Winter/Spring
2019

COLUMBIA PATHOLOGY AND CELL BIOLOGY REPORT

## Featured Article
How Exercise May Protect Against Alzheimer's

## The Body Scientific
You Can Observe A Lot Just By Looking

## Featured Article
Confessions of a Pathologist


# IN THIS ISSUE




**Columbia Pathology and Cell Biology Report**

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**ON THE COVER:** Abstract background (Source: rawpixel on freepik.com)

# Precision medicine and the future

Kevin A. Roth, M.D., Ph.D., Chair
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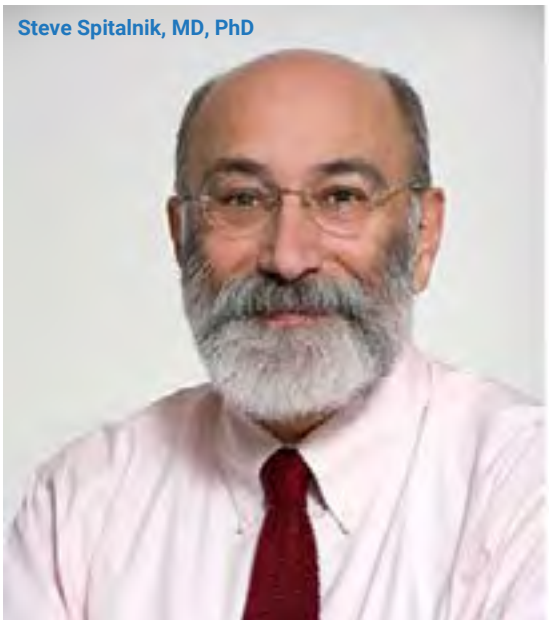
Significant progress is being made at CUIMC in enhancing an excellent precision oncology program that will significantly impact cancer patient care and oncology research. The Department of Pathology and Cell Biology and in particular, our Personalized Genomic Medicine (PGM) Laboratory, have played a key role in this effort. Under the leadership of its Medical Director, Mahesh M. Mansukhani, M.D., and with the efforts of outstanding physician, laboratory, and administrative personnel, the PGM Laboratory has been a pioneer and innovator in the oncology-related clinical genomics space. PGM has over five years' experience in advanced, high-quality cancer related somatic and constitutional genomics testing, all performed in a CLIA-certified, CAP-accredited, and New York State Department of Health (NYS DOH)-approved laboratory.

Since the PGM launch of clinical constitutional whole exome sequencing (WES) in 2013 and clinical cancer WES and transcriptome sequencing in 2014, more than 3000 samples have undergone constitutional WES analysis, over 500 cancer specimens have been analyzed by WES, and whole transcriptome (RNA) sequencing. Recently, with support from the Sohn Foundation, clinical cancer WES with transcriptome analysis has been routinely offered to high-risk pediatric cancer patients treated at participating institutions in the tri-state area.

In addition to this, PGM offers several next generation sequencing (NGS) cancer gene panels, including the Illumina TruSeq Amplicon Cancer Panel and the 467 gene Columbia Combined Cancer Panel (CCCP) that provides sequence, copy number, and gene fusion information. The CCCP is approved for determining patient participation in the National Cancer Institute MATCH clinical trial. In total, these panels have tested over 4000 cancer specimens in the last five years. This past year, PGM received NYS DOH approval for Darwin OncoTarget/OncoTreat analysis of transcriptomes, a powerful and novel systems biology approach that assesses activity of potentially targetable master regulators (developed by Dr. Andrea Califano's laboratory, Department of Systems Biology), which will further advance precision oncology efforts at CUIMC. PGM is also the only academic laboratory currently providing tumor whole transcriptome sequencing for both fresh/frozen and paraffin embedded tissue. In addition, PGM is actively engaged in new cancer-related test development, including more sensitive and specific cancer panels and the detection of circulating tumor DNA..

The PGM Laboratory has partnered with the Herbert Irving Comprehensive Cancer Center (HICCC) in pursuing several significant precision oncology initiatives. Most notably, PGM faculty and staff members participate at CUIMC in pediatric and adult molecular tumor boards and nationally in the American Society of Clinical Oncology's Targeted Agent and Profiling Utilization Registry (TAPUR) study molecular tumor board. The PGM bioinformatics team has led CUIMC involvement in Project GENIE, an American Association for Cancer Research program for aggregation of cancer genomics and clinical outcome data in a HIPAA compliant registry with the goal of catalyzing novel clinical and translational cancer research. PGM also supports the HICCC with a variety of industry- and grant- funded clinical research studies designed to accelerate the development of cancer therapeutics and to improve patient access to cost- effective and potentially life-extending personalized therapies. In total, the Department of Pathology and Cell Biology is committed to enhancing the PGM Laboratory's capabilities as a critical component of the CUIMC precision oncology community.◆

# Honors and Awards


Steve Spitalnik, MD, PhD


Matthias Szabolcs, MD

## *Dr. Steven Spitalnik and Dr. Matthias Szabolcs Receive ColumbiaDoctors' Patient Safety Recognition Awards*

Two Pathology faculty have earned special recognition as part of ColumbiaDoctors' Patient Safety Recognition Award Program.

Dr. Steven Spitalnik, MD, PhD, Professor of Pathology and Cell Biology, is the winner of the annual Leadership/Stewardship award for 2019. This annual award honors any ColumbiaDoctors leader who fosters a just culture and supports a culture of safety. The award was presented during an annual recognition luncheon at the Faculty Club on March 13.

Dr. Matthias Szabolcs, MD, Professor of Pathology and Cell Biology, is a co-winner of the Team Building Award. This quarterly prize honors individuals who are selected by their peers for consistently demonstrating teamwork in action and encouraging others to do the same. Dr. Szabolcs received this award at a recognition luncheon on March 6.

"This is excellent news. It's wonderful that great faculty in both AP and CP are being recognized!", said Dr. Kevin Roth, the department chair.

Congratulations to Dr. Spitalnik and Dr. Szabolcs for receiving these remarkable awards.

## Updates on Construction Projects

- Fenoglio Library - The construction, which started in November 2018, is expected to be completed in early April 2019.
- Labs renovation on VP&S 14 and 11 - VP&S 14 will be completed by April 1st and VP&S 11 is expected to be done by June.
- Office space construction on VP&S 11 and 16 - Construction is expected to be done by June.

# Honors and Awards

## *The Shelanski Research Innovation Award*

The Shelanski Research Innovation Award in Pathology, established in honor of Herman Alder Shelanski, the brilliant developer of povidone-iodine, is a competitive award program designed to support the development of innovative research ideas and concepts contributed by fellows and residents within the Department of Pathology and Cell Biology.

The Herman Shelanski Memorial Fund and Ralph Abrams Fund will provide up to $5,000 to defray cost for supplies and services for research projects that further our understanding of mechanisms of biology and pathophysiology of the disease.

We are proud to announce **Chun-Chieh (Paul) Lin, MD** as the winner of the 2018 Shelanski Research Innovation Award in Pathology for his proposal tiled: **Deciphering Multifactorial Genetic Contributions for Motor Neuron Development.**

Dr. Lin will work under the mentorship of Richard Mann, Ph.D., Higgins Professor of Biochemistry and Molecular Biophysics and Professor of Neuroscience (in Systems Biology).

