was pleasantly therapeutic.

Our Far-Flung Photographers



*Flowers in Thailand
by Patricia Tiscornia-Wasserman, MD*

Galahad Syndrome

Richard Kessin

Nothing improves writing like a newspaper column on science. The writer has 750 words to explain science to people who last took biology in 1959, so any word or paragraph that is not essential must be slashed. Adverbs die, as do most adjectives and the passive voice. For five years I have been writing a column called *The Body Scientific* for *The Lakeville Journal* and its associated papers in Northwest CT. I cover all manner of subjects but most columns recently have been about infection or disease. There are 8000 potential readers, one excellent editor, a couple of fact-checkers, and no reviewers. What a relief! Here is an example. I thought that vaccine denial is a collection of beliefs that should have its own name so I called it Galahad Syndrome:



The Lakeville Journal in Lakeville CT. Janet Manko, Editor-in-Chief.

Vaccine denial comes in several forms: those who think that vaccines give people the disease they are supposed to prevent; those who think vaccines cause autism in children; and those who think that healthy children don't need them. A central theme of vaccine deniers is that strength, health and virtue (include piety, if you like), suffice to stop any illness. Some parents think that vaccines are unnecessary for healthy children; it is an Arcadian return to a philosophy of rural bliss. The idea is that there is some ordained state of good health and perfect parenting that renders children immune. The idea is pernicious, but it has been hard to fight — as shown in a recent Republican candidate debate where Donald Trump espoused the debunked theory of autism caused by the measles, mumps and rubella vaccine.

Perhaps it is time to give this rejectionist approach to modern science and medicine a name. I suggest Galahad Syndrome. Let me explain.

Sir Galahad was a Knight of the Round Table and is a purely literary figure, but at least metaphorically, he too was certain that virtue and strength were sufficient for any challenge. The person who gave life to Sir Galahad was Alfred Lord Tennyson, a romantic if ever there was one. His poem, "Sir Galahad" (1832), was incorporated in "Idylls of the King," his rumination on the Arthurian legend. According to Tennyson, Sir Galahad could slash and thrust better than other knights because: "My strength is as the strength of ten/Because my heart is pure."

The poem espoused a faith in purity and strength, a martial manliness that charged first and asked questions later. We find it in "The Charge of the Light Brigade," immortalized in another Tennyson poem in which almost everyone dies.

My favorite alternative portrayal of the Arthurian legend is by Mark Twain. Twain's character, the Connecticut Yankee in King Arthur's Court, was a foreman at the Colt Arms Factory in Hartford who, after an unfortunate brawl with one of his workers, was knocked into the 8th century by a crowbar to the head. Waking up, he gradually sized up the situation, realized that King Arthur's court was populated with amiable dolts and decided to take charge.

With 19th century Connecticut ingenuity, he does take charge, but not without opposition from Merlin the Magician, whose stock, naturally, was sinking as the Yankee blew things up and predicted solar eclipses. To save his credibility, Merlin convinced King Arthur to do the sensible thing and to test the Yankee in a joust. He was to fight all of the mounted knights of

the roundtable, one at a time. The Connecticut Yankee knew a losing proposition and so he appeared, dressed in pink tights, with a lariat on a nimble quarter horse. He deftly lassoed each charging knight, including Sir Galahad, and yanked them off their horses. (Read this great satire for details.)

Let us define Galahad Syndrome as denial or overconfidence in the face of a threat that is not understood. Modern people suffering from Galahad Syndrome take a rejectionist approach to science and modern medicine, relying on virtue (pure hearts, in the Galahad metaphor) and healthy habits to protect them. For daily life that is fine practice, but faced with the flu virus or the measles virus your strength is not the strength of 10; a virus or bacterium does not care how healthy or virtuous its victim is. The flu virus of 1918 killed many thousands of soldiers, all young and healthy, then millions of other people. Tuberculosis seemed to have an affinity for the privileged of 19th century society. Polio downed millions of healthy people, including the vigorous Franklin Roosevelt, before science in the form of vaccines stopped it cold. Measles spread from a single infected child at Disneyland and affected hundreds of healthy children. According to records of the Centers for Disease Control, before 1963, when the vaccine was introduced, measles affected hundreds of thousands of American kids a year, practically every child got measles at some point. About 20 percent had serious complications and more than four hundred died in a typical year. People my age who had measles before 1963 will sometimes say it was not so bad, but more than 400 people are not here to agree.

