

DECEMBER 2022

THE LEADING MAGAZINE FOR ● ENDOCRINOLOGISTS

Endocrine news

Endocrine Innovations

2022 Was a Great Year for Endocrine Science and Scientists!

Endocrine science has proven once again that it is on the leading edge of new discoveries that will improve the lives of patients around the world for generations to come.

- **EUREKA! 2022:** Endocrine Society journal editors share their top picks for the biggest advances in endocrine research throughout the year.
- **LEADING THE WAY:** The Endocrine Society continues to pioneer research and awareness of endocrine-disrupting chemicals.
- **MASTERING THE MASTER GLAND:** By remapping the landscape of the pituitary gland, researchers have unlocked its secrets while creating a worldwide database.
- **LAB PARTNERS:** Antentor Hinton, Jr., PhD, is revolutionizing the endocrine lab and dispelling myths along the way.

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Hormone Science to Health

Endocrine news

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14 | EUREKA!

The Top Endocrine Discoveries of 2022

Now that more and more research labs across the globe have swung open their doors, even more groundbreaking endocrine research seems to be getting published than ever before. For the eighth year running, *Endocrine News* talks to editors from Endocrine Society publications to unearth the endocrine nuggets of 2022.

BY KELLY HORVATH

24 | Repainting the Pituitary Landscape

Always mystifying and a bit mysterious, the pituitary sends out orders to the other glands in the body, from regulating the adrenals and the thyroid to coordinating reproduction. However, thanks to a worldwide collaboration and a new database, we are slowly but surely unlocking the “master gland’s” secrets. **BY DEREK BAGLEY**

30 | MythBuster: The Many Passions of Antentor Hinton, Jr., PhD

After years of being told that there were no other scientists out there “who looked like him,” Antentor Hinton, Jr., PhD, made it his mission to increase diversity in research labs everywhere he could. By mentoring up-and-coming scientists; championing diversity, equity, and inclusion, and even creating the *1,000 Inspiring Black Scientists of America* list in the process, he still finds time to pursue his “big idea of being able to use 3D reconstruction as a vehicle to be able to understand the cell, through looking at mitochondria.”

BY GLENDA FAUNTLEROY SHAW

36 | Q&A: Ghada El-Hajj Fuleihan, MD, MPH, and Matthew T. Drake, MD, PhD

Endocrine News talks with Ghada El-Hajj Fuleihan, MD, MPH, and Matthew T. Drake, MD, PhD, co-chairs of the guideline development panel that created the latest Endocrine Society Clinical Practice Guideline on treating hypercalcemia of malignancy.

38 | Leading the Way: How the Endocrine Society Continues to Pioneer Endocrine-Disrupting Chemicals Research

The Endocrine Society was the first such organization to recognize the threat endocrine disruptors posed to human health. *Endocrine News* shares the story of how that came to pass over the course of several years, through prolific research, meetings, symposia, and forums as well as an advocacy effort that reaches around the world.

BY ANDREA C. GORE, PHD; R. THOMAS ZOELLER, PHD;
AND JERRY HEINDEL, PHD

2 | PRESIDENT'S VIEWPOINT

Taking Stock of Our Achievements

4 | FROM THE EDITOR

What a Phenomenal Year for Endocrine Science and Scientists!

6 | TRENDS & INSIGHTS

How nuclear medicine could help target neuroendocrine cancers; and Hormone discovery could predict long-term health of men.

BY DEREK BAGLEY

8 | INTOUCH

Endocrine Society condemns Florida's ban on gender-affirming care; Three Questions With: Bulent Yildiz, MD; and EndoBridge 2022 has a successful tenth year!

11 | DASHBOARD

Highlights from the world of endocrinology

12 | ENDOCRINE ITINERARY

Scientific meetings of interest to endocrinologists from around the world

43 | ADVOCACY

Looking back at 2022 in Endocrine Society advocacy; Endocrine Society urges Congress to complete NIH appropriations; and the Society weighs in on MPFS.

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Hormone Science to Health



Taking Stock of Our Achievements

After the stress of the past two years, 2022 felt like we were starting back into the world again. Despite ongoing pandemic pressures at work and home, we came together as a community this year to advance science and make a difference for patients.

We have so much to celebrate — our first in-person annual meeting in two years, the launch of our newest journal *JCEM Case Reports*, a new focused scientific meeting delving into the latest research in stress biology, a major advocacy win to reduce insulin costs, rising Impact Factors for our journals, and the launch of new Special Interest Groups dedicated to topics such as oncoendocrinology. But our most direct impact on public health came from our local EndoCares health fair events.

Our revitalized Patient Engagement initiative offered screenings and other health services to more than 500 people in Clarkston, Ga.; Seattle; Phoenix; and Baltimore this year. More than 100 people received COVID-19 vaccinations during our Clarkston EndoCares event alone. I am so proud of our inspiring EndoCares hosts and the impact their work is having in underserved communities: Nicole Ehrhardt, MD; Lorena Alarcon-Casas Wright, MD; Subbulaxmi Trikudanathan, MD, MRCP; Sonya Haw, MD; Priyathama Vellanki, MD; Melanie Haines, MD; Ricardo Correa, MD; and Rana Malek, MD.

This year was a noteworthy one for events! We hosted our first hybrid **ENDO** program, with thousands of attendees joining us in person in Atlanta, Ga., for the first time in two years. It was thrilling to be face to face again at **ENDO 2022** and at our new basic science events.

Our Basic Science Advisory Group has championed the idea of holding intimate, in-depth meetings, and the group's efforts resulted in us cohosting "The Mechanisms of Allostasis Conference: Stressed or Stressed Out" with FASEB this fall. The event yielded insightful discussions about the science of stress biology. In the new year, we will continue to facilitate conversations about emerging science and valuable networking among basic scientists.

Important conversations are also unfolding in the pages of our journals. In 2022, we launched *JCEM Case Reports*, an open access, online-only journal spotlighting reports on clinical cases and clinical problem solving from across the endocrinology field. Past president William F. Young, Jr., is leading the new journal, which is a terrific addition to our journal portfolio. *Endocrine Reviews*, *The Journal of Clinical Endocrinology & Metabolism*, and *Endocrinology* all had significant gains in their Impact Factors this year.

We also made important strides in diversity, equity, and inclusion (DEI) during 2022. Building on the long-time success of our FLARE program supporting researchers from underrepresented minorities, we held our first Excellence in Clinical Endocrinology Leadership (ExCEL) workshop in Washington, D.C., last spring. The ExCEL program is

designed to provide comprehensive leadership training and mentorship to early-career physicians from underrepresented minorities. Our member leaders also published a policy perspective this year on the need to eradicate racism from the endocrine workforce and ensure equal access to care for patients. I commend our community's commitment to DEI.


This year, our voices helped convince Congress to finally take action to address soaring insulin prices. The Inflation

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”

Reduction Act caps monthly insulin costs to \$35 for Medicare beneficiaries. While this is a major advocacy win, we know expanding insulin caps to individuals with private insurance would improve insulin access for even more of our patients. I appreciate so many of our U.S.-based members taking a few minutes to participate in our campaign pressing Congress to do more for those with private insurance.

As we reach the end of 2022, we can be proud of our many accomplishments. When we come together, we can improve public health and elevate research. I look forward to seeing what lies ahead in 2023. 

*– Ursula B. Kaiser, MD
President, Endocrine Society*

2024 LAUREATE AWARDS

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Our Laureate Awards are the highest honors bestowed in recognition of the paramount achievements in the endocrinology field including, but not limited to, seminal research, clinical investigation, translational research, mentorship, and non-traditional activities to support developing countries.

Nominate on your own schedule—nominations for the 2024 awards cycle are now being accepted until January 20, 2023.

Get started now by visiting
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Questions? Contact us at
laureate@endocrine.org.



FROM THE **EDITOR**

Another Great Year for Endocrine Science and Scientists!

As we wrap up another year, endocrine laboratories; endocrine science; and, of course, endocrine scientists take over the December issue! For the eighth consecutive year, we are running “Eureka! The Year’s Biggest Discoveries in Endocrine Science.” This year’s roundup is once again artfully compiled by Kelly Horvath, who spoke with more than a dozen editors from the Endocrine Society’s scientific journals for their input on new discoveries that could easily affect the future of endocrine science for years to come. She commented that the editors were all very excited about all the research that had been done throughout the year now that more labs are back to research as usual. So, dive into this year’s edition on page 14, which clocks in at well over 4,000 words. That’s what happens when endocrine science gets revved up, and we are ALL here for it!

I’ve often said that each year, **ENDO** proves to be the “gift that keeps on giving” because it seems to supply an endless array of topics to feature in the pages of *Endocrine News*. That tradition lives on in a most compelling way, but not due to what was presented in one of the many scientific sessions; it was due to a chance encounter in a hotel coffee shop in Atlanta. While I was getting water during the pre-conference Early Career Forum at **ENDO 2022**, I ran into Andrea Gore, PhD, and she asked me if I thought it would be worth pursuing a story about the Endocrine Society’s efforts to champion the importance of endocrine-disrupting chemicals (EDCs). I loved the idea, and on page 38 we feature “**Leading the Way: How the Endocrine Society Continues to Pioneer Endocrine-Disrupting Chemicals Research.**” Authored by Gore; R. Thomas Zoeller, PhD; and Jerry Heindel, PhD, they explain how the Endocrine Society was the first such organization to recognize the threat EDCs posed to human health, and they take us on a journey of how that came to pass over the course of several years, through prolific research, meetings, symposia, and forums as well as an advocacy effort that reaches around the world, raising awareness about these pesky chemicals.

On page 30, Glenda Fauntleroy Shaw’s “**MythBuster: The Many Passions of Antentor Hinton, Jr., PhD**” is a true Endocrine Society success story. A graduate of the Society’s FLARE (Future Leaders Advancing Research in Endocrinology) program and a recent recipient of a \$1.15

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Executive Editor: **Mark A. Newman**
mnewman@endocrine.org

Senior Editor: **Derek Bagley**
dbagley@endocrine.org

Art Director/Production: **Anthony S. Picco**

Art Director/Design: **Catherine C. Neill,**
CNJ Creative, saLLC
www.cnjcreative.com

Prepress & Printing: **The Sheridan Group**
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Endocrine News informs and engages the global endocrine community by delivering timely, accurate, and trusted content covering the practice, research, and profession of endocrinology.



President: **Ursula B. Kaiser, MD**
president@endocrine.org

President-Elect: **Stephen Hammes, MD, PhD**
stephen_hammes@urmc.rochester.edu

Past-President: **Carol H. Wysham, MD**
chwysham@comcast.net

Secretary-Treasurer: **Jeffrey Boord, MD**
jeffrey.boord@parkview.com

Chief Communications Officer: **Aaron Lohr**
alohr@endocrine.org

The mission of the Endocrine Society is to advance excellence in endocrinology and promote its essential and integrative role in scientific discovery, medical practice, and human health.

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million, five-year grant from the Chan Zuckerberg Initiative's Science Diversity Leadership program, Hinton has made it his mission to increase diversity in laboratories, well, everywhere! As assistant professor of molecular physiology and biophysics at the School of Medicine Basic Sciences at Vanderbilt University in Nashville, Tenn., Hinton certainly practices what he preaches: "At Vanderbilt, I utilize my laboratory as a way to demonstrate what could be the standard at Vanderbilt and other universities across the nation with hiring diverse talent," he says, adding that the talent in his laboratory includes Black and Hispanic researchers, and a Hmong scientist with a PhD in development biology.

Last month, the Society for Neuroendocrinology held its annual meeting in sunny San Diego, and senior editor Derek Bagley made the cross-country trip to see what new research our readers would find interesting. On page 24, he writes about new research on the "master gland" itself, the pituitary, in "**Repainting the Pituitary Landscape**," where he discusses the latest cutting-edge research into this mystifying little gland, as well as a new worldwide collaboration to create a new pituitary database, that can be "a resource for the community," according to Frédérique Ruf-Zamojski, PhD, a biomedical experimental scientist and associate professor in neurology at the Icahn School of Medicine, Mount Sinai in New York, N.Y. "With our database, any researcher or clinician without any knowledge in coding or software can go and query any genes of interest and find where it is expressed (which cell type), its chromatin accessibility profile, and its methylation pattern in the specific cell type in mice."

Of course, this issue only touches on the ice chips at the very tip of the endocrine science iceberg; there's so much going on in endocrine labs around the world. All of these efforts, while often disparate in the details, all contribute to the broad scope of improving human health worldwide.

If you have any thoughts, comments, or even ideas for future *Endocrine News* articles, please feel free to reach out to me at: mnewman@endocrine.org. 

— Mark A. Newman, Executive Editor, *Endocrine News*

THE ENDOCRINE SOCIETY
IS THRILLED TO ANNOUNCE
AND CONGRATULATE THE

2023 LAUREATE AWARDS WINNERS

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Mitchell A. Lazar, MD, PhD

EDWIN B. ASTWOOD AWARD FOR OUTSTANDING RESEARCH IN BASIC SCIENCE

Holly A. Ingraham, PhD

GERALD D. AURBACH AWARD FOR OUTSTANDING TRANSLATIONAL RESEARCH

Myles Brown, MD and Márta Korbonits, MD, PhD, DSc, FRCP

INTERNATIONAL EXCELLENCE IN ENDOCRINOLOGY AWARD

Tasnim Ahsan, MRCP, FRCP, FCPS

OUTSTANDING CLINICAL INVESTIGATOR AWARD

Peter J. Snyder, MD

VIGERSKY OUTSTANDING CLINICAL PRACTITIONER AWARD

Mihail Zilbermint, MD, MBA

OUTSTANDING EDUCATOR AWARD

David Stephen Cooper, MD

OUTSTANDING MENTOR AWARD

William Rainey, PhD

OUTSTANDING SCHOLARLY PHYSICIAN AWARD

Bryan Haugen, MD

RICHARD E. WEITZMAN OUTSTANDING EARLY CAREER INVESTIGATOR AWARD

Rana K. Gupta, PhD

ROY O. GREEP AWARD FOR OUTSTANDING RESEARCH

Joseph Bass, MD, PhD

SIDNEY H. INGBAR AWARD FOR DISTINGUISHED SERVICE

Beverly M.K. Biller, MD

AWARDS WILL BE PRESENTED AT ENDO
2023: THE ANNUAL MEETING & EXPO IN
CHICAGO, IL, JUNE 15–18, 2023.

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BY DEREK BAGLEY
Senior Editor

TRENDS & INSIGHTS



PET Tracer Shows Promise for uPAR-Targeted Therapy of Neuroendocrine Neoplasms

A novel positron emission tomography (PET) radiotracer can accurately assess the presence of a biomarker that indicates the level of tumor aggressiveness in neuroendocrine neoplasms (NENs), according to research published in the *The Journal of Nuclear Medicine*. The detection of the biomarker provides useful information for physicians to provide personalized care for patients with NENs and may also serve as a potential target for peptide radionuclide therapy (PRRT) for NEN patients.

NENs originate from the neuroendocrine cells and are found primarily in the gastrointestinal tract, pancreas, and lungs. The treatment for patients diagnosed with NENs ranges from indolent (causing little or no pain) to highly aggressive. Treatment is dependent upon the grade, or severity, of the disease, which makes accurate risk stratification important.