## *Alex Chavez, MD, PhD Appointed as a Gerstner Scholar*

Dr. Alejandro Chavez has been appointed to a three-year term as a Louis V. Gerstner Jr. Scholar effective July 1, 2019 through June 30, 2022. As a Gerstner Scholar, Dr. Chavez will receive $70,000 per year, for a total of $225,000, to support and enhance his research.

Designed to support junior physician-scientist in their goal of bringing new treatments to patients, the Gerstner Award program began in 2008. Every year, the winners have the potential to touch a significant portion of our patient population with their varied fields of focus. The selection committee recognizes the potential impact of the work highlighted in this proposal and gave this candidate its most enthusiastic support.

## OTHER HONORS AND AWARDS (SINCE AUGUST 2018)

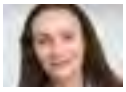
**Cory Abate-Shen,** PhD
was elected a fellow of the American Association for the Advancement of Science and named Chair of Pharmacology, effective April 1, 2019.

**Swarnali Acharyya,** PhD
was selected as a 2018-2021 Irving Scholar for "Diagnosing and Targeting Cachexia to Prolong Patient Survival".

**Richard Axel,** MD
was elected a fellow of the American Association for the Advancement of Science.

**Ibrahim Batal,** MD
was a winner of the Renal Pathology Society's mid-career achievement award, referred to as the Gloria Gallo Award.

**Joseph Schwartz,** MD
received the 2019 Hemphill-Jordan Leadership Award from the American Association of Blood Banks.



**Vivette D'Agati,** MD
received the prestigious "Distinguished Alumni Award" at the 2018 NewYork Presbyterian/Columbia Society of the Alumni Dinner.

**Clarissa Waites,** PhD
received RISE award for "Entropic Forces and SNARE Protein Ubiquitination in Synaptic Transmission and Plasticity"

# In Memoriam

## *Dept. Mourns the Loss of Donald West King, MD, Former Dept. Chair*

Columbia University Irving Medical Center and the Department of Pathology and Cell Biology mourned the passing of Donald West King, longtime chair of our Department of Pathology.

Dr. King completed his residency at Columbia, where he quickly earned a reputation as an outstanding clinician, gifted teacher, valued colleague, and trusted mentor. After serving on the faculties of Yale and the University of Colorado, Dr. King returned to Columbia in 1967, and chaired the department for fifteen years. His extensive record of publication makes him one of the true landmark figures in his field. We are fortunate to have benefited from his academic achievements, commitment to patient care and philanthropy. Dr. King and his wife, Dr. Mary Elizabeth King, established the Donald W. King, M.D. and Mary Elizabeth King, M.D. Professorship of Pathology and Cell Biology, which will carry on his distinguished legacy.

Memorial services were held for Dr. King at First Presbyterian Church on December 15, 2018.

## *VP&S Professor Emeritus Philip E. Duffy, MD Dies at Age 95*

Philip E. Duffy -- longtime professor at Columbia's College of Physicians and Surgeons and the discoverer of the mystery of ballet dancer George Balanchine's death – died on Friday morning, at his home in Easton. He was 95 years old.

As professor, and later Director of the Division of Neuropathology at Columbia Medical School, he was the author of a book called Astrocytes (Raven Press, 1983) which reviewed the functions of astrocytes, and presented new immunocytochemical of glial fibrillary proteins in those astrocytes in tissue and tissue culture. He also published over seventy articles in scientific journals in his field. In retirement, Dr. Duffy published three collections of short stories.

A memorial service was held on Thursday, September 27 at the First Presbyterian Church of Fairfield.

# It Happened Here: Dr. Charles Drew

- Dr. Steven Spitalnik talks about Charles Drew's tremendous contributions to blood banking in NYP's Health Matters

"The principle of banking blood so that you could use it later changed everything, and Charles Drew was an important part of that revolution," says Dr. Steven Spitalnik, director of Clinical Laboratories at NewYork-Presbyterian/Columbia University Irving Medical Center and executive vice chair of the Department of Pathology and Cell Biology at Columbia University Irving Medical Center. "Dr. Drew is an amazing figure who is recognized in our field as one of the forefathers of improving blood storage."

Click here to see the video and read the full story in NYP's newsletter Health Matters.

# Event Highlight

## *1st Annual International Symposium for the Global Eradication of Rh Disease*


Although Rh disease has virtually disappeared from Western Europe, Canada, the United States, and Australia, it remains dismayingly prevalent in other parts of the world, leading to hundreds of thousands of families affected by repeated miscarriages, stillbirths, and neonates with severe hyperbilirubinemia who then develop kernicterus.

Thus, although the cure for Rh disease already exists, this devastating disorder is still commonly seen in much of the world due to both a lack of awareness and a lack of access to appropriate care.

Our international consortium of physicians, scientists, epidemiologists, midwives, global health advocates, and industrial partners is committed to "doing something" by initiating a series of pilot projects in underserved settings to help families now, and to demonstrate proof-of-principle approaches that can be scaled up in the future to serve large populations.

To this end, Columbia University, on November 1, 2018, hosted a full-day symposium during which a roster of prominent speakers from around the world, representing multiple medical specialties and points of view, discussed these issues.

Nobel laureate Dr. Peter Agre, the Bloomberg Distinguished Professor at the Johns Hopkins Bloomberg School of Public Health, presented the 3rd Annual John Gorman Lectureship in Transfusion Medicine as part of the symposium. Although Dr. Agre won the Nobel Prize for his work on aquaporin, he also was one of the individuals who first cloned and sequenced the Rh gene. The title of his lecture on the day was "Aquaporin water channels – from Rh to Malaria". ◆

**Above: Dr. Spitalnik speaks at the symposium**

## Useful Information

**Updating online faculty profiles** – Faculty members can update their online profiles at http://columbiaprofiles.org/ or by emailing PathWebMast,0er@columbia.edu. Regularly updating your profile is strongly encouraged.

**Updating website content** - If you find any outdated, incorrect, or missing content on our department website (www.pathology.columbia.edu), and would like to have it updated, please contact PathWebMaster@columbia.edu.

**Posting images on touchscreen directories** - If you have interesting images (research, events, people, celebrations, etc.) that you wish to post on our three touch-screen directories located near the main elevators of the P&S and PH buildings, please contact PathNews@cumc.columbia.edu.

# New Graduate Students

**Kelsey Heavener** graduated from Simmons College with a B.Sc. in Biochemistry. After graduation, she was accepted to the Baylor College of Medicine PREP program, where she became interested in translational research. She also worked as a part-time technician in the Baylor Breast Center. Kelsey's research interests are in cancer biology and translational medicine and she is doing her first rotation in the laboratory of Dr. Marcus

**Nora Lam** received her BA from the University of California at Berkeley majoring in Molecular and Cell Biology. During her Junior year, Nora was awarded an NIH-funded fellowship, which allowed her to explore scientific research in the US and abroad. Following graduation, Nora worked in the laboratory of Dr. Arun Wiita (MD-PhD from Columbia) in the Department of Pathology at UCSF. Nora is interested in translational medicine, especially immunology and is doing her first rotation with Dr. Donna Farber.

**Joon Hyun Park** received his BA with Honors from the University of Pennsylvania, where he majored in Biological Basis of Behavior. After graduation, he worked for two years as a Research Specialist in the Department of Pathobiology at the University of Pennsylvania School of Veterinary Medicine. Joon is broadly interested in neurodegenerative disease research and is doing his first rotation in the laboratory of Dr. George Mentis.

