

RICARDO CORREA, MD, EdD, AND HIS LIFE'S JOURNEY TO ENDOCRINOLOGY

DECEMBER 2021

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine news

Looking Back at a Year of Endocrine Innovations

2021 VISIONARIES

● **A YEAR OF GROUNDBREAKING SCIENCE:**

Once again, Endocrine Society journal editors share their top picks for 2021's most significant advances in endocrine research.

● **A YEAR OF TREATMENT BREAKTHROUGHS:**

As endocrine science advances, so too do cutting-edge treatment options, therapies, and technology that will improve the lives of patients living with various endocrine disorders.

UNDER THE HOOD:

A look at the latest in laboratory hood technology

LAB NOTES Q&A:

David Katz, PhD, discusses potential new treatments for Cushing's

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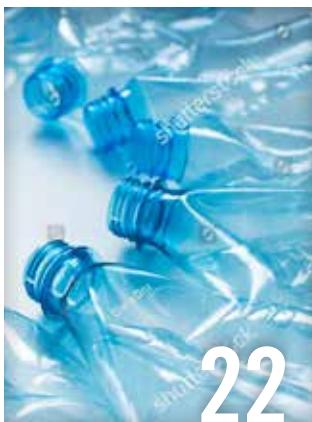
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Endocrine research remains at the forefront of medical breakthroughs, which has led to cutting-edge treatment options, therapies, and products. From remarkable new treatments for acromegaly, thyroid eye disease, hypoglycemia, and diabetes to new devices aimed at glucose monitoring in adults and children, a mail-in semen analysis, and much more, *Endocrine News* takes a closer look at some of these new innovations announced throughout 2021.

WRITTEN AND COMPILED BY DEREK BAGLEY

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Hormone Science to Health



Celebrating Success in a Challenging Year

It is hard to believe that another year has gone by in this new world of virtual meetings and remote interactions. Although it is far from optimal and most of us miss the personal, face-to-face interactions, I must say that we have made the best out of this situation. Despite the ongoing pandemic, we have many successes to celebrate.

The Society has adapted and developed virtual programs that have far exceeded everyone's expectations. Our fully virtual ENDO 2021 had more than 7,300 registrants, over 50 exhibitors, more than 2,200 scientific abstracts, and over 200 live and on-demand educational sessions. Thanks to our Annual Meeting Steering Committee and past-president Gary Hammer, MD, PhD, who developed an outstanding program that was hailed as a resounding success by participants and sponsors and exceeded all forecasted projections.

Similarly, the Clinical Endocrinology Update (CEU) and Endocrine Board Review (EBR) each broke attendance records when they were held virtually in September.

Last August we launched the new Center for Learning to remain current with trends in online education and to create a new central education "hub" that the community could regularly explore for new content.

On the publishing front, I am pleased to announce that the Board has approved the launch of a new Society journal in 2022: An online-only, Open Access journal focused on case reports. Member surveys have shown your growing interest in a case report journal, and we are thrilled it is coming to fruition.

The new journal, whose name will be announced later, will publish reports on clinical cases and clinical problem solving from across the field of endocrinology and around the world. We will feature educational cases with clear learning objectives on topics of special interest to early-career endocrinologists and members of endocrinology care teams. The journal will

be particularly interested in cases where learning relating to limited resources for investigation or management choices may have important implications for a wider audience. The journal's senior editors will offer guidance to early-career authors, reviewers, and editors.

These are just a few highlights from our extensive list of accomplishments of this past year. I am extremely proud of our Society. The passion and commitment of our members and staff are some of our greatest assets and the key to our success.

We are now accepting applications for an editor-in-chief to lead this new journal. We plan to announce the editor-in-chief at ENDO 2022 next June, with manuscript submissions opening by fall 2022.

We have also selected two wonderful new editors-in-chief for the *Journal of the Endocrine Society* and *Endocrine Reviews*. Zeynep Madak-Erdogan, PhD, (*Journal of the Endocrine Society*) and Ashley Grossman MD, FRCR (*Endocrine Reviews*) will formally take the helm next month.

This year marked the 100th anniversary of the discovery of insulin, and we have commemorated this landmark breakthrough throughout 2021, highlighting the many

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AND CONGRATULATE THE

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OUTSTANDING LEADERSHIP IN ENDOCRINOLOGY AWARD

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Shingo Kajimura, PhD

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AWARDS WILL BE PRESENTED AT ENDO 2022:
THE ANNUAL MEETING & EXPO IN ATLANTA, GA,
JUNE 11-14, 2022.



FROM THE **EDITOR**

DECEMBER 2021

Endocrine news

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Highlighting the Year in Endocrine Discoveries

As 2021 comes to a close, we wrap up the year with two articles that provide a somewhat comprehensive overview of what took place over the course of the year from an endocrine science and treatment perspective. Despite a year that was still feeling the wrath of the COVID-19 pandemic, there was definitely no lack of research activity from endocrine labs around the world as we are featuring over two dozen pages of major breakthroughs and innovations.

In “2021: A Progress Report” on page 38, senior editor Derek Bagley has compiled an exhaustive roundup of some of the new products, therapies, and treatments that hit the market this year, or were approved by the U.S. Food and Drug Administration. From remarkable new treatments for acromegaly, thyroid eye disease, hypoglycemia, and diabetes to new devices aimed at glucose monitoring in adults and children, a mail-in semen analysis, and much more, *Endocrine News* takes a closer look at some of these new innovations announced throughout 2021.

2021 was no different from previous years in terms of endocrine research breakthroughs. For the seventh consecutive year, we are running “Eureka! The Year’s Biggest Discoveries in Endocrine Science.” This year’s roundup on page 24 is once again put together 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. Cushing’s disease, hypothyroidism, all forms of diabetes, endocrine cancers, and many more endocrinopathies saw major breakthroughs while new research methods are proving to be more and more valuable with each passing year.

On page 52, Eric Seaborg talks to David Katz, PhD, founder of Sparrow Pharmaceuticals, who took his experience in the laboratory into the business world. In “Is It Time for a New Approach to Treating Cushing’s Syndrome?” Katz talks to Seaborg about his career path and the new therapies his company is working on that could foreseeably change the way people with Cushing’s syndrome and other disorders are treated. He also explains his reasons for founding Sparrow since so many large pharmaceutical companies have “de-prioritized many early-stage investigational drugs with strong clinical potential,” he says. “It’s good for patients that companies like Sparrow exist to bring those forward to the market. Excess corticosteroids play a central role in devastating diseases such as Cushing’s syndrome and autonomous cortisol syndrome (ACS),

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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.



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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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but treatment has been suboptimal. We identified a new approach that we felt larger companies have neglected."

On page 34, Ricardo Correa, MD, EdD, talks to *Endocrine News* about his passion for not only the practice of endocrinology, but the importance of education and reaching out to get more involvement from members of underrepresented communities, especially the Latinx

“Despite a year that was still feeling the wrath of the COVID-19 pandemic, there was definitely no lack of research activity of endocrine labs around the world as we are featuring over two dozen pages of major breakthroughs and innovations.”

community in “For the Love of Hormones: A Life’s Journey to Endocrinology.” “From being on the frontlines in many jobs to being scientists and physicians who are making significant changes in the way we deliver healthcare to patients,” he tells us, “I am proud of my heritage and proud of the things that we are developing. My hope is that more Latinos join us in our effort to grow our endocrine physician-scientist community.” You will definitely be inspired by his enthusiasm, I promise!