There is a way out of Galahad Syndrome, as it applies to vaccines. Learn how the immune system works. The immune system can be complicated, but important aspects, such as antibodies and how they are made, can be explained to non-scientists. We have known since Thucydides in 430 BCE that people who survived a plague in Athens became immune to it. Vaccines provide immunity and spare us the plague part. Thanks to the efforts of generations of scientists, we now know how to make that happen for many diseases.

See fifty other columns at:

<http://tricornernews.com/node/42798>.

If you have an idea for a guest column, contact Rich Kessin.

From the Archives-The First Women in Pathology



By Heidrun Rotterdam, MD

Many people have come into the Department since Dr. Heidi Rotterdam, now retired, wrote this article on women in pathology. We think people will find it interesting today.

In my office, there hangs an old photograph of the class of 1922 of the School of Medicine of Columbia University, still in its original frame, brown wood, faded and scratched and probably with its original glass. I rescued it from certain destruction one late evening when the garbage collector was about to take it together with piles of discarded office refuse. The brittle paper is cracked in many places but through the resulting geographic haze, I see 85 stern faces, 79 male, 6 female, all looking straight ahead, lips tightly closed, a faint smile here and there but a real smile with parted lips only on one face, a woman in the lower right corner. I don't know who she is, but I think she is right to smile: she is one of very few women allowed to study medicine, to graduate and perhaps to have a career thereafter. You've come a long way, baby.

I do recognize one of the other female faces: Dr. Virginia Kneeland Frantz, who became a well known pathologist; her office on the 14th floor of Vanderbuilt Clinic is still there, somewhat altered by repeated renovations, but still the same shape and size. Dr. Frantz does not smile, she looks as stern as most of her male colleagues. Remember, the first women in our profession needed to constantly prove that they could be as serious and devoted to their profession as men.

As I pursue my inquiry into women in pathology and descend to the "Archives & Special Collections" in the basement of the Long Health Sciences Library I come across some remarkable details related to Dr. Frantz and my photograph of her graduation. Indeed, 1922 was the first year that the School of Medicine of Columbia University graduated women. In 1917, three years into World War I, due to a drop

in male applicants, 13 medical schools, among them the College of Physicians and Surgeons of Columbia University, broke their all-male admission policy and allowed women to apply. Six women among 85 graduates seems a small number but it represents a big step forward.

Dr. Frantz was the first ever female intern in the Department of Surgery at Presbyterian Hospital from 1922 to 1924 when she advanced to surgical instructor. She branched out into surgical pathology (then a division of surgery) in 1926 and remained a surgical pathologist and researcher for the rest of her life. She was a thyroid specialist, wrote the first description of insulin-producing tumors of the pancreas, was the first to use radioactive iodine to demonstrate and treat metastatic thyroid cancer (both with Dr. Whipple) and wrote the AFIP fascicle on pancreatic tumors in 1959.

Not all Ivy League Medical Schools joined the initial group of 13. Harvard Medical School did not open their doors to women until World War II and women physicians were considered an oddity for quite some time thereafter. When I applied for a residency in Internal Medicine at Massachusetts General Hospital in 1968, I was told that I had three strikes against me: I was a woman, I was a foreigner, and I was married to a non-physician. "People like you go into pathology", someone suggested. And so I did. And I have no regrets.

Where are we today? As I look at our surgical pathology sign-out schedule there are 8 women and 11 men. Our Director of Surgical Pathology is a woman, our departmental administrator is a woman. As I look at the list of residents and fellows for the year 2011-2012, I see the mainly smiling faces of 18 women and 15 men. How did we get from there to here (there being a past of struggling individuals, here being a present of groups of curious and happy women who, more or less successfully, balance career and private lives)?