**Samantha Tener** graduated from Muhlenberg College with a BSc in Biology. Samantha has had multiple laboratory experiences at Muhlenberg College, as well as at a pharmaceutical company and is interested in a career in which she will explore the cellular and molecular basis of infection and disease. She is particularly interested in model organisms, such as Drosophila and is doing her first rotation with Dr. Mimi Shirasu-Hiza.

Photo by Alexander Andrews on Unsplash

# Confessions of a Pathologist

**BY HEIDRUN ROTTERDAM, MD,** Professor Emerita, Pathology and Cell Biology

***"I look at a slide like I look at a starry sky.***
***Has the starry sky changed since Adam and Eve?"***

In 1970, when I started my pathology residency at the Pieter Bent Brigham Hospital in Cambridge Massachusetts, one of my senior colleagues mentioned, in a tone of an irrelevant remark: "Well, you know, you chose the wrong specialty. There will be no need for pathologists in the near future. The computer will take over". I found this remark peculiar but not startling, since pathology, at that time, wasn't really a choice of mine: it was the only residency available, my real choice would have been internal medicine, a field I intended to pursue once I returned to Europe. Pathology was a good preparation for any of the clinical specialties, I thought then and still think today. But as I was told in those years, that seem a totally different era from today, "People like you go into pathology"; people like me, meaning foreigners and women.

Well, I never returned to Europe, became an American citizen, stayed in Pathology, and now, in my old age, can confess: I fell in love with Pathology.

How can this happen? A field rejected by many because you have to deal with flesh and blood, and other body fluids, have no contact with living patients, but only with the dead or the diseased tissues of the living? How can one ever fall in love with such a specialty? I remember a female first- year- resident, long time ago, who quit after a week admitting: I didn't know I had to touch these terrible things, I thought I would just sit at the microscope.

"***Per aspera ad astra***" is a popular Latin phrase, meaning "***through hardships to the stars***". Yes, there are hardships in pathology; autopsies after hours (at my time the autopsy service was available for 24 hours), ovarian cysts spraying their contents into your face when incised, slides breaking, special stains forgotten, surgeons yelling in the frozen section room, just to name a few hardships. But then there are the stars, the "astra". I look at a slide like I look at a starry sky. Has the starry sky changed since Adam and Eve? Have the layer of the gastric wall changed since humans appeared on this earth? I recognize some of the heavenly constellations, the Cassiopeia, Orion and the North Star, but the vast numbers of stars I cannot name but love to gaze at and wonder: Where do you come from? Where are you going? What are you (D'ou venons nous, que sommes nous, ou allons nous; the French title of a Gauguin painting). And the same questions arise each time I look at tissues, esophageal squamous mucosa or a colonic tubular adenoma or a signet ring carcinoma. I realize that the questions we ask in pathology and try to answer the best way we can, are in essence the same questions we ask ourselves in the rest of our lives. Training in Pathology is a very good preparation, not only for any carrier in medicine but for life. And let me not forget the visual beauty of histologic sections!! They are to be admired like a work of art.

And so I have to confess that the prejudice of past years was, for me, a blessing in disguise that I am grateful for. ◆


# Second Annual International Virtual Conference

On February 2nd and 3rd, 2019, the Anatomy Division's "International Collaboration and Exchange Program" held its annual virtual student conferences in the Health Hammer Sciences Library.

Approximately 200 students from 12 international universities participated. Students presented their international small group work covering various topics, including differences in healthcare education and systems, Public Health challenges (e.g., aging, addictions, mental health, environmental health), and health ethics and law (e.g., abortion, euthanasia, organ donation law, infertility, embryonic stem cell research law). The students will join research laboratories in the partner institutions during the summer.

The international program – led by the Pathology Department at VP&S - is a 12 school collaboration between Australia(University of Sydney), Austria (Medical University of Vienna), Canada (McGill University, Montreal, QC), Denmark (University of Copenhagen), Finland (University of Helsinki), Germany (1. Martin Luther University, Halle-Wittenberg, 2. Ludwig Maximilians University, Munich), Japan (1. Kyoto University, 2. Tokyo Women's Medical University), Taiwan (National Taiwan University, Taipei), the United Kingdom (King's College, London), and the United States (Columbia University, New York). ◆

**Transfusion Medicine**

## Drs. Sarah Vossoughi and Brie Stotler on Top Ten List for Patient Blood Management Articles of the Year

Congratulations to Sarah Vossoughi, MD (left), Fellow of Transfusion Medicine and Brie Stotler, MD (right), Assistant Professor of Pathology and Cell Biology, whose article "Analysis of Pediatric Adverse Reactions to Transfusions", made into the top ten list for patient blood management articles of 2018. This study aims to characterize differences between pediatric and adult patients regarding adverse responses to transfusions. The top ten list was announced at the annual meeting of the Society for the Advancement of Blood Management (SABM), which took place from September 13 to 15, in Brooklyn, New York.

# New Administrative Staff

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**Email: dp2657@cumc.columbia.edu**

**Danielle Pendrick, DrPH** joined the Department of Pathology and Cell Biology as the Administrative Director for Precision Pathology and Genomics. In this time of rapid acceleration in data driven healthcare, Danielle will facilitate the development, planning and organizational oversight of clinical and research applications for precision medicine in the Department.

Dr. Pendrick reports to Dr. Steven Spitalnik and Ms. Joann Li and provides administrative leadership and overall programmatic and operational support. She will contribute significantly to ongoing and future clinical and research projects aimed at building patient awareness and access to precision pathology and genomics through a variety of efforts including education and advocacy initiatives.

Dr. Pendrick comes to us from the CUIMC Division of Hematology, Oncology, and Stem Cell Transplantation, where she served as Program Manager for over four years. During her time there, she oversaw the creation and administration of an innovative, multi-disciplinary precision medicine program that aided in the establishment of CUIMC as a leader in next-generation sequencing efforts for pediatric oncology patients. She holds a master's degree in public health and recently earned a DrPH in health policy.

**Regina Cullen** joined the department as an Integration Project Manager with primary focus on the Epic implementation for the Department of Pathology and Cell Biology. In her role, Regina is our point person coordinating all efforts for our department with the Epic team, ensuring that Epic will integrate with our systems and meet the needs of the department.

Regina worked for 18 months at Atlantic Health System (AHS) in New Jersey as an Epic Implementation Manager overseeing the Orders, Beacon Oncology, and Willow Pharmacy team. Additionally, she assumed the LIS manager role during the project to lead the integration efforts of the lab team to ensure success.

Prior to her role at AHS, Regina was part of NYP IT from 2007 to 2016 working with teams across the organization. In her NYP role as the LIS Manager supporting the Clinical Labs, Regina was key to many successful system implementations, lab integration projects and process improvement initiatives with various customers, resulting in improved care for our patients and customer service for our clients.

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## *Study Reveals Genomics Sometimes See What Other Tests Can't in Prenatal Testing*

Vimla Aggarwal, MBBS

On January 31, The Lancet published a study titled "Whole-exome sequencing in the evaluation of fetal structural anomalies: a prospective cohort study" conducted by a group of Columbia researchers. Dr. Vimla Aggarwal, assistant professor of pathology and cell biology and director of Columbia's precision genomics laboratory, is one of the authors of the study. The study tries to investigate whether a new kind of genetic testing can improve the ability to diagnose the underlying causes of fetal anomalies found during prenatal ultrasounds, thus improving perinatal care for infants with genetic conditions and easing parents' fears by offering a clear diagnosis.