As we bid farewell to 2021, 2022 is looking even brighter. From our first hybrid ENDO 2022 in June to new topic areas in *Endocrine News* we’ve never covered in the past but we’re looking forward to bringing you in 2022! Stay tuned!

If you would like to share your own stories, please feel free to share your experiences with us. Don’t hesitate to contact me at: mnewman@endocrine.org. 

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



• H A P P Y •
Holidays

Your friends at the
Endocrine Society wish
you a Joyous
Holiday Season and a
Happy New Year.

ENDOCRINE
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Endocrine Society Celebrates House Passage of Build Back Better Act

Diabetes experts urge Senate to pass bill and send for president's signature

Biden Photo: lev radin/Shutterstock.com



The Endocrine Society hailed the House of Representatives for including provisions to improve insulin affordability in its version of the Build Back Better Act.

"This bill offers a once-in-a-generation opportunity to protect access to this life-saving medication," says Society President Carol H. Wysham, MD. "People with diabetes cannot wait any longer for Congress to take action. We urge the Senate to quickly follow suit."

For millions of Americans living with diabetes, including all people living with type 1 diabetes, insulin is a life-saving drug that must be taken to control blood sugar. Although insulin has been available for 100 years, its prices continue to increase and have nearly tripled over the past 15 years.

The Endocrine Society has prioritized the need for affordable insulin for years. Our members have worked to educate Congress about the barriers people with diabetes face in accessing affordable insulin. We have shared policy recommendations, testimony, and a collection of patient stories illustrating that people with diabetes continue to suffer due to the high price of insulin.

The House's version of the Build Back Better Act includes the following provisions that the Endocrine Society supports:

- ▶ Gives the government authority to negotiate the price of certain drugs, including insulin;
- ▶ Caps insulin co-pays at \$35 per month for Medicare beneficiaries; and
- ▶ Institutes an inflation cap ensuring that the price of insulin doesn't increase faster than inflation.

The inflation cap would apply to Medicare and the private insurance market to protect individuals with diabetes from price hikes.

"This bill has the potential to save the lives of people with diabetes," Wysham says. "We are thankful to President Biden and members of Congress who have persisted in prioritizing access to affordable insulin."



Society Launches Training Program for Minority Clinician Leaders

The Endocrine Society is launching the Excellence in Clinical Endocrinology Leadership (ExCEL) program, a multi-faceted training program offering comprehensive leadership training and mentorship to early-career physicians of communities underrepresented in medicine and science.

ExCEL is just one of the Society's many efforts to increase diversity, equity, and inclusion (DEI) in the endocrinology field. The initiative is designed to train the next generation of physicians and clinicians to treat individuals with endocrine conditions.

"Diversity and inclusion in medicine is extremely important as it creates a safer workplace, builds patient trust, and reduces disparities in endocrine diseases," says ExCEL program director Rocio Pereira, MD, of the Denver Health Medical Center in Denver, Colo. "Having a wider range of perspectives and more minority clinicians in leadership roles generates better health outcomes for patients and helps eliminate bias in healthcare settings."

The ExCEL program caters to clinical endocrinology fellows, while the Future Leaders Advancing Research in Endocrinology

(FLARE) program provides leadership training for early-career endocrine scientists from underrepresented minority communities. FLARE was founded in 2013.

The ExCEL Program includes:

- ▶ A leadership training workshop;
- ▶ A structured year-round mentoring network to build relationships between participating fellows and dedicated mentors; and
- ▶ A Society-based internship program for fellows that includes service opportunities within the Society and informal mentoring of medical students through a Visiting Faculty Seminar Series.

For more information, go to: <https://www.endocrine.org/excel-program>. 





EndoBridge® 2021 Celebrates Nine Years of Crossing Borders

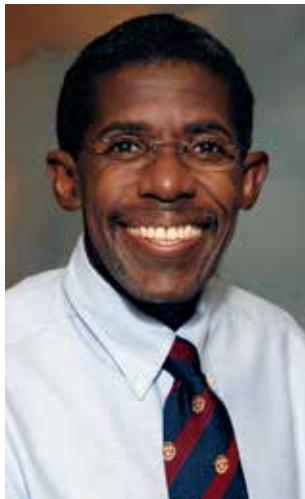
The 9th Annual Meeting of EndoBridge® was held from October 21 to 24, 2021, in an entirely virtual format and welcomed over 600 participants from 56 countries.

The four-day scientific program, which was accredited by the European Council, included state-of-the-art lectures and interactive expert discussion panels on challenging and interesting clinical cases. Delegates presented 139 clinical case e-posters. As usual, the event was conducted in English, with simultaneous translation into Russian, Arabic, and Turkish.

"EndoBridge 2021 took place as a fully digital, interactive meeting for the second time due to ongoing COVID-19 pandemic and it was freely available to all physicians and scientists in training," says Bulent Yildiz, MD, a faculty member at Hacettepe University School of Medicine, Ankara, Turkey, and founder and president of EndoBridge. "This year, for the first time, the American Thyroid Association and the Brazilian Society of Endocrinology and Metabolism joined EndoBridge as program partners. The initiative continues enhancing crosscultural dialogue and collaboration beyond the borders in the world of hormones."

Next year's EndoBridge will take place in Antalya, Turkey, October 20 – 23, 2022. Further information can be found at: www.endobridge.org.

E. Dale Abel, MD, PhD, Takes on New Role at UCLA



Endocrine Society past-president E. Dale Abel, MD, PhD, has been appointed chair of the Department of Medicine at the David Geffen School of Medicine at UCLA and executive medical director of the UCLA Health System's Department of Medicine.

Abel, currently chair and executive officer of the Department of Internal Medicine and professor of medicine, biochemistry, and biomedical engineering at the University of Iowa, will assume leadership of UCLA Health's largest department on Jan. 1, 2022. As chair, Abel will oversee a total staff of more than 3,000.

"I am proud of my contributions to the University of Iowa and thrilled to be joining UCLA Health and the David Geffen School of Medicine at UCLA, a leading academic health system that provides exceptional patient care, supports innovative research and trains top medical professionals, all in service to a vibrant metropolis and our larger world," Abel says.

Under Abel's leadership as department chair at Iowa over the past six years, research funding rose 31%, clinical revenues increased nearly 23%, and the number of faculty jumped 16%. In addition, the department's residency program remained nationally ranked under his watch.

During his eight-year tenure as director of Iowa's Fraternal Order of Eagles Diabetes Research Center, Abel grew faculty membership from an initial five to 110 today. More than 780 research grants were secured, and National Institutes of Health (NIH)-funded research rose to \$23.4 million last year. Communications to build a sense of community, provide strategic direction, and address issues of diversity, equity, and inclusion were a central focus of his work at Iowa, including a biweekly "Views from the Chair."

Abel's research has been continually funded by the NIH since 1995, with additional support from the American Heart Association, the American Diabetes Association, and others. His pioneering work on glucose transport and mitochondrial metabolism in the heart guided his research interest in molecular mechanisms responsible for cardiovascular complications of diabetes. Abel's laboratory has provided important insights into the contribution of mitochondrial dysfunction and aberrant insulin signaling to heart failure risk in diabetes.

