COLUMBIA PATHOLOGY AND CELL BIOLOGY
SPECIAL REPORT

Anniversary Issue 1987-2012

Celebrating 25 years of education, clinical service, and research

Dear Colleagues and Friends,

Over the years, my wife Vivien and I have enjoyed having members of the department to our home for festive evenings. Years ago, this meant having 25, then 50 and finally about 70 to our home in Brooklyn. As the Department of Pathology and eventually the Department of Pathology and Cell Biology grew, our home could no longer keep up and even division dinners became large. It has become clear that "hospital based" departments are also not fêted at Annual Galas at the Waldorf or the Plaza. Thus it became clear that if we were to have a party, we would have to throw it ourselves.

In the past 25 years we have worked together to bring the Department to a new level of excellence in clinical service, in scientific research and in education. We have built upon the base established by those who have gone before us – Stout, King, Lattes and Murray among others – and enjoyed the continuity of those who were here longer than 25 years ago and still work with us including Drs. Perzin, D'Agati, Hibshoosh, Marboe, Gershon, Axel, Richart and O'Toole and the critically important Pat Pringle. The heavy lifting of the past quarter century has depended almost entirely on those present in this room tonight. Credit belongs to those who have gone the distance, those who have come and gone and those who have only recently joined. Each of you has made a difference and it is the contributions of each of you and all of you that we celebrate this evening. Each physician, each scientist, each administrator, each student, postdoc and resident has contributed a vital thread to the fabric of our department.

A department does not stand alone. We depend on our colleagues, on the other departments and on the administration of the medical school, university and hospital for our success. I am delighted that so many of our friends and supporters from throughout the Medical Center could be with us this evening. I am also glad that representatives of our sister departments have been able to join and would like to personally acknowledge my own mentors and students who are here tonight.

For many of you this may be your first exposure to the grandeur of Low Library. I hope you will have many more chances to return. Our purpose here is rare – to honor all of us, not just one person, for our work and accomplishment. No funds are being raised, no books published. We are here to enjoy each other's company, to eat, to drink and to dance.

I raise my glass to all of you
with deepest gratitude. *Mike*

The Accomplishments of the Last 25 Years...

Michael Shelanski, MD, PhD

Migrants fromNYU
Michael Shelanski, Ron Liem, Mary Beth Hatton, Lloyd Greene, Carol Mason, Fred Maxfield

Yuan Chang
and
Patrick Moore

Department of Anatomy & Cell Biology
Michael D. Gershon, MD

1767

Studies of enteric nervous system and cell biology

The Motor Neuron Center co-directors: Drs. Christopher Henderson, Darryl De Vivo and Serge Przedborski are in the foreground. In the background are Dr. Lewis Rowland and former Dean Gerald Fischbach.

1986 PhD Programs in Pathobiology restarted

1987 Dr. Ron Liem

1988

1989 Dr. James Goldman

1990

1991

1992

1993 Discovery of the BCL6 proto-oncogene Riccardo Dalla-Favera

1994

1995 Kaposi Sarcoma Virus (HHV8) discovered by Chang and Moore

1996

1997 Discovery of the PTEN tumor suppressor by Ramon Parsons

1998

1999 Institute of Cancer Genetics formed from Oncology Division

2000 Role of acetylation in p53 regulation *Wei Gu

2001

2002 Taub Institute for Research on Alzheimer's Disease and the Aging Brain founded

2003

2004 Professor Richard Axel wins Nobel Prize for studies on olfaction

2005 Department of Anatomy & Cell Biology joins Pathology to form the Department of Pathology & Cell Biology

2006

2007 Discovery and therapeutic targeting of activated notch in T-cell leukemia by Adolfo Ferrando

2008

2009

2010 Motor Neuron Center joins Pathology & Cell Biology

Med into Grad Program initiated

2011 Howard Hughes Med-to-Grad grant received

Annual number of tests exceeds 6 million

New fellowship program in Molecular Genetic Pathology

2012 NIH grant revenues exceed $30 million

Graduate program training grant renewed

WHY IS THIS NIGHT DIFFERENT...

In the year 5738 we were a small and young people who sought refuge from the raging giants of the metropolis of the north and migrated to the East Side and found shelter at NYU. For seven years our people prospered. Our numbers increased with students and postdocs, the chronicles were filled with our work and the NIH rained blessings upon us. But, in the fullness of time our labs became cramped and our students overflowed and we beseeched Dean Saul (Shaul HaDean) to loosen our bonds and grants us more space. But the heart of Dean Saul hardened toward us and he gave us gornicht (and bubkes as well). We donned sackcloth and ashes but his heart remained hard.

So it was that in 5747 (1987 outside of New York), Dean Saul said לאזן זיי גיין (lassn sie geh'n) in the language of the East Side, and Moishe's movers came and packed the reagents, and the freezers and the equipment, and the traffic parted and our people, led by Moishe's moved slowly up the East Side on our way to Mount Sinai. There we encamped and entreated and waited. We ate lousy bread that tasted like cardboard and waited longer, but the prophecy was false. The bush did not burn, the calf was made of brass, there was no thunder, no lightning, no nada and schmutz all over the streets. This was not the promised land; in fact it smelled of ether and carbolic acid – no milk and no honey

So we journey on across across the wilderness of the Cross Bronx and Riverside Drive past Dead Dog Park to pitch camp on 168th Street.

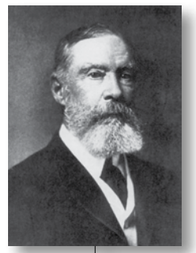
Welcomed by Dean Henrik, we built labs and the Angel Nih once again blessed us and our people grew in number and prospered by the work of their hands and of their minds. And Dean Henrik was followed by Dean Herb whose rule was a Pardes and for 10 more years the people were blessed by peace and prosperity. In the fullness of time Dean Herb left to conquer distant lands and Deans David, Tom and Gerry came and they went. Finally, we have entered the Gold(en)man Age if not the promised land and are AIMing HIgher each day.

Thus it has been ordained that every 25 years the people should gather in a place of celebration to retell the tales of our glory, to feast and to dance and to drink.

Let us proclaim
"Next Year in
Washington Heights"

Depend on the Past

1847-1883
Alonzo Clark
First professor
of Pathology
P&S



1883-1893
Francis Delafield, MD
Chair of Pathology

1893-1909
T. Mitchell Prudden, MD

1906
First
Accession Book

1922
Pathology Staff
Arthur Purdy Stout, MD
Virginia Frantz, MD,
Margaret Murray, PhD

Human Cancer
Arthur Purdy Stout, MD

1948-1979
Raffaele Lattes, MD

Karl Perzin, MD

Donald McKay
Chair

Donald West King

Sugical Pathology

William MacCallum
Chair

1848 1849 1850 1851 1852 1853 1854 1855 1856 1857 1858 1859 1860 1861 1862 1863 1864 1865 1866 1867 1868 1869 1870 1871 1872 1873 1874 1875 1876 1877 1878 1879 1880 1881 1882 1883 1884 1885 1886 1887 1888 1889 1890 1891 1892 1893 1894 1895 1896 1897 1898 1899 1900 1901 1902 1903 1904 1905 1906 1907 1908 1909 1910 1911 1912 1913 1914 1915 1916 1917 1918 1919 1920 1921 1922 1923 1924 1925 1926 1927 1928 1929 1930 1931 1932 1933 1934 1935 1936 1937 1938 1939 1940 1941 1942 1943 1944 1945 1946 1947 1948 1949 1950 1951 1952 1953 1954 1955 1956 1957 1958 1959 1960 1961 1962 1963 1964 1965 1966 1967 1968 1969 1970 1971 1972 1973 1974 1975 1976 1977 1978 1979 1980 1981 1982 1983 1984 1985 1986

23rd Street and
4th Avenue

First antiseptic
surgery at P&S

First bacteriology
course taught in
Pathology at P&S

Prudden and
others introduce
diphtheria and
tetanus antisera

1887-1928
P&S
West 59th Street

Affiliation of
Presbyterian
Hospital
and P&S

A. Purdy Stout
and others
serve in
WWI

Construction of
current campus

Surgical Pathology moves
from Department of Surgery
to Department of Pathology

Anti-Rh Treatment developed by Freda, Gorman and Pollack
Many thousands of lives saved!
(See article by Eldad Hod)

John Fenoglio
Acting Chair

The Early Days of Columbia Pathology

Richard H. Kessin, PhD

Reviewing the history of our department from the 19th century could lead to a list of names, but in creating the timeline you see above and from what I know of 19th century biology and medicine (forgive me, I was a history major), several trends emerge. The first has to do with the emergence of American medicine and science and how closely it followed Europe. Rudolf Virchow (1856) wrote *omnis cellula e cellula* – all cells from preexisting cells – a thought on which pathology and cell biology depends. We also depend on the germ theory of disease, which evolved in the same period. These ideas penetrated the United States slowly until, after the Civil War, many young physicians left the United States to study in French and German universities and brought them back.

The Newsletter has done a series of vignettes on important pathologists, including the early Chairs of our Department. The even earlier Chairs of Anatomy, whose history we share, are covered by Mike Gershon in the next article. Alonzo Clark (1847-1883) was the first Pathology Professor of whom we have much knowledge. His career spanned a revolution in medicine including the germ theory of disease and major advances in histology and microscopy, but he is not much remembered. He probably did not have a large department – perhaps only an assistant, according to our archivist Steve Novak. Yet the next Chairs, Francis Delafield and T. Mitchell Prudden played an enormous role in American medicine and Public Health. Delafield wrote A Manual of Physical Diagnosis and with his student, Prudden, he coauthored A Handbook of Pathological Anatomy and Histology. Both studied in Europe, but Prudden worked with Robert Koch and brought the science of bacteriology - and the germ theory of disease - to New York.

Prudden was appointed special assistant in Pathology at P&S in 1878. It was the first full time appointment in Pathology in the country. He later reminisced: *Finally there appeared on the horizon in this country a few anomalous individuals who cherished the notion that the science of disease, even in its etiological and morphological aspects alone, was broad and deep enough to command the exclusive attention of its devotees.*

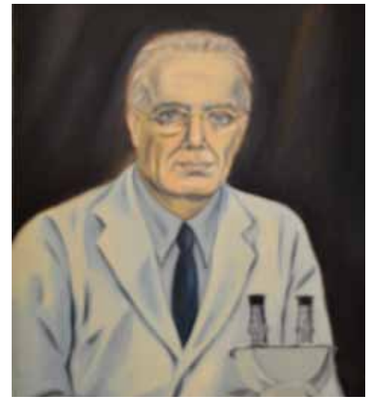
In 1885, at P&S, Prudden taught the first American course in bacteriology, funded by the P&S Club. He had a leading role in introducing the germ theory of disease to New York and the United States. In 1894 Prudden was attending a medical conference in Budapest when he learned that horse antisera against diphtheria toxin could arrest the course of diphtheria in children. He wired to New York asking his colleagues to buy horses and start to make diphtheria and tetanus vaccines. To get them used, he, Herman Biggs and others started the New York Board of Health. He wrote many books on pathology and bacteriology, some with Delafield. It was Prudden, who gave a start, in 1906, to Surgical Pathology, which has figured so heavily in the Department's history. His biography, available on the web, is worth reading. He retired in 1909 and a portrait, currently hanging outside Alumni auditorium, was commissioned by his students and colleagues.

The College of Physicians and Surgeons allied with the Presbyterian Hospital in 1910, but were not in the same location. The College was near the present Roosevelt Hospital and the medical school was across town so pathologists had to travel back and forth. It was not until 1928 that the present campus was built. By that time, another important event had occurred – the arrival of women, including the extraordinary Dr. Virginia Kneeland Frantz, as elegantly described by Heidi Rotterdam later in this booklet.

During the interwar and postwar periods, perhaps the most important figure was Arthur Purdy Stout, one of the founders of surgical pathology. A previous history written by Dr. Raffael Lattes and also published in 1997 contains much information on Dr. Stout and others from that period. Dr Stout's autobiography, published in 1997, describes Pathology in the 1930's and 40's and his personal experiences-particularly a haunting trip through Nazi Germany.

Dr. Karl Perzin discusses the period from 1955 to 1987, including Doctors Nathan Lane, John Fenoglio and Raffaele Lattes. This is a story that is too long for the current publication, but one that will be continued on our Website, with a new page dedicated to the history of Pathology and the role of our Department in it. The Lattes history will appear there as well. There are many gaps left here, which the Newsletter will try to fill in future issues.

Finally, it is important to note that Pathology was practiced in a number of clinical departments and it was not until 1960 that it was unified when Donald McKay became Chairman. The Department became an excellent clinical provider, but did not support much basic research, until 25 years ago, when the power of cell biology and neuroscience arrived in force, as described by the authors included below.



A painting of Dr. Lattes by current Pathology professor Jay Lefkowitch done in the 1970's

History of Anatomy at Columbia from Genesis to Merger

Michael D. Gershon, M.D.

The histories of biology and medicine begin with anatomy. Early humans observed the living machinery with some care because it was necessary for them to do so. Cuisine and faith each required it. Whether animals were butchered for food or sacrifices were made for gods, it was important that practitioners knew, at least in relative terms, what they were doing. The earliest anatomists were diviners who forecast the fates of kings and nations from the shapes of the liver of a ram. That necessitated a working knowledge of the hepatic location, relations, and gross morphology. Mummification in Egypt involved considerable dissection of organs and, as early as 1920 BCE, regulations of what might, with some charity, be called the medical profession appeared in the Code of Hammurabi. All of this activity, however, was driven by a belief in gods, capricious demons, and the supernatural.