For more details of the study, visit the CUIMC Newsroom.

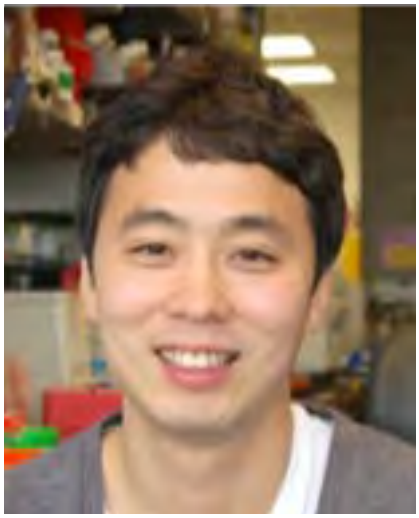
## GRANTS AWARDED (SINCE AUGUST 2018)

| PI | Sponsor | Title |
|---|---|---|
| Corey Abate-Shen | National Cancer Institute | Modeling Bladder Cancer Patholgenesis and Tumor Evolution |
| Dritan Agalliu | National Institute of Neurological Disorders and Stroke | miR Regulation of the Neurovasculature Function in Health and Disease |
| Ottavio Arancio and Russell Nicholls | National Institute on Aging | The Role of Methylation-Sensitive PP2A Isoforms in Regulating the Pathological Response to Tau |
| Ottavio Arancio and Russell Nicholls | BrightFocus Foundation | Tau-Induced Damage at Hippocampal Tripartite Synapses |
| Peter Canoll | Emerson Collective Cancer Research Fund | Targeting Treatment-Resistant Glioblastoma Cells with Ferroptosis Inducing Drugs |
| Catherine Clelland | Army Research Office | Negative Symptoms in Clinical High-Risk and First-Episode Psychiatric Illness: Investigation of a New Candidate for Targeted Treatment and Apathy in Alzheimer's Disease: Investigation of the Interaction Between Proline |
| Catherine Clelland | National Institute on Aging | The Role of Methylation-Sensitive PP2A Isoforms in Regulating the Pathological Response to Tau |
| Qing Fan and Matthias Quick | National Institute of General Medical Sciences | Mechanism of Activation and Modulation in Human GABA(B) Receptor |
| Rebecca Haeusler | National Institute of Diabetes and Digestive and Kidney Diseases | Bile Acids and Insulin Sensitivity |
| Ulrich Hengst | National Institute of Neurological Disorders and Stroke | Mechanism of Activation and Modulation in Human GABA(B) Receptor |
| Ulrich Hengst | National Institute on Aging | Mechanism of Activation and Modulation in Human GABA(B) Receptor |
| Tae-Wan Kim | National Center for Advancing Translational Sciences | Effects of ApoE-Enhancing Compounds on Alzheimer's Disease Phenotypes In Vivo |
| Tae-Wan Kim | National Institute of Neurological Disorders and Stroke | Chemical Biology of Tau Missorting in Alzheimer's Disease |

## GRANTS AWARDED (SINCE AUGUST 2018)

| PI | Sponsor | Title |
|---|---|---|
| George Mentis | National Institute on Alcohol Abuse and Alcoholism | Mechanisms of Synaptic Loss by the Classical Complement Pathway in Motor Circuit Development and Disease |
| Umrao Monani | Cure SMA | Restoring Function at the NMJ: A Novel Means to Treat SMA |
| David Owens | New York State Department of Health | Role of Epithelial Stem Cells in Age-Related Loss of Tactile Acuity |
| Liza Pon | National Institute on Aging | The Role of Actin in Cellular Aging |
| Serge Przedborski | National Institute of Neurological Disorders and Stroke | Mechanisms of Axon Pathology in ALS |
| Markus Siegelin | National Institute of Neurological Disorders and Stroke | Targeting Mutant IDH1 for a Novel Synthetic Lethal Interaction in Malignant Gliomas |
| Ira Tabas | National Heart, Lung, and Blood Institute | Mechanisms of Atherogenesis in Insulin Resistance |
| Andrew Teich | National Institute on Aging | A Translational Bioinformatics Approach to Rescuing Synaptic and Neurophysiologic Dysfunction in Alzheimer's Disease |
| Stephen Tsang | Abeona Therapeutics | Chromosome-Specific ChopStick Therapy for Best Vitelliform Macular Dystrophy & ChopStick Therapy for Autosomal Dominant Retinitis Pigmentosa (adRP) |
| Stephen Tsang | National Eye Institute | Defining Barriers to Gene Therapy |
| Stephen Tsang | National Eye Institute | Translational Gene Therapy for CNGB1 Retinitis Pigmentosa |
| Stephen Tsang | New York State Department of Health | Comparative Effectiveness of CRISPRn, CRISPRd, and CRISPRi in Patient-Specific Stem Cells |
| Stephen Tsang | Alcon Research Institute | CRISPR Single-Nucleotide Polymorphism (SNP) Editing for Autosomal Dominant Disorders |

# New Faculty



## Hee Won Yang, PhD

Hee Won Yang earned his Ph.D. from Korea Advanced Institute of Science and Technology and completed his postdoctoral work at Stanford University. Using an automated microscope and multiple bio-sensors to monitor signaling processes at the single-cell level, Hee Won has previously studied the molecular mechanisms underlying the decision of cell migration and proliferation. Currently, Hee Won is studying how proteins regulating proliferation are wired into circuits to carry out the decision of proliferation in normal as well as cancer cells.

## Minah Kim, PhD

Minah Kim received her Ph.D. at Korea Advanced Institute of Science and Technology (KAIST), where she worked on chemoresistant tumor cell metastasis and organ-specific angiogenesis with Dr. Gou Young Koh. She pursued her postdoc work at Donald McDonald's lab of UCSF where she studied vascular abnormalities under disease models and cancer immunology. Her research will focus on identifying the molecular mechanisms that drive immune and vascular changes to provide new therapeutic targets and better therapeutic strategies in cancer.

## Krystalyn Hudson, PhD

Krystalyn Hudson earned her Ph.D. from Emory University, where she studied how prior pathogen infections regulate alloantibody production against antigens on red blood cells under mentorship from Dr. James Zimring. She pursued her postdoctoral work with Dr. David Nemazee at The Scripps Research Institute where she worked on elucidating how B cell tolerance mechanisms modulate HIV vaccine efficacy. Krystal was an Assistant Member at Bloodworks Northwest Research Institute prior to joining the Department of Pathology & Cell Biology and the Laboratory of Transfusion Biology; her laboratory research will continue focus on autoimmune and alloimmune responses to antigens on RBCs, which will provide insight for better prophylactic and therapeutic treatments thereby leading to better patient care.