The prospective clinical phase II trial included 116 patients with NENs of all grades. Of these patients, 96 had whole-body ⁶⁸Ga-NOTA-AE105 urokinase-type plasminogen activator receptor (uPAR) PET/CT performed with evaluable lesions. Images were analyzed, and the uPAR target-to-liver ratio was used to identify lesions as uPAR positive. Patients were then followed for at least one year to assess progression-free and overall survival. uPAR expression was seen in most patients with both low-grade and high-grade NENs. uPAR-positive lesions were noted in 68% of all patients and in 75% of patients with high-grade NENs. High uPAR expression was associated with a worse prognosis with regard to progression-free and overall survival.

“When ⁶⁸Ga-NOTA-AE105 PET was used to image uPAR in patients with NENs, uPAR-positive lesions were seen in most patients, notably in patients with both low-grade and high-grade NENs,” the authors conclude. “Furthermore, uPAR expression was associated with a worse prognosis. We suggest that uPAR PET is relevant for risk stratification and that uPAR may be a promising target for therapy in patients with NENs.”



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”

Hormone Discovery Could Predict Long-Term Health of Men

Scientists from the University of Nottingham have discovered that the novel insulin-like peptide hormone INSL3 is consistent over long periods of time and is an important early biomarker for prediction of age-linked disease and published their findings in *Frontiers in Endocrinology*.

Researchers led by Richard Ivell, PhD, and Ravinder Anand-Ivell, PhD, FRSB, point out that INSL3 is made by the same cells in the testes that make testosterone, but, unlike testosterone, which



fluctuates throughout a man's life, INSL3 remains consistent, with the level at puberty remaining largely the same throughout a man's life, decreasing only slightly into old age. This makes it the first clear and reliable predictive biomarker of age-related morbidity as compared to any other measurable parameters.

The results show that the level of INSL3 in blood correlates with a range of age-related illnesses, such as bone weakness, sexual dysfunction, diabetes, and cardiovascular disease.

The discovery of the consistent nature of this hormone is very significant as it means that a man with high INSL3 when young will still have high INSL3 when he is older. But someone with low INSL3 already at a young age will have low INSL3 when older, making him more likely to

acquire typical age-related illnesses, opening up possibilities for predicting age-related illnesses and finding ways to prevent the onset of these diseases with early intervention.

The research is the latest of three recent studies into this hormone. Anand-Ivell explains: "The holy grail of aging research is to reduce the fitness gap that appears as people age. Understanding why some people are more likely to develop disability and disease as they age is vital so that interventions can be found to ensure people not only live a long life but also a healthy life as they age. Our hormone discovery is an important step in understanding this and will pave the way for not only helping people individually but also helping to ease the care crisis we face as a society."

The team analyzed blood samples from 3,000 men from eight regional centers in the north, south, east, and west of Europe, including the UK, with two samples taken four years apart. The results showed that, unlike testosterone, INSL3 remains at consistent levels in individuals

The study also showed that the normal male population, even when young and relatively healthy, still shows a wide variation between individuals in the concentration of INSL3 in the blood — almost 10-fold.

Ivell adds: "Now we know the important role this hormone plays in predicting disease and how it varies amongst men, we are turning our attention to finding out what factors have the most influence on the level of INSL3 in the blood. Preliminary work suggests early life nutrition may play a role, but many other factors such as genetics or exposure to some environmental endocrine disruptors may play a part."



“

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Endocrine Society Condemns Florida's Ban on Gender-Affirming Care

Anti-science rule threatens to harm transgender and gender-diverse minors and sets a dangerous precedent for all healthcare decisions.



The Endocrine Society rebukes the Florida Board of Medicine's decision to ban gender-affirming care for transgender and gender-diverse teenagers and calls on the Florida Board to reverse the ban and allow physicians to provide evidence-based care and protect the lives of minors.

The Florida ban is blatantly discriminatory and contradicts medical evidence followed by the Endocrine Society, the American Academy of Pediatrics, the American Medical Association, the American Psychological Association, the Pediatric Endocrine Society, and other mainstream medical organizations.

When an individual's gender identity is not respected and they cannot access medical care, this can result in higher psychological problem scores and can raise the person's risk of committing suicide or other acts of self-harm. Research has found denying access to puberty-delaying medication and/or hormone therapy raises the risk of suicidal ideation and self-harm.

According to the Endocrine Society's globally recognized evidence-based Clinical Practice Guidelines, only reversible treatments to delay puberty are recommended for adolescents. Puberty-delaying medication is safe, reversible, and the conservative approach that gives teenagers and their families more time to explore their options. The same treatment has been used for decades to treat precocious puberty.

Teenagers who continue to demonstrate gender incongruence and who demonstrate the ability to provide informed consent can be offered gender-affirming hormone therapy, which is partially reversible. The Florida Medicaid ban prevents teenagers from accessing these important treatment options.

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Medical evidence, not politics, should inform treatment decisions. The Endocrine Society submitted comments earlier this year during the abbreviated public comment period on the Board's guidance on “treating gender dysphoria for children and adolescents,” yet the Florida Board of Health opted to rely on controversial research that is not recognized by the mainstream medical community in crafting its ban on gender-affirming care. Consequently, the state blocked transgender residents from receiving gender-affirming care through Medicaid coverage.

Twenty states have proposed legislation to limit access to care during the 2022 legislative session, according to Freedom for All Americans. The Endocrine Society is alarmed that misinformation about medical care recommended for transgender and gender-diverse adolescents is fueling efforts to limit access to gender-affirming care.

The move by the Florida Board of Health to ban gender-affirming care based on a political agenda rather than on science sets a dangerous precedent for all healthcare decisions.



EndoBridge Celebrates a Decade of Bridging the Worlds of Endocrinology

Celebrating its tenth anniversary, EndoBridge 2022 brought together global leaders of endocrinology and welcomed over 400 delegates from 36 countries.

As usual, the meeting was held in English with simultaneous translation into Russian, Arabic, and Turkish. Accredited by the European Council, the three-day scientific program took place from October 20 to 23 and included state-of-the-art lectures and interactive case discussions covering all aspects of endocrinology and metabolism. The abstracts of clinical cases presented by the delegates in oral and poster sessions will be published as a supplement of *JCEM Case Reports*, the Endocrine Society's newest journal.



(Top) Attendees to the 10th Annual EndoBridge Conference that took place in Antalya, Turkey, Oct. 20 – 23, 2022.
(Above) The distinguished faculty of EndoBridge 2022 came to Turkey from around the world.

Supported by the Endocrine Society, European Society of Endocrinology, and Society of Endocrinology and Metabolism of Turkey, EndoBridge welcomed the American Thyroid Association and the Brazilian Society of Endocrinology as program partners this year.

“In our first face-to-face meeting after the pandemic era, we are proud to celebrate the tenth anniversary of EndoBridge,” says Bulent O. Yildiz, MD, a faculty member at Hacettepe University School of Medicine in Ankara, Turkey, and the founder and president of EndoBridge®. “Since we first launched EndoBridge® in 2013, the initiative brought together more than 6,000 physicians and scientists from 95 countries to share their experience and expertise and participate in discussions with world-renowned leaders of endocrinology. I am excited and pleased to see that we have moved forward together to enhance cross-cultural dialogue, understanding, and collaboration beyond the national borders in the world of hormones.”

The 11th Annual EndoBridge® will take place in Antalya, Turkey, October 19 – 22, 2023. Additional information can be found at www.endobridge.org.



Bulent Yildiz, MD

Like so many Endocrine Society members, Bulent O. Yildiz, MD, wears many hats. Aside from being the founder and president of EndoBridge®, the world-renowned endocrinology conference that takes place in Turkey each autumn, he is also a professor of medicine and endocrinology at Hacettepe University School of Medicine in Ankara, Turkey.

Yildiz is also a well-regarded researcher in the field of polycystic ovary syndrome (PCOS), for which he was recently recognized with the Walter Futterweit Clinical Research Excellence Award from the Androgen Excess and PCOS Society. This annual award recognizes individuals who have made significant contributions to education, research, and/or practice in androgen excess disorders, including PCOS, over a sustained period through scholarly endeavors, teaching excellence, educational innovation, advocacy, and/or service.

1 WHAT DID IT MEAN TO YOU TO RECEIVE THE WALTER FUTTERWEIT CLINICAL RESEARCH EXCELLENCE AWARD FROM THE ANDROGEN EXCESS AND PCOS SOCIETY?

This year, we are celebrating the twentieth anniversary of the Androgen Excess and PCOS Society. I have been involved with the Society since it was first established, and I had the pleasure and privilege to interact with Dr. Walter Futterweit for many years as a mentor, colleague, and friend. Walter was an outstanding clinician and researcher in the field of PCOS, so it is a great honor for me to receive this award in his name. Connecting with Anaheim, Calif., and giving my award lecture online at 1:30 a.m. from Antalya during our EndoBridge Annual Meeting will always be memorable for me.

2 CAN YOU GIVE US SOME DETAILS ABOUT YOUR OWN PCOS RESEARCH?

Our research focuses on better understanding phenotypic features of PCOS in clinical and unselected populations as well as potential effects of oral contraceptives and other treatments on obesity and cardiometabolic and psychological disturbances in the syndrome. We are particularly interested in the gut-brain axis and metabolism in PCOS including regulation of orexigenic and anorexigenic peptides, as well as the composition and function of adipose tissue and, more recently, gut microbiota.

3 WHY DO YOU THINK PCOS IS SO UNDERAPPRECIATED?

PCOS is a lifelong metabolic, reproductive, and endocrine disorder affecting millions of women worldwide, yet it is underrecognized, underappreciated, and underfunded. The main reason for this is the difficulty in defining and diagnosing it. PCOS is a syndrome but not a disease you could diagnose by a number such as diabetes, obesity, or hypertension. There is still confusion over diagnostic criteria, and half of the patients with PCOS report seeing three or more physicians before finally receiving their diagnosis. The name does not reflect the disorder's full spectrum and might also be misleading since many women with PCOS do not have polycystic ovaries, whereas up to one third of the population will show polycystic ovarian morphology without having PCOS. Furthermore, we are far from fully understanding the etiopathogenesis, the new drug pipeline is very thin, and many current guidelines lack rigorous evidence-based recommendations aside from those for infertility management. **EN**

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This year, our voices helped convince Congress to finally take action to address soaring insulin prices. The Inflation Reduction Act caps monthly insulin costs to \$35 for Medicare beneficiaries. While this is a major advocacy win, we know expanding insulin caps to individuals with private insurance would improve insulin access for even more of our patients, **I appreciate so many of our U.S.-based members taking a few minutes to participate in our campaign pressing Congress to do more for those with private insurance.**”

— Endocrine Society President **Ursula B. Kaiser, MD**, discussing how getting involved in the Society’s advocacy efforts can make a real difference (President’s Viewpoint, page 2).

26%

Among people with chronic kidney disease, metabolic syndrome was not only common, but also increased the risk for mortality by 26%.

— SOURCE: JOURNAL OF INTERNAL MEDICINE



81% Percentage of endocrine clinicians who would still choose this specialty if they had to do it all over again.

— SOURCE: MEDSCAPE PHYSICIAN COMPENSATION REPORT 2022

ENDOCRINOLOGY



28%



Percentage of U.S. youth ages 12-19 living with prediabetes. This number more than **doubled** in the last 20 years.

— SOURCE: MEDPAGE TODAY



In stage B heart failure, uncontrolled diabetes was linked with more than a **7.5-fold** higher risk for heart failure progression.

— SOURCE: JOURNAL OF AMERICAN COLLEGE OF CARDIOLOGY

16

Number of states that now officially have high obesity prevalence rates, defined as at least 35% of residents having obesity.

— SOURCE: ENDOBREAK



17%

Percentage of nursing home residents with type 2 diabetes who met criteria for glycemic overtreatment in a recent study.

— SOURCE: JOURNAL OF THE AMERICAN GERIATRICS SOCIETY



ENDO 2023

June 15 – 18, 2023 • Chicago, Illinois/Virtual Event

REGISTRATION OPENS: January 11, 2023

ABSTRACT DEADLINE: December 19, 2022

We hope to see you at **ENDO 2023**, taking place June 15 – 18, 2023, in Chicago, Ill. With over 7,000 attendees, nearly 2,000 abstracts, and over 200 other sessions, **ENDO** is the top global meeting on endocrinology research and clinical care. **ENDO** provides the opportunity to collaborate with an unparalleled list of endocrinologists, healthcare practitioners, and leading scientists from around the world. Through sharing our experience, advice on patient care, and new advances in research, we move the needle forward in hormone health and science. Our outstanding slate of world-renowned speakers will showcase the most cutting-edge advances in research and medicine, with presentations spanning the spectrum of science, clinical care, and social implications. www.endocrine.org/endo2023



3rd International Conference on Diabetes, Endocrinology and Obesity

Virtual Event

March 20 – 21, 2023

The conference will focus on the latest and exciting innovations in all areas of diabetes research, which offers a unique opportunity for investigators across the globe to meet, network, and perceive new scientific innovations. This year's annual congress highlights the theme, "New Technologies and Practical Approaches: Diabetes and Endocrine Disorders," which reflects the

innovative progress in diabetes disease research. The two-day conference includes special keynote sessions conducted by eminent and renowned speakers who excel in the field of diabetes.

<https://www.diabetesmeet.com/>

43rd American Association of Endocrine Surgeons Annual Meeting

Birmingham, Alabama

April 29 – May 3, 2023

The 2023 AAES Annual Meeting will be an in-person event in Birmingham, Ala.

All presentations (podium and poster) will be given in person. New for #AAES2023 is an entire Scientific Session dedicated to health equity. Examples include but are not limited to: healthcare workforce disparities; differences in patient access based on social and cultural determinants of health; population-level factors, such as socioeconomic determinants, and disparities in healthcare coverage, and more.

<https://www.endocrinesurgery.org/2023-annual-meeting>



Endocrine Society Webinars

The Endocrine Society holds webinars throughout the year on many topics, from clinical practice and basic research to career development, advocacy, and more. Check below for information on upcoming webinars and links to previous events. Visit our Center for Learning for a full list of Society educational offerings.

Past webinars have included The Complexities of Cushing's Syndrome: Diagnosing and Managing Patients; Utilizing Nurse Practitioners and Physician Assistants to Optimize Patient Care: How to Build Effective Teams; Genetics in Pituitary Disease; Facts and Controversies of Testosterone Replacement Therapy in Male Hypogonadism; and so much more! Most of the webinars are free for Endocrine Society members, but some do require a small registration fee.

<https://education.endocrine.org/Public/Catalog/Main.aspx>

Obesity Research Conference Los Angeles, California/Virtual May 1 – 3, 2023

The main objective of this conference is to bring researchers together to share their ideas and provide a critical review of the present state of the field. It is designed in such a way that it provides an opportunity to meet up with people from both industry and academia and establish a scientific network between them. The 7th annual meeting (ORC-2023) will feature the same high-quality lectures as in past years, discussing the current trends in treatment options for obesity, chronic diseases associated with obesity, the epidemic of childhood obesity, the prevention methods, and the care and management of obese patients. This three-day online event will provide a dedicated platform to share cutting-edge scientific findings, medical practices, and caregiver initiatives related to obesity and various chronic diseases associated with it. It is dedicated to creating a stage for exchanging the latest research results and advanced research methods.

<https://obesity.unitedscientificgroup.org/>

18th International Pituitary Congress Chicago, Illinois June 12 – 14, 2023

The 18th International Pituitary Congress will present an exciting group of speakers expert in normal and disordered pituitary function. Our faculty includes distinguished clinicians and investigators, fellows in training, and basic scientists. As usual, we will present cutting edge in-depth topics that will permit our attendees to become familiar with the latest trends in pituitary endocrinology. The plenary format of the meeting is intended to facilitate maximum interaction and free exchange of ideas among participants and speakers.