"I was motivated to consider the UCLA opportunity because of the strength of the clinical and research operations of the department and the opportunity to leverage those resources and those of the strong faculty to set new standards regarding what success in academic medicine across all of its missions of clinical care, education, research, and community engagement should look like in the next decade," Abel tells *Endocrine News*. "I was also impressed by their strong commitment to diversity, equity, and inclusion and the desire of the organization to work towards increasing these values in their missions, particularly given the diversity of the greater Los Angeles area."

Prior to the University of Iowa, Abel held faculty positions at Harvard Medical School and at the University of Utah.

Abel has been recognized for a longstanding commitment to mentoring the next generation of endocrine researchers and biomedical scientists. He has served as the program chair

“

I am well aware that endocrinologists are relatively under-represented among chairs of academic departments of Internal Medicine. That said, I believe that endocrinologists are uniquely positioned to understand the complexity of Academic Medical Centers and to appreciate the importance of integration, collaboration, and synergy across all of their missions of patient care, research, and education.”

”

for the annual Network of Minority Investigators workshop sponsored by the National Institute of Diabetes and Digestive and Kidney Disorders to increase the success of minority biomedical researchers. Since 2012, he has been a principal investigator for the Endocrine Society’s FLARE program, which has successfully increased the pipeline of underrepresented groups into productive careers in endocrinology and diabetes research.

“I believe that my time serving in the presidency of the Endocrine Society prepared me in many ways to take on this role,” Abel says. “The strategic planning and focus of the Endocrine Society to be the global voice for endocrinology representing the cutting edge of innovation and patient care, and its commitment to diversity provided with me with essential perspectives that will inform my role at UCLA. I am particularly proud of the success of the Endocrine Society’s FLARE program, which I have led for the past nine years, and the lessons learned regarding strategies to provide life-long mentorship to the next generation of biomedical innovators, particularly those from backgrounds that have been traditionally under-represented in medicine.”

In recognition of his unwavering commitment, Abel has received mentorship awards from the University of Utah and the University of Iowa, as well as the Network of Minority Health Research Investigators Medallion from the National Institute of Diabetes and Digestive and Kidney Disorders.

“An important goal at UCLA will be to strengthen and diversify the physician scientist pipeline and I believe that my prior experiences in this realm will inform our strategy,” Abel says. “As president of Association of Professors of Medicine, I am well aware that endocrinologists are relatively under-represented among chairs of academic departments of Internal Medicine. That said, I believe that endocrinologists are uniquely positioned to understand the complexity of Academic Medical Centers and to appreciate the importance of integration, collaboration, and synergy across all of their missions of patient care, research, and education.”

Abel earned a medical degree from the University of the West Indies in Kingston, Jamaica, and a doctorate in physiology from Oxford University in England, where he was a Rhodes Scholar. He trained in internal medicine and served as chief resident at Northwestern University in Chicago, followed by a fellowship in endocrinology and metabolism at the Harvard Medical School, Beth Israel Deaconess Medical Center in Boston. EN



BY DEREK BAGLEY
Senior Editor



“
What's novel in this paper is that we used genomic sequencing.
We specifically looked at changes in the liver cells with the addition of the pathway preferential estrogens, and how it compares to what happens when you give estrogen.
”

Postmenopausal Women May Benefit from Estrogen Compound Research

Postmenopausal women have increased risk of non-alcoholic fatty liver disease due to loss of estrogen from metabolic changes. A high-fat diet further exacerbates the disease, which can progress to cirrhosis and liver failure. Hormone replacement therapy (HRT) is an effective treatment, but it carries increased risk of breast cancer, uterine cancers, and cardiovascular disease.

Researchers led by Zeynep Madak-Erdogan, PhD, associate professor in the Department of Food Science and Human Nutrition at the University of Illinois, identified a novel estrogen compound, pathway preferential estrogens, which provides benefits similar to HRT but without the risk factors and published their findings recently in *nutrients*.

Previous research had shown that the compound activated specific signaling pathways, particularly in the metabolic tissues. Now, the researchers explore the effects of pathway preferential estrogens on liver and uterine health in mice.

“Estrogens are important for the reproductive system and metabolic tissue. Hormone replacement therapy can address some of the metabolic issues associated with onset of menopause. But we know it also increases the risks associated with exposure to the hormones,” Madak-Erdogan says. “We removed the ovaries of the mice to mimic the loss of estrogen that happens in menopausal women. We also placed the mice on a high-fat diet, and they gained weight pretty quickly. We treated one group of mice with hormone replacement therapy, and another group of mice with the pathway preferential estrogens.”

The researchers observed the mice for six weeks, measuring their food intake and body composition. At the end of the trial, they collected liver and uterine tissues for analysis. “Normally, estrogen will cause an increase in uterine weight, but this did not happen with the pathway preferential estrogens. That is a good thing,

because it suggests there are no negative effects on the uterus,” Madak-Erdogan says.

Treatment with either estrogen or pathway preferential estrogens can help reduce excess lipid deposition in the liver. That much was already known, Madak-Erdogan says. “What's novel in this paper is that we used genomic sequencing. We specifically looked at changes in the liver cells with the addition of the pathway preferential estrogens, and how it compares to what happens when you give estrogen,” she says. “We found there was an increase in the generation of new mitochondria with pathway preferential estrogens. Mitochondria is a powerhouse, and you need healthy new mitochondria so your cells can continue functioning. This is particularly important for the liver cells, the hepatocytes.”

As a result, even though the mice were receiving more calories, they were also burning more when they received pathway preferential estrogens. The compound can also prevent the progression of fibrosis. “As the non-alcoholic fatty liver disease progresses from lipid deposition to cirrhosis, it causes further damage to the liver cells, and fibrosis begins. As you accumulate more lipids, it will cause oxidative stress and it will start damaging hepatocytes,” Madak-Erdogan says.

“When we treated the animals with the pathway preferential estrogens, the reduction in fibrosis was much greater compared to estrogen,” she continues. “The compound causes higher utilization of what's coming from the diet, but it also protects against the damage from the excess diet itself and from the lipid deposition. This means pathway preferential estrogens prevent further fibrosis, which is the path that leads to liver failure and metabolic problems.”

John Katzenellenbogen, PhD, a research professor of chemistry at the University of Illinois, developed the pathway preferential estrogens in his research lab.

Safe, Non-Invasive Treatments Could Combat Obesity Epidemic

Novel obesity treatments such as modulation of the gut microbiome and gene therapy are underutilized and could help fight the obesity epidemic, according to a new manuscript published in *Endocrine Reviews*.

Researchers led by Christos S. Mantzoros, MD, ScD, of Beth Israel Deaconess Medical Center in Boston, Mass., point out that nearly half of the adults and 20% of children in the U.S. have obesity, yet doctors are under-prescribing effective weight loss medications and many patients are not receiving the treatment they need. The weight stigma that exists in healthcare settings makes people with obesity hesitant to seek care until comorbidities develop and reach a dangerous stage. Lack of insurance coverage and cost issues are other factors that create barriers to obesity treatment. “Yearly deaths attributable to a high body mass index (BMI) have been estimated to be 4 million, and this number includes persons who are overweight, which account for 40% of this toll,” the authors write.

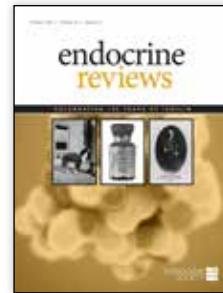
“Obesity is the epidemic crisis of our time. The disease leads to serious comorbidities such as diabetes, fatty liver disease, and cardiovascular disease and significantly shortens a person’s length and quality of life,” Mantzoros says. “Until recently we did not understand the genetic and hormonal causes of obesity and how obesity leads to these comorbidities. We have recently started to understand the causes of obesity in humans, which is a big discovery that has led to designing effective therapies.”