Nobody who was anybody seems to have thought that natural events might be significant until Thales of Miletus (624 BCE-546 BCE), the man to whom Bertrand Russell attributes the origin of western philosophy, began to do just that in Ionia (the western coast of what is now Turkey). Thales introduced "rationalism", which proposed the then novel idea of causality, a concept that had not previously colored the reasoning of ancient minds. Under rationalism, events were attributed to a natural cause, whether or not that cause was known or understood; moreover, a particular cause was thought to reproducibly produce the event to which it was linked without change by the intervention of a capricious will. To rationalists, there was a law that governs the universe, but it was a natural law that human minds could ultimately, if not immediately, understand.

Rationalism, after Thales, was quite popular in the ancient world and peaked in then contemporary medicine with the works of Hippocrates about 400 BCE. Because the fame of Hippocrates was so transcendent, many authors, no doubt out of deference to the master signed his name to their work; therefore, whether or not Hippocrates was actually responsible for his oath is not clear. Another man with the same name might have written it. The success of rationalism, however, was transient. Both rationalism as an ideal and observation of anatomical detail were eventually suppressed. Greeks, and later Romans, became more concerned with warfare, conquest, and its moral philosophical rationalizations than with natural philosophy. Anatomical observation was condemned in Judeo-Christian tradition because dissection desecrated the human body, which was, the bible maintains, created in the likeness of G_d. Egyptians agreed, although they thought it was necessary to avoid dissection in order to keep the body fit and trim for life after death.

Rationalism staged a comeback in the seventeenth century, beginning in Flanders, the fields of which became notorious for other reasons in 1914-1918. Andreas Vesalius was born in Brussels in 1514 into a family with a medical tradition. Vesalius acquired an interest in anatomy during the beginning of his medical education in Paris, where he was often observed contemplating bones at the Cemetery of the Innocents. At that time, barber-surgeons conducted dissections, the practice of which had been revived, but lecturers directed the dissections and students watched. The goal of the exercise was not to observe and describe what one saw, but to find what Galen, the ancient Roman, had written should be seen. A problem, unsuspected prior to Vesalius, was that faith in Galen, which was absolute, had been misplaced. Human dissection was forbidden in ancient Rome, so Galen worked and described Barbary apes, which he thought were close enough (perhaps a precocious inkling of the coming of Darwin). Apes, however, are not humans, a difference that Vesalius noticed and thought was significant. When Vesalius did his own dissections, therefore, his observations naturally differed from those of Galen. Vesalius' former teachers became formidable enemies, which was fine in the sense that in order to refute Vesalius, they too had to dissect and observe. It is one thing to read a book (by Galen or anyone else) and ask people to see what does not exist on the grounds that the book claims that it exists; it is yet another to search and find it. The story of Vesalius can be understood as a precocious example of a critical anatomical maxim, as valuable to modern cell biologists as to early anatomists; it is the principle of Yogi Berra, "Never can tell what you might see just by looking". Vesalius' enemies may have been after his scalp, but they went a long way toward validating his work. Unfortunately for Vesalius, however, science in his day was hard. Peers did not conduct peer reviews, but religious and secular authorities conducted reviews. Vesalius was driven to make a pilgrimage to the Holy Land, which led, in 1564, to a shipwreck and his death as a pauper on the island of Zakynthos in the Ionian Sea. The death of Vesalius did not end rational anatomical science because a flowering of microscopy followed it.

Thomas Hooke used the word "cell" in 1665, describing chambers he observed in cork. Anton von Leewenhoek polished lenses of short focal length to get microscopy going and described bacteria and protozoa. These developments were eventually to transform medicine and come to underlie the fields of pathology and cell biology; however, they affected virtually nothing in New York on June 10, 1760 when the first law regulating medicine was passed in this city. On that day, a certain Cadwalder Colden, a physician who was repeatedly elected the Lieutenant Governor of the New York province (colony), pushed through a law that stated that: "No person whatsoever shall practice as a physician or surgeon …before he shall first be examined in physick or surgery and approved of and admitted…" Those legal regulations implied that some form of training and coursework was going to be necessary. Examination, approval, and admission provide a fine rationale for a college, the establishment of which soon followed. The right people were available and Vesalius had set a precedent that traveled across the Atlantic, even to what appeared to European contemporaries as a land that was distant, somewhat strange, and very fierce. New York had recently been engaged with the British and French in their customary activity, war. Colonial physicians were therefore gaining practice in the surgical treatment of wounds; moreover, the absence of sterile technique, sewers, or an adequate supply of clean water in cities provided an endless supply of sick patients. Doctors had to be trained and that meant that anatomy, which was the one form of medical knowledge at the time that was linked to reality, was in demand.

Peter Middleton, M.D., who had been trained at St. Andrews University of Dundee, Scotland teamed with a local doctor, Samuel Bard (of Hall fame) to give anatomical demonstrations and lectures to interested New Yorkers. They used the bodies of convicted and executed murderers that they had injected with dye to enable blood vessels to be visualized. These lectures, which evidently were very popular, were supplemented by clinical training given at the "House of Correction". It is best to keep the morality of that age and not the current age in mind while considering these historical events. One cringes to imagine what constituted clinical training after the French and Indian War and why the House of Correction was deemed a suitable place for it to occur. In any case, while these activities were in full sway, an impressed James Jay, the older brother of John Jay (who was to graduate with a degree in law from New York's King's College and become first Chief Justice of the United States Supreme Court) took it upon himself to medically improve the colony. Jay, who was a physician who had been trained in Edinburgh, went abroad in 1762 to raise funds and lift the profile of King's College. George III took to Jay and made him a knight in 1763, which gave Jay standing to petition the governors of King's college. Jay urged the governors to make King's College a university, which included a college of medicine "…which will add such reputation as will give it preeminence in every respect above every institution in America". This was an appealing suggestion, preeminence being then the same desirable trait that it is today. Jay thought that 5 professors would be needed. Because 5 professors, however, seemed overly expensive, Jay thought that King's College could start with 3. The fields of the new medical school would be anatomy and midwifery, the theory and practice of physick, and chemistry and materia medica. On June 23, 1763 the governors of King's College approved Jay's plan in principle, but stated that the project could not be launched until the funds became available. In an age that predated the NIH, Medicare, and Medicaid, raising funds for teaching and medicine presented a challenge, but it was one that enthusiasm for anatomy helped to solve.

Samuel Clossy, M.D. emigrated to New York City from Dublin in 1763. Clossy had trained in medicine at Trinity College in Dublin and published meticulous works of dissection in which he correlated anatomical findings with disease. The politics of the hospital at Trinity College, however, drove him out of Dublin. He began teaching in New York at King's College soon after his arrival and he very quickly began to give anatomical lectures. He wrote back on August 1, 1764 to a former colleague, George Cleghorn, the anatomist who had taught Clossy back at Trinity College, that "…You would be amazed with what delight…" his lectures were received (this delight has passed on through multiple successors to Paulette Bernd today).

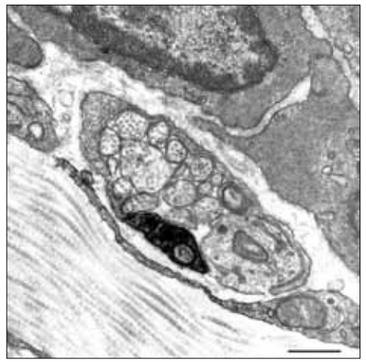
Samuel Bard, MD, one of the founders of King's College

Clossy was appointed a Professor of Natural Philosophy at King's College in 1765 and established a course in anatomy under the official countenance of the President and Board of Governors. This was the very first course in Anatomy given as part of the curriculum of any college in America. Two years after Clossy began to "delight" New Yorkers with his anatomical lectures, King's College was petitioned on August 4, 1767 to launch a real medical school in the winter term. On August 14, 1767 King's College decided to comply and one-upped the penurious James Jay by exuberantly appointing 6 Professors, which kept King's College, at least in respect to faculty numbers, competitive with Edinburgh. Among the stalwart 6 was Professor Samuel Clossy, who held down the chair of Anatomy, joining Peter Middleton in Physiology and Pathology, Samuel Bard in Physick, John Jones in "Chirugery", John Tennant in Midwifery, and James Smith, in "Chymistry", Materia Medica. Peter Middleton gave the opening lecture on Monday, November 2, 1767, with considerably more fanfare than is currently our practice. Students, of course, must have attended, but the New York "Mercury", which may not have noticed them, reported that the Board of Governors, all of the professors, the president of the college, members of the Supreme Court in full robes and regalia, as well as his "Excellency, the Governor, Sir Henry Moore", were all present to hear, and presumably learn, about the history of the "…ancient and present state of medicine". Clossy followed Middleton in the afternoon and introduced the human body. King's was the second medical school to be established in colonial America but it worked quickly; King's was the first school to graduate a medical class, Robert Tucker and Samuel Kissam, which it did in 1769. Robert Tucker went on to receive America's first doctorate in medicine, from King's College in 1770. Transformative events were brewing in New York, however, which would soon end, in 1776, the initial burst of medical energy at King's College.

Samuel Clossy may have come from Dublin,

History of Anatomy at Columbia from Genesis to Merger and Acquisition *continued*

but he was a devoted Tory. His students were something else. Classes became tumultuous as ties with England became tenuous. Controversial wars, like a later one fought by Americans in Vietnam, complicate the calm and concentration needed



Neuronal elements in the gut. This is of a small nerve in the submucosa of the bowel wall, immunostained to show tyrosine hydroxylase. The markers = 500 nm.

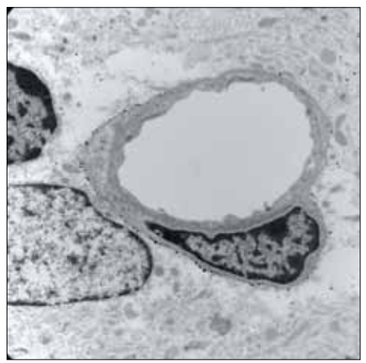
to study academic subjects, like anatomy. Clossy's lectures might once have been greeted with "delight", but with the coming of the Redcoats, he found lectures impossible to present and he was forced to cancel classes while he raged in his diary about radicals (not the Red Sox) descending on his adopted city from Boston. In 1776, the old King's College of medicine suspended activity for the duration as British troops occupied New York. The school re-opened in 1784, now as Columbia College, and in December of that year, classes in the medical school re-started. Samuel Bard was named dean in 1791 but no more was heard, at least in the Columbia context, of Samuel Clossy.

I was the last Professor of Anatomy at Columbia and had no idea that I was to assume that status when I moved to Columbia from Cornell. Moving across town was easy, but that was the only easy part. My immediate predecessor had been fired from his role as Chairman but stayed on as a disgruntled professor. Curricular changes had been imposed on an un-accepting faculty and teaching was not going well in any of the courses assigned to the department. Hours devoted to the teaching of anatomy, histology and neuroanatomy had drastically been curtailed, but the material presented was not. Teachers spoke faster. No one was happy; students blamed the faculty in surveys and the faculty blamed the students, who they thought had lost interest in learning. Research within the department was moribund and anything other than description was suspect. The search committee discovered that replacing an angry leader with a new Chair was not easy; a succession of distinguished candidates came, looked, and left. The department drifted in its discontent but by the time it was my turn to be interviewed, the former Chair had died and the major impediment to rebuilding the department was no longer present. The Chair had become an attractive one. I understood that whatever I did would be a success; virtually anything that changed would have to be for the better, worse was not possible.

The tenured faculty met with me upon my arrival at Columbia and assured me that while they all thought I might be quite stellar, I was the wrong person for this job. Dean Tapley disagreed with this assessment and let me make changes, the most important of which was to introduce Cell Biology to Anatomy at Columbia and to alter the composition of the faculty. New people, both junior and senior were recruited, research began in earnest, grants were obtained, the graduate program was revived and the material taught was made to correspond to the time available to teach it. Faculty and students ceased to be at odds with one another. Joint appointments facilitated collaborations with cell biologists across departmental boundaries, particularly with the new and very different Department of Pathology rebuilt by Michael Shelanski. Cell biology was thriving at Columbia and disciplinary boundaries were blurring.

While the first Professor of Anatomy at the school that was to become Columbia University P&S, Samuel Clossy, went out with the bang of the American Revolution, the last Professor, Michael Gershon, went out without a whisper as the Department that started the school merged out of a free-standing existence. Before the merger, Cell Biology had become integral to Anatomy, which was reflected officially when department's name was changed from Anatomy to Anatomy and Cell Biology. Cell Biology had also been incorporated into Pathology albeit not into the name of that department. The merger thus made sense, two departments with cell biology as a common activity became one, Pathology and Cell Biology. In union, moreover, there is strength. The merger leaves the original vision of Samuel Clossy intact; he searched for the anatomical basis of disease and thus would have been quite comfortable had he been a member of today's Department of Pathology and Cell Biology. The Department's teaching of the tradition of Vesalius can "delight" students today just as Clossy's lectures in that tradition used to delight students in his time. Microscopic research within the newly merged Department produces images that Leewenhoek would have appreciated. Columbia may now lack a department of Anatomy but anatomy is still alive and well at Columbia.