<https://www.pituitarysociety.org/events>

INTERNATIONAL ITINERARY

SSMC Congress on Endocrinology and Endocrine Surgery Virtual and Abu Dhabi, UAE

January 6 – 8, 2023

The Mayo Clinic International - SSMC Congress on Endocrinology and Endocrine Surgery will offer opportunities to explore breakthroughs in research, share creative and stimulating ideas, make valuable connections, and obtain inspired perspectives from all members of the multidisciplinary team who are key to the management of patients with complex endocrine disorders, both medical and surgical.

<https://www.menaconference.com/>

ATTD 2023

Berlin, Germany

February 22 – 25, 2023

The 16th International Conference on Advanced Technologies & Treatments for Diabetes (ATTD 2023) to be held on February 22 – 25, 2023, in Berlin, Germany, is the leading international forum where clinicians, diabetes care providers, researchers, industries, start-ups, investors, reimbursement authorities, regulators, and people with diabetes; assemble with the goal to ameliorate the care of people with diabetes at the fastest possible pace. Presentations and discussions will be given by many distinguished professionals in the field and will include topics such as artificial intelligence-based decision support systems; glucose sensors; closed-loop systems; artificial pancreas; devices for diabetic prevention; new medications for the treatment of diabetes, insulins, delivery systems, and insulin pumps; and many more.

<https://attd.kenes.com/>

50th European Calcified Tissue Society Congress Liverpool, UK

April 14 – 18, 2023

The European Calcified Tissue Society (ECTS) and Bone Research Society (BRS) join forces to provide a unique platform for sharing the most relevant and cutting-edge science and innovation in calcium, bone and mineral metabolism in Europe. We aim to provide excellent learning and networking opportunities to basic, translational and clinical scientists, specialists, trainees and allied health professionals.

<https://www.ects2023.org/>

WCO-IOF-ESCEO 2023

Barcelona, Spain

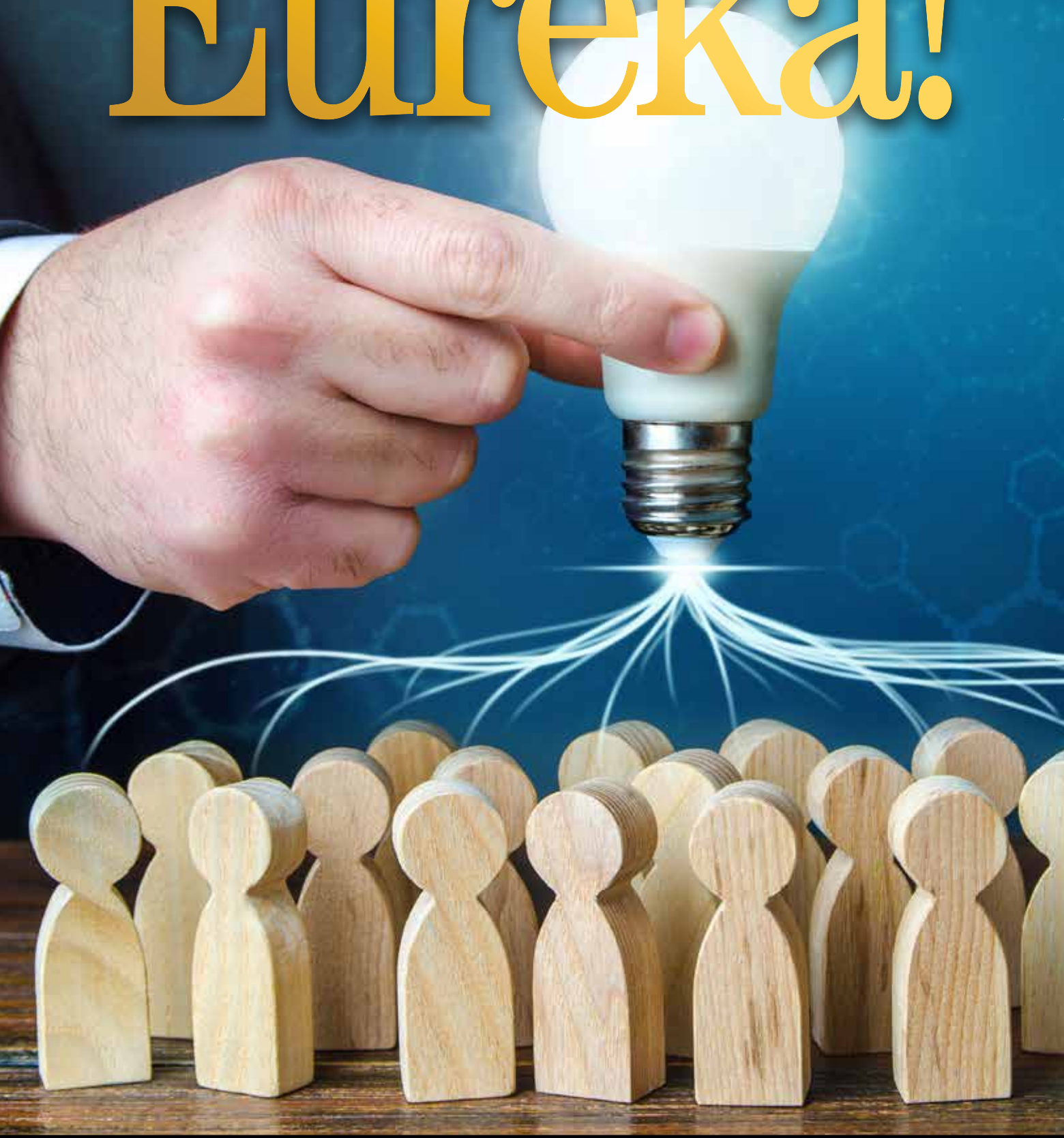
May 4 – 7, 2023

After more than two years of virtual editions, the World Congress on Osteoporosis, Osteoarthritis, and Musculoskeletal Diseases will take place from May 4 – May 7, 2023 in Barcelona, Spain. The members of the Committee of Scientific Advisors of the International Osteoporosis Foundation (IOF) and the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) are developing a scientific program that will bring together the world's best in the field of musculoskeletal health and disease. It is hoped that this Congress will move the field one step forward on all fronts, from new understanding of bone metabolism and pathology to new strategies and options in prevention, diagnosis, and treatment.

<https://www.wco-iof-esceo.org/>

Eureka!

BY KELLY HORVATH





THE TOP ENDOCRINE DISCOVERIES OF 2022

Now that more and more research labs across the globe have swung open their doors, there seems to be even more groundbreaking endocrine research getting published than ever before. For the eighth year running, *Endocrine News* talks to editors from Endocrine Society publications to unearth the endocrine nuggets of 2022.

This may go down as the “Gold Rush of ’22.” Maybe because researchers were more fully able to return to their labs this year after facing pandemic-related challenges for so long, or maybe just because it has been a banner year for endocrinology research, they struck it rich. Whatever the reason, the number and quality of this year’s studies are better than ever.

More than a dozen editors from *Endocrine Reviews*, *Endocrinology*, *Journal of the Endocrine Society*, and *The Journal of Clinical Endocrinology & Metabolism* (JCEM) share what they consider the top endocrinology studies published in the last 12 (or so) months.

Their picks span just about every endocrine theme: new insights into endocrinopathies like hypogonadotropic hypogonadism, Cushing disease, all forms of diabetes, obesity, aldosteronism, and hypothyroidism are among the breakthroughs. Breast, thyroid, and adrenocortical cancers are now more fully understood. An array of molecules was discovered or further investigated. Endocrine disruptors were found to wreak yet more havoc than previously known. Pathophysiologic mechanisms and pathways were better elucidated, and links uncovered. Collectively, this research shows how study of patients with certain diseases can lead to improvement of care; addresses important and understudied clinical questions; and highlights areas of clinical uncertainty where additional, larger, trials are needed. The breadth of these study topics underscores how endocrinology touches every facet of life.



“ In thinking about the most significant publications in endocrinology over the past 12 months. I have been impressed by many ‘clinical approach’ articles and meta-analyses, but for the most part these have not greatly changed my clinical practice. As an active clinician, I am most interested in publications that are not directly concerned with the majority of my patients in my specialist field, but more in those offering novel data for patients whom I would only infrequently see, but whose management is troubling.”

— ASHLEY GROSSMAN, FMedSci, EDITOR-IN-CHIEF,
ENDOCRINE REVIEWS



From the Editor-in-Chief of *Endocrine Reviews*

Endocrine Reviews editor-in-chief **Ashley Grossman**, FMedSci, emeritus professor of endocrinology, University of Oxford; senior research fellow, Green Templeton College; consultant NET endocrinologist, Royal Free London; professor of neuroendocrinology, Barts and the London School of Medicine; and consultant endocrinologist at the London Clinic Centre for Endocrinology, in the U.K., chose **“Cytoreductive Surgery of the Primary Tumor in Metastatic Adrenocortical Carcinoma: Impact on Patients’ Survival”** from the April issue of *The Journal of Clinical Endocrinology & Metabolism* (JCEM) by Srougi, V. et al. This survey by nine international groups retrospectively analyzed the effects of cytoreductive therapy on survival in 239 patients with metastatic adrenocortical cancer (ACC), led by a center in São Paulo, Brazil.

“In thinking about the most significant publications in endocrinology over the past 12 months,” Grossman says, “I have been impressed by many ‘clinical approach’ articles and meta-analyses, but for the most part these have not greatly changed my clinical practice. As an active clinician, I am most interested in publications that are not directly concerned with the majority of my patients in my specialist field, but more in those offering novel data for patients whom I would only infrequently see, but whose management is troubling.”

For patients with ACC, this is especially true, he explains. “I see a steady stream of such patients, their outlook is generally (although surprisingly not always) horrid, and survival is poor in spite of chemotherapy and mitotane. New molecular therapies have not made any major impact.” In Grossman’s chosen study, however, “over a mean follow-up of just over five years, the hazard ratio of a beneficial effect of surgery was 3.18; there may also have been a positive effect of metastatectomy. Accepting all the caveats regarding a retrospective analysis, and the fact that survival in all patients is still sadly very poor, nevertheless this is one study that may affect my own management plans for this awful disease,” he says.



More From the Editors of *Endocrine Reviews*

Katrin J. Svensson, PhD, assistant professor (Department of Pathology) at Stanford University, Stanford School of Medicine, in Palo Alto, Calif., gives **“An Exercise-Inducible Metabolite that Suppresses Feeding and Obesity”** from the June issue of *Nature* by Li, V. L., et al. top billing.

“My top choice this year is the discovery of the exercise-inducible anti-obesity molecule lactoylphenylalanine (Lac-Phe), which was covered by more than 120 news outlets,” Svensson says. “By looking at the plasma metabolome from humans, horses, and mice, these researchers found the top metabolite elevated after exercise to be a molecule called Lac-Phe. Remarkably, the function of this metabolite is to suppress appetite. While exercise obviously burns calories, this study highlights a new mechanism by which physical activity is linked to obesity.”



From the Editor-in-Chief of *Endocrinology*

Editor-in-chief **Carol A. Lange**, PhD, professor of medicine (Division of Hematology, Oncology, and Transplantation) and pharmacology; Tickle Family Land Grant Endowed Chair of Breast Cancer Research; co-lead, Cellular Mechanisms of Cancer Program; and director, Molecular, Genetic, and Cellular Targets of Cancer Training Program at the University of Minnesota Masonic Cancer Center in Minneapolis chose several papers that cover topics she specializes in. “It was a great year,” Lange says, “our field is so vibrant!”

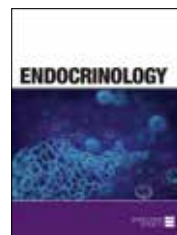
Although admittedly hard to choose, **“90 Years of Progesterone: Progesterone Receptor Signaling in the Normal Breast and Its Implications for Cancer”** published in the July 2020 issue of *Journal of Molecular Endocrinology* by Brisken, C. and Scabia, V. was her favorite: “This is likely a first to show progesterone receptors are drivers of metastasis in vivo,” she explains.

Another that rose to the top of her list is **“Insulin Action and Resistance Are Dependent on a GSK3-FBXW7-ERR Transcriptional Axis”** by Xia H., et al. in the April issue of *Nature Communications* that shows that nuclear receptors multitask by “sensing” multiple hormones.

Two focusing on mutant estrogen receptors — an area currently of great interest in the endocrine research sphere — are **“Steroid**

Hormone Receptor and Infiltrating Immune Cell Status Reveals Therapeutic Vulnerabilities of ESR1-Mutant Breast Cancer” by Williams M. M., et al., published in *Cancer Research* in February 2021, and **“ESR1 Mutant Breast Cancers Show Elevated Basal Cytokeratins and Immune Activation”** by Li, Z. et al., published in the April issue of *Nature Communications*.

Immunomodulation is another theme Lange has particular interest in, and **“Obesity Alters Pathology and Treatment Response in Inflammatory Disease”** by Bapat, S. P. et al., published in March in *Nature*, got her attention, as did **“Autocrine Vitamin D Signaling Switches Off Pro-Inflammatory Programs of TH1 Cells”** by Chauss, D. et al., published in the January issue of *Nature Immunology*. This one, says Lange, “shows how vitamin D modulates pro-inflammatory T cells, by shutting them down, which is relevant to COVID infection. It also may explain why it protects from a number of cancers and can protect from COVID.”



More From the Editors of *Endocrinology*

Several associate editors of *Endocrinology* also contributed. **Jennifer K. Richer**, PhD, tenured professor of pathology, University of Colorado Anschutz Medical Campus and co-leader, Tumor Host Interactions Program, University of Colorado Cancer Center, in Aurora, Colo., also appreciated Lange’s choices and selected four additional papers that shed light on hormones and immune modulation and metastasis in cancer themes.

“I really liked these articles in *Nature* from June: **“Androgen Receptor Activity in T Cells Limits Checkpoint Blockade Efficacy”** by Moran, A. E., et al., and **“Androgen Receptor Blockade Promotes Response to BRAF/MEK-Targeted Therapy”** by Vellano, C. P., et al. I also like these two in *Endocrinology*: from July, **“The Liver X Receptor Is Selectively Modulated to Differentially Alter Female Mammary Metastasis-Associated Myeloid Cells”** by Ma, L. et al. and **“T-cell Metabolism as Interpreted in Obesity-Associated Inflammation”** from October by Bharath, L. P. et al.

Hershel Raff, PhD, FAAAS, FAPS professor of medicine, surgery, and physiology and professor of Pharmacy School, at the Medical College of Wisconsin (MCW), and director of the Endocrine Research Laboratory at Aurora St. Luke’s Medical Center, in Milwaukee, Wis., chose **“Corticosteroid-binding Globulin (SERPINA6) Establishes Postpubertal Sex Differences in Rat Adrenal Development”** from the October issue of *Endocrinology* by Toews, J. N. C. “There is intense interest in the pubertal development of sex differences in the hypothalamic-pituitary-adrenal (HPA) axis,” he says. “Many researchers overlook how important plasma

corticosteroid-binding protein (CBG) is in all aspects of HPA axis function including development of sex differences. Using a novel rat model, the authors concluded that ‘...sex differences in adrenal growth, morphology and gene expression profiles that emerge during puberty in rats are dependent on concomitant increases in plasma CBG produced by the liver.’ The effects of CBG on the adrenal transcriptome has significant implications in clinically relevant sex differences in HPA axis dynamics and function.”