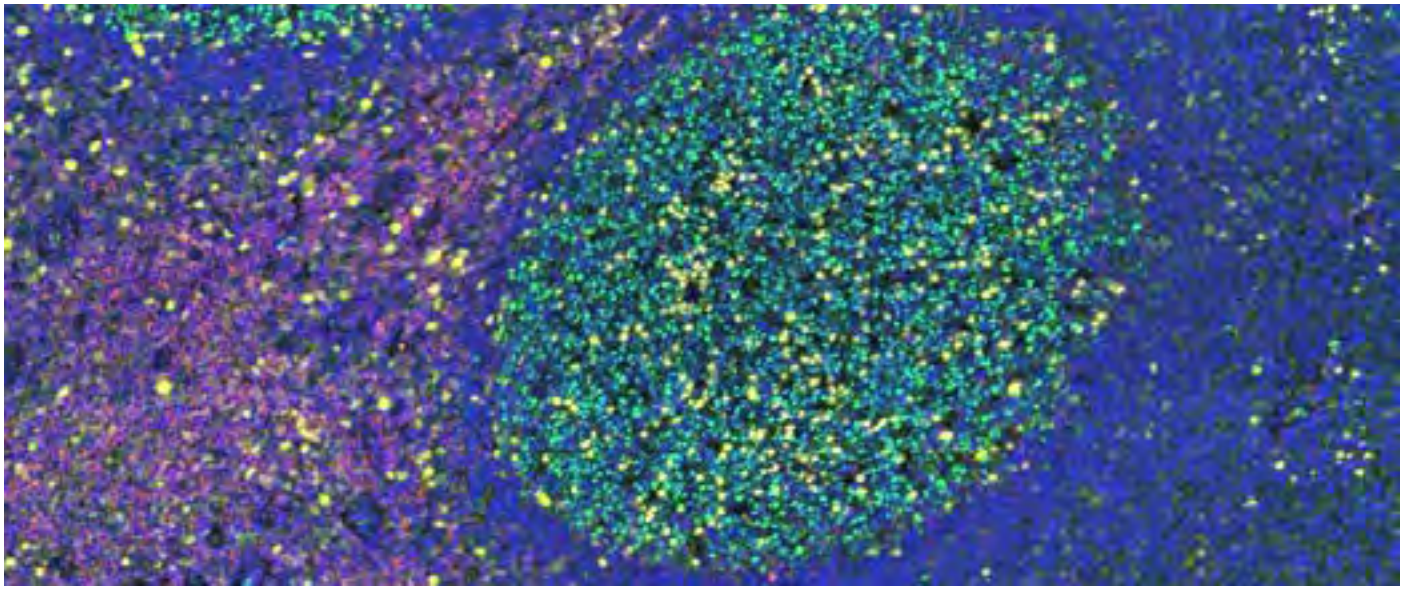


Image: High Magnification Germinal FL

## Digital and Computational Patholoy Laboratory (DCPL) Established

The Department of Pathology & Cell Biology Digital and Computational Pathology Laboratory (DCPL) was established in 2018, through a partnership with New York-Presbyterian Hospital, with a mission to facilitate the basic, translational and clinical research in pathology. DCPL specializes in slide digital image acquisition, web-based image management, and quantitative image analysis. DCPL is equipped with two cutting-edge Aperio whole slide scanners: Aperio AT2 scanner for high-throughput and high resolution (40X) bright-field imaging, and Aperio Versa 8 fluorescence scanner for multiplex applications ranging from UV to near Infrared. DCPL uses Aperio eSM for data management & remote sharing. For advanced quantitative image analysis, DCPL provides stations for consultation and training for image analysis using: Aperio Imagescope, HALO (including HALO AI), Visiopharm and Qupath.

DCPL Director and Faculty Supervisor is Dr. Kevin Gardner (contact email: klg2160@cumc.columbia.edu).

For any service or training inquiries, please contact DCPL Image Data Analyst Zhong Wang at zw2568@cumc.columbia.edu, or DCPL Assistant Ambar Caban at ac4344@cumc.columbia.edu.

DCPL is located at PH 1582.

## Dr. Kevin Gardner Was a Guest Speaker at Medgar Evers College in February in Celebrating Black History


In February 2019, in honor of Black History Month, CUNY's Medgar Evers College presented an exciting array of events that aimed to be both celebratory and informative.

Senior Vice Chair of the Department of Pathology and Cell Biology of Columbia University Irving Medical Center, Kevin L. Gardner, MD, PhD, joined the #MedgarEversFamily in celebrating the event as the feature speaker for the Frank Ragland Lecture Series.

THE BODY SCIENTIFIC

# You Can Observe a Lot Just By Looking

## Microscopes in grade school

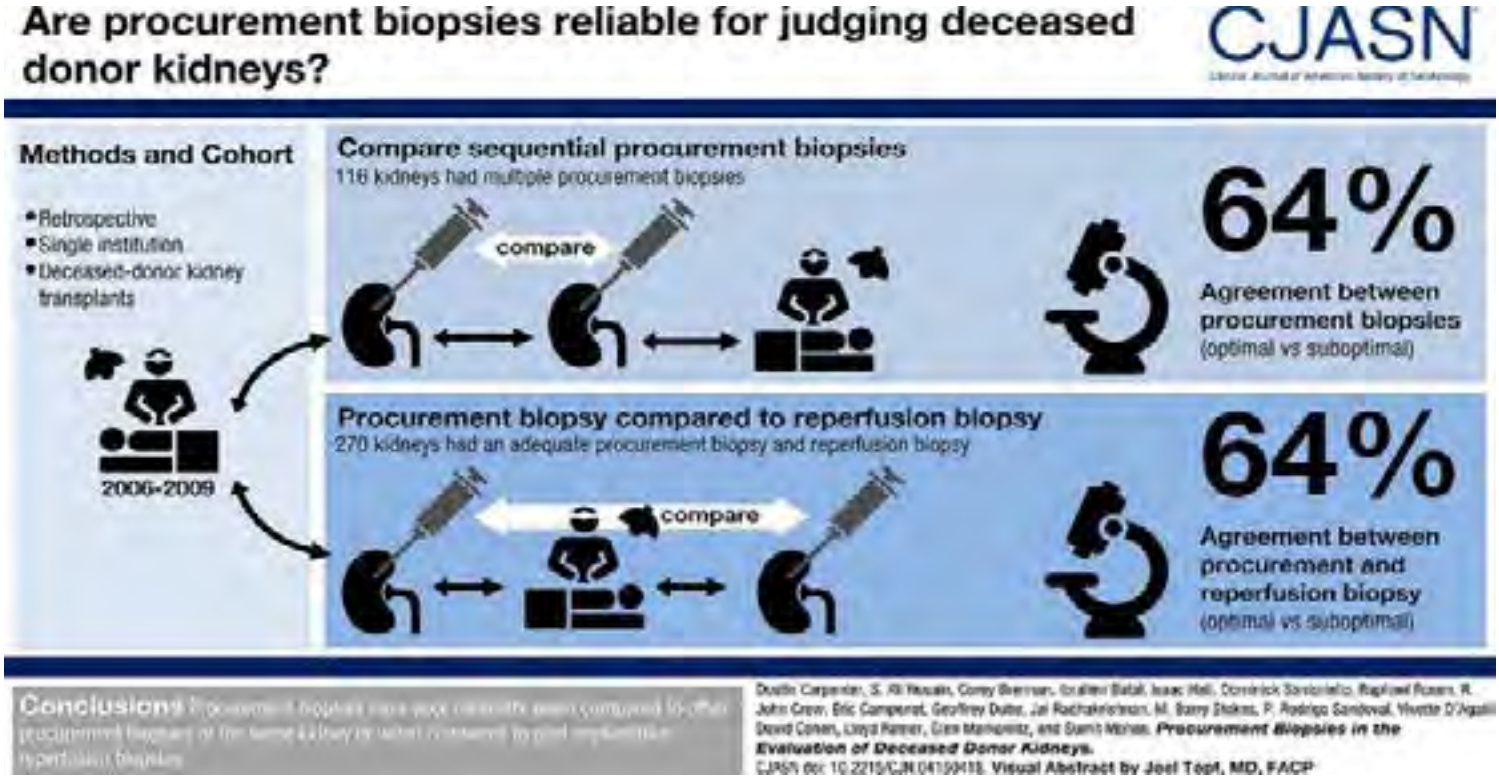
BY RICHARD H. KESSIN, PHD
Professor Emeritus and Special Lecturer, Pathology and Cell Biology

You can observe a lot just by looking" is an aphorism by Yogi Berra, folk philosopher and long-time catcher for the New York Yankees. The statement may seem more malapropism than aphorism, but Yogi knew what he was saying. Yogi caught Don Larsen's perfect game in the 1956 World Series against the Dodgers, and was later a manager, so he had a certain authority. Dee Dao, a former graduate student in my lab, now at NYU, surprised me with this gem when she used it as the first slide of her thesis defense, which, as you might imagine, involved a lot of microscopy.