From the Doetsch Lab- the site of stem cells in the brain



Neuronal Stem Cells in the Brain
Immunogold labeling for Aquaporin 4 reveals astrocyte endfeet around blood vessels in the adult subventricular zone neural stem cell niche. Courtesy of Masoud Tavazoie and Fiona Doetsch and Kristy Brown

A Tradition of Teaching Gross Anatomy at The College of Physicians and Surgeons

By Paulette Bernd, PhD

It may seem a little strange that I was asked to write this piece on the past 25 years of Gross Anatomy since I only joined the faculty less than 4 years ago. However, I earned my PhD from Columbia's Department of Anatomy in 1980 and therefore have the perspective of both student and faculty. Let me begin by saying that I received a superb education in Gross Anatomy here and was lucky to be mentored by many of the Gross Anatomy teaching faculty. The course that I took was created by Mel Moss and Ernie April with the intention of stressing the functional and clinical importance of Gross Anatomy rather than minutiae. This approach was revolutionary at the time and transformed Gross Anatomy into a course that was both relevant and exciting for students.

The commitment of the Gross Anatomy faculty to Columbia has been incredible. For example, the current faculty include Ernie April and Phil Brandt, both of whom were my teachers and have taught the course for more than 40 years. Tuan Pham, a relative newcomer to the group, has only taught for 26 years. This dedication is also true of former faculty, such as Rick Ambron, Mel Moss, Chuck Ely and Fritz Agate. All of the Gross Anatomy faculty have been lauded by medical and dental students over the decades, receiving many awards.

My onerous task upon arriving back at Columbia was to create a Gross Anatomy course for the new curriculum that necessitated shortening a 6-month course to a 4-month one. My primary goal was to maintain the functional and clinical focus of the original course but to also emphasize team-based learning both in and out of the dissection lab, as well as modern imaging techniques, the primary way most clinicians see the inside of the body. The renovation of teaching space allows us to conduct small group sessions that are in turn benefited by the recent addition of numerous models.

I have also been able to expand upon the involvement of clinicians in the course as a result of the generous cooperation of many medical school faculty who provide their clinical expertise in the form of correlation lectures and laboratory demonstrations. We are also very fortunate to have three surgeons teaching throughout the course, Warren Widmann, Anette Wu and Mark Erlich. All of these individuals add a clinical perspective to Gross Anatomy that is valued by both students and the Anatomy faculty.

The new Gross Anatomy course has been running for three years and has been well received by students. Columbia can be proud of the anatomical knowledge that our graduates carry forward with them, both now and for the past several decades.

Dr. Paulette Bernd joined the Department of Pathology and Cell Biology in 2008 after a 21-year career at the SUNY Downstate Medical Center, where she was a Distinguished Teaching Professor of Anatomy & Cell Biology. She earned a PhD under the guidance of Dr. Michael Gershon. Paulette then did a postdoctoral fellowship in the laboratory of Dr. Lloyd Greene at NYU. Paulette has won several teaching awards during her career but is particularly proud of the "Golden Scissors" award presented by the P&S Class of 2013, the first to take her new Gross Anatomy course.

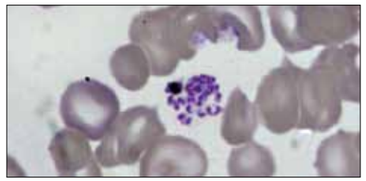
Lowe Library. Photo by Charles Manley

Columbia
The New Millenium

By Alain Borczuk, MD
Vice-Chairman for Anatomic Pathology

It is hard to have a 25 year perspective after only 17 years in pathology with 12 at Columbia. By all descriptions, anatomic pathology went from separate units to a more unified division with a centralized laboratory in the first part of the last 25 years. By 1999, when I joined the department, much of this had already occurred. Some of the major changes since then have included an increase in volume requiring an emphasis on quality assurance. For example, the immunohistochemistry laboratory went from a mixture of manual staining and semi-automation to a high throughput automated service. The continuous barcoding through the laboratory has allowed for an unprecedented ability to track and organize, assuring specimen integrity. The faculty and staff have shown incredible resilience in the face of such major changes.

But the ultimate measure of anatomic pathology progress is diagnostic accuracy. As we strive to improve our diagnoses through continuous education and development of subspecialization, new methodologies have evolved requiring incorporation. Our immunohistochemistry panels are more complex and increasingly likely to resolve difficult cases. We regularly incorporate new technologies to better establish our initial impressions, and it is clear that diagnostic uses of molecular biology will continue to enhance this process. All of this added complexity and a reduction in turn around time – progress indeed!



Diagnosis: malaria

"Next Gen" Columbia Anatomic Pathology

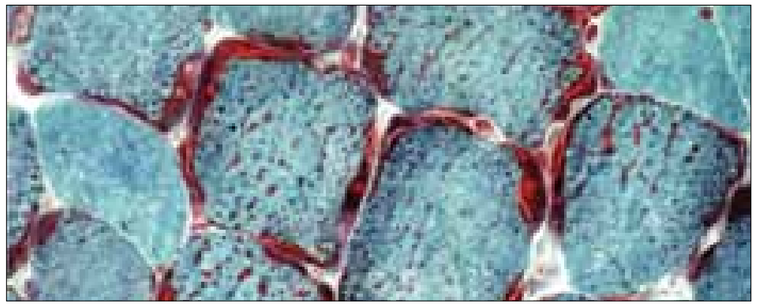
Glen Markowitz, MD, Vice-Chairman for Operations

I came to Columbia University Medical Center as a renal pathology fellow in 1997 and joined the faculty as an Assistant Professor of Clinical Pathology in 1998. It has been an honor and pleasure to be a part of this Department for the past 15 years.

Although it is difficult to summarize the events in Columbia Anatomic Pathology over the past 15 years, the simple theme has been progress. I can remember an antiquated gross room filled with the odor of formalin; we now have excellent fumigation and an expanded, twice renovated facility. I can recall an old residents' room with a dilapidated red leather coach; we now have a wonderful facility for residents, equipped to meet all of their needs. There have been various challenges with respect to staffing and office space, and these have been largely corrected. I can recollect numerous complaints with respect to the autopsy service, and these have all been remedied under the guidance of Doreen Hebert. We have markedly upgraded technology and quality in tissue processing, immunohistochemistry, and in situ hybridization. Quality assurance has emerged as a major focus for our department, and we have invested in the "next gen" of QA, advanced barcode technology.

Rather than becoming a department with pure subspecialty sign out, we have maintained a hybrid environment that appears to best meet the needs of the faculty and residents. While the renal, neuro-, hemato-, gynecologic, and oral pathologists are ensconced in their subspecialties, the majority of the department continues to work as both general pathologists and subspecialists. In my narrow "15 year view", it is hard to imagine that Anatomic Pathology at Columbia existed before the likes of Drs. Perzin, Richart, O'Toole, Lefkowitch, Rotterdam, Goldman, Tanji and D'Agati, to name a few.

Our colleagues speak of next generation ("Next Gen") DNA sequencing; my focus in this entry is on the "Next Gen of pathology" or, more specifically, the pathologists who have begun their careers in our department during these 15 years and benefited from the modern environment. We have recruited excellent young assistant professors, some of whom have risen to full professor. We have watched one of our residents, Dr. Bhagat, similarly ascend. We have others who are on the same trajectory, and a promising group of young assistant professors. During these 15 years, we have watched some of our "Next Gen" of residents and young faculty depart for green pastures, with former colleagues holding faculty positions at Cornell, Mount Sinai, Memorial Sloan Kettering, University of Pittsburgh, Stanford University, University of Michigan, and the Mayo Clinic. The department has created a supportive environment for the "Next Gen", and the "Next Gen" has flourished.



Ragged red fibers in a diagnosis of muscle disease. Courtesy of Kurenai Tanji, MD

Division of Hematopathology, the past 25 years *By Govind Bhagat M.B.B.S*

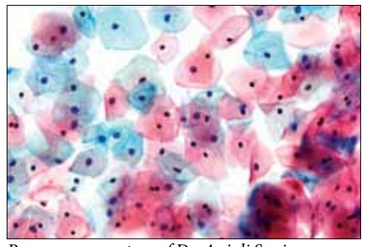
Despite seminal work performed in the Department of Pathology at Columbia University over the last century, leading to the characterization of epithelial and mesenchymal tumors, comprehending the diversity of hematopoietic and lymphoid neoplasms had to wait till the 1980s when the techniques of immunohistochemistry were developed and molecular biologic tools began to be used for diagnostic purposes. The last 25 years have seen major advances in the field of hematopathology, many spearheaded by members of our faculty. Dr. Daniel M. Knowles was an early adopter of immunohistochemical techniques to study the immune architecture of lymphoid tissue by applying reagents developed for flow cytometry to frozen and later formaldehyde fixed tissue specimens. In collaboration with other faculty members, he also characterized ectopic lymphoid tissue developing in states of chronic inflammation. Taking advantage of the diverse and unique types of specimens that come through the Department of Pathology, faculty members of the Division of Hematopathology have made contributions in the field of neoplastic disorders of the hematologic system. Drs. Knowles and Chadburn developed one of the first classification systems for lymphomas arising after solid organ transplantation in the mid 1990s and with the help of Drs. Dalla-Favera and Inghirami characterized molecular lesions associated with lymphomas occurring in HIV infected individuals and also described new lymphoma entities.

Members of the division assisted Drs. Chang and Moore in the discovery of the Kaposi sarcoma associated Herpes virus (KSHV/HHV8) in 1994. Since 1995, the division has been led by Drs. Barbara Osborne, Anne Matsushima, Attilio Orazi, Bachir Alobeid, and Govind Bhagat. Over the past 15 years, the division has grown from a one member operation handling 1200 cases/year to three full time faculty members and a technologist diagnosing over 4000 cases/year. Although a fellowship program in Hematopathology had been in existence for over two decades, formal ACGME accreditation was obtained in July 2000 to train two fellows per year. The fellowship program has grown in stature to be recognized as one of the preeminent training programs, attracting the finest candidates in the country. The hematopathology faculty has contributed to over 200 presentations at national and international meetings and workshops over the past decade and its members have had a prodigious scholastic record, publishing over 150 peer reviewed manuscripts and book chapters over the same time period. Both Drs. Bhagat and Alobeid have been invited to present at state, national, and international meetings. The Division has been an early adopter of new technology. Over the past decade, Southern Blots have given way to PCR-based assays for diagnosing hematologic disorders and next generation sequencing is around the corner. Having access to state of the art laboratories in the Department of Pathology and Cell Biology has allowed integration of information from the immunogenetics, molecular diagnostics, and cancer cytogenetics laboratories, enabling timely and accurate diagnoses and opening avenues for research in the field of hematologic neoplasia.

The Ob/Gyn Division and its Dedication to Women's Diseases

By Ralph Richart, MD, Former Division Director

The Division of Obstetrical & Gynecological Pathology was established in the 1960s as part of a national wave of subspecialty surgical pathology units in major American hospitals and medical schools. Cytology, an up-and-coming discipline, was added to the Division in 1965.



Pap smear, courtesy of Dr. Anjali Saqi

The Division's major academic interests revolved around gynecologic cancer with a special interest in neoplasia of the lower anogenital tract (LGT). The Division was a world leader in the study of LGT disease for 50 years and made major contributions to the understanding of the natural history of LGT, its etiology, its epidemiology, and its clinical management.

The Division was a magnet for attracting fellows and associates from the U.S. and abroad whose presence was a constant joy and whose work and publications led to subsequent careers as division directors in other institutions, chairpersons, and even deans. The level of research was consistently world class and led to the Division's publications of more than 700 peer reviewed articles, not to mention at least ten books, countless contributions to LGT courses, the establishment of specialized treatment modality clinics, and numerous honors bestowed on the faculty by their peers.

The level of science practiced by the Division, the skills and dedication of the faculty and fellows, and the support of the Hospital and the Department of Pathology made the Division a consistently challenging and exciting place to work. It was fun to come in every morning.

None of these Divisional accomplishments would have been possible without the dedication of a smart, hard-working, involved support staff who were an integral part of the team.

The Division has now been merged with others. However, all the faculty, fellows, and staff will have garnered their small place in history and can be proud of their contributions in creating new knowledge and passing it on. We were all privileged to play our part and to make major contributions to improving the health care of women-our ultimate goal.

A Short History of the Renal Pathology Division

By Vivette D'Agati, MD

The Renal Pathology Division of Anatomic Pathology at Columbia University, which was founded in 1973 by Dr. Conrad L. Pirani, actually has its roots in Chicago. Dr. Pirani, a pioneer in nephropathology based at the University of Illinois, had been studying percutaneous renal biopsies since they were introduced as a new diagnostic technique in 1952. He tried to make sense of these small specimens using thin light microscopic sectioning and the application of special stains (such as periodic acid Schiff, trichrome and Jones methenamine silver) to highlight renal basement membranes and immune deposits. Over the next decade, the application of direct immunofluorescence and electron microscopy would become invaluable tools in the diagnostic armamentarium of the renal pathologist.