Patricia L. Brubaker, PhD, FRSC, professor, Departments of Physiology and Medicine; Banting & Best Distinguished Scholar at the University of Toronto, in Ontario, credits **“Beta-Hydroxybutyrate Suppresses Hepatic Production of the Ghrelin Receptor Antagonist, LEAP2”** by Holm, S. et al., published in *Endocrinology* in June. “This study provides exciting new insight into the regulation of hunger signals during fasting, through studies in humans exposed to a variety of different environmental conditions, as well as in animal models,” she explains. “The findings indicate that signaling by the orexigenic hormone, ghrelin, is modulated by a fasting-induced metabolite (β -hydroxybutyrate) through actions on a hepatic ghrelin receptor antagonist.”

Daniel J. Bernard, PhD, professor, Department of Pharmacology and Therapeutics; director, Centre for the Study of Reproduction, at McGill University in Montreal, Canada, selected **“TGFBR3L Is an Inhibin B Co-Receptor that Regulates Female Fertility”** published in December 2021 by Br  l  , E. et al. in *Science Advances*. “At the end of 2021, the orphan protein TGFBR3L was discovered to be the long sought-after inhibin B receptor,” says Bernard, who was a coauthor of the paper. “Inactivation of the *Tgfr3l* gene in female mice led to increases in follicle-stimulating hormone levels and litter sizes. TGFBR3L’s restricted expression to pituitary gonadotropes makes it a novel target to similarly regulate FSH and fertility in humans.”



From the Editor-in-Chief of the *Journal of the Endocrine Society*

For JES editor-in-chief **Zeynep Madak-Erdogen**, PhD, associate professor of nutrition; Sylvia D. Stroup Scholar at the University of Illinois Urbana-Champaign, **“Operation of a TCA Cycle Subnetwork in the Mammalian Nucleus”** was a stand-out, published in *Science Advances* in June by Kafkia, E. et al. “It is fascinating to see how key metabolic pathways are present and functional in the nucleus to change posttranslational modification of key proteins to impact cellular programs,” she says. “There are many implications for how nuclear receptor activities might be directly modulated by metabolic states.”

Madak-Erdogen also appreciated **“Gut Bacterial Nutrient Preferences Quantified In Vivo”** published in September in *Cell* by Zeng, X. et al. “This paper is important because they elegantly delineate the nutrient sources for gut microbiota. It makes one reconsider what diet is, how a body’s ecosystem utilizes it, and how one can potentially use diet as a tool to revamp gut microbiota to support health.”



More from *Journal of the Endocrine Society* Editors

Ana Claudia Latronico, MD, PhD, head professor of the Endocrinology and Metabolism Division of S  o Paulo University in Brazil, nominates **“MC3R Links Nutritional State to Childhood Growth and the Timing of Puberty,”** published in *Nature* in November 2021, by Lam, B. Y. H. et al., for demonstrating a new pathway link between the reproductive and metabolism systems. “It was known that common variants in the vicinity of MC3R (melanocortin receptor type 3) were associated with both adult height and age at menarche,” she explains. “In this study, loss-of-function mutations in MC3R (heterozygous and homozygous) were associated with later onset of puberty in humans. In addition, mice lacking MC3R had delayed sexual maturation and an insensitivity of reproductive cycle length to nutritional perturbation. These findings suggest that MC3R primarily regulates the disposition of calories into growth, lean mass, and the timing of sexual maturation.”

“An Exercise-Inducible Metabolite that Suppresses Feeding and Obesity” by Li, V.L., et al., published in *Nature* in June got a second nod, this one from **Stephen R. Hammes**, MD, PhD, Louis S. Wolk Distinguished Professor of Medicine; chief, Division of Endocrinology and Metabolism; and executive vice chair, Department of Medicine at the University of Rochester School of Medicine and Dentistry in Rochester, N.Y. “It turns out that Lac-Phe reduces food intake in animals, including mice, humans, and racehorses, without affecting energy expenditure,” he says. “Interestingly this compound is only produced with vigorous aerobic exercise, and may be the reason why, when we exercise hard, our appetite acutely goes down. In animals, administration of Lac-Phe decreases body weight and improves glucose metabolism, whereas reduction of Lac-Phe synthesis in mice increases food intake and obesity following exercise.”

Jodi A. Flaws, PhD, professor, Department of Comparative Biosciences, at the University of Illinois Urbana-Champaign, liked **“Correlates of Positive Thyroid Peroxidase Antibodies Among Firefighters: A Cross-Sectional-Study”** by Ogunsina, K. et al., published in August in JES. “I was interested in the paper because



it is a very novel study on the potential impact of endocrine-disrupting chemicals (EDCs) in flame retardants on thyroid function in firefighters,” she says. “We know that humans are being exposed to EDCs on a daily basis and that firefighters have an increased exposure in flame retardants. However, we have limited information on the impact of such exposures on thyroid function. The paper contains new and important data showing thyroid peroxidase antibodies are high in firefighters, suggesting that we may need to screen/monitor thyroid function in firefighters.”

Roberto Salvatori, MD, professor of medicine and neurosurgery; medical director, Pituitary Center at Johns Hopkins University in Baltimore, Md., chose **“Long-term Safety of Growth Hormone in Adults with Growth Hormone Deficiency: Overview of 15 809 GH-Treated Patients”** by Johannsson, G. et al. from the June issue of JCEM. “This is the largest cohort of subjects treated with growth hormone (GH) replacement therapy (with the longest follow up) showing that in both adult-onset and childhood-onset GH deficiency, replacement therapy was not associated with increased risks or new cancer or of recurrence of pituitary adenomas,” he said.

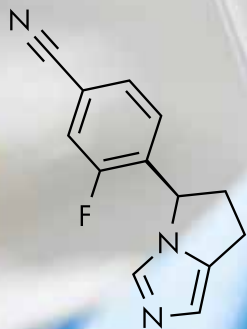


From the Editor of *The Journal of Clinical Endocrinology & Metabolism*

Editor-in-chief of JCEM, **Paul M. Stewart**, MD, FRCP, FMedSci, executive dean and professor at the University of Leeds School of Medicine in the United Kingdom says he “wanted something of an evidence to a decision that flags a couple of great papers from the nearly 500 that JCEM publishes each year” and highlights two: **“Effects of Tirzepatide, a Dual GIP and GLP-1 RA, on Lipid and Metabolite Profiles in Subjects with Type 2 Diabetes,”** by Pirro, V. et al. from February, and **“Randomized Trial of Osilodrostat for the Treatment of Cushing Disease,”** by Gadelha, M. et al. from June. “For me, both highlight a real strength of JCEM — the publication of innovative phase 2 clinical studies that are multicenter in design, partnered with industry, informed by state-of-the-art experimental medicine, and that will undoubtedly shape future clinical practice,” Stewart says.

“ We know that humans are being exposed to EDCs on a daily basis and that firefighters have an increased exposure in flame retardants. However, we have limited information on the impact of such exposures on thyroid function. The paper contains new and important data showing thyroid peroxidase antibodies are high in firefighters, suggesting that we may need to screen/monitor thyroid function in firefighters.”

— JODI A. FLAWS, PHD, PROFESSOR, DEPARTMENT OF COMPARATIVE BIOSCIENCES, UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN, ILL., ON THE PAPER “CORRELATES OF POSITIVE THYROID PEROXIDASE ANTIBODIES AMONG FIREFIGHTERS: A CROSS-SECTIONAL STUDY” BY OGUNSINA, K. ET AL., PUBLISHED IN AUGUST IN *THE JOURNAL OF THE ENDOCRINE SOCIETY*



osilodrostat



“ JCEM is known for publishing papers that alter our approach to clinical management of endocrine diseases. However, JCEM has also been one of the leading journals that publish basic physiologic observations and mechanisms of metabolism in humans.”

— RAGHU G. MIRMIRA, MD, PHD, PROFESSOR OF MEDICINE; VICE CHAIR FOR RESEARCH; DIRECTOR, TRANSLATIONAL RESEARCH CENTER AT THE UNIVERSITY OF CHICAGO, CHICAGO, ILL.

The first study describes the effect of the novel glucagon-like peptide 1 receptor (GLP-1R) agonist tirzepatide on lipid and metabolic profiles in patients with type 2 diabetes mellitus. “Highly effective in improving insulin action and often weight reduction, GLP-1Rs have become the standard care for many patients. Recent work has focused on dual agonists that, in addition to their action on the GLP-1R also stimulate the glucose-dependent insulinotropic polypeptide receptor (GIPR). In this double-blind placebo-controlled study involving over 300 patients and utilizing novel mass spectrometric analyses, dual agonist therapy with tirzepatide significantly improved metabolomic and lipidomic profiles in addition to glucose control compared to placebo or GLP-1R agonist alone. Although the mechanisms are not yet fully understood this dual agonist approach offers the exciting possibility of reversing the metabolic dysregulation associated with type 2 diabetes mellitus while also addressing glucose control.”

The second study demonstrates the effectiveness of osilodrostat, a potent oral inhibitor of 11β-hydroxylase, an enzyme involved in the final biosynthetic pathway of cortisol within the adrenal cortex. “Without control of hypercortisolism, Cushing syndrome has a high morbidity and mortality,” Stewart explains. “Although surgery remains the mainstay of treatment for most patients, up to one third of patients with the commonest cause — pituitary-dependent Cushing syndrome (Cushing disease) — are unsuitable for surgery or not cured postoperatively. Several drugs are licensed to treat such patients in an attempt to normalize cortisol hypersecretion, but to date, all with variably efficacy. In this randomized placebo-controlled study of 73 patients with Cushing disease, osilodrostat normalized urinary free cortisol in 77% and 81% of patients receiving the drug after 12 weeks and 36 weeks, respectively. The drug was well tolerated with anticipated ‘side effects’ that we typically observe in patients undergoing ‘steroid withdrawal.’”

“These outstanding clinical studies highlighting the clinical benefit of new therapeutics have provided pivotal information to improve the management of our patients with type 2 diabetes mellitus and separately those with Cushing disease,” Stewart adds.



More from JCEM Editors

David J. Handelsman, PhD, professor of medicine, Concord Clinical School, ANZAC Research Institute, at the University of Sydney; Department of Andrology, Concord Hospital, in Australia, liked two JCEM hypogonadism papers. **“Reproductive Phenotypes in Men with Acquired or Congenital Hypogonadotropic Hypogonadism: A Comparative Study”** was published in June by Maione, L. et al. “This is a comprehensive, large study of congenital and acquired hypogonadotropic hypogonadism outlining their differences and will be a definitive reference for this condition,” Handelsman says. Stamou, M. I. et al. published **“Prevalence and Phenotypic Effects of Copy Number Variants in Isolated Hypogonadotropic Hypogonadism”** in July. “This large study describes the prevalence and impact of copy number variation as a genetic cause of congenital hypogonadotropic hypogonadism and brings to attention the importance of this overlooked genetic mechanism in this condition,” he says.

Elizabeth N. Pearce, MD, MSc, Boston University School of Medicine, Section of Endocrinology, Diabetes, and Nutrition, Boston, Mass., says, “I opted to highlight two thyroid papers (since, as a thyroidologist, these are the ones I get most excited about). The first is the most highly cited thyroid trial in JCEM, and the second is the most highly cited JCEM thyroid paper overall.”

By Brose, M. S. et al., **“A Randomized Study of Lenvatinib 18 mg vs 24 mg in Patients with Radioiodine-Refractory Differentiated Thyroid Cancer”** came out in February. “The multikinase inhibitor lenvatinib has been shown to prolong survival in patients with advanced, non-radioactive iodine-avid differentiated thyroid cancer,” Pearce says. “However, at the recommended starting dose of 24 mg daily, it is poorly tolerated, and most patients will require treatment interruptions or dose reduction. This randomized, blinded clinical trial in 152 patients aimed to determine whether starting lenvatinib at 18-mg/day leads to reduced toxicity and similar efficacy compared to the 24-mg/day dose. Disappointingly, this did not prove to be the case, as response to therapy at 24 weeks was significantly lower in the 18-mg/day group, and adverse effects did not differ. This trial clearly supports starting lenvatinib at the labeled 24-mg daily dose.”

Her second choice, **“SARS-CoV-2 Vaccine-induced Thyroiditis: Safety of Revaccinations and Clinical Follow-up,”** by Oğuz, S. H. et al. that came out in April, stands out despite being about COVID, which has been studied extensively the last two years. “It is now reasonably well established that both SARS-CoV-2 infection and SARS-CoV-2 vaccination may trigger subacute thyroiditis or Graves’ hyperthyroidism,” said Pearce. “This study was the first to address the very practical question of whether it is safe to provide repeated SARS-CoV-2 vaccination in patients who have already experienced vaccine-related thyroiditis. In this small series in which cases were meticulously defined, it is reassuring that only two of nine patients with prior vaccine-linked thyroiditis developed recurrent thyroiditis with subsequent vaccine doses.”

Sangeeta Kashyap, MD, professor of medicine; associate program director for Endocrinology, Diabetes and Metabolism Fellowship at the Cleveland Clinic Lerner College of Medicine in Ohio, also chose two JCEM papers. **“Twin Study: Genetic and Epigenetic Factors Affecting Circulating Adiponectin Levels,”** published in September by Hasegawa, M. et al., “highlights that fat hormones are under the influence of the environment thru epigenetic modifications and not just genetic factors that one would expect in monogenic twins.” Thanks to **“Mapping Cord-Blood Transcriptome of Early Pregnancy Maternal Anemia to Identify Signatures of Fetal Programming”** by Hatem, G. et al. in April, says Kashyap, “We have a better sense of which genes in fetal development are linked to diabetes from mothers with anemia.”

Raghu G. Mirmira, MD, PhD, professor of medicine; vice chair for research; director, Translational Research Center at the University of Chicago, Chicago, Ill., also gave two JCEM papers top billing. **“Ketone Body Infusion abrogates Growth Hormone Induced Lipolysis and Insulin Resistance,”** by Høgild, M. L. et al., was just published in October. “JCEM is known for publishing papers that alter our approach to clinical management of endocrine diseases. However, JCEM has also been one of the leading journals that publish basic physiologic observations and mechanisms of metabolism in humans. This study provides new insight into human metabolic disease. It has been observed that ketone body administration (notably β -hydroxybutyrate) reduces glucose and free fatty acid (FFA) levels in humans, but the underlying mechanisms, and if the two are linked, has remained unknown. In this study, the authors induced elevations in FFAs through infusion of growth hormone, along with infusions of either saline or β -hydroxybutyrate in healthy subjects. They studied insulin sensitivity using a clamp technique and followed glucose levels using a tracer. They found that the mechanism by which β -hydroxybutyrate reduces glucose levels is not a direct effect on improving insulin sensitivity, but a secondary effect via the suppression of FFAs. The authors hypothesize that this effect on FFA suppression might be mediated through the HCA2 receptor. This study provides an important

new insight into the mechanism by which ketone bodies improve insulin resistance and lower blood glucose.”