In the article, the researchers map out the molecular and hormonal pathways that lead to obesity and the disease’s related comorbidities. This data gives researchers the insights they need to

design, test, and implement new obesity therapies. The researchers highlight the need for safer and more effective obesity therapies, including new drug delivery systems, vaccines, modulation of the gut microbiome, and gene therapy. Novel medications, including combinations of gastrointestinal hormones and other molecules, are being tested and are expected to lead to significant percentages of weight loss with fewer side effects once available. As our understanding of obesity improves, more effective medications with fewer side effects will be developed.

Recently approved medications such as semaglutide, a modified gastrointestinal hormone administered once a week, can lead to 15% weight loss when combined with lifestyle changes. Bariatric surgery can lead to up to 40% weight loss, but it is invasive and linked to complications. “Ultimately, advancements in our understanding of the pathophysiological basis and the interindividual variation of obesity will hopefully lead to multimodal, personalized approaches to obesity treatment that result in safe, effective, and sustainable weight loss, which, in turn, would also result in the decreased prevalence of obesity comorbidities such as T2DM, NASH, CVD, OSA, and obesity-related malignancies,” the authors write in their conclusion.

“Insurance companies need to pay attention to data from studies and the scientific progress we are making and start covering the medications that are and will be approved soon, given that currently only a small minority of patients with obesity have coverage for the medications and medical care they need,” Mantzoros says. “It would be much more cost effective to cover treatments early instead of waiting for comorbidities and their complications to develop.”



“Until recently we did not understand the genetic and hormonal causes of obesity and how obesity leads to these comorbidities. We have recently started to understand the causes of obesity in humans, which is a big discovery that has led to designing effective therapies.”



“Importantly, the bone age to chronological age ratio advanced similarly in both groups, suggesting that the increased rate of longitudinal growth did not occur at the expense of accelerated skeletal maturation.”

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Lonapegsomatropin Shows Promise in Treatment-Naïve Children with GHD

The investigational long-acting, once-weekly prodrug lonapegsomatropin (TransCon hGH) may be more beneficial to treatment-naïve pediatric patients with growth hormone deficiency (GHD) than daily somatropin of equivalent weekly dose, according to a paper recently published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Aimee D. Shu, MD, of Ascendis Pharma (who funded the trial), point out that children with GHD have been treated with daily injections of somatropin (recombinant human GH) since 1987, and although the drug is safe and does help children achieve normal height, results don't always match expectations. Children and their caregivers don't particularly like daily injections, leading to noncompliance rates ranging from 5% to 82%. “In 2015, the Growth Hormone Research Society recognized the need for a long-acting growth hormone (LAGH) and agreed that by decreasing injection frequency and offering different pharmacokinetic properties, a LAGH would potentially improve adherence and outcomes,” the authors write.



The Phase 3 heiGHT trial enrolled 161 treatment-naïve, prepubertal patients with GHD, and randomized the children 2:1 to receive lonapegsomatropin 0.24 mg hGH/kg/week or an equivalent weekly dose of somatropin delivered daily. The researchers found that after 52 weeks, patients taking lonapegsomatropin had a an ANCOVA-adjusted least squares (LS) mean (SE) annualized height velocity (AHV) of 11.2 cm compared to 10.3 cm for the children taking somatropin. The observed AHV range was 5.9 to 18.0 cm/year and 4.7 to 16.3 cm/year for lonapegsomatropin and daily somatropin, respectively.

“The Phase 3 heiGHT trial of weekly lonapegsomatropin in treatment-naïve pediatric patients with GHD demonstrated superior AHV and statistically greater change in height SDS from baseline compared to a commercially available daily somatropin of equivalent weekly dose, with a similar safety and tolerability profile,” the authors write. “Importantly, the bone age to chronological age ratio advanced similarly in both groups, suggesting that the increased rate of longitudinal growth did not occur at the expense of accelerated skeletal maturation.”

The researchers go on to conclude the fundamental challenge of developing a LAGH is to create a more convenient dosing regimen while retaining the excellent safety, efficacy, and tolerability of daily somatropin. “Building on the concept of releasing unmodified somatropin to maintain physiologic distribution, weekly lonapegsomatropin is the first LAGH with data demonstrating superior efficacy compared to a daily somatropin, while maintaining similar bone age advancement, AE profile, and immunogenicity,” they write. “Lonapegsomatropin may represent an important therapeutic option for children with GHD.”

Highest Rates of Severe Hypoglycemia Crises Are in Patients with Diabetes and ESKD

In patients who have diabetes and end-stage kidney disease (ESKD), the rates of severe hypoglycemia crises requiring emergency department visits or hospitalizations are the highest so far reported, according to a nationwide study recently published in *Diabetes Care*.

Researchers led by Rodolfo J. Galindo, MD, associate professor of medicine at Emory University School of Medicine in Atlanta, in collaboration with Rozalina McCoy, MD, MS, associate professor of medicine at Mayo Clinic, analyzed data from 521,789 adults (56.1% male, 46% white) with diabetes and ESKD from the United States Renal Data System registry, from 2013 to 2017, looking at annual rates of emergency department visits or hospitalizations for hypoglycemic and hyperglycemic crises, reported as number of events/1,000 person-years, adjusting for patient age, sex, race/ethnicity, dialysis modality, comorbidities, treatment regimen, and U.S. region.

The researchers found that the overall adjusted rates were 53.64 hypoglycemic crises per 1,000 person-years to 18.24 hyperglycemic crises per 1,000 years. Notably, younger patients (18 – 44 years) had the highest rates of severe hypoglycemic crises, with 120.07 events (95% CI 114.84 – 125.30) per 1,000 person-years, compared with 42.07 events per 1000 person-years among patients >=75 years old. These findings demonstrated the high burden of disease, vulnerability, and complexity of care of young patients with diabetes on dialysis. They must “manage their diabetes and ESKD in the context of other life demands like family, education, and employment. In addition, they are most likely to have type 1 diabetes, end-stage diabetes-related complications, and/or childhood causes of ESKD.”

The researchers also found that most patients were treated with insulin therapy, up to 63.8%, and insulin therapy was associated with a 34% increased risk for hypoglycemic crises compared to non-insulin therapy, and 40% increased risk compared to no therapy. Interestingly, compared with patients treated with insulin, patients treated with noninsulin

medications had a 72% lower risk of hyperglycemic crises, while patients treated with lifestyle therapy had a 56% lower risk. The study highlights that insulin therapy, considered the “safest therapy” for dialysis patients, may not be the best anti-diabetic therapy, particularly with the development of newer agents with lower hypoglycemic risk.

Galindo and his team point out that it will be important for Endocrine Society members and others treating these patients to be aware of the burden of severe hypoglycemia. This is the highest burden of all previous reports, compared to pre-dialysis CKD, and other comorbidities, by more than three to fivefold, Galindo tells *Endocrine News*.

The authors write that the reported rates of severe hypoglycemia are higher than previous for high-risk populations, including elderly patients, elderly patients with longstanding (40 years) type 1 diabetes, patients with long-standing (15 years) type 2 diabetes treated with complex insulin regimens, and patients with diabetes and non-dialysis CKD.