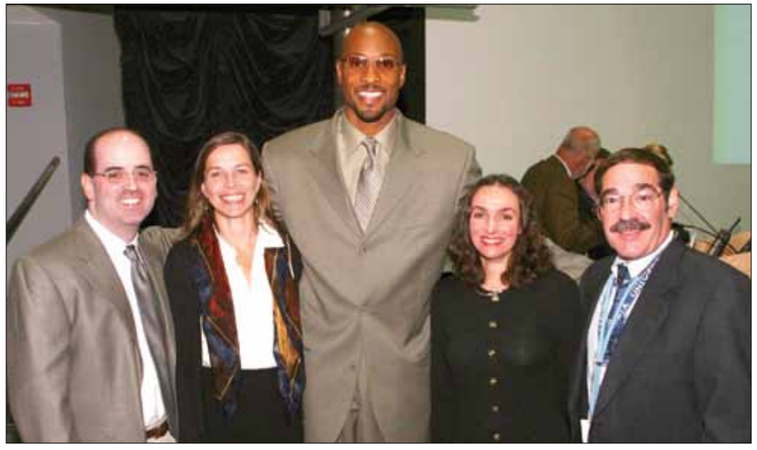
At the time Dr. Pirani was recruited to Columbia University by our former chairman, Donald West King, he was one of the few renal pathologists in the country. Dr. King was a strong advocate of organ-specific sub-specialization within anatomic pathology and aimed to create a center of excellence for medical renal pathology that would be distinct from urologic pathology. (Prior to this time, the urologic pathologist, Dr. Myron Tannenbaum was reading the medical renal biopsies by light microscopy only.) Dr. Pirani once confessed to me that his main impetus to leave the intellectually stimulating environment he had enjoyed at University of Illinois was not the prospect of working at Columbia, but Dr. King's promise that he would have his own personal secretary. In those days before the use of dictaphones or computers, a dedicated secretary was critical to a professor's clinical and academic productivity. So as chance would have it, the future of the renal pathology division of Columbia University would turn on a personal secretary, who in those days was none other than Eileen Erceg.

Dr. Pirani trained many fellows in his tenure at Columbia, including Fred Silva, who would become the executive secretary and director of the United States and Canadian Academy of Pathology. In 1983, as Dr. Silva was about to leave Columbia to become Director of Surgical Pathology at University of Texas Southwestern, I was just completing my Pathology Residency at Columbia. I had already taken an unusual route by doing a year of specialization in renal pathology as a first year resident (which I volunteered for because Dr. Pirani had no fellow that year and my group of incoming residents was large). I did a second year of specialization in 1983 through a National Kidney Foundation Research Fellowship Grant to study lupus nephritis. As it turned out, I was to be Dr. Pirani's last fellow and succeeded him as Division Director upon his retirement in 1984. I guess you could say I was fortunate to be in the right place at the right time.

When I became division director in 1984, the renal pathology laboratory was located on the 14th floor of the Black Building (Room 1428). Because this large room had been designed as a chemistry lab, much of the space was unusable for our purposes. In fact our histology technician and IF facilities had to be housed in neighboring space (Room 14-503), which was an inefficient way to work. One of the first things Dr. Shelanski did upon becoming chair in 1987 was to relocate the lab to VC-14 in order to centralize the diagnostic divisions and provide more bench space for the

Visiting Italian nephrologist Dr. Belgioioso, and Vivette D'Agati (renal fellow) in 1984 (in the original renal pathology laboratory BB1428).

basic scientists he was recruiting. This was convenient for me because I was also signing out in Surgical Pathology in those early days. In 1987, the renal pathology laboratory moved to a small portion of the space now occupied by the surgical pathology secretaries, followed by a brief sojourn of nearly 2 years on the 16th floor in Ob-Gyn pathology while the current laboratory in VC14-224 was under construction. The new laboratory was completed in 1996, at which time I was the sole renal pathologist handling a case load of approximately 750 biopsies per year (3-fold more biopsies than in Dr. Pirani's time but without a renal secretary!). We had only 2 very energetic and dedicated technicians at that time: Llewellyn ("Tony") Ward performed light microscopy and immunofluorescence, while Hildegard Gutwil did the embedding and grid preparation for



The legendary basketball player Alonzo Mourning received a kidney transplant and has graciously helped our department. From left: Glen Markowitz, Agnes Fogo (Vanderbilt University), Vivette D'Agati and Gerald Appel.

electron microscopy. All EM scoping was performed by the pathologist. In the days before digital imaging systems, it could take hours to scope a single case because the negatives had to be developed by hand, the plates reloaded and the vacuum re-established multiple times in a day. As the size of the laboratory grew, all this was to change rapidly in the years to follow.

The laboratory now has 5 full-time dedicated renal pathologists, with the additions of Dr. Glen Markowitz in 1998, Dr. M. Barry Stokes in 2002, Dr. Samih Nasr in 2005 (who left to join the Mayo Clinic in 2009), Dr. Leal Herlitz in 2009 and Dr. Eric Campenot in 2011. Drs. Markowitz, Nasr and Herlitz received renal pathology fellowship training at Columbia; Dr. Stokes did his fellowship at University of Washington and was an attending at New York University before joining Columbia, while Dr. Campenot was trained in nephropathology at the University of North Carolina, Chapel Hill. In addition to a secretary, Rozanne Xavier, and 2 transcriptionists, Robin Miller and Ava Scanlon, the laboratory staff includes 8 technicians skilled in the processing of renal biopsies by light, immunofluorescence and electron microscopy. Much of the technical work continues to be done by hand, with minimal automation, ensuring maximal quality control.

The laboratory now receives approximately 3700 renal biopsies per year, including native and allograft biopsies, of which approximately 800 originate within Columbia Presbyterian Medical Center and 2900 are sent as wet tissue from over 400 nephrologists at academic and community-based medical centers within 12 states (spanning a broad geographic base that extends from Rhode Island to Florida, and as far west as Indiana). Because most of our material comes from outside the medical center, we report our findings by telephone to the referring nephrologist, at which time we provide clinical-pathologic correlations and discuss treatment options. This personal approach defines the style of our practice, which is one of the largest in the country. Our biopsy database provides a valuable resource for fellowship training, clinical-pathologic studies and basic research using archival human renal tissue.

Drs. Conrad Pirani and Fred Silva signing out renal biopsies circa 1976

Major areas of research include pathogenesis of focal segmental glomerulosclerosis, HIV-associated nephropathy, lupus nephritis and drug toxicities. NIH-funded research is directed to mechanisms of podocyte injury and glomerulosclerosis in focal segmental glomerulosclerosis and HIV-associated nephropathy as well as the identification of new biomarkers in chronic kidney disease (CKD). The Columbia Renal Pathology Division has hosted several important international consensus conferences on the classification of renal diseases, including the first working group classification of focal segmental glomerulosclerosis and a revision of the WHO classification of lupus nephritis.

The Renal Pathology Division runs an annual postgraduate course "Renal Biopsy in Medical Diseases of the Kidney", which is now in its 35th year. The 4-day course, which is given jointly with the Division of Nephrology, provides a comprehensive update of major diagnostic entities in nephropathology, with emphasis on clinical correlations and pathogenesis. The longest running CME course at Columbia University Medical Center, it is attended annually by approximately 250 registrants from over 30 countries.

The Division hosts a weekly in-house renal biopsy conference, which has been ranked by the nephrology fellows as their most valuable teaching conference in the medical center. The tradition of the weekly clinical-pathologic conference was instituted by Dr. Pirani in the 1970's and has followed in a similar format to this day (even as Powerpoint has replaced the old Kodachrome projectors). Drs. Markowitz, Stokes and Herlitz also provide continuing education to the many referring nephrologists throughout the tri-state area through regional renal biopsy conferences. Committed to advancing education in the field, the Columbia renal pathologists are invited regularly to lecture at annual meetings of the American Society of Nephrology (ASN), the United States and Canadian Academy of Pathology (USCAP), and the World Congress of Nephrology, among others.

Dr. Shelanski has guided the renal pathology laboratory into the modern age of molecular pathology while preserving the legacy of specialized clinical-pathologic diagnosis using the traditional (but updated) tools that Dr. Pirani introduced nearly 4 decades earlier. He has appreciated the particular demands of practicing medical, as opposed to surgical, pathology and has supported the laboratory's continued specialization and growth to become one of the largest and most influential laboratories of its type in the country.

A Transformative Quarter Century for Surgical Pathology

By Kathleen O'Toole, MD

When I began reflecting on the last 25 years, I was dumbfounded by all the changes that had occurred. For those of us who were around back then, the changes were gradual. However, the cumulative changes have been so profound that the Division of Surgical Pathology has undergone a complete transformation in a relatively short time.

By far the most obvious change is in the number of specimens processed. In 1987, there were 15,488 cases accessioned in Surgical Pathology; in 2011, that number totaled 33,647. This dramatic increase reflects not only the absorption into Surgical Pathology of all cardiac and pediatric surgical specimens, but also the striking increase in the number of hospital procedures. Whether performed in operating rooms or in endoscopy, cystoscopy, mammography, cardiac catheterization or interventional radiology suites, procedures generally generate tissue specimens.

It's even more complicated because the number of cases accessioned doesn't convey the actual number of specimens we are dealing with. Back then, a prostate biopsy consisted of one or at most two containers. Today, the typical prostate biopsy includes twelve containers, each containing one or more cores from a uniquely designated site. This counts as one case, but in reality, there are twelve different biopsies, each of which must be evaluated and reported on. Similarly, back then breast cancer was treated with mastectomy or sometimes lumpectomy. Now, we will frequently receive a lumpectomy accompanied by one or several sentinel node biopsies and six additional margin resections. Again, one case, but infinitely more complicated, requiring additional labor in the gross room and histology lab, not to mention the pathologists' time spent signing out.

While we do see some simple, straightforward cases, we have a very high percentage of large and extremely complex cases reflecting the hospital's role as a quaternary care referral center. At the opposite end of the spectrum, we are seeing increasing numbers of fine needle biopsies not much thicker than thread. These biopsies usually represent an attempt to diagnose a deeply situated tumor using a minimally invasive approach. The irony is that these tiny specimens often require an extensive panel of immunohistochemical stains for accurate diagnosis, and it's not uncommon that we run out of material.

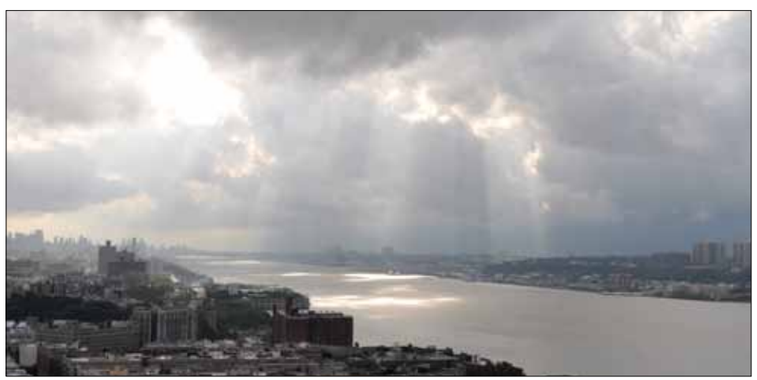
Other changes have come about largely because of the ever increasing role played by various regulatory bodies. Back in 1987, the only manuals we had included binders containing recipes for the stains used in histology, instruction manuals that accompanied our equipment, and crude diagrams in the gross room illustrating how tissue sections were to be labeled. In preparation for our first CAP inspection in 1995, we had to create highly detailed procedure manuals for each of the functional units in the division. Those manuals must be constantly updated by our lab supervisors as they are the primary focus of any lab inspection. Also because of increased regulations and government mandates, our reports have become highly standardized. Particularly for cancer cases, there are numerous items that must be included for a report to be considered an acceptable one. The quality of our reports is a key factor in determining the hospital's eligibility for various accreditations including that of the JCAHO.

Regulatory activity has also impacted our turnaround time. In the old days, biopsies were generally reviewed and signed out the next day. Big resections, on the other hand, were often left fixing in the gross room for days until the resident found time to submit sections, and no one got too upset. Now, all specimens are on a fairly rigid timetable whereby all but a small subset of diagnostically difficult cases are completed within three working days of their arrival in the division.

Finally, the financial aspects of the division have undergone a sea change since 1987. Back then, we were completely dependent on the hospital for all revenue, a fact that was reflected in our salaries. We had a primitive system whereby specimens were classified into four categories: small or large, and inpatient or outpatient. The triplicate copy of the requisition slip was stamped with the appropriate category, and those were sent to the hospital to be processed for eventual payment to the Pathology department. Beginning around 1990 with the creation of an incorporated practice plan, the revenue began increasing.

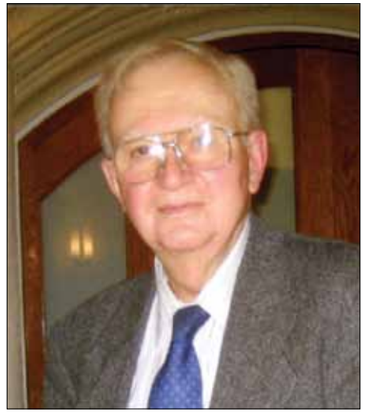
These are just a few of the many changes that have taken place, but they're the ones I consider most significant. For me and probably for others of my vintage, the Surgical Pathology of today is a totally different entity as compared to what it was 25 years ago. People who have only recently joined us have no idea how far we've come. This positive trajectory will surely continue.