From September, **“Lower Blood Oxygen Saturation is Associated with Microvascular Complications in Individuals with Type 1 Diabetes,”** by Laursen, J. C. et al., focuses on determinants of complications in the setting of type 1 diabetes, a topic that has received less attention compared to type 2 diabetes. “Nevertheless,” Mirmira says, “complications such as retinopathy, nephropathy, neuropathy, and cardiovascular disease occur in individuals with type 1 diabetes, and determinants beyond glycemic control have not been intensively investigated. These authors have previously shown that hypoxemia is more prevalent in individuals with type 1 diabetes compared to controls and hypothesized that low blood oxygen may contribute to the pathogenesis of diabetic complications. The authors performed a cross sectional study of low versus high blood oxygen saturation in patients with type 1 diabetes, adjusting for variables such as age, diabetes duration, sex, smoking, physical activity, body mass index, systolic blood pressure, and blood hemoglobin, then calculated odds ratios (ORs) for developing complications. They show that individuals with low blood oxygen saturation exhibit significantly higher ORs for traditional ‘microvascular’ complications (nephropathy, retinopathy, neuropathy), but not for cardiovascular disease. These findings suggest that low oxygen saturation in individuals with type 1 diabetes may be a contributing factor for the development of complications, a finding not previously appreciated. This study points to the need to conduct prospective cohort studies to examine the association, and whether correcting hypoxemia might lower risk of complications.”


Whitney S. Goldner, MD, professor, Division of Diabetes, Endocrinology & Metabolism, at the University of Nebraska Medical Center in Omaha chose **“Thyroid Cancer and Pesticide Use in a Central California Agricultural Area: A Case-Control Study,”** by Omidakhsh, N., et al. that published in JCEM in July. “I liked this article because it investigated the possible association between





residential exposure to pesticides and its association with thyroid cancer,” she says. “There has been an increasing amount of information about endocrine disruptors and their association with overall endocrine health and thyroid cancer in recent years. Many of the studies have evaluated agricultural or occupational exposure to pesticides. This article focuses on exposure that can occur within urban areas from residential pesticide exposure. This highlights the importance of further research in the area of endocrine disruptors and thyroid and other endocrine cancers.”

Felix Beuschlein, MD, director, Department of Endocrinology, Diabetology and Clinical Nutrition; director, Center for Obesity and Metabolic Surgery, Universitäts Spital Zürich, in Germany, picked a paper out of *Nature Communications* from September by Le Floch, E. et al. “**Identification of Risk Loci for Primary Aldosteronism in Genome-Wide Association Studies**” identifies the first risk loci for primary aldosteronism and suggests new mechanisms involved in the development of aldosterone-producing adenoma and bilateral adrenal hyperplasia in accordance with accumulating evidence for a continuum between the two conditions,” he says.

Hirota Watada, MD, PhD, professor, Department of Metabolism and Endocrinology, at Juntendo University in Tokyo, Japan, found “**Microbiota Imbalance Induced by Dietary Sugar Disrupts Immune-Mediated Protection from Metabolic Syndrome**,” by Kawano Y. et al., published in September in *Cell*, particularly interesting. “There have been many reports on how metabolic abnormal obesity causes insulin resistance, regarding the involvement of inflammation in adipocytes and abnormal secretion of adipocytokines,” he says. “It has been reported that a high-fat diet causes intestinal inflammation, resulting in endotoxemia and adipocyte inflammation, but the mechanism of this process has not been elucidated. These authors reported that in mice, Th17 cells in the intestinal epithelium release IL17 under a normal diet, which is involved in the maintenance of normal fat absorption, but that high sugar intake along with a high-fat diet alters the intestinal microbiota that changes in the intestinal microflora. This change reduced the number of Th17 cells, resulting in increased fat absorption from the intestinal tract. If this result would be applicable for humans, it will greatly contribute to the elucidation of the pathogenesis of metabolic abnormal obesity as well as to the development of a new therapy.” 

“ **There has been an increasing amount of information about endocrine disruptors and their association with overall endocrine health and thyroid cancer in recent years. Many of the studies have evaluated agricultural or occupational exposure to pesticides. This article focuses on exposure that can occur within urban areas from residential pesticide exposure. This highlights the importance of further research in the area of endocrine disruptors and thyroid and other endocrine cancers.**”

— WHITNEY S. GOLDNER, MD, PROFESSOR, DIVISION OF DIABETES, ENDOCRINOLOGY & METABOLISM, AT THE UNIVERSITY OF NEBRASKA MEDICAL CENTER, OMAHA, NEBRASKA, ON “THYROID CANCER AND PESTICIDE USE IN A CENTRAL CALIFORNIA AGRICULTURAL AREA: A CASE-CONTROL STUDY,” BY OMDAKHSH ET AL. FROM THE JULY 2022 JCEM

HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE ABOUT THE OFTEN-CONFOUNDING CONDITION OF BONE FRAGILITY IN DIABETES IN LAST MONTH'S ISSUE.

Repainting the **PITUITARY LANDSCAPE**



Always mystifying and a bit mysterious, the pituitary sends out orders to the other glands in the body, from regulating the adrenals and the thyroid to coordinating reproduction. However, thanks to a worldwide collaboration and a new database, we are slowly but surely unlocking the “master gland’s” secrets.

BY DEREK BAGLEY

The pituitary — the master gland that produces hormones controlling the functions of many other organs, ranging from blood pressure to sexual maturation and reproduction — has been left out of major single-cell atlases and consortia, and therefore it has not been characterized at single-cell resolution until very recently. There are a couple of reasons for this: animal models can be elusive, since the pituitary gland, about the size of a chickpea in humans, is obviously much smaller in mice. Moreover, contrary to other organs included in human databases and atlases, the pituitary can only be studied postmortem in humans, which complicates the access to samples.

However, over the past couple of years, researchers at the Icahn School of Medicine at Mount Sinai in New York, along with other laboratories in the U.S., Canada, and the United Kingdom, have been mapping the landscape of the pituitary gland, looking at the gland's cell types using single-nucleus (sn) multi-omics assays, first in murine pituitaries, then in archived post-mortem human pituitaries, and adding their findings to a growing database. They hope this pituitary database will be a resource for others seeking to get a better understanding of this complex and important organ. The investigators published their mouse model-related findings in *Nature Communications* in May 2021, and followed with a *Cell Reports* article in March 2022 describing the results obtained in human pituitary samples. .

“Pituitary cell types have been well-established for years,” says Frédérique Ruf-Zamojski, PhD, a biomedical experimental scientist and associate professor in neurology at the Icahn School of Medicine at Mount Sinai in New York. “We know they consist of hormone-producing cells as well as non-hormone producing cells. However, determination of the exact composition, and cell type-specific characterization of the pituitary at the transcriptomic and epigenetic levels to look into potential cell states or subtypes had yet to be achieved.”

Using Single-Nucleus Atlases

Ruf-Zamojski and her colleagues developed single-nucleus atlases instead of single-cell ones because access to healthy pituitary samples is made more feasible from frozen archived samples stored in biobanks and, as such, can only be analyzed using nuclei. She says that her laboratory developed and optimized specific protocols for frozen pituitaries, since, at the time, very few groups were using nuclei, and no commercial protocols for nuclei were published or even supported by commercial single-cell platforms.

Ruf-Zamojski says that there were three main reasons to build single-nucleus atlases of murine and human pituitaries. First, the lab of Stuart C. Sealfon, MD, with whom she is working, focuses on the regulation of gonadotrope cells, which represent only 5% of pituitary cells. She explains that there



Frédérique Ruf-Zamojski, PhD

“Interestingly, we found stem cells at different stages, with many uncommitted stem cells, but also detected committed progenitors at all ages. Using pseudotime trajectory analyses, we further characterized their gene expression changes with age and sex differences. Our sample size in this study was small, and additional studies will be needed to complete a multi-omics characterization of human pituitary stem cells.”

— FRÉDÉRIQUE RUF-ZAMOJSKI, PHD, BIOMEDICAL EXPERIMENTAL SCIENTIST AND ASSOCIATE PROFESSOR IN NEUROLOGY, ICAHN SCHOOL OF MEDICINE, MOUNT SINAI, NEW YORK, N.Y.

are cell culture models of gonadotrope cells that, although proven useful to tackle some underlying mechanisms, remain imperfect, and do not represent physiological gonadotropes in their environment. “Having single-cell atlases of pituitaries enables the study of gonadotropes in vivo, revealing molecular aspects we cannot get from cell cultures,” she says.

Next, Ruf-Zamojski describes the need to have normal reference atlases for comparing and getting a better understanding of the molecular pathogenesis of neuroendocrine pituitary tumors/adenomas. These tumors may arise from any pituitary cell types; they represent heterogeneous and complex systems composed of different cell types and subtypes; they often recur, and recurrence

may be from a single cell. “Having single-cell/nucleus atlases and single-cell resolution data is critical for elucidating the molecular mechanisms underlying pituitary tumor development,” she says.

Finally, Ruf-Zamojski says, it is important to have cell-type specific transcriptomic and epigenetic information to study any gene in the genome and get basic information on its expression and regulation.

Finding Lost Signals

This past summer, Ruf-Zamojski presented some of her lab’s work at ENDO 2022 in Atlanta, Ga. During the session,

RESEARCH RESOURCE: Connecting Collaborators Around the World

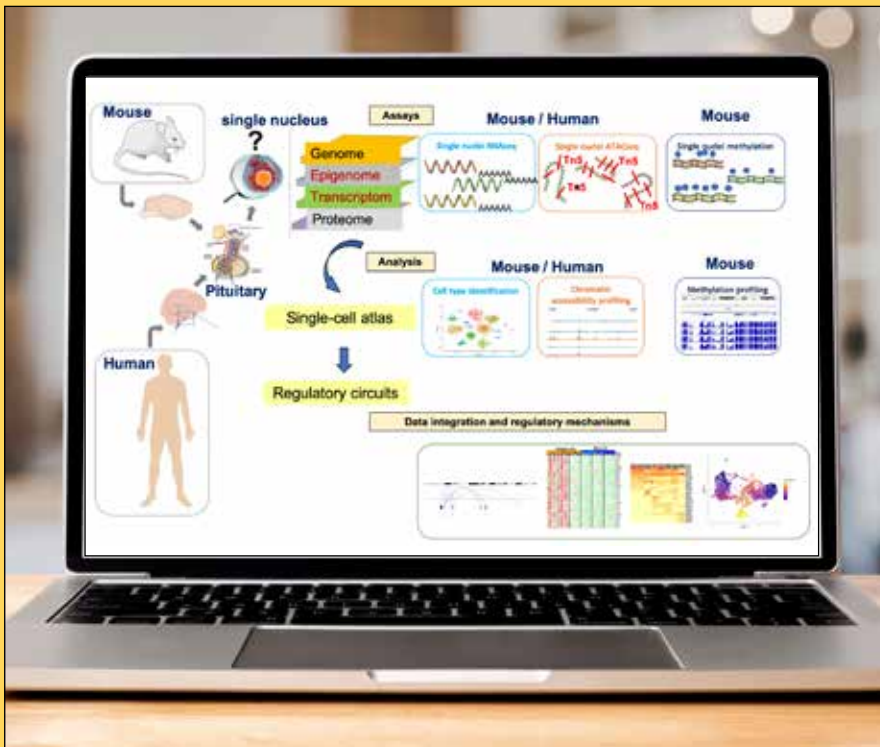
To help researchers develop additional studies to reach more definite conclusions, Ruf-Zamojski and her colleagues developed and presented their datasets and analyses as a resource for the research community, which can be accessed at snpituitaryatlas.princeton.edu. Ruf-Zamojski says that the datasets relied on the contribution of many wet lab and dry lab scientists in her group as well as collaborators around the world. “These projects were very collaborative and have shown the importance of bringing together

teams from different fields and subfields to tackle an important project,” she says. “We are lucky to have collaborators from around the country and around the world join our lab meetings, thus providing diverse expertise that helps in the design and interpretation of these studies.”

Ruf-Zamojski says that their human study set the stage for analyzing human pituitaries at single-cell resolution, an important first step,

since it showed how studying postmortem samples can give important information on pituitary cell types and can be used for additional targeted studies. She thinks studies will now focus on different age groups, probably comparing normal with diseased pituitaries, and trying to understand the molecular mechanisms underlying any pituitary dysfunction with the objective to establish better prognosis tools and improve therapeutic options.

“We hope our datasets can be a resource for the community,” Ruf-Zamoski says. “We believe sharing datasets and resources (pipelines, algorithms, reagents, protocols) is critical for research to move forward. With our database, any researcher or clinician without any knowledge in coding or software can go and query any genes of interest and find where it is expressed (which cell type), its chromatin accessibility profile, and its methylation pattern in specific cell types in mice.”



“Breakthroughs in Understanding Pituitary Networks,” she pointed to the power of multi-omics assays for studying the regulatory network and gene control mechanisms relevant to physiology and disease. “We are at a stage where single-cell resolution studies are finally possible, reliable, and reproducible for a detailed characterization of cell types in complex tissues,” she tells *Endocrine News*. “Our single nucleus multi-omics assays of murine and archived postmortem human pituitaries represent references of normal pituitaries. It finally brings insights into the characterization of pituitary cell types and cell states in selected conditions.”

In past investigations, researchers used bulk approaches to examine the pituitary, yet those studies had limitations. Ruf-Zamojski likens those approaches to analyzing a bowl of different types of fruits. The bulk approach would be the equivalent of turning that fruit bowl into a smoothie; all the fruits would still be present, but the smaller or less tasty fruits would not be as discernible in the smoothie. “Imagine, for example, having a single blueberry in it: you will probably not identify it, although it’s present in your drink,” she says. “In a parallel way, we have been able to analyze pituitary responses in bulk approaches, but some signals are lost and cannot be detected even though they are important.”

In her lab’s analysis of pituitary gonadotropes, Ruf-Zamojski and her colleagues focus on the transcription of *Fshb*, a gene expressed in gonadotropes only. A requirement for *Fshb* gene transcription is that the chromatin be open at the *Fshb* promoter for the recruitment of transcription factors and for transcription to initiate. “However, if you use a whole pituitary approach, you cannot detect any opening at the level of the *Fshb* promoter,” Ruf-Zamojski says. “This is not that the chromatin is not accessible in gonadotropes, but it is simply because the signals coming from around 5% of gonadotrope cells within the whole pituitary are too low to be detected in a bulk experiment.”

Single cell and nucleus assays are again the equivalent of a bowl of fruits, but now more like a fruit salad, in which each ingredient can be easily identified and classified — even a single blueberry could be seen and picked up. “The same is true for pituitary analyses at the single-cell level, where even rarer cell types are identified,” Ruf-Zamojski says. “Now we can characterize specifically our gonadotrope cells among all the pituitary cells, computationally extract them from all the other cells analyzed, and we can look specifically at the accessibility of *Fshb* within the gonadotrope cluster. Unsurprisingly, when *Fshb* is expressed, we also find that the *Fshb* promoter is accessible in gonadotropes only, something we could not detect in a bulk assay, although the same cells/signals were there.”

“So, using single-cell/nucleus atlases, one can now look specifically at any pituitary cell types or subgroups of cells within the pituitary, and get a better understanding of the cellular functions within the cell type of interest,” she continues. “We generated our atlases in normal healthy pituitaries, and these could now be extended to diverse conditions and samples.”



The researchers found stem cells at different stages, with many uncommitted stem cells, but also detected committed progenitors at all ages, according to Ruf-Zamojski.