A list of residents that passed through our department starting in 1967 reveals some interesting statistics: During the 20 years before our last chairman, Dr. Michael Shel-

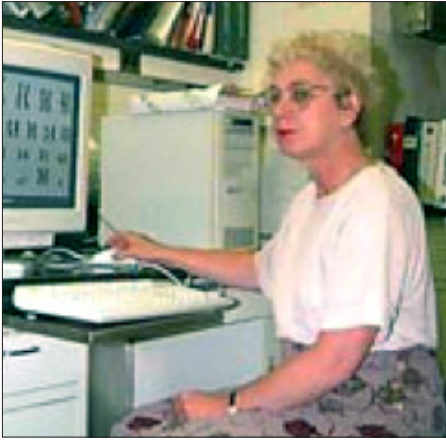
anski, arrived, there were 19 female residents and 65 male residents (M/F ratio 3.4). After his arrival in 1987, the ratio changed remarkably: during the next 20 years, between 1987 and 2007, there were 57 female residents and 74 male residents (M/F ratio 1.3) and between 2007 and 2011 there were 18 female residents and 15 male residents (M/F ratio 0.83). Yes, we have come a long way. We have come to be equals as far as opportunity and achievement are concerned. But is there something unique we, the women in pathology, can offer?

In 1957, when Virginia Frantz was offered the "Elizabeth Blackwell Award", given to women for distinguished service in medicine, research and teaching, she considered rejecting the award, because it identified her as a "female" doctor. "I am not a medical oddity", she is quoted as having said, before she accepted it. On the topic of medical education, she remarked that "teaching is much more philosophical speculation than formal pedagogy, much more art than science, much more fun than work". So perhaps it is this element, we the women in pathology, can contribute to our profession: to infuse the science, the service, the teaching with beauty and with joy.

Dr. Heidi Rotterdam was the last trainee in surgical pathology of Dr. Raffaele Lattes from 1974 to 1975. She returned to CUMC as an attending pathologist in July 1991 and recently retired.



In Memoriam – Dr. Dorothy Warburton



Dorothy Warburton was one of the pioneers of Clinical Genetics and had been at P&S and associated with our Department since 1964. We shared her with several others, including Genetics and Development and Pediatrics. Her specialty was in fetal chromosomal abnormalities and from 1969 to 2005 Dorothy was the director of The Genetic Diagnostic Laboratory. She was a heroine of cytogenetics and was awarded the William Allan Award by the American Society of Human Genetics in 2006. She received many other awards.

My own memory of Dorothy was of her teaching first-year medical and dental students how to analyze karyotypes. This was back in the day when chromosomes could be stained for banding patterns but there was no fancy fluorescence in situ hybridization. Students cut out chromosomes with the kind of scissors used by fourth graders. It was not so easy to arrange them into karyotypes and to detect translocated segments and aneuploidy, but eventually they got the idea. I remember a combination of concentration and of laughter. That was Dorothy Warburton. (RHK)

National Laboratory Workers Appreciation Day



We recently celebrated Laboratory Worker Appreciation Day. Our staff carry out many critical functions and we are only too happy to celebrate them. As usual in New York, this involves food, particularly bagels. Some relatively foreign foods seem to have snuck in, like croissants (see photo). We hear they are excellent. Next year in Paris.

Omnis Cellula e Cellula Rudolf Virchow and the Beginnings of Pathology

The Department's History of Science and Medicine Column

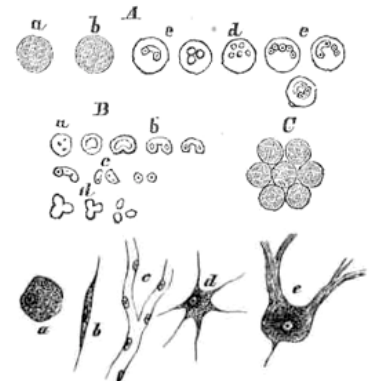
The great French microbiologist and Nobel Prize winner once said that it is dangerous to parachute young scientists into a field whose history they do not know.