Kathleen O'Toole began her residency in Anatomic Pathology at Columbia in 1978. Except for a 10 month fling with community hospital pathology in 1989, she's been here ever since.



The view looking south from the medical center. Photo by Richard Miller

Dr. Karl Perzin's History of the Department is an extensive work in progress. Here we present the first few paragraphs. Details of the years that followed these will appear on the Pathology and Cell Biology Website for which we are planning a new History Section and then a publication. Dr. Perzin's many years of teaching have been recognized by the Perzin Teaching Award, given to Attendings for their efforts in teaching Residents.



In this essay, I describe some of the major events that occurred during the years 1955-1987, before Dr. Shelanski became chairman. In speaking with various current members of our Department, I have found that most are unaware of these events. I will concentrate on the structure of Pathology services, especially on the major reorganization that occurred in 1960. I will also describe the changes that have occurred in the teaching of Surgical Pathology to our medical students. I also reminisce about several individuals I knew during this period, including Drs. Virginia Kneeland Frantz, Arthur Purdy Stout, Raffaele Lattes, Nathan Lane, and Donald West King.

I first came to the Medical Center in September, 1954 as a first year medical student. My first encounter with the Pathology Department was in September, 1955. On the first laboratory day, the Chairman of the Pathology Department, Dr. H. P. Smith, told us that we had to buy coloring pencils, smudge sticks, and an unlined notebook, into which we were to make, in each lab session, a drawing of something we examined from one of our slides. The drawings were part of our final grade. Many students were offended (imagine – a coloring book in medical school!) but, in retrospect, those exercises helped us to critically examine what we were supposed to be seeing through the microscope.

My first encounter with the Division of Surgical Pathology was in the spring of the second year (1956), in a course called "Introduction to Surgery", in which we were taught about granulation tissue and the principles of wound healing. At that time, the Division of Surgical Pathology was part of the Department of Surgery and my instructor in the lab was Dr. Virginia Kneeland Frantz, a Professor of Surgery.

At P&S, the third year was a full 12 month year, without vacations. (Three months Medicine, three months Surgery, divided between General Surgery and Surgical Subspecialties, three months divided between Neurology and Psychiatry, and three months divided between Pediatrics and Ob-Gyn). During the six week General Surgery rotation, students came to the Surgical Pathology Laboratory twice a week. There was a classroom where the Pathology Residents Room is now, with the blackboard wall facing the Humphreys Auditorium, and with five rows of benches containing cabinets in which we locked our microscopes. Each of us was given a box of glass study slides. I remember being given a metal tray containing a formalin fixed gall bladder to examine. My instructor in the lab again was Dr. Virginia Kneeland Frantz.

In the third year, in addition to the Laboratory, there was a Surgical Pathology lecture course, which was given every Saturday morning, starting in September and lasting until March. The setting was the Humphrey's Auditorium, which was twice the size it is now, room enough for the entire class. The first part of each lecture consisted of a discussion of an entity by a surgeon, followed by a presentation of the pathologic findings by a Surgical Pathologist. One example was Crohn's Disease with the surgeon Dr. Frank Gump, discussing its clinical aspect, and Dr. Raffaele Lattes describing the pathologic features. The Surgical Pathology discussors were Drs. Frantz, Lattes, Lane, and Ozzello. This course was ended in the late 1960's. During the student rebellion years of that time, almost all Saturday teaching functions were terminated.

When the Columbia Presbyterian Medical Center was established in 1928, each Hospital or Division had its own pathologist. The Medical School had a Pathology Department. These pathologists did autopsies, taught the second year pathology course, conducted research, and participated in various conferences, such as the CPC (the clinico-pathologic conference, which was a major weekly event for many years). The Pathologist at Babies Hospital was Dr. Dorothy Anderson, who, I was told, first showed that Celiac Disease and Cystic Fibrosis were different entities. The Pathologist at the Neurologic Institute was Dr. Abner Wolff; at the New York Orthopedic Hospital was Dr. Zent Garber, at the Squire Urologic Clinic was Dr. Meyer Melicow, at the Sloan Hospital for Women was Dr. Engler, and at the Eye Institute was Dr. Reese. Surgical specimens removed by Surgeons in General Surgery (and ENT) were studied by the Pathologists in the Division of Surgical Pathology, which was part of the Department of Surgery. In the late 1950's, when I was a medical student, the Surgical Pathologists were Dr. Frantz, Dr. Lattes, and Dr. Lane. Dr. Arthur Purdy Stout had retired in about 1950, at the mandatory retirement age of 65, but he continued to act as consulting Pathologist until 1968, when he died at age 83.

I graduated from P&S in June 1958, and returned in July, 1961. While I was gone, Dr. H. P. Smith had retired as Chairman of the Pathology Department. Dr. Donald McKay was recruited from Boston to be the new Chairman, but he only came with the proviso that all the various Pathology Laboratories be unified into the Pathology Department. The merger of the various laboratories resulted in a unified Pathology Training program. As far as I can remember, Dermatopathology and Eye Pathology remained separate entities. These changes were crucial to the Department we know today.

The remainder of Dr. Perzin's recollections will appear on the Website and in other forms.

A Treatment for Rh disease

By Eldad Hod, MD

Rh disease, a form of hemolytic disease of the fetus and newborn, used to claim the lives of approximately 10,000 babies annually in the United States alone. However, it was virtually eradicated in the 1960's thanks to the efforts of Drs. Vincent Freda and John Gorman at Columbia Presbyterian Hospital. Dr. Freda, an obstetrician, and Dr. Gorman, who completed his residency training in Anatomic and Clinical Pathology at Columbia in 1960 and who was the Blood Bank Director at Columbia, were awarded the Albert Lasker Award for Clinical Medical Research in 1980 for their role in virtually eliminating this devastating disease.

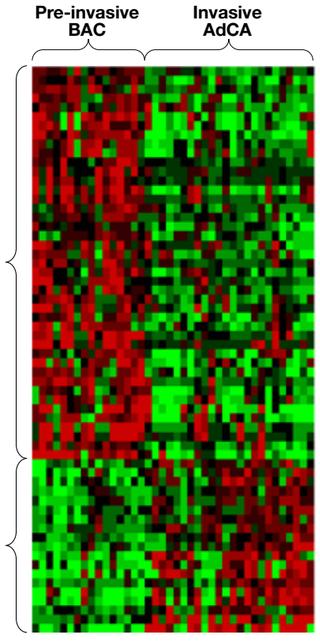
Rh disease results from a blood group incompatibility between the mother and paternally-inherited antigens on fetal red blood cells. Although it can be caused by antigens other than the Rh(D) antigen, this was the most common cause at the time; this would still be true today had it not been for Freda and Gorman's invention of Rh-immune globulin treatment. Historically, an Rh-negative mother (i.e., the mother does not express the Rh(D)-antigen on her red blood cells) becomes immunized to the Rh(D)-antigen during pregnancy when Rh(D)-positive fetal red blood cells cross the placenta into the maternal circulation. During subsequent pregnancies, maternal IgG anti-Rh(D) antibodies can cross the placenta into the fetal circulation and destroy the red blood cells of an Rh(D)-positive fetus. This red blood cell destruction (i.e., hemolysis) can produce hydrops fetalis (i.e., heart failure due to the severe hemolytic anemia). In addition, hemolysis leads to production of bilirubin in the fetus as a by-product of hemoglobin degradation. After delivery, bilirubin is no longer cleared by the placenta and can accumulate in the newborn, which can cause permanent brain damage (i.e., kernicterus).

Although NIH Study Sections failed to fund the project on two separate occasions, commenting that their idea was "nonsense and

Eldad Hod and Steven Spitalnik studiy the stability of red blood cells. Dr. Spitalnik is Vice Chair and the Director of the Clinical Pathology Division.

will never work," Drs. Freda and Gorman persisted in their research. In a landmark study published in Science in 1966, they showed that passive immunization of pregnant women, by injection of exogenous antibodies to Rh(D) (i.e., Rh-immune globulin), within 72 hours of delivery successfully prevented active maternal immunization to Rh(D). This led to the current standard of practice of providing pregnant Rh-negative women with Rh-immune globulin injections twice during pregnancy and also at delivery. This treatment effectively prevents women from making anti-Rh(D) antibodies in virtually every case, thereby preventing Rh disease. The most fascinating aspect of the story scientifically is that we still do not have a complete, mechanistic understanding of how this therapy works. The original hypothesis that Rh-immune globulin functions by clearing fetal Rh(D)-positive red blood cells from the maternal circulation, thereby hiding this foreign antigen from the maternal immune system, is inconsistent with the fact that passive immunization with Rh-immune globulin guides the fetal red blood cells directly to antigen presenting cells, the same cells responsible for initiating an immune response to foreign antigens. Thus, the story is much more complex than initially thought. In addition, perhaps because of this lack of mechanistic understanding, the use of Rh-immune globulin remains the only antigen-specific "immunosuppressive" therapy currently approved for use in humans. Investigation into the mechanisms underlying immunization to red blood cell antigens and immune-mediated hemolytic reactions continues in the Department of Pathology & Cell Biology at Columbia University Medical Center; the additional insights gained may allow this type of immunomodulatory therapy to be used in other clinical settings.

Typing Lung Cancers



Microarray technology reveals genes that are up-regulated (in red) and down regulated (in green) for pre-invasive bronchioloalveolar carcinoma (on the left) and invasive mixed subtype adenocarcinoma (on the right). Each column is an individual tumor. Squares across represent individual genes expressed in one tumor type relative to the other.

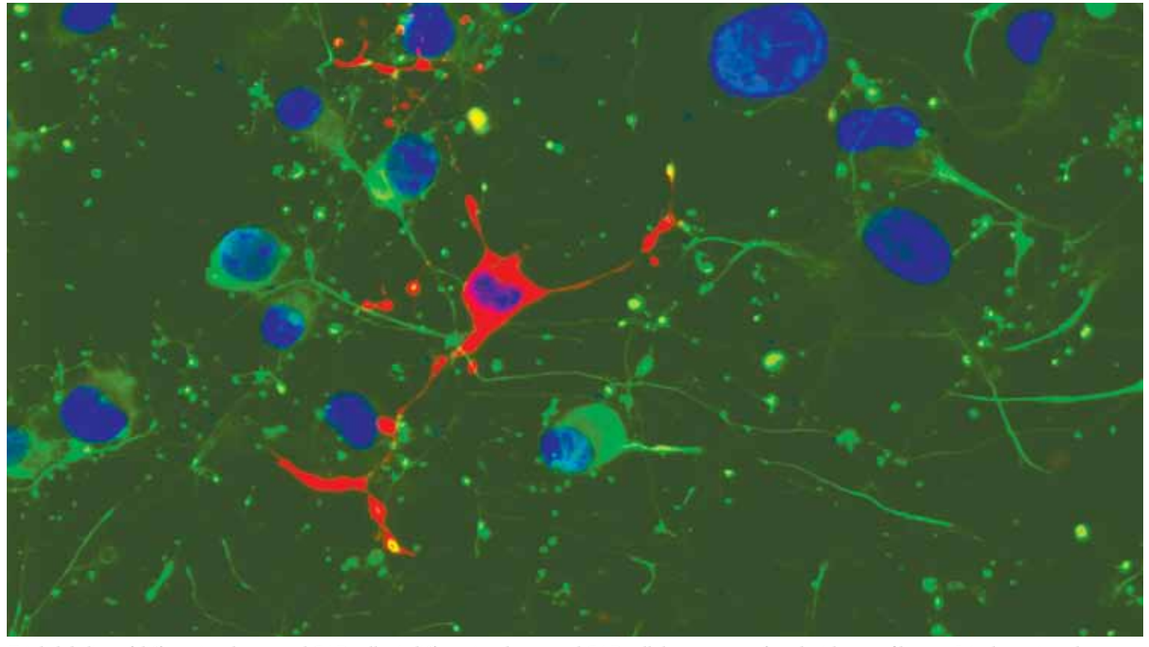
Courtesy of Alain Borczuk, MD

By Richard Baer, PhD

The Institute for Cancer Genetics (ICG) was established in 1999 from a nucleus of cancer researchers in the Department of Pathology. The goal of the ICG was to elucidate the biological processes that cause human cancer, and translate these discoveries into new strategies for improved prevention, diagnosis, and therapy. To achieve these aims, Dr. Riccardo Dalla-Favera, the founding ICG Director, assembled a strong group of investigators who would pursue independent cancer-related research programs while exploiting a shared organizational and cultural framework. With the early support and encouragement of Dr. Shelanski, the initial ICG laboratories were comprised entirely of faculty from the Department of Pathology, including Drs. Benjamin Tycko, Ramon Parsons, Wei Gu, and Richard Baer. The ICG originally occupied space in the Russ-Berrie Pavilion (1999-2005), before moving to the Irving Cancer Research Building in 2005. With the recruitment of key investigators (Antonio Iavarone, Anna Lasorella, Adolfo Ferrando, Jean Gautier, Jose Silva, Shan Zha, and Bin Zheng), the scope of ICG research now encompasses many of the critical areas of human oncology and represents the largest concentration of cancer-related science at Columbia University. One simple measure of this expansion is the level of funding from peer-reviewed grants for research and training, which has increased from ~$1.5 million in 1999 to over $10.0 million in 2012 (annual direct costs). As most of its current faculty still enjoy primary appointments in the Department of Pathology & Cell Biology, the ICG maintains close ties to its origins after thirteen years of growth.