AT A GLANCE

- ▶ The pituitary has, until very recently, been uncharacterized at single-cell resolution, having been left out of major single-cell atlases and consortia.
- ▶ A coalition of researchers have been mapping the landscape of the pituitary gland’s cell types using single nucleus multi-omics assays, first in murine pituitaries, then in archived postmortem human pituitaries.
- ▶ The researchers developed and presented their datasets and analyses as a resource for the research community, which can be accessed at snpituitaryatlas.princeton.edu.



We are at a stage where single-cell resolution studies are finally possible, reliable, and reproducible for a detailed characterization of cell types in complex tissues. Our single nucleus multi-omics assays of murine and archived postmortem human pituitaries represent references of normal pituitaries. It finally brings insights into the characterization of pituitary cell types and cell states in selected conditions.”

— FRÉDÉRIQUE RUF-ZAMOJSKI, PHD, BIOMEDICAL EXPERIMENTAL SCIENTIST AND ASSOCIATE PROFESSOR IN NEUROLOGY, ICAHN SCHOOL OF MEDICINE, MOUNT SINAI, NEW YORK, N.Y.

Potential of Stem Cells


For their work published in *Nature Communications*, the researchers profiled the transcriptome, chromatin accessibility, and methylation status of more than 70,000 single nuclei from adult murine pituitaries and provided a multi-omics resource to investigate transcriptional regulatory mechanisms. “Our study identified epigenetically defined cell type composition, cell type-specific and sex-specific differences in transcriptional and epigenetic programs, an experimentally supported *cis*-regulatory domain, and epigenetic mechanisms contributing to cell type-specific and sex-specific regulon composition,” the authors write. “Our work lays the foundation for characterizing the general epigenetic regulatory principles that control cell type-specific animal-specific and sex-specific gene expression programs.”

In the *Cell Reports* paper, the researchers describe a human single-nucleus RNA-seq and ATAC-seq resource from pediatric, adult, and aged postmortem pituitaries and characterize cell type-specific gene expression and chromatin accessibility programs for all major pituitary cell lineages. Human pituitary stem cells (PSCs) have been incompletely characterized, the authors write, and they were able to identify uncommitted PSCs, committing progenitor cells, and sex differences as well as distinct deterministic mechanisms that contribute to heterogeneous marker expression within PSCs. “These findings characterize human stem cell lineages and reveal diverse mechanisms regulating key PSC genes and cell type identity,” they write.

“Without high-throughput single-cell approaches, studying these cells remained challenging,” Ruf-Zamojski says. “But there were already studies and interest in PSCs for years, including from our collaborator Dr. Cynthia Andoniadou.

Stem cells and their regenerative potential are a very active area of investigation. Studies have started to characterize murine PSCs, but human PSCs have largely not been analyzed. Our recent paper in *Cell Reports* is part of that effort. We found PSCs at all ages in human postmortem pituitary samples, and they express similar markers as observed in the mouse (including *SOX2*, *SOX9*, *WWTR1*, *YAPI*, etc.)”

“Interestingly we found stem cells at different stages, with many uncommitted stem cells, but also detected committed progenitors at all ages,” she continues “Using pseudotime trajectory analyses, we further characterized their gene expression changes with age, and sex differences. Our sample size in this study was small, and additional studies will be needed to complete a multi-omics characterization of human pituitary stem cells.”

Ruf-Zamojski is careful here, noting that the researchers included only six pituitaries in their human postmortem study — three from male donors and three from female donors, all very different ages. The researchers detected significant heterogeneity across the different samples, which could be attributed to age, but also to other factors, since humans do not live in controlled environments. The pituitary samples were all considered “healthy,” but Ruf-Zamojski says that just means without neurological or pituitary disorders. “But other factors like diabetes, drug use, medication, and obesity may contribute to the variation observed, and, unfortunately with postmortem samples from biobanks, we have to work with de-identified samples, meaning that we have only access to basic metadata and information, not the full medical history,” she says. “Thus, a larger cohort, with, if possible, access to metadata for subgroup classifications, should be studied to make more definite conclusions.” 

— BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. IN THE NOVEMBER ISSUE, HE WROTE ABOUT “REBRANDING” DIABETES INSIPIDUS WITH A NEW NAME.



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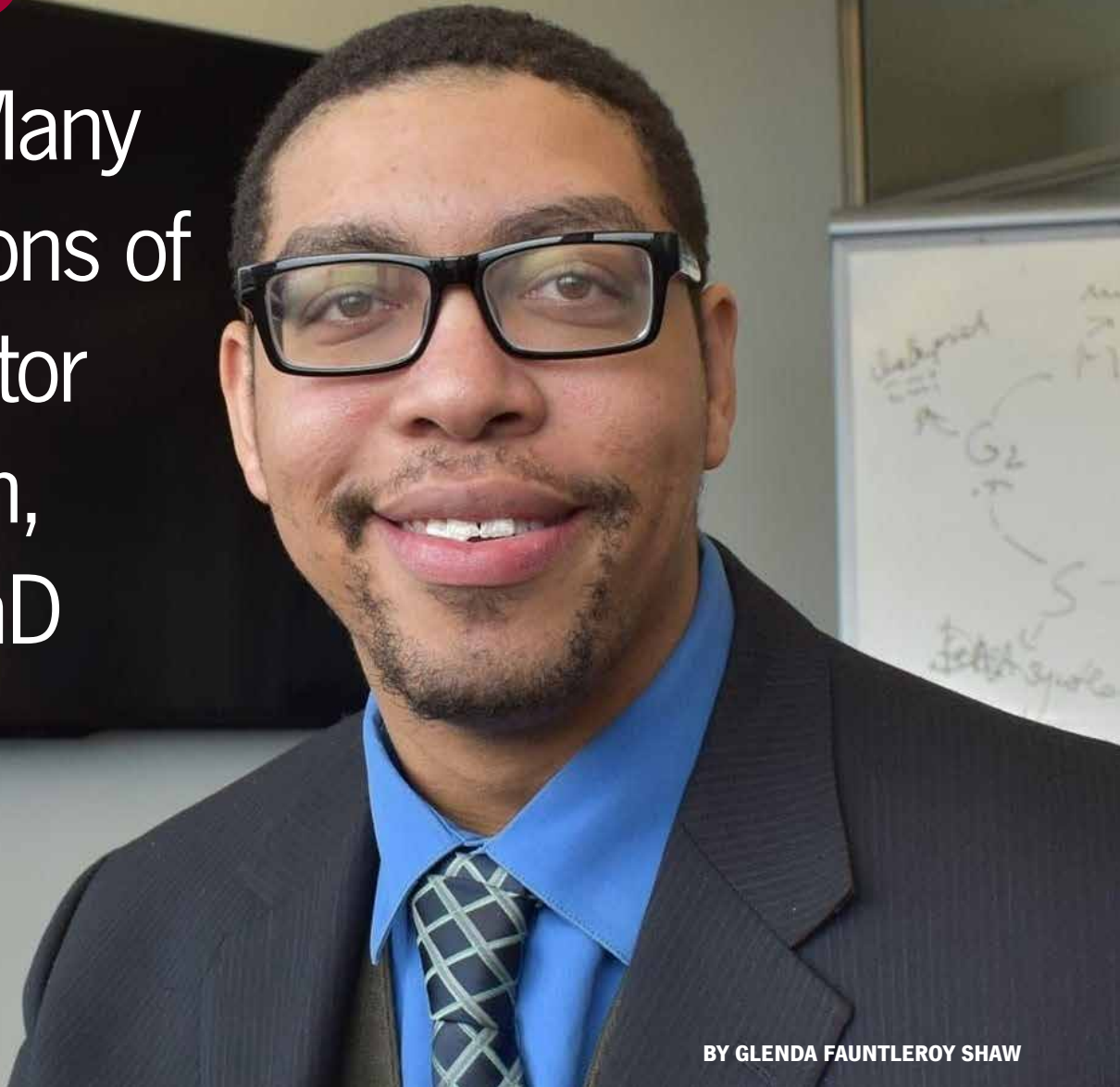
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MythBuster:

The Many Passions of Antentor Hinton, Jr., PhD



BY GLENDA FAUNTLEROY SHAW

After years of being told that there were no other scientists out there “who looked like him,” Antentor Hinton, Jr., PhD, made it his mission to increase diversity in research labs everywhere he could. By mentoring up-and-coming scientists, championing diversity, equity, and inclusion (DEI), and even creating the *1,000 Inspiring Black Scientists of America* list in the process, he still finds time to pursue his “big idea of being able to use 3D reconstruction as a vehicle to be able to understand the cell, through looking at mitochondria.”



Hinton Laboratory members and undergraduate interns celebrate a publication at Slim & Husky's, the first Black-owned restaurant on Nashville's Broadway.



Hinton Laboratory members and undergraduate interns celebrate several publications, honors, and awards during the summer of 2022 at Martin's Bar-B-Que Joint.

Antentor Hinton, Jr., PhD, has made it a life mission to make sure the world knows he's not an anomaly — that there are thousands of other scientists in America doing amazing work who look like him. He's even published lists with the proof.

Hinton, an assistant professor, and Ernest E. Just Early Career Investigator in the Department of Molecular Physiology and Biophysics at Vanderbilt University in Nashville, Tenn., was recently awarded for his mission with a \$1.15-million, five-year grant from the Chan Zuckerberg Initiative's Science Diversity Leadership program. The program honors researchers who have shown a history of promoting diversity and inclusion in their fields through outreach, mentoring, and leadership, and nothing describes Hinton's work better. He's also the principal investigator in his Vanderbilt laboratory where his diverse team is working to find organelle contacts in human tissue across ethnicities to increase representation in research.

While Hinton was at the University of Iowa from 2016 to 2021, his primary investigator (PI) and mentor there was Endocrine Society past-president, E. Dale Abel, MD, now chair of the Department of Medicine at the David Geffen School of Medicine at UCLA. Abel, who was then the director of the Division of Endocrinology & Metabolism in the Department of Internal Medicine at the University of Iowa, first met Hinton in 2015 at the Society's Future Leaders Advancing Research in Endocrinology (FLARE) meeting. "One of the exercises was an individual career development plan. A.J. [Hinton's nickname] confidently asserted that within 10 years he planned to be tenured professor and funded



New postdoctoral fellow, Dr. Dominique Stephens (back, left) being welcomed to the lab via a team-building activity of candle making. Other lab members pictured on left side include Dr. Zer Vue (senior postdoc, middle) and Heather Beasley (EE Just funded post-doc, left, front). Right side (Hinton, front), Ms. Amber Crabtree (grad student, middle), and Dr. Andrea Marshall (staff scientist, back).

“ I hope societies that have the power will create more programs that mentor minority scientists, like the [Endocrine Society’s] FLARE program, that I once participated in, for example. Institutions can create programs that give junior faculty access to senior faculty for help in writing their first R01 grant, and help to demystify the process. Sometimes it’s just about getting the first grant, and then the rest will come, right?!”

— ANTENTOR HINTON, JR., PHD,
ERNEST E. JUST EARLY CAREER INVESTIGATOR;
ASSISTANT PROFESSOR, DEPARTMENT OF
MOLECULAR PHYSIOLOGY AND BIOPHYSICS,
VANDERBILT SCHOOL OF MEDICINE BASIC
SCIENCES, VANDERBILT DIABETES RESEARCH AND
TRAINING CENTER, NASHVILLE, TENN.

by the Howard Hughes Medical Institute (HHMI)!” Abel recalls. “Fast forward seven years. After spending five years in my laboratory as a post-doc, A.J. is now a tenure track assistant professor at Vanderbilt University, who has been incredibly successful in garnering multiple extramural awards including from the Burroughs Wellcome Foundation, the United Negro College Fund, and the National Institutes of Health.”

While a post-doc in Abel’s lab, Hinton was fiercely committed to investing in the future and diversity of life sciences and mentored dozens of undergraduate students from diverse backgrounds, including many who were first-generation students and others from groups that have been historically underrepresented in science, and he received multiple University-level awards for his commitment to mentorship, according to Abel. “Therefore, I was very thrilled to learn that he was awarded a prestigious and competitive Chan Zuckerberg Initiative Award that will be used to decipher racial differences in the mitochondrial responses to heart failure, while using this as an avenue to increase diversity in science, through his commitment to mentorship,” he says. “I am incredibly proud of A.J. and honored to have played a small role in his meteoric rise and ongoing success.”

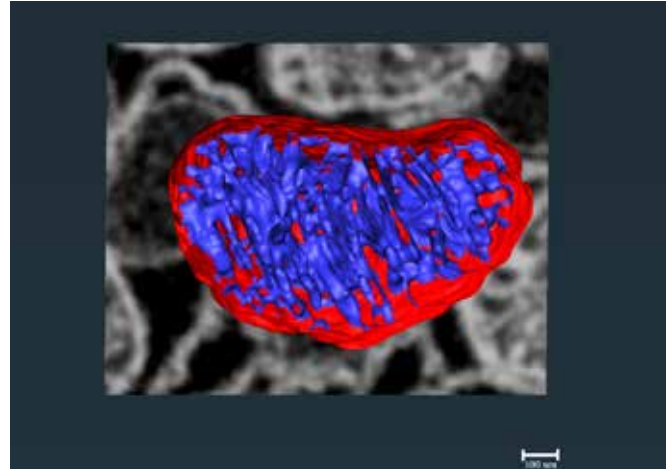
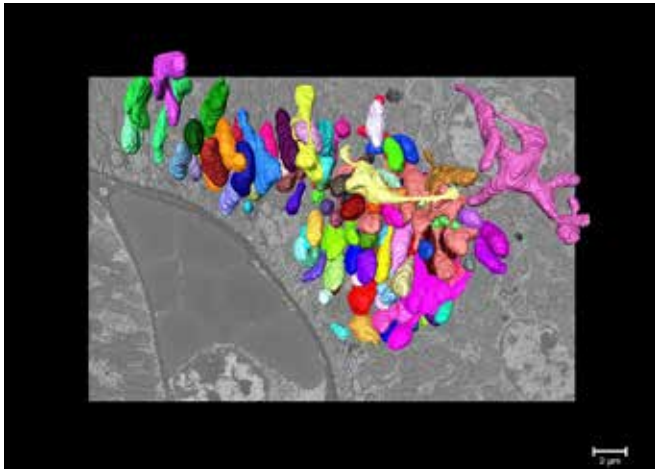
Endocrine News caught up with Hinton via Zoom during his busy Spain vacation to find out how the award will impact both his lab research and mission to elevate minority scientists across the country.

***Endocrine News:* Congratulations on such a tremendous award. How do you hope the grant will impact your work in the lab and beyond?**

Hinton: The grant will allow me to keep pace with my big idea of using 3D reconstruction as a vehicle to understand the cell, through looking at mitochondria. I’m curious if



Hinton working in E. Dale Abel’s laboratory during his postdoctoral period at the University of Iowa.



Serial block-face scanning electron microscopy (left) of a mouse kidney sample and focus ion beam scanning electron microscopy (right) 3D reconstructions of mitochondria of a mouse kidney sample.

mitochondria could reveal differences between a normal state and a disease state. I believe that when mitochondria change their morphology, this is marked by changes in pathology. So, understanding how the context and structure looks will give us clues about how pathology occurs, and, as they change shape, maybe we could detect disease and ultimately prevent it.

EN: Your laboratory uses a technology known as Focus Ion Beam Scanning Electron Microscopy (FIB-SEM) that allows for 3D reconstruction and for you to observe the mitochondria. How might FIB-SEM impact patients with diabetes or obesity?