Omnis cellula e cellula—all cells from [pre-existing] cells—was Rudolf Virchow's starting thought in his development of pathology. In the 1840's and 1850's most physicians and scientists believed cells formed spontaneously. Virchow brought clarity and technical expertise to pathology and made many contributions to medicine: he discovered leukemia and defined the life cycle of *Trichinella*. He coined the terms, chromatin, agenesis, parenchyma, osteoid, amyloid degeneration, and spina bifida. The journal he founded still exists.

He was an ardent liberal who established many of the principles of public health in Germany and believed that poor social conditions led to disease. He ran for public office and was elected, confronting Otto von Bismarck, the man who unified Germany. Bismarck reportedly challenged Virchow to a duel, which was never fought. Virchow had widespread interests, published 2000 papers, but never believed in evolution, calling Darwin and Ernst Haeckel fools. He had equal contempt for the germ theory of disease.

Others who want to write on the history of biology and medicine should contact the editor.

R Virchow's Cellular Pathology

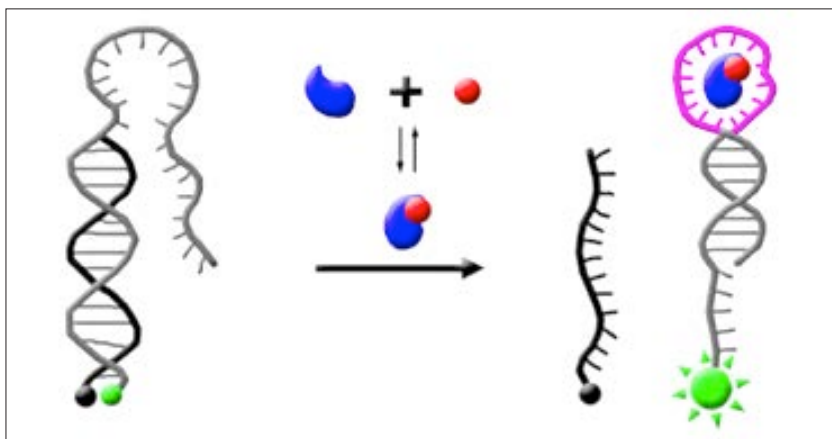


The Labmedicine Aptamer Initiative

Developing a point-of-care device to care for patients with phenylketonuria

By Tilla Worgall MD, PhD* and Milan Stojanovic, PhD

The Stojanovic lab at CUMC has developed high-affinity DNA aptamers that enable accurate quantification of small molecules. Aptamers are short strands of DNA that form receptors to targets. They are chemically selected from large pools of DNA aptamers by a process called SELEX technology ('systematic evolution of ligands by exponential enrichment'). A specific aptamer permits an immediate readout by fluorescence. These high affinity binding aptamers are suitable for measuring small molecules in human specimens. We focused on phenylalanine, because there is a long-standing clinical need for this patient group that no other technology has been able to satisfactorily tackle.



*High affinity aptamers (left) were selected to detect CP*III Rho-bound phenylalanine. CP*III Rho (blue) is added to the detection buffer where it binds phe (red). The complex is recognized and bound by the aptamer. This binding causes the release of a fluorescence quencher. The fluorescence (green star) is proportional to phe concentration.*

The inability to catabolize phenylalanine causes phenylketonuria (PKU), the most prevalent inborn error of amino acid metabolism. Patients must adhere to a life-long diet to maintain blood phenylalanine below 360 micromolar to prevent irreversible mental disability. There is, however, no home monitoring system because enzyme based methods proved inaccurate, while proven technologies such as HPLC and mass spectrometry cannot be miniaturized. Turn-around times for sample testing of more than 3 days are stressful to parents and patients, and preclude compliance and timely adjustment of therapy.