Those were the days my friend. Riccardo Dalla-Favera studies a sequencing gel, back in the day.

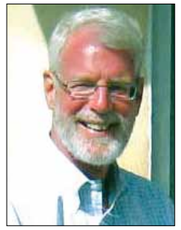
Neuronal Cells in Tissue Culture



Triple labeling of differentiated neuronal CAD cells. A differentiated neuronal CAD cell that was transfected with neurofilament L is shown in red. The endogenous expression of the neuronal intermediate filament alpha-internexin is labelled in green. Nuclei are labelled in blue. Courtesy of Dr. Ron Liem

The Residency Training Program

By Charles Marboe, MD



The Department of Pathology has a long history of training men and women for careers in the clinical practice of pathology and laboratory medicine and for leadership roles in diagnostic, academic, and research pathology. The training programs have flourished with the support and guidance of Mike Shelanski in his tenure as Chair. The ACGME- accredited program has 21 positions in Anatomic and Clinical Pathology as well as ACGME-accredited fellowship programs in Hematopathology, Molecular Genetic Pathology, and Neurpathology as well as Assistant Attending Pathologist "Fellowships" in Surgical Pathology and GI/liver pathology.

Graduating residents are now in positions spanning the country, from Brigham & Womens Hospital in Boston, to the Hospital of the University of Pennsylvania, the University of Pittsburgh, East Carolina University, the University of Florida, the University of Miami, the USAF in Biloxi, Mississippi, M.D. Anderson Cancer in Houston, the Mayo Clinic in Rochester, Cleveland Clinic, University of Wisconsin, University of Michigan, UCLA, Cedars Sinai, and UCSF in California, Fred Hutchinson in Seattle, University of Colorado, and the University of Utah, among others. Many graduates are in the greater New York area including New Jersey.

The department has also heartily populated other departments of pathology in New York City, including Cornell (Drs. Knowles (chairman), Cesarman, Pirog, Renwick, Shaknovich, Shevchuk). At Mt. Sinai we have Dr. Singh, vice chair for CP and Dr. Thaker, vice chair for AP, as well as Dr. Foitl and Dr. Pessin-Minsley. At NYU we have Drs. Barisoni, Littman, O'Neill, Simsir, Singh. Our beloved colleague Dr. Yee past away last year. Our graduates are also at Memorial Sloan Kettering Cancer Center, Downstate Medical Center, Albert Einstein, Winthrop-University Hospital, Long Island Jewish Medical Center, and St. Luke's-Roosevelt.

Among graduates of the program since 2004, 66% are in academic faculty positions.

For graduates of 2004 through 2011, the department has the gratifying, and we believe unique, experience of 100% first time pass on the certifying examinations in anatomic pathology, clinical pathology, neuropathology, and hematopathology of the American Board of Pathology.

Today is Better!

The new One World Trade Center, now visible from the Medical Center

The Residency Training Program

Sneaking Up on Pathology *Patricia Raciti, MD*

In spite of being raised by a pathologist mother and surgeon father, I lacked a focused curiosity for science and biology. Instead my interests wandered, first to history and literature and then finance and consulting, before they were finally piqued by medicine. It was only after I opened the pages of Robbins and Cotran's Pathologic Basis of Disease that I became mesmerized by Pathology. Suddenly I needed to learn more about one half of my "family business."

Having taken the last several years to understand pathology in more detail, I retroactively appreciated three "keys to success" my mother displayed: she approaches her interactions with other pathologists and clinicians with humility; she has genuine curiosity about every case that comes across her scope; and finally, she is constantly aware that there is a patient behind every slide and test tube.

As my first year of combined AP-CP residency draws to a close at Columbia-Presbyterian, one aspect of the Pathology Department I have witnessed and appreciate is the parallel between the culture of our department and my mother's "keys to success."

The hallmark of the department is unquestionably teamwork. As a junior resident, I have seen this characteristic displayed most evidently in the time and care senior residents take to help newcomers navigate the environment. And, after a year here, I can see a culture of teamwork that pervades all levels in both Anatomic and Clinical Pathology. There is a mutual understanding that problems are best solved as a team and that ego must be subordinated in order to deliver the best patient care.

The goal of Pathology is often to give an accurate, definitive diagnosis, yet at Columbia there is a tremendous amount of discussion, thought and analysis dedicated to seemingly straightforward cases. It is through this curiosity, open-mindedness and commitment to correct diagnosis in every case that observations are noted, patterns are noticed and critical discoveries are made. As a first year resident, I have sought to categorize cases, clinging to what I know. Over and over, I have been challenged to accept cases that sit uncomfortably in a "gray zone" and to view these cases as opportunities to advance my knowledge and knowledge in the field.

Pathologists are by their nature imaginative. Where others see a flat pink and blue image, we see a range of colors from gray to purple and sometimes, three-dimensionality. This imagination serves us well – it helps us imagine our patient standing before us when only their cells are present. At Columbia, I have found this imagination, resulting in patient care, underlies the care given to every aspect of work in the department, whether grossing an organ, viewing a slide, performing an autopsy or signing out a molecular test.

As the Department celebrates its achievements over the last 25 years and its basic science discoveries continue to drive our understanding of medicine, I am proud to be part of a Department that emphasizes a collective, collaborative approach in diagnosing and treating difficult diseases while maintaining what is fundamentally a patient-centered attitude.

And Representing the Younger Faculty

Andy Teich, MD, PhD

In terms of my perspective as a junior pathologist, I think that one of the strongest themes in my training and early career has been the rapid pace of change in the field. Not just scientifically, although there certainly is that, but also in terms of the shifting landscape of health care, the future role of the government in health care, and how our relationship with other physicians will change as a result of all of this. The pace of change is so rapid that I don't even have any conclusions, other than to simply note that things are changing. On the scientific side, the rise of molecular diagnostic testing is changing everything, especially in tumor diagnosis. In my own field, every few months another mutation is found in a neurologic neoplasm that has some predictive or therapeutic significance, and the pace of this discovery is increasing. I've heard from older attendings that there used to be fellowships in "immunohistochemistry" when this technique was first available. Of course, now everyone incorporates IHC into their daily routine. I suspect the same will be true of molecular diagnostics in a decade. On the health care side, it's clear that our country can't afford the current health care system as it stands. How will this be resolved? Where will pathology fit into the new order (whatever that will be)? I have no idea. All of these themes together give me the sense of great potential as well as great uncertainty for our field. I suspect that this is always the case in a field when great things are happening. It's exciting; that's for sure.

Pathology *and* Cell Biology

Liza Pon, PhD

Mike Shelanski is well known for his interest in molecular mechanisms of neurodegenerative diseases. However, many in the Department may not know that Mike was the first to purify "a subunit from microtubules" (tubulin) which has colchicine-binding activity. He is also one of the first to identify a role for tubulin and microtubules in neuronal transport, and the first to detect cross-bridges between microtubules and mitochondria in axons. In light of this, it is not surprising that Cell Biology is well-represented in the Department. I am happy to report that Cell Biology continues to flourish, and to describe some recent advances in Cell Biology in the Department.

New mechanisms for intracellular movement: Richard Vallee's lab has worked out the mechanism for the century-old mystery of interkinetic nuclear migration in radial progenitor cells in the developing brain. They have also worked out the complete mechanism explaining how adenovirus recruits cytoplasmic dynein to travel to the nucleus.

Gregg Gundersen's lab discovered TAN lines (for transmembrane actin-dependent nuclear lines), the first structure to be identified in the nuclear envelope since the identification of nuclear pores. TAN lines may transmit force into the nucleus and drives actin-dependent nuclear movement, which leads to centrosome alignment and polarization of migrating cells.

Checkpoint control during cell division: All previously characterized checkpoints monitor inheritance of the nucleus and nuclear DNA. The Pon lab has identified two novel checkpoints that block cell cycle in response to defects in the inheritance of mitochondria and mitochondrial DNA.

Yinghui Mao's lab found that the formin mDia3 can regulate microtubules, independently of its effect on actin. They also identified links between the state of microtubule attachment to mitotic checkpoint signaling at the kinetochore and accurate chromosome segregation.

News from the second brain: Mike Gershon's laboratory identified stem cells of neural crest origin that give rise to enteric neurons in the bowel (see the figure in his article). They also identified dopaminergic neurons in the enteric nervous system, and that enteric neurons produce oxytocin, which acts to oppose stress.

Molecular mechanisms of disease and drug discovery: Ron Liem's laboratory found that pathogenic mutations in a neurofilament gene lead to protein aggregation in cell culture models. They have used these mutations to develop a mouse model for Charcot Marie Tooth Syndrome, the most common inherited neurological disorder.

Howard Worman's lab has elucidated pathogenic mechanisms of diseases caused by mutations in nuclear envelope genes and are developing novel drug treatments for cardiomyopathy caused by mutations in the lamin A/C gene.

Gil Di Paolo's lab identified lipid enzyme Phospholipase D2 as a key factor in Alzheimer's disease-linked synaptic dysfunction and cognitive deficits. They also found that the signaling lipid PI(4,5)P2 is a target for Aβ oligomers, and that trisomy at synaptojamin 1 gene is a key contributor to brain dysfunction in Down Syndrome.

Rick Ambron's laboratory has identified a signaling mechanism that transmits information from sites of nerve injury and inflammation to nociceptive neuronal cell bodies, which in turn leads to long term hyperexcitability, an event that is associated with chronic pain. They have also developed drugs that target this pathway, which may ultimately be used to treat chronic pain without sedation, tolerance or addiction.

With the recruitment of new investigators including Julie Canman, who admits that she is obsessed with cell division and building new microscopes, Ulrich Hengst, who studies intra-axonal mRNA translation, signaling pathways that control growth cones, neurodegenerative disorders and neuronal repair, and Clarissa Waites, who studies the role of ubiquitination in synaptic function, it is clear that Cell Biology will continue to thrive.

Reinventing the PhD Program

By Ron Liem, PhD

When the new Chair and his team arrived at the Department of Pathology in 1987, the Graduate Program had lost accreditation. There was only one NIH grant in the whole department. Part of the problem was that the students in the program were typically not working in laboratories in the Department, had not partaken in any organized curriculum, did not receive stipends, and often even paid tuition, which in excellent PhD programs, is paid by the program. To remedy these defects, we proposed a curriculum of courses in basic cell and molecular biology as well as the mechanisms of human disease, student seminars, laboratory rotations and guaranteed support for the students. We were provisionally approved for accreditation, and admitted our first class in 1988. Since that time we have developed into a vibrant and rigorous graduate program.

Among the graduates from our program are Wei Gu, Professor of Pathology and Cell Biology at Columbia and Geri Kreitzer Associate Professor of Cell Biology at Cornell. Dr. Stefan Pukazki is an Assistant Profressor of Biology at the University of Alberta and works on cholera infection. Chung-Liang Chien is Professor of Anatomy and Associate Dean of Student Affairs and International Affairs, National Taiwan University. Several of our students have won the Weintraub Graduate Student Award at the national level and the Dean's Award at the university level.

The Graduate Programs at Columbia University Medical Center are now consolidated under the Coordinated Doctoral Programs in Biomedical Sciences. Our graduate program is now called the Program in Pathobiology and Molecular Medicine and is part of the Graduate Programs in Molecular Basis of Health and Disease. There are currently 25 students in the Pathobiology and Molecular Medicine Program (average five per class), including MD-PhD students. The number and the quality of applicants have steadily increased over the years. The students have a rigorous curriculum that includes basic science courses in biochemistry, cell and molecular biology and molecular genetics, as well as a one year course in Mechanisms of Human Disease and a course in Histopathology. All students receive serious training in the Responsible Conduct of Research. A number of our students participate in the Med into Grad Program, a Howard Hughes Medical Institute supported program that gives graduate students clinical experience. The directors of the program are Drs. Ron Liem, Steve Spitalnik, Howard Worman and Patrice Spitalnik. The perspective of one of our students, Mike Badgley, appears elsewhere in The Newsletter.

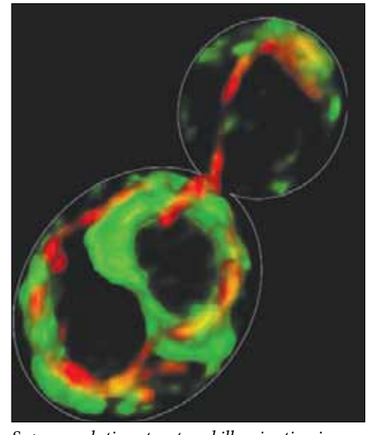
Over the years, our faculty members have participated heavily in several other graduate programs at the Columbia University Medical Center. In addition to the Med into Grad Program, both the Integrated Program in Cellular, Molecular and Biomedical Studies and the MD-PhD programs are run by Drs. Liem and Shelanski. Both programs have long-standing training grants that have just been renewed. The Cell Biology Program is now a subdivision of the Integrated Program, which is directed by myself with the critical assistance of Zaia Sivo, who also administers the Pathobiology Program. The Vision Training Grant and the Cancer Training Grant are directed by Drs. Carol Mason and Richard Baer, respectively. Dr. Mason is also one of the co-directors of the Neurobiology and Behavior graduate program. Faculty in our department have students from many different graduate programs in the Basic Medical Sciences, in addition to students from the Pathobiology and Molecular Medicine Program, the Integrated Program, the Neurobiology and Behavior Program and the MD-PhD Program, and the Pharmacology, Nutrition and Genetics programs.