Hinton: The hope is to build a large mitochondrial database that allows us to take biopsies from any muscle or organ and be able to compare, after doing structural changes with FIB-SEM, to every other tissue that's in the database to determine if the pathology is leading towards disease. So, that's the first part.

In particular, for heart disease and diabetes, how it relates depends on the insulin-resistant tissue. So, if we're looking at liver or skeletal muscle, we can take a biopsy and look at the structure. If we're looking at how type 2 diabetes might be associated with cardiovascular complications, we cannot. So, the way that we would have to do that is through autopsy cases. If someone has donated their tissue, we can focus on structural changes and determine what's the degree of difference in normal, healthy hearts compared with those in pathological states.

From there, if we can get an overview of what the mitochondrion looks like in very different human patients who are healthy, and

across different ethnicities, this can allow us to look at molecular clues by comparing the structure and function of those genotypes. This will allow us a better understanding of the mitochondrial structure and help us delve deeper into other mechanisms that may be indicative of these structural changes, such as mutated mitochondrial DNA (mtDNA) or molecular pathways involved in morphology. My ultimate goal is to find a biological marker that could be used to identify these structural changes. For example, if we think that the MICOS complex (a multi-subunit complex present in the inner mitochondrial membrane) or the expression of these genes, may be important for these structural changes in any tissue of interest, we can use these genes as a panel to interrogate any mutations that might occur. Additionally, we can also take a biopsy of the tissue to confirm its structure.

EN: Could what you've described happen in the next five or 10 years?

Hinton: We're now using FIB-SEM, and there's also another scope that's used for 3D called serial block facing-scanning electron microscopy; they're both based off SEM technology, but are used in different ways. So, it is very new as far as technology and the application in which we're doing it, but since around the early 2000s, people were starting to make improvements on the scope to obtain higher resolution.

The key becomes having enough samples in the database to be able to use the power of the FIB-SEM. So, if we have enough individuals across different ethnicities to collect biopsies and donate their tissues, we could set up that large mitochondrial database. It's kind of like setting up the genome-sequencing

“ I’m curious if mitochondria could reveal pathology between a normal state and a disease state. I believe that when mitochondria change their morphology, this is marked by changes in pathology. So, understanding how the context and structure looks will give us clues about how pathology occurs, and, as they change shape, maybe we could detect disease and ultimately prevent it.”

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project, where everybody kind of pooled in and did this thing. So, if a lot of the imaging scientists across the world were able to mill a bunch of different samples, and collect them into a database, we could easily have this free access, because that’s the goal of the actual grant — make it free access to everyone.

The idea is to be able to put that knowledge out there so that we all can use it freely and help diagnose individuals. The whole point is really to save lives.

EN: The Chan Zuckerberg award honors you for your history of outreach and mentoring to minority, especially Black, scientists. What makes up your outreach in the Nashville community?

Hinton: It actually started in Iowa and at the Baylor College of Medicine. I really learned how to develop grassroot efforts from Dr. Gayle Slaughter at Baylor, who was the senior associate dean of diversity at the time. She allowed me the chance to be the president of the Association of Graduate Student Diversity, and so that allowed me opportunities to really understand how diverse backgrounds could work together and what was required for them to be successful.

So, from that knowledge base, when I was recruited to Iowa, my PI, E. Dale Abel, MD, PhD, taught me that you must speak about what is your passion, and not only is science your passion, but if mentoring and DEI are also your passions, you should be able to pursue those also. So, while at Iowa, I accepted a position as the academic and career development instructor and created the “100 Inspiring Black Scientists in America” and the “100 More Inspiring Black Scientists in America” because there was a myth that there were no Black scientists out there. Later, I partnered with the Community of Scholars and created the “1,000 Inspiring Black Scientists in America” list.

From the 1,000 Black scientists list, so many Black scientists were recognized or acknowledged because people didn’t realize there were so many scientists who looked like me and who were doing amazing discoveries in science.

At Vanderbilt, I utilize my laboratory as a way to demonstrate what could be the standard at Vanderbilt and other universities across the nation with hiring diverse talent. For example, I have three African American individuals (one staff scientist and two post-docs, Dr. Andrea Marshall, Dr. Heather Beasley, and Dr. Dominique Stephens) working in my lab. I also have one Hispanic/Latino individual in the laboratory conducting biomedical research (Edgar Garza Lopez).

I’ve also created opportunities for individuals who are from Hmong backgrounds. For example, I hired the very first Hmong scientist, Zer Vue, who received a PhD in development biology.

EN: You also published an article in *Cell* about how predominantly white institutions (PWIs) can utilize the practices of historically Black colleges and universities (HBCUs) to better mentor and support Black students in the Science, Technology, Engineering, Math, and Medicine (STEMM) fields. Do you really think the nurturing environment at HBCUs can be replicated?

Hinton: So, leadership at PWIs must be able to read articles like mine and change their minds to be able to lead their peers and their departments. Creating nurturing culture is going to bring in more resources! I also use my platform to raise awareness around topics of mentoring, career/professional development, and DEI. Currently, I have written 24 commentaries on these topics and conducted research studies in mentoring, career development, and DEI.

Additionally, I'm hoping that PWIs would strengthen their relationships with HBCUs to provide the opportunity for individuals to acquire real resources. For instance, when HBCU individuals are applying for grants, half the time they do not obtain the respect because they're not at a PWI. Some funding agencies say they cannot do it because they are under resourced, or they're not actively doing cutting-edge research, or don't have a librarian, etc. But it's all a lie that's been passed down.

Notably, HBCU's are leading science education in many areas. They're turning over large numbers of undergraduates with science degrees, and these students are going on to graduate school at PWIs and doing well. A few other Zuckerberg award winners graduated from HBCUs, like myself, or were trained by individuals who went to an HBCU.

One other thing is that I hope societies that have the power will create more programs that mentor minority scientists, like the [Endocrine Society's] FLARE program, that I once participated in, for example. Institutions, can create programs that give junior faculty access to senior faculty for help in writing their first R01 grant and help to demystify the process. Sometimes it's just about getting the first grant, and then the rest will come, right?! 🙏



Co-mentors with Dr. Dominique Stephens (center), post-doc fellow in the Hinton and Damo laboratory. Stephens is an HHMI Hanna Gray Finalist and BWF PDEP Fellow. Dr. Steven Damo (left), professor of chemistry, biochemistry and molecular biology, Chair, Department of Life and Physical Sciences, Fisk University; member of the Center for Structural Biology at Vanderbilt University, and Hinton (right).



The Hinton Lab presenting its research on changes in mitochondria morphology at the 13th World Congress on Targeting Mitochondria in Berlin, Germany. Pictured (l to r) Dr. Zer Vue (senior postdoc), Dr. Andrea Marshall (staff scientist), Hinton, Dr. Edgar Garza Lopez (staff scientist), and Larry Vang (senior research technician).



The Hinton Lab presented its research on changes in mitochondrial morphology at the Multifaceted Mitochondria Cell Symposia in Seville, Spain. Pictured (l to r) Mein Vue (Amira research tech), Dr. Zer Vue (senior post-doc), Dr. Edgar Garza Lopez (staff scientist), Dr. Stefanie Alexander (resident/post-doc fellow, MD/PhD), Hinton, Larry Vang (senior research technician), Dr. Andrea Marshall (staff scientist), Dr. Neng Vue (scientific artist/editor, and research technician), and Ms. Chia Vang (visiting graduate student/intern).

– GLENDA FAUNTLEROY SHAW IS A FREELANCE WRITER BASED IN CARMEL, IND. SHE IS A REGULAR CONTRIBUTOR TO ENDOCRINE NEWS.

Q&A

Ghada El-Hajj Fuleihan, MD, MPH

Matthew T. Drake, MD, PhD

Endocrine News talks with **Ghada El-Hajj Fuleihan, MD, MPH**, and **Matthew T. Drake, MD, PhD**, co-chairs of the guideline development panel that created the latest Endocrine Society Clinical Practice Guideline on treating hypercalcemia of malignancy.



**Ghada El-Hajj Fuleihan,
MD, MPH**



**Matthew T. Drake,
MD, PhD**

Hypercalcemia of malignancy (HCM) is the most common metabolic complication of cancer, but its incidence may be declining due to potent chemotherapeutic agents. The high mortality associated with HCM has declined markedly due to the introduction of increasingly effective chemotherapeutic drugs. Despite the widespread availability of efficacious medications to treat HCM, evidence-based recommendations to manage this debilitating condition are lacking.

To guide physicians treating this condition, the Endocrine Society is publishing a new practice guideline. “Treatment of Hypercalcemia of Malignancy in Adults: An Endocrine Society Clinical Practice Guideline,” will be published this month and will appear in the March 2023 print issue of *The Journal of Clinical Endocrinology & Metabolism*.

The co-chairs of the guideline development panel are Ghada El-Hajj Fuleihan, MD, MPH, at the Department of Internal Medicine, American University of Beirut, in Lebanon, and Matthew T. Drake, MD, PhD, at the Department of Internal Medicine, Mayo Clinic, Rochester, Minn. They share their thoughts with *Endocrine News* about how this guideline will provide the latest in evidence-based recommendations for treatment, and how it should be a valuable tool for primary care physicians and other practitioners.

Endocrine News: What was the main reason for the publication of the hypercalcemia of malignancy guideline – what drove the decision and why now?

Ghada El-Hajj Fuleihan: Hypercalcemia of malignancy (HCM) is the most common metabolic complication of malignancies. Its presence carries a poor prognosis and, if left

untreated, it can be life threatening. While several published clinical practice guidelines (CPGs) target the treatment of cancer patients with bone metastases, multiple myeloma, and parathyroid carcinoma, we are unaware of any guidelines that are specific for the treatment of HCM. HCM treatment substantially and rapidly alleviates symptoms; improves quality of life; and importantly, provides an opportunity to administer therapies targeting the primary malignancy.

EN: What are your hopes for the impact of the guideline on endocrine standards of care for adults with hypercalcemia of malignancy?

Matthew T. Drake: We hope these guidelines will provide a structured framework to guide care pathways in various clinical HCM scenarios. The guidelines illustrate common presentations of HCM, with regards to the etiology and severity of HCM, and presence of symptoms. They are based on a systematic approach using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology which was used to scrutinize the evidence available to date, its quality as well as its limitations.

EN: How do you expect other medical specialties to be affected by the Guideline Development Panel's recommendations?

GEHF: We anticipate these CPGs and the related workflow/care pathways will streamline the clinical care of patients with HCM across medical specialties. If implemented, they may provide opportunities for data pooling of future case series from various disciplines. They will hopefully stimulate the development of clinical trial protocols aiming at closing knowledge/care gaps identified during the development of these guidelines.

EN: What are the key take-home messages for patients in this guideline?

MTD: The key messages to patients are that the guideline's recommendations are driven by disease etiology, severity, clinical manifestations, and resources/healthcare systems available. In addition to the universal use of potent anti-resorptive medications such as intravenous zoledronic acid and subcutaneous denosumab, regardless of HCM disease etiology, the utilization of disease-specific drugs such as calcimimetics for parathyroid carcinoma and glucocorticoids for some tumors such as lymphoma, are useful adjuncts that can be added in sequential or combination protocols. **EN**

“ While several published clinical practice guidelines target the treatment of cancer patients with bone metastases, multiple myeloma, and parathyroid carcinoma, we are unaware of any guidelines that are specific for the treatment of HCM.”

— GHADA EL-HAJJ FULEIHAN, MD, MPH, DEPARTMENT OF INTERNAL MEDICINE, AMERICAN UNIVERSITY OF BEIRUT, BEIRUT, LEBANON



Leading The Way

How the Endocrine Society Continues to Pioneer Endocrine-Disrupting Chemicals Research

The Endocrine Society was the first such organization to recognize the threat endocrine disruptors posed to human health. *Endocrine News* shares the story of how that came to pass over the course of several years, through prolific research, meetings, symposia, and forums as well as an advocacy effort that reaches around the world.

BY ANDREA C. GORE, PHD; R. THOMAS ZOELLER, PHD; AND JERRY HEINDEL, PHD

In 2006, we published an article entitled “Endocrine disruption for endocrinologists (and others)” in the June issue of *Endocrinology* in which we wrote: “The Endocrine Society should continue to be a leader in research on endocrine disruption...[and] should also inform government policy and regulatory rules as well as scientists, physicians, the public, and the media.”

Much has happened in the subsequent 16 years, including the recent launching of a new Endocrine Disruptor Special Interest Group (SIG). This SIG provides a significant opportunity for the Endocrine Society to expand its influence and expertise on the mechanisms of endocrine diseases, and to apply knowledge to clinical practice. For the endocrine disruption field, this new SIG signals that endocrine-disrupting chemicals (EDCs) have an actual home for its research at the Endocrine Society.

Here, we give a brief history of EDCs in the context of the Society, discuss where we are today, and articulate plans for the future.

No Home of Their Own

The Endocrine Society formally defines an EDC as an exogenous chemical or mixture of chemicals that interferes with any aspect of hormone action. Exposure to EDCs is ubiquitous; babies are born pre-polluted with endocrine disruptors. EDCs are found in everyday products such as personal care and household products, food preservatives, clothing and furniture, plastics and plasticizers, and pesticides.

When exposure occurs in utero or in early development, their effects lead to permanent alterations in gene expression and epigenetic programming, leading to increased susceptibility to a variety of diseases and dysfunctions. EDCs are linked to a greater risk of hormone-dependent cancers, diabetes, reproductive, metabolic, immune, learning and behavior, and cardiovascular and liver diseases.

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...to our knowledge there are no PhD programs in endocrine disruption; in fact, there are few (if any) such programs in endocrinology itself, **although the discipline may be subsumed within other programs. This can also create a bottleneck in translation to clinical understanding and practice.**”



Members of the Endocrine Society's EDC SIG — Andrea Gore, PhD (far left) and Leo Trasande, MD, MPP (far right) — had a lively discussion at **ENDO 2022** during the All SIG Reception with Heather Patisaul, PhD; Ruth Keri, PhD; Taylor Baker; and Lindsey Trevino, PhD.



The Endocrine Society's representative to the Roundtable on the Chemicals Strategy, Anne-Simone Parent, MD, PhD.



On Sept. 21, 2016, Andrea C. Gore, PhD, spoke at the Congressional briefing celebrating 25 years of research on endocrine-disrupting chemicals at the Dirksen Senate Office Building in Washington D.C.



Endocrine Society member Abby Fleisch, MD, MPH, speaking about the effects of EDCs on bone health at a Congressional briefing.



Endocrine Society EU EDC Task Force Chair Barbara Demeneix presents at a briefing in Brussels about EDCs in 2019.

There are currently about 1,000 known endocrine disruptors, likely just the tip of the iceberg.

There have been several impediments to getting EDCs on the radar. One is that there is no endocrine disruption society. Scientists interested in endocrine disruption work in many classical fields like cancer, reproduction, thyroid, neuroscience, and toxicology and attend those society conferences. But they have no home of their own. This is a particular problem in basic endocrinology: to our knowledge, there are no PhD programs in endocrine disruption; in fact, there are few (if any) such programs in endocrinology itself, although the discipline may be subsumed within other programs. This can also create a bottleneck in translation to clinical understanding and practice.

Early ENDO Connections

Enter the Endocrine Society, slowly and cautiously at first. This story started in the early 2000s. The proposition at the time that EDCs were a human health problem was quite controversial, and endocrinologists were minimally involved in research in this area. EDC research was not present at the Endocrine Society other than occasional symposia talks delivered at the annual meeting. These talks were difficult to get on the program due to the controversy surrounding whether EDCs were a genuine concern for endocrinologists and a problem for human health.