“For instance, the study by Lipska, et. al. 2011 was a landmark study making us aware of the increasing hypoglycemia crises in the elderly, but in our study, the rates among young (18 - 44 years) adults on dialysis were extremely higher (150 compared to ~20-30 events per 1,000 person-years among other cohorts with high-risk comorbidities),” Galindo says.

The study exposed health disparities. Black patients were more affected by hypoglycemic crises, as well as those with a history of amputation. “In this nationwide study of patients with diabetes/ESKD, hypoglycemic crises were threefold more common than hyperglycemic crises, greatly exceeding national reports in non-dialysis patients with chronic kidney disease,” the authors conclude. “Young, Black, and female patients were disproportionately affected.” EN



In this nationwide study of patients with diabetes/ESKD, hypoglycemic crises were threefold more common than hyperglycemic crises, greatly exceeding national reports in non-dialysis patients with chronic kidney disease.

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ENDO 2022

June 11 – 14, 2022 • Atlanta, Georgia/Virtual Event

ADVANCE REGISTRATION:

Early Bird: January 12, 2022 – March 4, 2022

Advanced: March 5, 2022 – May 18, 2022

Late/Onsite: May 19, 2022 – June 14, 2022

ABSTRACT DEADLINE: January 17, 2022

HOUSING DEADLINE: May 20, 2022

ENDO 2022, taking place June 11 – 14, will be the Society's inaugural hybrid meeting; attendees can participate in Atlanta, online ... or both! This increased flexibility will foster expanded connectivity, community, and knowledge sharing among the diverse, international endocrine community. Each format has intrinsic benefits, and when the time comes, attendees will have the option to select the best format that suits their desires and needs when June 2022 rolls around.

Attendees can expect top-flight education at **ENDO 2022**, as well as a new vibrancy and contemporary conference experience with expanded networking. Learners can expect a range of carefully curated sessions in a variety of delivery formats spanning the endocrinology journey from bench to bedside and back again. **ENDO 2022** attendees will have the opportunity to tailor their learning experience to fit their precise professional and personal development needs. Further, the Society is also ramping up its investment in technology-forward learning enhancements to align the **ENDO** learning experience with the reality of day-to-day life in the 21st century.
www.endocrine.org/endo2022



CDEI 57th Annual CME Conference

**Snowmass, Colorado
January 22-25, 2022**

The 57th Annual Clinical Diabetes and Endocrinology Institute (CDEI) CME Conference will address insulin on its 100th birthday, thyroid nodule evaluation, hypercalcemia work-up and management, diabetes technology, cholesterol-lowering therapy, post-op management of pituitary tumors, insulins: how they work, menopausal hormone therapy, and more. The faculty will be comprised of known experts, will offer insights, latest research, case presentations and clinical guidelines. To reinforce knowledge gained from the course and ensure lasting value to each attendee's practice, CDEI will provide access to course presentation

slides and recorded live presentations after the completion of the course. Ideally suited for endocrinologists, primary care physicians, and other healthcare professionals with an interest in diabetes, endocrinology, and metabolism.

<https://www.cdei-snowmass.com/>

Medical Management of the Metabolic-Bariatric Surgery Patient

**February 15, 2022
10:00 a.m. – 5:20 p.m. (ET)
(Webinar)**

Severe obesity and its complications are best managed by an interdisciplinary team including both surgical and medical providers. This webinar will feature presentations by leading experts, panel discussions, and dedicated time for interactive Q&A to

cover best practice recommendations for the pre- and post-operative management of patients undergoing metabolic-bariatric surgery. Topics include optimizing pre-operative care as well as recognizing and developing approaches to the variability in post-operative weight loss and remission rates of obesity-related complications in both adult and pediatric patients. All registrants will receive on-demand access to recordings throughout 2022.

<http://www.obesity.org/meetings-education/webinars/>

BPS 2022: 66th Biophysical Society Annual Meeting

**San Francisco, California
February 19 – 22, 2022**

The Biophysical Society annual meetings are the largest annual gathering of biophysicists around the world. The

meetings include symposia, workshops, 15 subgroup programs, over 500 platform speakers selected from submitted abstracts, the Biophysical Society Lecture, more than 4,000 packed poster presentations, as well as educational exhibits, exhibitor presentations, and career development sessions.

www.biophysics.org/2022meeting#/

Clinical Endocrinology 2022

Live Streaming

April 6 – 10, 2022

Clinical Endocrinology 2022, a live streaming CME program, has been optimized for remote learning. All sessions and workshops will be live streamed and include online, live chat, where participants can pose their specific questions to faculty. All sessions and workshops will be recorded and made available to participants for online viewing, at their convenience, via a course archive. As a participant, you will be able to access these recordings for 60 days after the conclusion of this course. For nearly 50 years, renowned experts in endocrinology at Harvard Medical School and Massachusetts General Hospital have delivered the CME course Clinical Endocrinology — the acclaimed annual update of current endocrine diagnostic and management strategies. If you provide care to patients with endocrine disorders, this course will be invaluable to your medical decision-making and patient care.

<https://endocrinology.hmscme.com>

AAES 2022

Cleveland, Ohio • May 22 – 24, 2022

(Virtual Event) • May 22 – 24, 2022

As the leading endocrine surgery association in North America, the American Association of Endocrine Surgeons (AAES) Annual Meeting is the premier event to connect with professionals and leaders across the globe in the field of endocrine surgery while receiving high-level education on the latest advancements in science and research. The 2022 Annual Meeting will be a hybrid event taking place in Cleveland, Ohio, but with virtual opportunities. While in-person podium presentations are preferred, exceptions will be made, and the ability to travel to the meeting venue is not a prerequisite for abstract acceptance.

<https://www.endocrinesurgery.org/2022-annual-meeting>

ATTD 2022

Paris, France

March 8 – 11, 2022

Join us in Paris for the 15th International Conference on Advanced Technologies & Treatments for Diabetes. For 15 years, ATTD has stood at the forefront of diabetes innovation. Remarkable developments keep coming at full speed, and ATTD 2022 will again be the platform to present, review, and discuss the latest changes. We aim to move the diabetes field forward with an ever-growing community that promotes and enhances novel technologies and treatments to change the lives of people with diabetes.

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

WCO-IOF-ESCEO 2022

Berlin, Germany

March 24 – 27, 2022

For this 22nd Edition of the World Congress on Osteoporosis, Osteoarthritis, and Musculoskeletal Diseases (WCO-IOF-ESCEO) Congress, the members of the Committee of Scientific Advisors of the IOF and the members of the Scientific Advisory Board of ESCEO are developing a very exciting Congress' scientific program that will bring together the world's best in the field of musculoskeletal health and disease.

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

3rd World Congress on Diabetes & Endocrinology

Dubai, UAE

May 9 – 10, 2022

The 3rd World Diabetes Congress 2022 brings together a unique international mix of experts, researchers, and decision makers both from academia and industry across the globe to exchange their knowledge, experience, and research innovations. This conference is a unique international platform that's a confluence of all stakeholders of the ecosystem — industry, academia, research, innovators, regulators — coming together to present and discuss current topics in diabetes and endocrinology, gestational diabetes, epidemiology and public health, obesity, pediatric endocrinology, diabetes and immunology, diabetic neuropathy, and many more. Join us to network with your peers, exchange expertise and experiences, and arm yourself with the latest information to take your department to the next level.