Our students are the reason we come to work in the morning and, although managing a student's training is often not simple, it is one of the most fulfilling experiences we can have.

The Forbidden Fruit –Cell Biology in the Department of Pathology (1987-2005)

By Lloyd Greene, PhD

It seems that for most of my career I've had Cell Biology envy. Cell Biologists always seem to be the coolest folks around. Maybe this comes from studying the fundamental unit of life. Words like Golgi, centrosome and endoplasmic reticulum effortlessly roll off their tongues. They understand the optics on their fancy microscopes for which the prices go up as the photon numbers go down. Ok, I'm a neurobiologist, but hey, neurons are cells too! Undergraduate Chem major, graduate degree in Chemistry, post-doc in the Heart Lung and Blood Institute (not as bad as it sounds, but not a "Cell Biology" lab either), first job in a Department of Neuropathology. Met a quintessential Cell Biologist along the way who polymerized and depolymerized microtubules at will – and what did he offer? A job in a Department of Pharmacology. Finally the quintessential Cell Biologist decided to take on a new Chair across town and again offered a job. Horror of horrors, it was in a Department of Pathology. The hallways were stacked with those bottles of pickled malformed innards that populate nightmares. I looked out the window from my new office the first week and noticed some guys in white coats across the way in the P&S building hunched over something that fortunately did not and could not rise to view. Were my Cell Biological aspirations about to be sliced up, embedded and warehoused? Ron Liem and Carol Mason also made the ride across town. Somehow they got joint appointments in the *bone fide* Department of Anatomy and Cell Biology. And they didn't even have the where-with-all to be smug about it. It's said that when you're drowning you'll grab at anything to stay afloat. Janus-faced Ron and Carol were a good start. Then there were fellow Pharmacologist-Pathologists-really Cell Biologists Fred Maxfield, Ekkhart Trenkner and Mary Beth Hatten. Flailing about a bit more in the Department one struck neuropathologist cum Cell Biologist Jim Goldman and and then an expanding throng of Cancer (nee Cell) Biologists like Riccardo Dalla-Favera, Ramon Parsons, Jan Kitajewski, Srikumar Chellapan, Antonio Iavarone and Richard Baer. Other bona fides like Chloe Bulinski and Gregg Gundersen reached out to join us. In good time, Richard Vallee came aboard and lent a mighty Cell Biological hand along with recruits Gil Di Paolo and Yingui Mao. So did generations of our offspring including Carol Troy, Ben Tycko, Wei Gu, Darrell Yamashiro, and Peter Canoll. Many more came, left their Cell Biological imprints and then moved on including John Krolewski, Tim McGraw, Paul Fisher, Takaaki Sato, Wilma Friedman, Brett Lauring, Gene Marcantonio, Yuan Chang, and Patrick Moore. And there was always Chairman Quintessential himself. As a result, my long-sought Cell Biological identity not only failed to sink in that dreaded mire of pathology, but was buoyed up and flung onto the fertile ground prepared by this host of co-Departmentists (no unkind thoughts please about the nature of fertilizer – we're talking here about intellectual sustenance). Perhaps there were equal, but there were certainly no better places on this planet to dissect the Biology of Cells, those basic units of living matter. We hadn't the name, but that mountain, *par la force des choses*, would eventually come to us. To the whirring of saws and clanking of microtomes, Chairman Q had forged an Eden of Cell Biology. And not entirely in his own image!



Super-resolution structured illumination image of mitochondria (red) and ER (green) in the budding yeast. See previous article by Lisa Pon.

A Graduate Student's Perspective

Angela Yuanyuan Jia

Why do we make the commitment to a life in science? As any graduate student will tell you, there is a huge cost in terms of labor and perseverance. So why do we do it? Certainly not for the money or lifestyle!

For me, a big part of the answer is this: If we think creatively, if we plan efficiently, and if we execute skillfully at the lab bench ... there will be a few rare moments when we learn something new and surprising that nobody else in the world knows. This is the payoff. There is so much more that we need to do and to learn; that's what draws me to lab every day.

I want to thank my advisor, Dr. Cordon-Cardo, for providing me with a challenging and exciting research problem, and the Department of Pathology for welcoming me into an outstanding research environment. There are a few aspects of the Department of Pathology that I want to highlight as especially important to me. Of particular significance is the commitment to translational research, and by that I mean the use of knowledge from model systems and model organisms to understand the pathogenesis in human disease. Across the department, we have many examples of this approach, and in my personal experience, I have been able to build on the expertise from Dr. Dalla-Favera's lab, whose members have helped with miRNA analysis methodology and to apply this knowledge to understand why some bladder cancer metastasizes aggressively and why some is relatively benign. Similarly important are the large number of faculty members working across multiple disciplines, who serve as teachers and role models. Beyond the bench, weekly student seminars in our program provide an integrated and friendly environment for dialogue and keep us aware of current research spanning various fields. These group discussions have created a close-knit community from which we develop support networks among fellow students and faculty – when experiments fail, as inevitably they do, it is comforting to know that there are half a dozen professors interested and eager to assist.

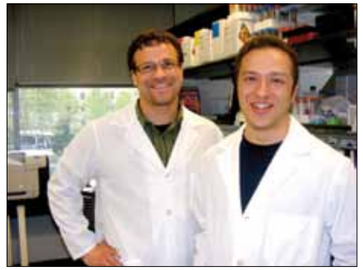
In our department, we are united in the goal of elucidating molecular mechanisms of disease, for the sake of knowledge and ultimately to improve medical care. I am committed to build on the scientific strengths that I have acquired over the last few years. Wherever I go and whatever I do, the experiences from the Department of Pathology will be part of me, and I am grateful.

Angela Jia is a fifth year graduate student. She studies the role of microRNAs in the development of bladder cancer, and additionally serves as the President of the Graduate Student Advisory Council for the entire University.

The Med-into-Grad Program: A Grad Student Tackles Pancreatic Cancer

By Michael Badgley

The desire to carry out scientific research springs from a variety of sources. Some aim to satisfy curiosity regarding the "hows" and "whys" of the natural world. Others may enjoy the prestige and trust offered by a respected profession. Some can find comfort in the scientific method and the systematic unpacking of research questions. And then there are those of us who value not only the elegance of scientific study, but also its profound utility; especially as applied to the management and treatment of human disease.



Michael Badgley (right) and his PhD advisor Ken Olive study pancreatic cancer.

While most researchers likely derive motivations from an amalgamation of these motivations, I have found that the final description is aptly suited to myself and to the other students of the Pathology department. It is rare that a program's mission, faculty, and students complement one another so well in the pursuit of a singular goal: the improved treatment of human disease through the understanding of basic biology. Even rarer still is the graduate program that seeks to buttress this objective through the facilitated interactions of working clinicians, translational researchers, and basic scientists. As this publication shows, this dedication has developed over many decades and I am happy to be a part of it.

Students in the Med-into-Grad Program

Recently, Columbia has begun to support the direct interaction of student researchers and its clinical community in an institutional way. In 2004, the Howard Hughes Medical Institute (HHMI) established a grant-based initiative whose primary goal would be to bridge the so-called bench-bedside gap, and create a new generation of basic researchers who would be not only familiar with the terminology and processes of the clinic, but would also develop an understanding of important scientific questions in modern medicine. This initiative would come to be known as the Med-into-Grad program. Columbia was among the 2010 grant awardees. In a mere two years, Columbia has established a new, clinically focused curriculum for 1st year Pathology students as well as coordinated the pairings of a growing number of Med-into-Grad participants and clinicians to mentor them. The program continues to mature as students maintain contact with their clinical mentors and spend time interacting with patients.

From a more personal perspective, I will say that this nascent program was one of the major draws for me during my application to Columbia. Establishing a working knowledge of basic clinical principles as taught by an expert staff of doctors, research faculty, and my clinical mentor has provided me with a depth of knowledge that will grow and inform my future research. Interacting with like-minded students and finding a laboratory whose work aims to translate directly into clinical use motivates my research. And finally, it bears special noting that in the grind of daily lab experiments, researchers in the biomedical field may forget that human stories populate the landscape of what they consider primarily a research problem to be tackled from the bench. For me, this program and the Department of Pathology and Cell Biology serve as reminders that scientific work becomes all the more critical and satisfying in the context of the human lives. Mike Badgley is a second year graduate student.

By Patrice Spitalnik, MD

The MD-PhD program accepts some of the most exceptional students in the country. The goal is to produce the next generation of leaders in medical research with an emphasis on the qualities of both medical and scientific training. This training will enable our graduates to be innovative at the bench and to play a vital role in the translation of scientific findings to clinical research. The most important ingredients, therefore, are the student and the interactions of the student with his or her mentors, both in medical and in graduate training.

This is easily said and not so easily done. At Columbia we have been able to attract highly able students and our large faculty is involved in a broad range of research and clinical care. MSTP training opportunities are exceptionally broad and include not only the traditional biomedical sciences, but also Chemistry, Bioengineering, Biomedical Informatics and Epidemiology. We encourage interdisciplinary work-one of our students undertook a productive collaboration in bacterial evolution with experts at the Museum of Natural History.

We seek a unique student. Our ideal student will have had an in depth, often multi-year research experience as an undergraduate during which he or she would develop a passion for research and a good idea of the direction in which the work might lead. Objective evidence might include publication and participation in scientific meetings as well as knowledge of the work that extends beyond experimental details and methods.

The MD-PhD curriculum includes 18 months devoted to the basic science courses of the Medical School and to one major graduate school course. This is followed by 3 to 4 years of graduate study, which is supplemented by an ongoing clinical tutorial and by a final 13-14 month "Clinical Year."

The MSTP at Columbia is a close collaboration between faculty and students with the single aim of training outstanding young physician-scientists who will lead to coming generations of biomedical research.

One of the worries about four years of research is that medical skills learned in the first two years of medical school will be lost. We avoid this by a clinical competence training during the research years, in which students learn clinical medicine and see patients one day a month.

Although the Medical Science Training Program that funds the program has been in existence for 37 years, our Department's role dates from 1998, when, with the help of Dr. Ron Liem and Dr. Ira Tabas, we became responsible for its administration. When we became its administrators, there were 70 students in all years and now there are 105. We could not support this number of students without the generous support of the Medical School and Dean Goldman. In the past 15 years, the time to completion has been shortened.

There have been other changes. The integration between medical and graduate schools is now better, partly because we are blessed with a number of accomplished educators and administrators, MDs and PhDs, who watch over students and make sure that all progress on schedule. We do not presume that we have reached perfection, but, with nearly 500 applications a year for 15 places, we are confident that our MSTP program is one of the best in the country.

Cell Biology

An MD-PhD student perspective *by Kimberly Robinson*

Kimberly Robinson and her advisor Gil Di Paolo

Physician scientists are expected to integrate clinically relevant research with proficient patient care. This integration is underscored in the Medical Scientist Training Program at Columbia University administered through the Department of Pathology and Cell Biology. The program, directed by Dr. Michael Shelanski, ultimately aims to prepare the next generation of leaders in medical research. Students matriculate into the College of Physicians & Surgeons and then enter the Graduate School of Arts and Sciences to complete degrees in both schools in 7-8 years. Dr. Shelanski, as well as assistant directors Drs. Ron Liem and Patrice Spitalnik, have structured the training plan to provide a realistic time frame to complete an uncompromised doctoral dissertation. Training at Columbia fosters the interdisciplinary relationships physician scientists sustain throughout their careers to merge clinical responsibilities with research.

Walking onto campus to begin my studies in 2007, I was pleasantly surprised at the diversity and camaraderie I observed in the program. From welcoming my family during orientation and the White Coat Ceremony to stories shared over various tantalizing ethnic foods during MD/PhD Fall and Spring dinners, program administrators have personally made me feel comfortable and valued. As an aspiring researcher, I chose the program to engage in a rigorous clinical curriculum, and I was not disappointed. During the pathophysiology course at P&S, I was fascinated by the knowledge and passion shown by so many faculty members from this department. Many of these individuals practice medicine and do basic research- a combination that I wish to emulate. I later joined the department as a graduate student to enjoy the equally stimulating immersion into the world of translational research that I had sampled during medical school.

As I think about selecting a clinical specialty, I find pathology to be the most interesting and amenable to my research goals. I have observed graduates of the MD/PhD program return to this department after residency to continue their career as faculty; this is likely due to the way the department encourages translational research by establishing provisions for physician scientists to have bench space and time for clinical responsibilities. As a student in this department I have been nurtured, challenged, and endowed with the skills I need. I have no doubt that the faculty, staff, and administrators will continue to provide an excellent training environment for budding physician scientists in years to come.

Kimberly Robinson did her undergraduate degree in biochemistry at Andrews University. She came to Columbia in 2007 and is currently doing her PhD work titled, "The role of phospholipase D1 in trafficking and processing of amyloid precursor protein" with Dr. Gil Di Paolo.

From the Archives: Some Recent Awards

Dr. Michael D. Gershon received the 2008 Masters Award for Sustained Achievement in Digestive Science.