Four hundred years ago scientists and artists learned a lot with telescopes and microscopes, just by looking. Using a microscope can still be exciting even if you are in fourth grade—there is a virtue to observing your own pond water, or callow lily pollen, or a tick that was about to bite you. Ideally, no one else chose the object for you; it did not come from a slide or a video, and there is not going to be an exam. A child takes ownership of the image and questions flow. How big is that pollen? What's it for? Why does that ticky-thing have 8 legs? Don't bugs have six legs? Can I make this butterfly wing photo into art?

The extraordinary primary school teachers I have met cover all subjects, including a new integrated science curriculum, which progresses from K to 12. There have microscopes but they can be a challenge to use. Teachers are not trained to use various kinds of microscopes.— the power magnification are most useful because students and see a bigger object that can be lit from various angles. It would be useful to be able to photograph what they see, which has traditionally involved expensive equipment. These schools have almost no discretionary money. As I understand it, the $250 tax deductible amount that teachers could spend from their own pockets has been eliminated by so-called tax reform.

There are always ways around these problems. Most of us carry the most expensive part of a microscope around with us. Any smart phone can attach to a magnifying lens that will make a tick or a pollen grain 50 times bigger and then photograph it. The zoom lens of my iPhone magnifies 4-fold and a snap on lens magnifies another 12.5 times, giving a total magnification of 50-fold. It is not the 400-fold of a research microscope, but 50X with a good camera is useful for photographing nature, or study small creatures. The camera is also fast enough that it can be used outside, photographing a bee on a flower, say and it does time-lapse. I have found one (Xenvo.com) that attaches to any smartphone or iPad. It has a dual use lens that will do wide-field or magnified images. The kit costs between $20 and $30 and comes with a light and a set of plug-in instructions in which a pleasant PhD from Wisconsin explains how to set it up. I do not know these people, but they sound like fun. ◆




# Procurement Biopsies in the Evaluation of Deceased Donor Kidneys

**AUTHORED BY** Carpenter D1, Husain SA2,3, Brennan C4, Batal I5, Hall IE6, Santoriello D6, Rosen R2, Crew RJ2, Campenot E5, Dube GK2, Radhakrishnan J2, Stokes MB5, Sandoval PR1, D'Agati V5, Cohen DJ2, Ratner LE1, Markowitz G5, Mohan S

New research indicates that many kidneys obtained for transplantation from deceased donors are discarded because of biopsy findings which are unreliable and unreproducible. The findings, which appeared in the December issue of Clinical Journal of The American Society of Nephrology (CJASN) and was published at ASN Kidney Week 2018, suggest an urgent need to reduce reliance on such biopsies in determining the quality of procured kidneys.

The study, conducted by a team led by Sumit Mohan, MD, MPH and S. Ali Husain, MD, MPH, which included pathologists from Pathology and Cell Biology, examined data on nearly 300 deceased-donor kidneys that were transplanted at a single center from 2006-2009. The organs had undergone both a procurement biopsy and a reperfusion biopsy, the latter being the gold standard high quality biopsy for measuring kidney quality. On average, they followed patients for nearly six years after transplantation.

The study found that the agreement between the procurement biopsies and the reperfusion biopsies was not good: the procurement biopsy and the high-quality biopsy produced the same result in only 64 percent of cases. Also, while standard biopsy results were associated with the success of the transplanted organ, procurement biopsies were not. In addition, procurement biopsies of the same organ often conflicted with each other.

The findings call into question the value of procurement biopsy for adjudicating kidney quality for transplantation. As indicated by Dr. Sumit Mohan, limited reliance on procurement biopsy histology will likely result in an improvement in organ utilization by reducing the discard of kidneys attributable to the findings. This has the potential to improve organ allocation efficiency and dramatically increase the number of kidney transplants being performed in the United States.

The study noted that efforts to improve the predictive value of biopsies could include requiring biopsy review by experienced kidney pathologists, standardizing biopsy techniques and biopsy reporting, and better integrating biopsy data with other clinical information. For more information, visit the CUIMC Newsroom. ◆