<https://diabetes.inovineconferences.com/>

“

I would like for institutions to care more about producing strong research regarding health disparities. This, alone, would bring in more Latinx patients as subjects in clinical trials. **At this time, there is reluctance due to prior episodes in medicine and the only way of changing it is if more principal investigators are from the same culture and can explain the processes and the procedures to the patient in their native language.”**

— Ricardo Correa, MD, EdD, discussing how to get members of the Hispanic community more involved in scientific research in “*For the Love of Hormones: A Life’s Journey to Endocrinology*” on page 34.



35

The age overweight adults should begin screening for type 2 diabetes. This is five years earlier than currently advised, experts recommended. This means more than 40% of the adult population in the U.S. should now be screened, according to one estimate.

— SOURCE: NEW YORK TIMES

91,000 to 107,000



The number of premature deaths each year among people ages 55 to 64 years in the U.S. that may be linked to phthalates, the common endocrine-disrupting chemicals.

— SOURCE: CNN

MEMBER SPOTLIGHT

Ricardo Arrais, MD, PhD



Ricardo Arrais, MD, PhD, received his medical degree at Federal University of São Paulo (UNIFESP-EPM) Escola Paulista de Medicina in 1985. In 1988, he completed his medical residency in pediatrics and went on to receive a pediatrics focused master's degree in 1994. Arrais earned a PhD in clinical endocrinology in 2005, along with all degrees at EPM.

Arrais was born and raised in São Paulo, but in 1997, he moved to Natal, Brazil, to provide pediatric endocrinology services. In 2003, he started a residence program of pediatric endocrinology. Since then, more than 30 professionals are trained to provide services at the Federal University of Rio Grande Do Norte, where Arrais is an associate professor. He also is a research collaborator at the LAIS (Laboratório de Inovação Tecnológica em Saúde - Technology Innovation on Health Laboratories).

For 10 years, he has worked alongside a group of very diverse professionals in health, technology, informatics, and communication to develop tools to enhance electronic health, such as recording data applications and programs, diabetes-related devices, and other subjects in pediatric endocrinology including growth and puberty disorders.

Read more about your fellow Endocrine Society's members at: www.endocrine.org/member-spotlight

12 hours

In “time-restricted eating,” the window for all calorie intake is restricted to a consistent interval of less than 12 hours without overtly attempting to reduce calories. This is an emerging behavioral intervention approach based on the understanding of the role of circadian rhythms in physiology and metabolism.



— SOURCE: ENDOCRINE REVIEWS

45

Menopause before age 45 is a risk factor for fractures, but menopause occurs at age ≥ 45 years of age in nearly 90% of women.

— SOURCE: THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

\$8 billion

The estimated cost to treat and diagnose polycystic ovary syndrome (PCOS), the most common hormone disorder affecting women of reproductive age nationwide in 2020.

— SOURCE: THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM





eureka!

the top
endocrine discoveries
of 2021

For the seventh year running,
Endocrine News talks to
editors from Endocrine
Society publications to get the
endocrine discoveries of 2021
worth their weight in gold.

BY KELLY HORVATH

Research never stops. Despite facing challenges related to social distancing, supply chain disruptions, and other pandemic-related problems this past year, scientists dug deep in the mines of endocrinology and struck the mother lode.

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

Endocrinopathies like Cushing's disease, all forms of diabetes, and hypothyroidism; breast and thyroid cancers; and liver disease are now better elucidated in these studies, and editors also favored studies that developed or used new assays, sophisticated testing methods, and machine learning to make important breakthroughs.

From the Editor of *Endocrine Reviews*



Endocrine Reviews editor-in-chief Daniel J. Drucker, MD and senior scientist at the Lunenfeld Tanenbaum Research Institute of the Mt. Sinai Hospital in Toronto, Ontario, Canada, points to "Convergent somatic mutations in metabolism genes in chronic liver disease," by Ng, S.W.K., et al. published in *Nature* in October.

"Metabolic liver disease is increasingly common in people living with type 2 diabetes or obesity. The complications of excess fat in the liver may include hepatic inflammation (NASH) leading to fibrosis, cirrhosis, and rarely, hepatocellular carcinoma. NASH is also associated with increased rates of cardiovascular disease. The intrahepatic metabolic adaptations ensuing from liver injury are only partly understood," explains Drucker.

"In this paper, Dr. Stanley Ng and colleagues studied the genomes of multiple segments of the human liver from people with alcohol-related or non-alcohol-related fatty liver disease," Drucker continues. "Remarkably, they found areas of the liver with clonal expansion of liver cells that harbored acquired somatic mutations in genes regulating carbohydrate and lipid metabolism. Moreover, these genetic changes would be predicted to protect the liver cells from excess fat accumulation. Hence these intriguing studies highlight a potential new mechanism by which injured liver cells may adapt to self-protect from metabolic insults."

From the Editor 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

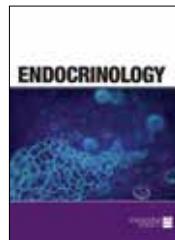
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Dr. Stanley Ng and colleagues studied the genomes of multiple segments of the human liver from people with alcohol-related or non-alcohol-related fatty liver disease. Remarkably, they found areas of the liver with clonal expansion of liver cells that harbored acquired somatic mutations in genes regulating carbohydrate and lipid metabolism. **Moreover, these genetic changes would be predicted to protect the liver cells from excess fat accumulation. Hence these intriguing studies highlight a potential new mechanism by which injured liver cells may adapt to self-protect from metabolic insults.”**

— DANIEL J. DRUCKER, MD, EDITOR-IN-CHIEF, ENDOCRINE REVIEWS; SENIOR SCIENTIST, LUNENFELD TANENBAUM RESEARCH INSTITUTE OF THE MT. SINAI HOSPITAL, TORONTO, ONTARIO, CANADA

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 “ER α is an RNA-binding protein sustaining tumor cell survival and drug resistance,” by Xu Y., et al., published in the September issue of *Cell*. “This is not only a new function for ER- α as an RNA-binding protein that regulates steps in RNA metabolism, but also this novel function has biological roles that contribute to progression of breast cancer,” Lange says.

More From the Editors of *Endocrinology*



Several associate editors of *Endocrinology* also contributed. Hershel Raff, PhD, FAAAS, FAPS professor of medicine, surgery, and physiology and of the 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, chose two papers that are quite close to home. First, “O-GlcNAcylation Is Essential for Rapid POMC Expression and Cell Proliferation in Corticotropic Tumor Cells,” by Massman L.J., et al., published this month in *Endocrinology*, is not only from his journal, but the team of researchers is also at MCW. Although Raff did not participate in the studies, he had an insider’s peek into this study’s development. “I think this is a very important ‘aha’ paper for many of us who were unaware of the O-GlcNAcylation pathway, which regulates proteins in critical signaling pathways, and its deregulation is involved in cancer progression and endocrine diseases such as diabetes,” Raff says. “This pathway is amenable to medical therapy, possibly of corticotroph tumors causing Cushing’s disease.”