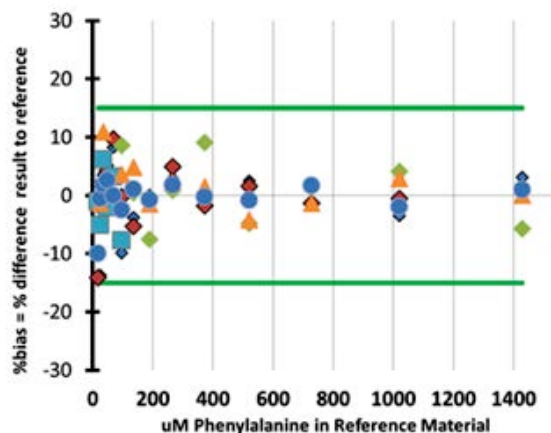
Having selected an appropriate aptamer, we are proceeding to the clinical applicability of this novel technology. Accuracy, precision and robustness of the technology were evaluated in actual patients' samples over a range of 50 – 1500 micromolar. The analysis is linear, requires a very small sample volume (1 microliter), costs less than 50 cents per sample and is robust to temperature. The technology, if clinically proven, will allow patients to determine blood phenylalanine from a drop of blood within 1 h and would signify a paradigm shift in treatment and monitoring of PKU.



Milan Stojanovic



Tilla Worgall



Excellent accuracy in buffer. Buffer was spiked and analyzed twice a day over three days. All measurements are well within the upper and lower limits of acceptance (green lines at 15 %).

The Vagelos Education Center at Columbia University



Exterior view of the south facade and study cascade.

New Grants–2016

PI	Sponsor	Title
Canman,Julie	Revson (Charles H.) Foundation	Uncovering how polarity controls cell division in a multicellular environment
Canman,Julie	National Institute of General Medical Sciences/NIH/DHHS	Cell polarity and cytokinesis
Gundersen,Gregg G.	American Heart Association	Mechanisms of nuclear positioning during muscle differentiation GRA fellowship predoc – Ruijuin Zhu
Bartolini,Francesca	AMERICAN HEALTH ASSISTANCE FOUNDATION	Formin-induced stable microtubules in alzheimer s disease
Vallee,Richard	American Heart Association	A Role for Centrosome Positioning in Controlling Neural Progenitor Division
Pon,Liza A.	Muscular Dystrophy Association	A newly identified congenital muscular dystrophy: mechanisms and interventions
Clinical Trial – Micro Research Lab	Sponsor: CURETIS AG	Detection of Microorganisms and Antibiotic Resistance Genes in Lower Respiratory Tract (LRT) samples using the Curetis Unyvero LRT55 Application
Clinical Trial - ClinPath	Sponsor: SIEMENS CORPORATE RESEARCH, INCORPORATED	SIEMENS Clinical Study - External Performance Evaluation of assay applications on CS-2100i and CS-5100 Analyzer (Wave B)
Goldman,James E.	Department of the Army	Molecular mechanisms underlying the epileptogenesis and seizure progression in Tuberous Sclerosis Complex 1 deficient mouse models
Qiang,Li	National Institute of Diabetes and Digestive and Kidney Diseases/NIH/DHHS	Brown Remodeling of White Adipose Tissue by Pargamma Deacetylation
Berman,Diego	DENALI THERAPEUTICS	Validating new retromer stabilizing compounds for Alzheimer s disease therapeutics. Columbia Technology Ventures
Przedborski,Serge	BIOGEN IDEC	Biogen Grant Title - Columbia Technology Ventures
Kim,Tae-Wan	ONO PHARMACEUTICAL CO. LTD	Discovery of small molecule inhibitors for a novel Alzheimer s disease target. Columbia Technology Ventures
Monani,Umrao	Sanofi S.A.	AAV9-based treatment for Glut1 DS. Columbia Technology Ventures
Waites,Clarissa	IRMA T HIRSCHL TRUST	Elucidating the molecular mechanisms of synaptic protein degradation.
Vlad,George	BRISTOL-MYERS SQUIBB PHARMACEUTICAL RESEARCH INSTITUTE	Expression of LAG3 in Human B cell Malignancies
Pellizzoni,Livio	Muscular Dystrophy Association	Role of Defective U7 snRNP biogenesis in spinal muscular atrophy