FEATURED ARTICLE

# HED: How Exercise May Protect Against ALZHEIMER'S

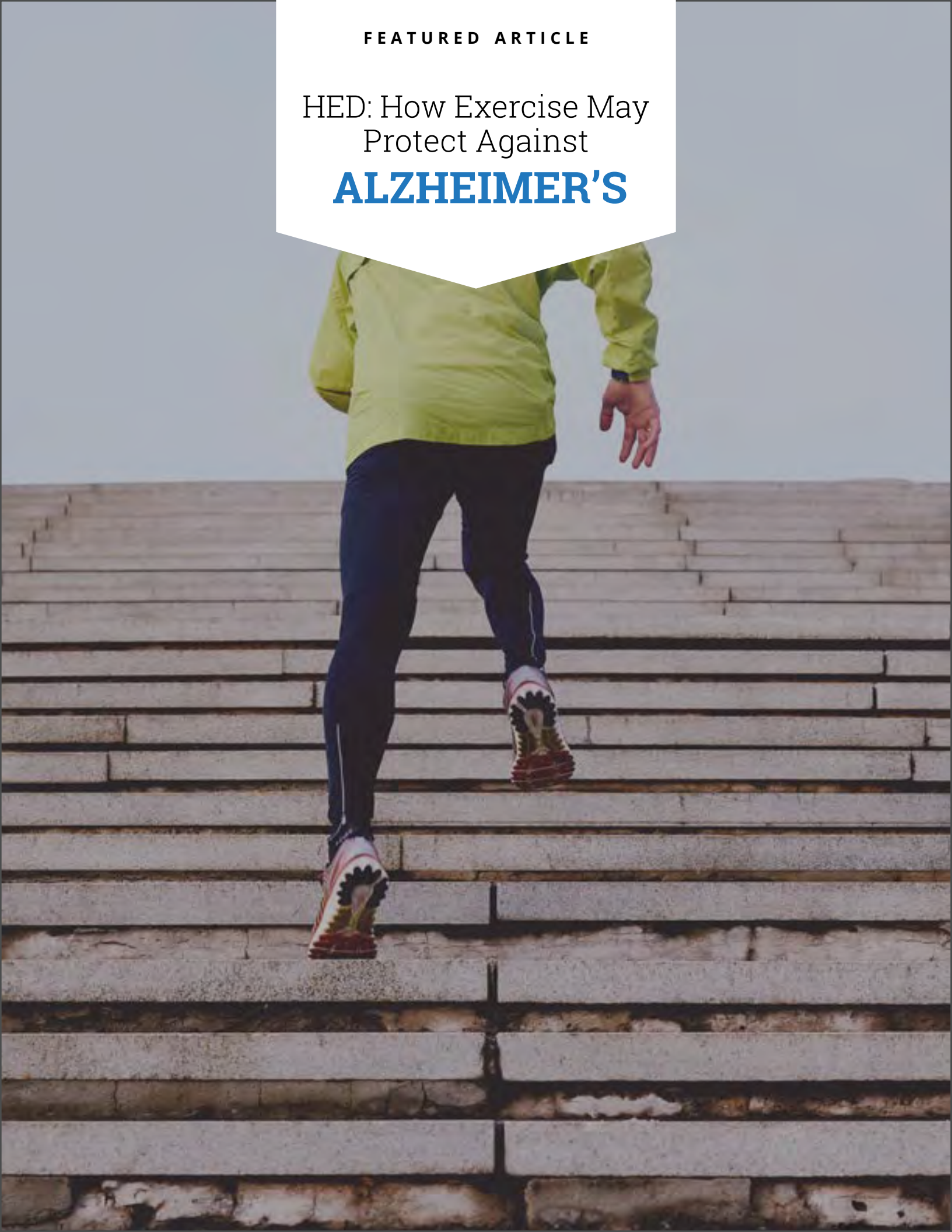


Photo by Clique Images on Unsplash

A hormone called irisin – produced during exercise – may protect neurons against Alzheimer's disease. Athletes know a vigorous workout can release a flood of endorphins: "feel-good" hormones that boost mood. Now there's evidence that exercise produces another hormone that may improve memory and protect against Alzheimer's disease, according to a study co-led by **Ottavio Arancio, MD, PhD**, a researcher at Columbia University's Vagelos College of Physicians and Surgeons and Taub Institute for Research on Alzheimer's Disease and the Aging Brain.

The study, which is titled, "Exercise-linked FNDC5/irisin rescues synaptic plasticity and memory defects in Alzheimer's models", was published in Nature Medicine.

Physical activity is known to improve memory, and studies suggest it may also reduce the risk of Alzheimer's disease. But researchers don't understand why.

A few years ago, exercise researchers discovered a hormone called irisin that is released into the circulation during physical activity. Initial studies suggested that irisin mainly played a role in energy metabolism. But newer research found that the hormone may also promote neuronal growth in the brain's hippocampus, a region critical for learning and memory.

"This raised the possibility that irisin — if present in people — may help explain why physical activity improves memory and seems to play a protective role in brain disorders such as Alzheimer's disease" says Arancio, who is a professor of pathology and cell biology and of medicine at Columbia University Vagelos College of Physicians and Surgeons.

**Irisin is reduced in brains of people with Alzheimer's**

In the new study, Arancio and his colleagues at the Federal University of Rio de Janeiro in Brazil and Queens University in Canada first looked for a link between irisin and Alzheimer's in people. Using tissue samples from brain banks, they found that irisin is present in the human hippocampus and that hippocampal levels of the hormone are reduced in individuals with Alzheimer's.

To explore what irisin does in the brain, the team turned to mice. These experiments show that irisin, in mice, protects the brain's synapses and the animals' memory: When irisin was disabled in the hippocampus of healthy mice, synapses and memory weakened. Similarly, boosting brain levels of irisin improved both measures of brain health.

**Swimming boosts irisin, protects memory in mice**

The researchers then looked at the effect of exercise on irisin and the brain. In the study's most compelling experiments, the researchers found that mice who swam nearly every day for five weeks did not develop memory impairment despite getting infusions of beta amyloid — the neuron-clogging, memory-robbing protein implicated in Alzheimer's.

Blocking irisin with a drug completely eliminated the benefits of swimming, the researchers also found. Mice who swam and were treated with irisin-blocking substances performed no better on memory tests than sedentary animals after infusions with beta amyloid.

Together the findings suggest that irisin could be exploited to find a novel therapy for preventing or treating dementia in humans, Arancio says. His team is now searching for pharmaceutical compounds that can increase brain levels of the hormone or can mimic its action.

"In the meantime, I would certainly encourage everyone to exercise, to promote brain function and overall health," he said. "But that's not possible for many people, especially those with age-related conditions like heart disease, arthritis, or dementia. For those individuals, there's a particular need for drugs that can mimic the effects of irisin and protect synapses and prevent cognitive decline." ◆

**MORE DETAILS** The study is titled, "Exercise-linked FNDC5/irisin rescues synaptic plasticity and memory defects in Alzheimer's models." The other contributors are: Mychael V. Lourenco (Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, and CUIMC); Rudimar L. Frozza (Federal University of Rio de Janeiro and Oswaldo Cruz Institute, Oswaldo Cruz Foundation, FIOCRUZ, Rio de Janeiro); Guilherme B. de Freita (Federal University of Rio de Janeiro and Queen's University, Kingston, Ontario, Canada); Hong Zhang (CUIMC); Grasielle C. Kincheski (Federal University of Rio de Janeiro); Felipe C. Ribeiro (Federal University of Rio de Janeiro); Rafaella A. Gonçalves (Queen's University, Kingston, Ontario, Canada); Julia R. Clarke (Federal University of Rio de Janeiro); Danielle Beckman (Federal University of Rio de Janeiro); Agnieszka Staniszewski (CUIMC); Hanna Berman (CUIMC); Lorena A. Guerra (Federal University of Rio de Janeiro); Letícia Forny-Germano (Federal University of Rio de Janeiro); Shelby Meier (University of Kentucky, Lexington, KY); Donna M. Wilcock (University of Kentucky); Jorge M. de Souza (Federal University of Rio de Janeiro); Soniza Alves-Leon (Federal University of Rio de Janeiro); Vania F. Prado (University of Western Ontario, London, Ontario, Canada); Marco A. M. Prado (University of Western Ontario); Jose F. Abisambra (University of Kentucky); Fernanda Tovar-Moll (D'Or Institute for Research and Education, Rio de Janeiro, Brazil, and Federal University of Rio de Janeiro); Paulo Mattos (D'Or Institute for Research and Education and Federal University of Rio de Janeiro); **Ottavio Arancio (CUIMC);** Sergio T. Ferreira (Federal University of Rio de Janeiro); and Fernanda G. De Felice (Federal University of Rio de Janeiro and Queen's University).

This work was supported by grants from Alzheimer Society of Canada, the Weston Brain Institute (to F.G.D.F.), National Institute for Translational Neuroscience (INNT/Brazil), Human Frontier Science Program, International Society for Neurochemistry, National Institutes of Health (R01NS049442), Canadian Institutes of Health Research, and from the Brazilian funding agencies Conselho Nacional de Desenvolvimento Científico e Tecnológico and Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro.