Fierce advocacy to the Endocrine Society's Annual Meeting Steering Committee for more EDC programming led to the opportunity to organize a special meeting on EDCs in association with the ENDO annual meeting. This culminated in the Forum on EDCs in 2005, an



EDC Advocacy Around the World

The Endocrine Society's advocacy has elevated the issue of EDCs in policy discussions around the world and ensured that our members are able to advise policymakers on technical and scientific issues that inform legislative and regulatory decisions.

In the U.S., the Endocrine Society has worked with legislators to eliminate EDCs in personal care products; this led in 2016 to a hearing in which Senator Dianne Feinstein (D-CA) expressed her personal concern about EDCs in cosmetics and other consumer products and included special considerations for specific EDCs in the Personal Care Products Safety Act, introduced with Senator Susan Collins (R-ME).

In 2018, then-Senator Kamala Harris (D-CA) introduced the Environmental Justice Right to Know Act that called for a greater accounting of the endocrine-disrupting effects of chemicals in products that disproportionately impact women, in particular women of color.

In the European Union, the Endocrine Society successfully advocated for provisions in the Chemicals Strategy for Sustainability that would eliminate EDCs from consumer products in the EU and worked to improve the scientific criteria that defined EDCs in pesticides and biocides laws.

As the Society's influence grows, our members are even better positioned to make an impact. We now hold a seat on a roundtable to advise the European Commission on the implementation of the chemicals strategy, and we are accredited to the United Nations Environment Assembly (UNEA) giving us the opportunity to provide expert guidance on the public health effects of EDCs in plastics as UN delegates develop an international treaty to end plastic pollution. – Joseph M. Laakso, PhD, director, science policy, Endocrine Society

unprecedented full-day meeting that took place the day before ENDO in San Diego, Calif. It was a full house, attended by basic scientists and clinical endocrinologists alike. This Forum included state-of-the-art talks by leading researchers in the field, and there was electricity in the room as connections began to be made between research and the clinic, and endocrinologists realized that this was their bailiwick.

A Scientific Statement Debut

The Endocrine Society's Research Affairs Committee noted the Forum's success and the growing recognition that EDCs were, at heart, intrinsic to endocrinology. The committee agreed to convene a group of EDC experts to write a white paper on the subject to review the evidence and determine whether there was a critical mass of evidence. At the same time, then-Endocrine Society President, Robert Carey, MD, had developed an initiative for the Society to publish Scientific Statements intended as comprehensive reviews that would bring cutting-edge topics to the Endocrine Society.

The timing was propitious: the white paper on EDCs was invited to be the Society's first Scientific Statement. This statement noted that the Endocrine Society should be the de facto home for EDC researchers. Held to a higher bar because of the potential prominence of a Scientific Statement, the paper went out for first internal committee review and then a full Society commenting period.

The Endocrine Society published its first Scientific Statement on EDCs in the June 2009 issue of *Endocrine Reviews*. To date, it has been cited over 4,000 times. Fast forward, and based on an explosive increase in publications on EDCs, a second Scientific Statement on EDCs (referred to as EDC-2), was published in the December 2015 issue of *Endocrine Reviews*, following a similar review process.

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There have been several impediments to getting EDCs on the radar. One is that there is no endocrine disruption society. Scientists interested in endocrine disruption work in many classical fields like cancer, reproduction, thyroid, neuroscience, and toxicology and attend those society conferences. **But they have no home of their own.**”

Together, the two Endocrine Society Scientific Statements were transformative in bringing EDCs into the mainstream. In 2012, in its Statement of Principles, the Society also articulated recommendations on how a deep understanding of endocrinology was essential for EDC science and policy. In 2014, the Endocrine Society and the International Pollution Elimination Network (IPEN) developed a guide to EDCs translated into eight languages. It is also notable that over this period, the Endocrine Society journals were increasingly a key publications venue for the field, and EDC science became a regular feature of the annual **ENDO** meetings.


Achieving a Unique Leadership Position

At this point, the Endocrine Society recognized its unique leadership position in EDCs. Ultimately, the Endocrine Society published a Position Statement on EDCs in 2018 in which, for the first time, the Society took a strong stand on EDCs as a significant public health concern and made recommendations for change to the regulatory system and policy. It is also notable that during this period, the Society's Advocacy and Public Outreach Core Committee began including EDCs on the agenda of talking points whenever Society members

visited Capitol Hill to represent the Endocrine Society on issues of key importance to public health (see sidebar).

Today, the Endocrine Society's new EDC SIG has the potential to remove barriers and silos between basic scientists, clinical investigators, and physicians-in-practice within the Society. This has been a key impediment, as the cause and effect between exposure to EDCs and the manifestation of a disease that may take years or decades to emerge, can only be revealed through the combination of fundamental research, clinical studies, and epidemiology.

This combination is reflected in the disciplines and training of the SIG coordinators: along with the three of us (basic researchers) are two physician-scientist experts in EDCs, Leonardo Trasande, MD, MPP, and Robert Sargis, MD, PhD. In its short existence, the SIG has held its first multidisciplinary webinar and already has over 200 members. Moving forward, we will work to have more EDC-focused sessions at **ENDO**; to develop a satellite meeting on EDCs and diseases, and, importantly, to train the next generation of EDC researchers.

Now EDCs have a home, and it is the Endocrine Society. 

– GORE IS PROFESSOR AND VACEK CHAIR IN PHARMACOLOGY, THE UNIVERSITY OF TEXAS AT AUSTIN, AUSTIN, TEXAS; AND A PAST EDITOR-IN-CHIEF OF THE ENDOCRINE SOCIETY'S JOURNAL, *ENDOCRINOLOGY* (ANDREA.GORE@AUSTIN.UTEXAS.EDU); ZOELLER IS PROFESSOR EMERITUS, BIOLOGY DEPARTMENT, UNIVERSITY OF MASSACHUSETTS AMHERST, AMHERST, MASS. (TZOELLER@BIO.UMASS.EDU); HEINDEL IS THE DIRECTOR, HEALTHY ENVIRONMENT AND ENDOCRINE DISRUPTOR STRATEGIES (HEEDS.ORG), A PROGRAM OF ENVIRONMENTAL HEALTH SCIENCES, (JERRYHEINDEL@GMAIL.COM).



2022 Endocrine Society Advocacy Year-in-Review

The Endocrine Society advocates on behalf of our members, the patients they treat, and the science they research. This year, in addition to continuing our virtual advocacy, we had the opportunity to reintroduce several in-person advocacy activities. With help from our members, we successfully advocated for our policy priorities and raised awareness of the value of endocrinology and endocrine research.

Let's review some of our advocacy wins from this year.

HISTORIC INSULIN LEGISLATION

In August, President Joe Biden signed into law the Inflation Reduction Act, which included several measures that would make insulin more affordable. Most notably, the law will institute a \$35/month cap on out-of-pocket costs of insulin for Medicare beneficiaries beginning in 2023. The law's passage is the result of years of Endocrine Society advocacy to make insulin more affordable. We provided recommendations to policymakers on policy options; we worked with representatives and senators on both sides of the aisle to find consensus; we shared patient stories with congressional offices; we conducted congressional briefings to educate policymakers; we testified before Congress; and we conducted Hill Days with our members. This outcome could not have been achieved without the help of our Society members, and we thank them for their work to make insulin more affordable. We will continue to urge Congress to pass a \$35/month cap on insulin for people with private insurance, so that all Americans with diabetes have access to this lifesaving drug.

INCREASING NIH FUNDING

We successfully advocated for funding increases of over \$2 billion for the National Institutes of Health (NIH) that were incorporated into the House and Senate versions of fiscal year (FY) 2023 funding legislation. Although the legislation has not been finalized as of this writing, we successfully educated many congressional offices about the importance of funding endocrine research. We shared testimony with the House and

Senate explaining why increased NIH funding is essential for propelling endocrine research forward. We joined with other medical and scientific organizations to participate in the Rally for Medical Research Hill Day, which took place in person, to tell Congress why continuing resolutions harm public health. We will continue to call on our members to participate in our online campaign urging Congress to pass a final funding bill with an increase for NIH as soon as possible.

TELEHEALTH EXPANSION

The Endocrine Society secured a victory this year in our effort to expand access to the telehealth services that our members provide. The House of Representatives passed the Advancing Telehealth Beyond COVID-19 Act, which provides a two-year extension of the telehealth waivers put in place during the COVID-19 public health emergency (PHE). The legislation, which passed overwhelmingly in the House, includes two-year extensions of audio-only services and a continued relaxation of the originating site requirement rule ensuring that patients can receive telehealth from home. This win was the result of Society advocacy, including Hill Days and meetings with congressional leaders. We applaud the House for taking action, but the Senate still needs to act on this important legislation. We will continue to advocate for this issue and will keep you updated as this process moves forward.

EDC ADVOCACY IN THE EUROPEAN UNION

Throughout the past year, the Endocrine Society has been a leader advocating for better regulation of endocrine-disrupting chemicals (EDCs) in the European Union. The Endocrine Society has a seat on an advisory body to the European Commission concerning the implementation of the Chemicals Strategy for Sustainability (CSS). In May, Society member Anne-Simone Parent, MD, PhD represented the Society at a meeting in Brussels to encourage the Commission and EU institutions to move quickly to develop effective legislative proposals that reduce exposure to EDCs as part of the CSS. Following the meeting,

the Commission proposed a new hazard class for EDCs in the regulation on Classification, Labeling, and Packaging (CLP). The hazard class includes multiple categories of EDCs depending on the strength of the available evidence, which was in alignment with the recommendations that we provided to the Commission. We recently received accreditation from the United Nations Environment Programme (UNEP), which positions us to give input on EDCs in the development of an international legally binding treaty on plastic pollution.

PFAS REGULATION

This year, the Environmental Protection Agency (EPA) added the most prevalent PFAS chemicals, which are endocrine disruptors, to the toxic release inventory. This inventory helps the EPA track potential sources of toxic exposures and to hold polluters accountable. The Endocrine Society provided feedback on a strategic plan for Federal coordination of PFAS research and development, and this proposed rule was in line with our recommendation to hold polluters accountable. There are over 9,000 known PFAS compounds, and this rule only recognizes two of them as hazardous. The Endocrine Society will continue to advocate for regulating PFAS as a class of chemicals, given the known toxicity and prevalence of chemicals with similar structures and activity.

TRANSGENDER HEALTH

The Endocrine Society continues to be the voice of science in discussions about transgender health and treatment for gender dysphoria. In October, the Endocrine Society was featured on an episode of “The Problem with Jon Stewart” that focused on access to gender-affirming care. Stewart interviewed Endocrine Society clinical practice guideline author Josh Safer, MD, to discuss the importance of gender-affirming care for minors. On the judicial front, the Endocrine Society continues to be a “friend of the court” in cases on the state level that challenges anti-trans laws or laws that criminalize

gender-affirming care. We provide the court with medical evidence about what it means to be transgender and what gender-affirming care is.

As you can see, Endocrine Society advocacy really does influence the policies affecting endocrine-related research and practice. This year’s successes would not have been possible without our members’ participation. Meeting with your elected representative, participating in an online campaign, and amplifying our message on Twitter really makes a difference. We appreciate your work this year and look forward to continued success in 2023.

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**With help from our members,
 we successfully advocated for our
 policy priorities and raised awareness
 of the value of endocrinology
 and endocrine research.**
 ”

Endocrine Society Urges Congress to Complete NIH Appropriations by December 16th Deadline

The Endocrine Society is committed to advocating for increases in the budget of the National Institutes of Health (NIH). Our Hill days, advocacy campaigns, and meetings with appropriators have contributed to increases in the NIH budget over the past seven years. Continued investment in the NIH is critical to further our understanding of endocrine disorders such as diabetes, obesity, cancer, and infertility, among many diseases affecting millions of Americans. Therefore, the Endocrine Society is advocating for Congress to provide at least \$50 billion for the NIH base budget in fiscal year (FY) 2023, which is a 7.9% increase from FY 2022 levels.

Unfortunately, Congress was not able to complete appropriations for FY 2023 by the September 30 deadline this year. Instead, it passed a short-term continuing resolution (CR) through December 16. As this issue of *Endocrine News* went to press, there was still no agreement on final appropriations, and we are concerned that the CR could be

extended further. While a CR averts a government shutdown, it continues to fund the NIH only at last year's funding levels and does not account for substantial increases in biomedical research inflation.

With a long list of legislative goals for members of Congress to complete during the "lame duck" session, we have been working hard to keep appropriations prioritized and prevent an extended CR. In November, the Endocrine Society sent a letter to Congressional leadership urging them to finalize a spending package for FY 2023 before the CR expires on December 16. In addition to an increase in the NIH budget, we recommended that any funding for the Advanced Research Projects Agency for Health (ARPA-H) supplement, and not supplant, funding for the NIH. While complementary, the NIH and ARPA-H have distinct and critical missions and should therefore be budgeted separately.

The most powerful form of advocacy, however, comes from you. Our policymakers want to hear what is important to their constituents, which is why we have launched an online

advocacy campaign that we encourage our U.S.-based members to participate in. With your help, we can keep appropriations

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Continued investment in the NIH is critical to further our understanding of endocrine disorders such as diabetes, obesity, cancer, and infertility, among many diseases affecting millions of Americans.

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at the top of the legislative agenda and secure much-needed funding for life-saving endocrine research. Please visit www.endocrine.org/takeaction to join our campaign today!

Endocrine Society Weighs in on Medicare Physician Fee Schedule and Urges Congress to Avert Scheduled Medicare Cuts

Each year, the Center for Medicare and Medicaid Services (CMS) releases the Medicare Physician Fee Schedule (MPFS) rule, which outlines the agency's payment and quality program policies for the upcoming year. Medicare policy often sets the bar for the private insurance market as well. Therefore, the payment policies and other revisions in the MPFS are important to our members, and the Society weighs in during the rulemaking process to ensure that our members' needs are addressed.

In September, CMS released the MPFS proposed rule for 2023. The Society provided feedback to the agency about the policies related to the conversion factor, Evaluation and Management (E/M) codes, continuous glucose monitoring (CGM) coverage, and other endocrinology issues. The full comment letter is on our website.

In November, CMS released the MPFS final rule for 2023. The final rule includes a 4.5% reduction in the conversion factor

for 2023. The rule also makes some important updates to E/M office code visits and extends some telehealth flexibilities put in place during the pandemic. There is a brief summary of the rule and its impact on endocrinologists on our webpage. (www.endocrine.org/improving-practice/macra).

Unfortunately, the proposed cut to the conversion factor is one of two cuts scheduled to go into effect on January 1, 2023. Together, these two cuts would result in an 8.5% reduction in payments to physicians. Only Congress has the power to avert these cuts, and the Endocrine Society has been urging Congress to act before the end of the year.

You can join our advocacy by visiting www.endocrine.org/takeaction to participate in an online campaign and tell your elected representatives how these cuts will impact you, your practice, and your patients. Congress will not take action if it doesn't hear from people who are affected. Join our online campaign today.

ENDO2023

JUNE 15-18, 2023 CHICAGO, IL

SHOWCASE YOUR RESEARCH

SUBMIT YOUR ABSTRACT BY WEDNESDAY, JANUARY 11, 2023

[ENDOCRINE.ORG/ABSTRACTS](https://endocrine.org/abstracts)

DEADLINE EXTENDED!