Pellizoni, Livio	FIGHTSMA	Role of SMN in Cytoplasmic mRNA Regulation
Santa-Maria Perez,Ismael	ALZHEIMER'S ASSOCIATION	Role of microRNAs in the regulation of tau pathology
Wichterle,Hynek	BIOGEN IDEC	**CTV** The role of PLD1 and PLD2 in Neurodegenerative Pathways Common to ALS and AD
Przedborski,Serge	Office of The NIH Director	Enhancing Animal Care in a New High-Throughput Rodent Behavior Analysis Core Facility
Wichterle,Hynek	PROJECT A.L.S.	Improving Drug Screening Methods in ALS and Identifying Therapeutic Targets **Gift to Emily Lowry in Wichterle lab**
Greene,Lloyd A.	SAPIENCE THERAPEUTICS	The role of ATF5 and its dominant negative forms in cancer. Columbia Technology Ventures
Ezratty, Ellen	Dr. Ines Mandl Research Fellowship	For her work in mechanotransduction in tissue stem cells of the skin
Monani, Umrao	Association Francaise Contre les Myopathies	Mediators of the spinal muscular atrophy NMJ phenotype
Cannoll, Peter D.	ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI	PlexinB2 function in glioma invasion and glioma stem cell maintenance
Cannoll, Peter D.	MAYO CLINIC--ARIZONA	The ENDURES Study: Environmental Dynamics Underlying Responsive Extreme Survivors of Glioblastoma
Gundersen, Gregg	National Institute of General Medical Sciences/NIH/DHHS	Role of Nucleo-cytoskeleton Interactions in Cell Migration (competitive renewal)
Wichterle, Hynek	PROJECT A.L.S.	Selective vulnerability of motor neurons in ALS - Phase II
Clark, Lorraine	National Institute of Neurological Disorders and Stroke/NIH/DHHS	Identification of Susceptibility Genes for Essential Tremor (competitive renewal)

Our Far-Flung Photographers



Brooklyn Bridge by Patricia Tiscornia-Wasserman, MD

A Note to Our Readers

Pathology and Cell Biology Reports (PCR) intends to inform all members of the Department about the work of each of our branches. These include Pathology and all of its divisions, Administration and all of their valuable functions, and also Cell Biology including neuroscience and cancer biology. We intend to publish the normal congratulations, retirements, and promotions, but also substantive short articles. We also publish photographs and artwork, scientific or otherwise, by our members. If you have an idea, please contact Rich Kessin (rhk2@columbia.edu).

In our next issue (tentatively)

Tumor Banking In the Era of Precision Medicine *Hanina Hibshoosh, MD*

Overcoming apoptotic resistance in recalcitrant neoplasms *Markus David Siegelin, MD*

New Anatomic Pathology Faculty

New Pathobiology PhD students

Profile of former Chair,
Dr. Donald W. King

Notes from the Residency Program

Notes from the Pathobiology PhD Program

Progress on the New Website

Our Diagnostic Services

The Department offers a very broad range of expertise and diagnostic services. We are available for consultation at the following locations.

Web:

www.pathology.columbia.edu

Email:

pathology@columbia.edu

Laboratory services:

1-800-653-8200/1-212-305-4840

Administrative Services:

1-212-305-7164

COLUMBIA PATHOLOGY AND CELL BIOLOGY REPORT

Summer 2016

Chairman

Dr. Kevin Roth, MD, PhD

Donald W. King, M.D. and
Mary Elizabeth King, M.D.
Professor of Pathology and Cell Biology
Chair, Department of
Pathology and Cell Biology
Pathologist-in-Chief,
Columbia University Medical Center

Editor

Dr. Richard H. Kessin

Professor of
Pathology and Cell Biology Emeritus

Design and production

Richard V. Miller

Columbia University Print Services

<http://pathology.columbia.edu/>

Senior Associate Proofreader

Ms. Casey Schadie
*Coordinator of Residency Programs
Department of Pathology and Cell Biology*

The Columbia Pathology and Cell Biology Report is a publication of the Department of Pathology and Cell Biology at the Columbia University Medical Center.

If you have comments or questions, contact:

Dr. Richard H. Kessin
at 860.542.3950

Email: rhk2@columbia.edu