## Recent Theses Defended

**Corentin Moevus,** Greene Lab, November 30, 2018
"Single-molecule visualization of nucleosome looping by condensing"

**Brian Ji,** Vitkup Lab, December 3, 2018
"Quantifying spatiotemporal dynamics of human gut microbiota and metabolic limitations of cancer cell growth"

**Nathan Johns,** Wang Lab, December 4, 2018
"Gene regulatory compatibility in bacteria: Consequences for evolution and synthetic biology"

**Jamie Yang,** Tavazoie Lab, December 5, 2018
"Yease survival under acute exposure to lethal stress"

**Ruth Singer,** Sussel Lab, December 7, 2018
"Long noncoding RNAs are critical regulators of pancreatic islet development and function"

**Edward Eckels,** Fernandez Lab, December 7, 2018
"Magnetic Tweezers for Probing Single Protein Physiology"

**Chelsea Dieck,** Ferrando Lab, December 11, 2018
"Mechanisms and therapeutic targeting of NT5C2 mutations in relapsed acute lymphoblastic leukemia"

**Jin Du,** Kitajewski Lab, December 11, 2018
"Genome-wide screening approaches identify novel Notch signaling targets as regulators of angiogenesis"

**Sway Chen,** Wang Lab, December 18, 2018
"Novel genetic engineering tools for functional studies of the gut microbiome"

**Claudia Tenen,** Greenwald Lab, December 20, 2018
"Function and tissue focus of daf-18/PTEN in maintaining blast cell multipotency and quiescence in Caenorhabditis elegans dauer larvae"

**David Thomas,** Tall Lab, January 17, 2019
"Single-molecule visualization of nucleosome looping by condensing"

**Enrique Garcia,** Pon Lab, January 28, 2019
"ER stress and lipid droplet-dependent proteostasis in response to lipid stress in S.cerevisiae"

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# CUIMC Announces New Partnership with Fulgent Genetics (Pathology Newsroom)

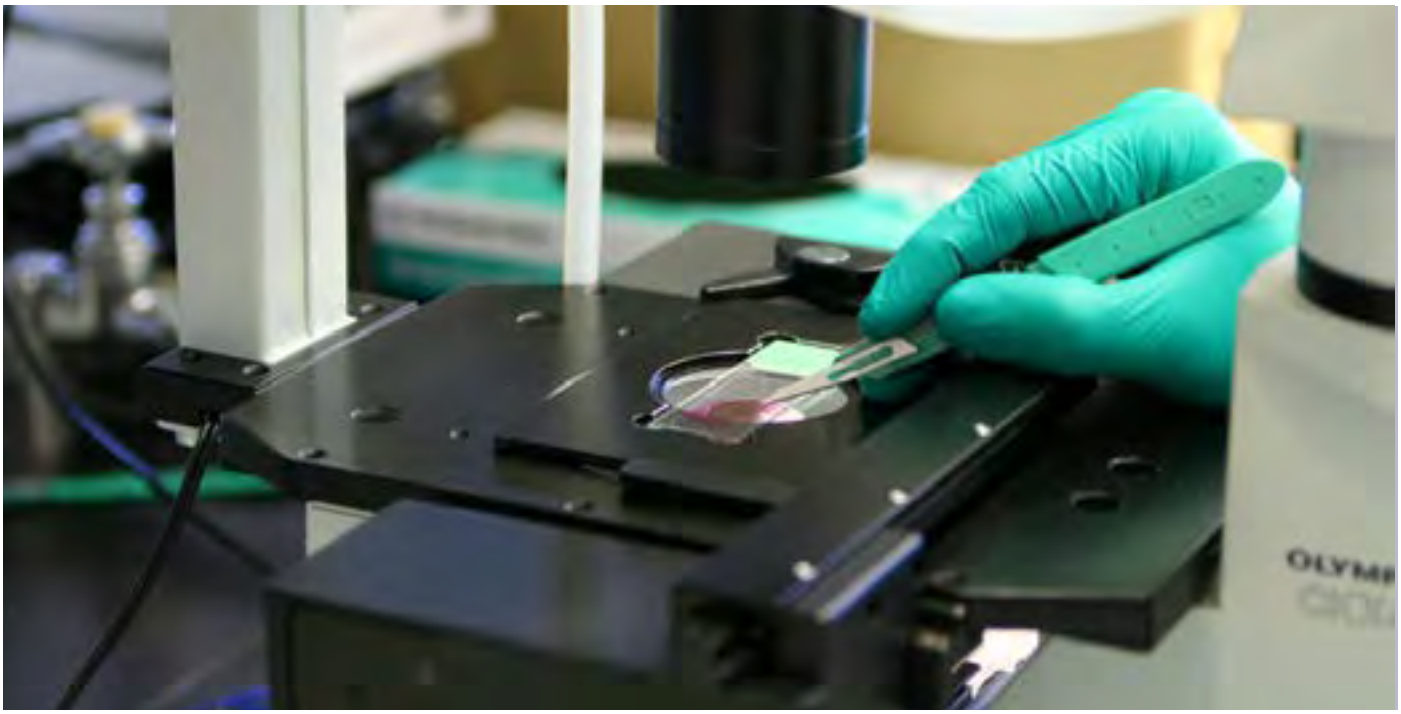

Image: Precision Genomics Laboratory at CUIMC

Fulgent Genetics and the Precision Genomics Laboratory (PGL), in collaboration with the Department of Obstetrics and Gynecology, at Columbia University Irving Medical Center (CUIMC) announced a new partnership to make on site performed, expanded carrier screening available to Columbia patients. This unique collaboration will leverage both parties' expertise in laboratory management, bioinformatics, clinical genetics and next-generation sequencing to deliver an expanded carrier screening test with many advantages over other currently available tests.

The PGL is jointly operated by the Institute for Genomic Medicine (IGM) and the Department of Pathology and Cell Biology and is designed to enhance patient care through genomic diagnostics, research, and education at CUIMC.

Carrier screening is a genetic test used to identify whether individuals and carrier couples are at risk for passing genetic disorders to their children. These genetic disorders may result in physical disabilities, cognitive impairment, and other severe health problems in newborn babies. Traditionally, carrier screening tests targeted couples of certain ethnic groups that have historically been at higher risk for specific genetic disorders. This approach has presented difficulties for patients who are multiracial, adopted, or are unsure of their ethnic backgrounds. To address this challenge, expanded carrier screening (ECS) was developed to test for mutations that cause hundreds of different genetic disorders regardless of a patient's ethnicity.

Professional medical associations like the American College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics and Genomics (ACMG) have published guidelines on ECS and its importance in reproductive care.

"We are extremely excited to partner with such a prestigious institution in a collective effort to help improve patient care by offering expanded carrier screening as a routine test to Columbia patients," said Brandon Perthuis, Vice President of Commercial Operations at Fulgent Genetics.

"This collaboration will help us to bring high-quality reproductive genomic testing to our patients," said the IGM's David Goldstein, "and will enable the Institute for Genomic Medicine and Fulgent Genetics to leverage our strengths in genomic medicine and clinical genetics to co-develop a range of new tests in the future."

"The Fulgent partnership is another exciting step in the evolution of precision medicine clinical testing at CUIMC and the PGL. The Department of Pathology and Cell Biology, in partnership with Fulgent, the IGM, and the Department of Obstetrics and Gynecology, looks forward to providing reproductive genomic testing to CUIMC patients," said Dr. Kevin Roth, Chair, Department of Pathology and Cell Biology.

"We are thrilled to partner with Fulgent Genetics to bring reproductive genomic testing to our patients," said Dr. Mary D'Alton, Chair of the Department of Obstetrics and Gynecology at CUIMC. "Prenatal diagnosis has significantly enhanced our ability to counsel patients at risk for genetic disease in advance of delivery, but carrier screening will transform our field even further. Patients who are eager to conceive are increasingly seeking genetic information to help them make informed decisions as they build their families, and our partnership with Fulgent will make this possible for many more women and couples." Dr. Ronald Wapner, Director of Reproductive Genetics in the Department of Ob/Gyn and the IGM added "this service will allow us to continue to lead the provision of personalized medicine care in women's health." ◆

More info at Pathology Newsroom