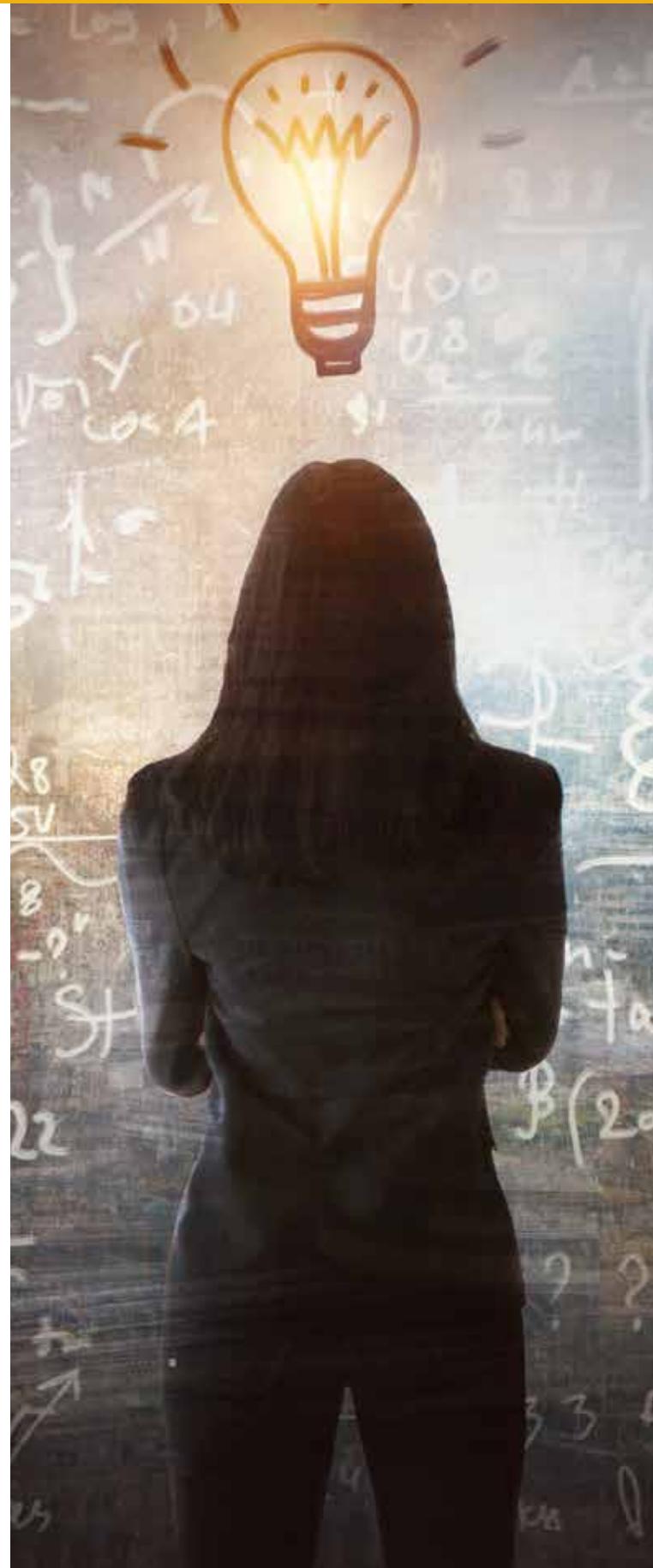
Raff co-authored his next choice: “Consensus on diagnosis and management of Cushing’s disease: a guideline update,” by Fleseriu M., et al., and published online in October ahead of print in *The Lancet Diabetes and Endocrinology*. “This extremely important publication resolves and clarifies many controversial and confusing issues in the diagnosis and treatment of Cushing’s disease — one of the most challenging in clinical endocrinology,” Raff says.

Patricia L. Brubaker, PhD, FRSC, professor, Departments of Physiology and Medicine at the University of Toronto, in Ontario,

credits "Evidence for Glucagon Secretion and Function Within the Human Gut," by Sun E.W., et al., from the April issue of *Endocrinology*. "Using sophisticated new approaches with human tissues, the authors have resolved the long-standing question as to whether glucagon can be produced by the intestinal tract, a question of relevance to patients following total pancreatectomy as well as with diabetes," Brubaker explains. "Although questions remain as to whether intestinal glucagon contributes to circulating levels of glucagon, the findings indicate a role for this peptide in regulating local intestinal function."

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, also appreciated Lange's top choice, "ER α is an RNA-binding protein sustaining tumor cell survival and drug resistance," and selected four additional papers that shed light on estrogen and breast cancer:

- ▶ "RAC1 Plays an Essential Role in Estrogen Receptor Alpha Function in Breast Cancer Cells," from the August issue of *Oncogene*, by Sun J., et al., identified the Rho family GTPase protein RAC1, an essential estrogen receptor (ER) cofactor, suggesting that RAC1 might be a druggable target in estrogen-receptor positive (ER+) breast cancer.
- ▶ In "Estrogen Regulation of the Molecular Phenotype and Active Translatome of AVPV Kisspeptin Neurons," from the September issue of *Endocrinology*, Stephens S.B.Z. and Kauffman A.S., isolated mRNA transcripts from *Kiss1* neurons to determine what other transcripts they co-express and how estradiol effects such expression levels. They view their findings as opening the door to understanding anteroventral periventricular nucleus (AVPV) kisspeptin cell regulation and functions.
- ▶ In "Exosomal miR-19a and IBSP Cooperate to Induce Osteolytic Bone Metastasis of Estrogen Receptor-Positive Breast Cancer," published in *Nature Communications* in August, Wu K., et al., uncover the mechanism underlying how ER+ breast cancer cells increase the likelihood of bone metastasis along with exosomal miR-19a and integrin-binding sialoprotein (IBSP), the presence of which can also predict risk of bone metastasis. Importantly, inhibiting IBSP binding with chlorogenic acid is a potential therapy to prevent recurrence.





► “Drivers and Suppressors of Triple-Negative Breast Cancer,” by Wu W., et al., from the August issue of *Proceedings of the National Academy of Sciences of the United States of America*, demonstrates that estrogen receptor β (ER β) agonists are not a viable therapy for triple-negative breast cancer because ER β may mimic the action of ER α and increase proliferation.

From the Editor of the *Journal of the Endocrine Society*



Journal of the Endocrine Society (JES) editor-in-chief J. Larry Jameson, MD, PhD, professor of medicine, dean of the Perelman School of Medicine, and executive vice president for the Health System at the University of Pennsylvania, in Philadelphia, highlights a February JES paper coauthored by *Endocrinology* editor Hershel Raff: “New Cutoffs for the Biochemical Diagnosis of Adrenal Insufficiency after ACTH Stimulation using Specific Cortisol Assays,” by Javorsky B.R., et al. “Ruling out adrenal insufficiency is a common clinical question in endocrinology. The adrenocorticotropin (ACTH) stimulation test is a long-standing, if imperfect, means to assess the hypothalamic–pituitary–adrenal axis,” Jameson says. “This article demonstrates that with the advent of newer cortisol assays, the cut-off point for discriminating normal versus abnormal adrenal function is reduced from the traditional threshold of 18 ug/dL to 14–15 ug/dL. I congratulate the authors for their rigorous approach to evolve and improve the data we use to manage patients.”