Dr. Joan Witkinwon the coveted Balmfolk Award for teaching excellence.

Dr. Janet Sparrow won the Research to Prevent Blindness Senior Scientist Award.

Women in Pathology

By Heidrun Rotterdam, MD

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 of 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 department 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 most recent chairman, Dr. Michael Shelanski, 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 has been here since.

Oral Pathology

By David J. Zegarelli, D.D.S.

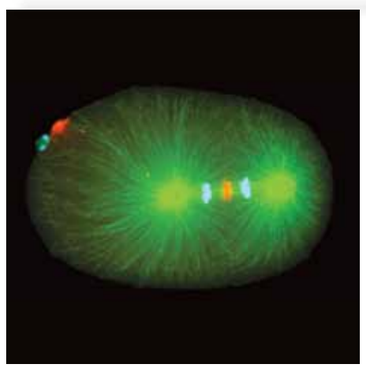
My first recollection of oral pathology begins way back in the 1960s when I was an undergraduate dental student in the College of Dental Medicine of Columbia University. Two part-time professors, later my mentors and friends, Drs. Lester Cahn and Melvin Blake, taught the 48 hour undergraduate course in oral pathology. It was classic clinical – radiographic – microscopic oral pathology. They initiated my interest in oral pathology and during my senior year I chose oral pathology as a specialty. I will not forget Dr. Cahn arriving every Wednesday wearing his Bowler hat and carrying his silver-tipped cane. Dr. Donald King offered me a residency position in general pathology stating that all subspecialties of pathology are based in general pathology. That was enough for me to commence my residency at CUMC on July 1, 1969 – although there were no full time oral pathologists then in this institution.

One year into my residency I learned that 2 of my 3 years had to be spent under the direct auspices of a full time oral pathologist. Consequently, I chose an oral pathology residency program at the College of Dental Medicine of S.U.N.Y. at Buffalo, NY. I shuffled up to Buffalo for 2 years spending an almost equal amount of time between the oral pathology residency at S.U.N.Y.A.B, and, being a resident in general pathology at Roswell Park Memorial Institute. Remembering Dr. King's words – I completed more than 90 autopsies during my 3 year program.

During the Spring of 1972 I was offered 2 full time positions in oral pathology. One, I could be the eighth oral pathologist in Buffalo, or, the first and only full time oral pathologist at CUMC. The choice was a no brainer and I returned to N.Y.C. and Presbyterian Hospital and began teaching, research and patient care activities. The Oral Diagnostic Biopsy Service was established on July 1, 1972 and continues to flourish– having processed more than 150, 000 surgical oral pathology specimens. I worked solo for 18 years and finally a second oral pathologist came aboard – Dr. Carla Pulse – a University of Tennessee graduate with a distinctive southern charm and an astute mind in pathology. She remained for 10 years sharing equal responsibility.

Our laboratory was then separate from the surgical pathology laboratory – and we ran it as a private practice under the auspices of the College of Dental Medicine and the Department of Pathology. For a variety of administrative reasons it became incumbent in the mid 1990s to align the laboratory service into the surgical pathology laboratory and an important event occurred. I broached the subject with Dr. Shelanski and he welcomed the oral pathology practice into surgical pathology. This further cemented the relationship of the dental school with the department of pathology and from my vantage point we appear to work well with one another.

Dr. Pulse left CUMC and moved to Florida. Eventually, we increased our staff through the help of Dr. Shelanski to 3 full time oral pathologists. This faculty increase allowed us to develop a 36 month Oral and Maxillofacial Pathology Residency Program supported by the Department of Hospital Dentistry but centered entirely in the Department of Pathology. This newly established program contributed one of our 3 current full time oral pathologists. Dr. Angela Yoon, our first resident graduate, passed her boards shortly after completing the program and currently serves as an assistant professor. She has been joined by Dr. Elizabeth Philipone, a recent graduate of the LIJ program. Together, we perform teaching, research and patient care activities.



Cell Division. A work of art by Dr. Julie Canman

Facts and Figures

By Joann Li, Department Administrator and Steve Russo, Deputy Department Administrator

In 1987, The Department of Pathology had been without a chairman for a period of over three years. It was housed in 35,000 sq. ft. of antiquated office and laboratory space in the College and Vanderbilt Clinical Buildings. It had 67 full-time faculty members who performed 25,000 surgical diagnoses per year, and its medical residency program accommodated 16 residents. Research grant funding to the department was less than $400,000 per year.

Today, after 25 years, the Department of Pathology & Cell Biology possesses nearly double the space with 63,000 sq. ft. of extensively renovated laboratories and offices across several CUMC buildings. We currently have over 93 full-time faculty (both clinical and basic science), 126 Research Officers, 19 Fellows, 21 Residents, 60 Officers of Administration and 120 SSA Union Employees. In 2011, we processed and reported on over 55,000 surgical specimens, 60,000 cytologies, 239 autopsies, 2,500 consults and nearly 40,000 physician reviews of nearly 6.7M laboratory clinical lab tests. The Department consistently ranks in the top 5 nationally among Pathology Departments (1st in New York and New England) in NIH funding. In 2011 there were 59 ($22million) NIH funded grants. This is all achieved with an overall operating budget of approximately $75M.

Against a background of uniform excellence, the Department is widely recognized for its clinical expertise in the diagnosis and understanding of diseases of the kidney, brain, liver, and female reproductive tract.

The clinical laboratories at the Presbyterian, Harkness, CHONY, Milstein, and Allen sites provide a wide array of STAT and routine services 24 hours per day/7 days per week and a broad menu of routine and specialty testing during regular weekday working hours. A wide array of point-of-care (POC) testing services is supported at all Hospital sites and throughout the Ambulatory Care Network. Clinical consultation services by our MD, PhD, and MD/PhD physicians, laboratory directors, fel-

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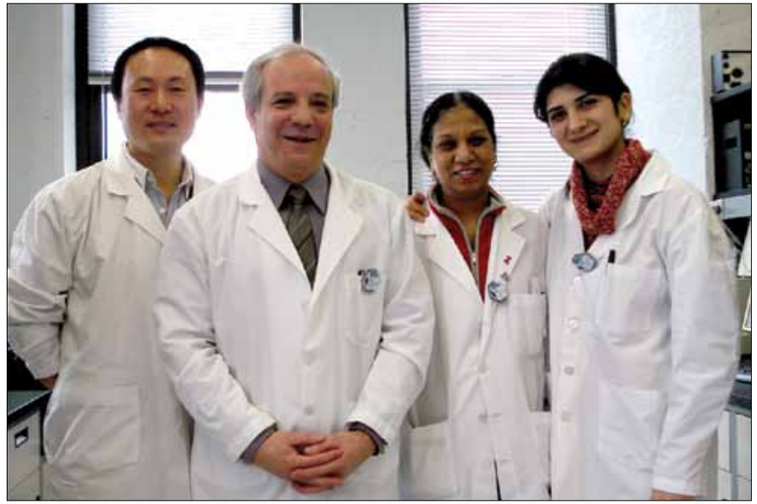
From the Archives: Around the Department

Our Neurogenetics Laboratory

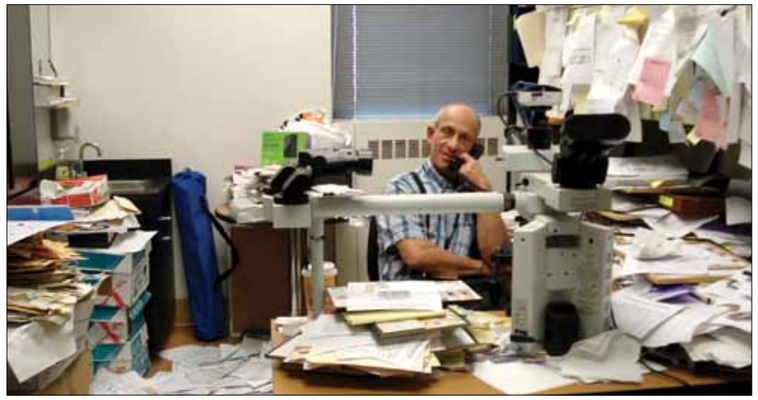


Members for the Laboratory: From left to right: Jiesheng Lu (Associate Research Scientist), Dr. Naini, Sindu Krishna (Senior Staff Associate) and Maryam Shirazi (Postdoctoral fellow).

Dr. Ann-Judith Silverman

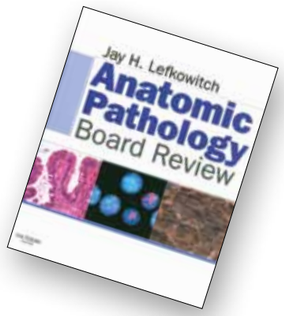
Grants administration staff

From left to right Josie Salcedo, Steve Russo, Irene D'Silva and Frances Antonetty



Dr. Jay Lefkowitch...yes, I know where everything is.

The Department's Antique Microscope, stored in dusty splendor in Mike Shelanski's office, is a Powell and Lealand monocular made about 1870. It may have been Delafield's.



One of many books from the department

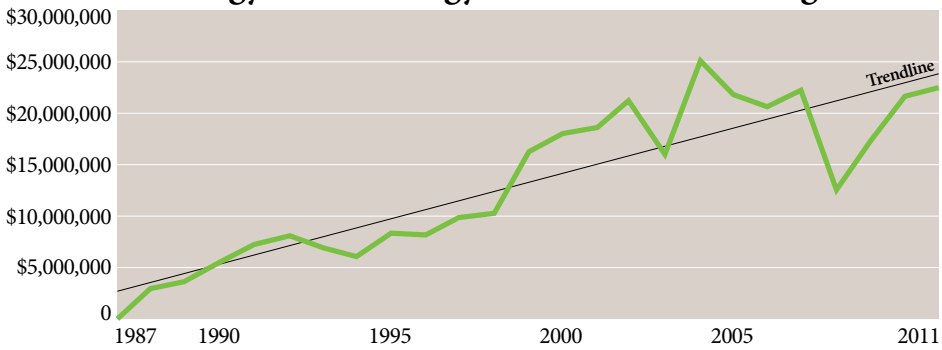
View of the George Washington Bridge from the new labs in the Black Building.

lows, and residents are available at all times to health care providers to provide support in clinical decision making and to resolve laboratory testing issues.

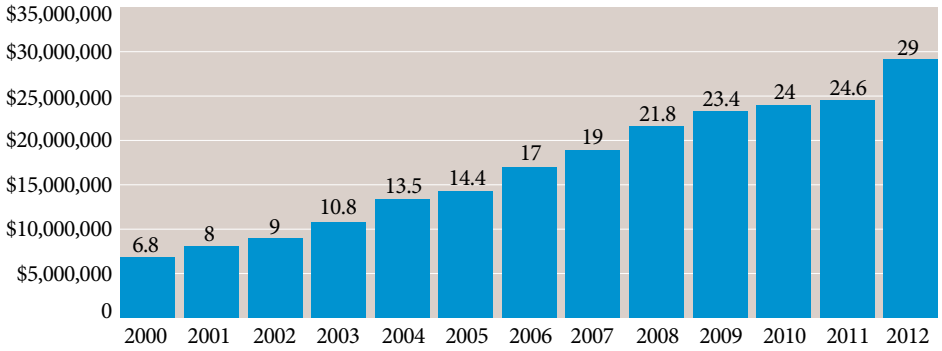
Divisions in Anatomic Pathology include Surgical Pathology, Autopsy, Neuropathology, Obstetric/Gynecologic Pathology, Cytopathology, Hematopathology, Immunopathology, and Renal Pathology. Practice sites are The College of Physicians and Surgeons of Columbia University, Presbyterian Hospital, and Vanderbilt Clinic. Frozen section diagnoses are provided in the Milstein Pavilion and the Allen Hospital. The divisions collectively process and report on more than 100,000 specimens each year.

The Department contributes significantly to the educational mission of the Columbia University Medical Center, with strong ACGME approved pathology residency and fellowship training programs, with leadership roles in medical student education, and with leadership positions in graduate biomedical education and the MD-PhD Medical Scientist Training Program. Departmental faculty members are consistently recognized with teaching awards from the medical school and several of them have been elected to the prestigious Glenda Garvey Teaching Academy. Finally, building on the success of a new course in graduate education aimed at encouraging PhD students to pursue medically-relevant research, members of the Department were recently awarded a prestigious "Med into Grad" grant award from the Howard Hughes Medical Institute.

Pathology & Cell Biology NIH Research Funding



Clinical Revenues



Twenty-five years ago there was one NIH research grant. The arrival of Mike Shelanski brought a cadre of researchers and a huge bump, going to about a dozen NIH grants in that first year and rising to the current 59 grants in the department. It also created a designation of Pathology as the only clinical and basic science department in the university. The rise in NIH funded research from less than a half million dollars in 1987 to last year's total of $22 million is almost constant. Looking at the graph we can see the impact of the Clinton initiated doubling of the NIH budget in 1998 and the fallout of the end of that doubling process in 2003.

COLUMBIA PATHOLOGY AND CELL BIOLOGY REPORT

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The Newsletter normally follows the activities of our administrative staff, lists new Honors, and new grants that have been awarded. We describe the work of new faculty. These standard Newsletter subjects will return in the fall issue.

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

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