More from JES Editors



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 three

“ This paper was particularly interesting to me because it is a harbinger of the increasing role and potential benefits that AI/ML will have in medicine/endocrinology. In addition, the paper has implications for both pediatric and adult endocrinologists. Moreover, the paper highlighted sex differences in growth and height, the mechanisms of which remain poorly understood. **The ability to predict an individual’s adult height by the age of six years provides a theoretical window of opportunity to influence final adult height. While this may be a potential medical or health benefit in some cases, it also raises important ethical issues for consideration.”**

—URSULA B. KAISER, MD, SENIOR PHYSICIAN, BRIGHAM AND WOMEN'S HOSPITAL; PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL, BOSTON, MASS.

papers. “Probably one of the major ‘discoveries’ in my area of pituitary and adrenal disorders,” Grossman explains, “was the identification of the germline mutation for food-dependent bilateral macronodular adrenal hyperplasia by two French groups.” “Loss of *KDM1A* in GIP-Dependent Primary Bilateral Macronodular Adrenal Hyperplasia with Cushing’s Syndrome: A Multicentre, Retrospective, Cohort Study,” by Chasselooup F. et al., published in the November issue of *The Lancet Diabetes and Endocrinology*, and one currently in press in *Genet Med* by Vaczlavik et al. “The lysine demethylase mutation identified was unexpected,” Grossman says, “and leads to a lot of new ideas and speculations, but does show how study of even a few patients with a very rare disease can lead to exciting new insights.”

“In another area,” he continues, “much less a ‘discovery’, but very commendable, is the study published in JCEM from major endocrine centers comparing patients with ‘confirmed Cushing’s disease’ and those in whom it was ‘unconfirmed’ (some 14% of their cohort).” “Diagnostic Pitfalls in Cushing Disease: Surgical Remission Rates, Test Thresholds, and Lessons Learned in 105 Patients,” by Mallari R.J., et al, came out in September. “Cushing’s syndrome remains problematic

and enigmatic, Grossman says, “and this study is exemplary for its honesty in frankly exploring and admitting areas of uncertainty; indeed, confirming that even now we don’t always have all the answers.”

Bülent O. Yıldız, MD, professor at the Hacettepe University School of Medicine in Ankara, Turkey, chose “Early Prediction of Gestational Diabetes Mellitus in the Chinese Population via Advanced Machine Learning,” published in March in JCEM by Wu Y., et al. “Hyperglycemia throughout pregnancy might adversely affect clinical outcome both for the mother and the baby,” Yıldız says. “Recently, different machine learning algorithms are being tested to establish risk prediction models for gestational diabetes, which might provide an opportunity for earlier intervention before the recommended screening with oral glucose tolerance test at 24 – 28 weeks of gestation. Using a machine learning–driven selection approach, Wu et al. provide new evidence that a clinically cost-effective 7 variable model could predict gestational diabetes in early pregnancy with high accuracy.”

Ana Claudia Latronico, MD, PhD, head professor of the Endocrinology and Metabolism Division of São Paulo

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— BÜLENT O. YILDIZ, MD, PROFESSOR,
HACETTEPE UNIVERSITY SCHOOL OF MEDICINE, ANKARA, TURKEY

University in Brazil, nominates “MKRN3 Inhibits the Reproductive Axis through Actions in Kisspeptin-Expressing Neurons,” by Abreu A.P, et al., and published in *The Journal of Clinical Investigation* in May 2020 that she coauthored. “My choice demonstrates the role of MKRN3, a central precocious causative gene,” she says.

Loss of *KDM1A* in GIP-Dependent Primary Bilateral Macronodular Adrenal Hyperplasia with Cushing’s Syndrome: A Multicentre, Retrospective, Cohort Study” got another nod, this one from Gérald Raverot, MD, PhD, professeur des Universités-Praticien Hospitalier, and Hospices Civils de Lyon Federation d’Endocrinologie du Pole Est, in France. Raverot also selected “Two Distinctive *POMC* Promoters Modify Gene Expression in Cushing Disease,” from the September issue of JCEM, by Araki T., et al., that identified a second *POMC* promoter in ACTH-secreting pituitary tumors, which could be a therapeutic target for suppressing excess ACTH production.

Published in October, “Obesity-Associated GNAS Mutations and the Melanocortin Pathway,” by Mendes de Oliveira E., et al., from *The New England Journal of Medicine*, caught the eye of Luca Persani, MD, PhD, professor of endocrinology at the University of Milan in Italy. “This study brings evidence that inheritable GNAS-inactivating variants can cause resistance to melanocortin and satiety signaling and isolated obesity in the presence of other mild features of Albright’s hereditary osteodystrophy, including higher TSH levels,” Persani says. “Therefore, more widely, monogenic diseases are clinically more variable than their classic descriptions suggest.”

Persani also thought “Severity of Proteinuria Is Directly Associated with Risk of Hypothyroidism in Adults,” by Kwong N., et al., from the February issue of JCEM, worthy of extra attention. “This study gives evidence on the relationships between thyroidology and nephrology. The results provide support to the systemic screening of thyroid function in patients with proteinuria, as well as to the evaluation of kidney function in patients with hypothyroidism,” he says.

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 U.K., selected a September paper from JCEM that is already getting a lot of traction. “Calcifediol Treatment and COVID-19-Related Outcomes,” by Nogues X., et al., “further highlights the close

interplay of the endocrine system in the pathophysiology of COVID-19 infection,” he says. “Stringent placebo-controlled clinical trials are now required to confirm if this well-known (and non-expensive) hormone is indeed beneficial in COVID-19 infected patients.”

More from JCEM Editors



Elizabeth N. Pearce MD, MSc, Boston University School of Medicine, Section of Endocrinology, Diabetes, and Nutrition, in Massachusetts, found two JCEM papers published in 2021 particularly interesting. From October, “Comparative Effectiveness of Levothyroxine, Desiccated Thyroid Extract, and Levothyroxine+Liothyronine in Hypothyroidism” by Shakir M.K.M., et al., “compared the effects of levothyroxine monotherapy, desiccated thyroid, and T3/T4 combination therapy in hypothyroid patients in a crossover randomized clinical trial,” she says. “Overall, symptom scores, quality of life, symptoms of depression, and memory scales did not differ by type of thyroid hormone replacement. However, among the third of the patients studied who had the highest level of symptoms at baseline, there was a preference for T3-containing therapies. I think this highlights an area of clinical uncertainty where additional, larger, trials are needed.”

She also selected “Pregnancy Does Not Affect the Prognoses of Differentiated Thyroid Cancer Patients with Lung Metastases,” by Xi C., et al., from July. “Although this study is relatively small and retrospective, it addresses an important and understudied clinical question,” Pearce says. “Of 124 women of reproductive age who underwent surgery and radioactive iodine treatment for differentiated thyroid cancers with lung metastases, 37 subsequently went on to become pregnant, and the study examined whether pregnancy worsened cancer outcomes. Reassuringly, 10-year overall and progression-free survival did not differ in the women who became pregnant compared to those who did not, strongly suggesting that a history of thyroid cancer (even advanced thyroid cancer) should not be a deterrent to subsequent pregnancies.”

Ragh G. Mirmira, MD, PhD, professor of medicine; vice chair for research, director, Translational Research Center at the University of Chicago, gave three JCEM papers top billing. “Dual GIP and GLP-1 Receptor Agonist Tirzepatide Improves Beta-cell





Function and Insulin Sensitivity in Type 2 Diabetes,” by Thomas M.K., et al., was published in January in JCEM. “Tirzepatide is a synthetic 39-amino acid peptide that is being developed for the treatment of type 2 diabetes,” Mirmira explains. “Tirzepatide has been shown to have effects on both glycemic control and weight loss that are significantly superior to GLP-1 receptor agonists. The study by Thomas et al. is a post-hoc analysis comparing tirzepatide to dulaglutide (a GLP-1 receptor agonist), in which the authors focused on the effects of these drugs on biomarkers of insulin resistance and β -cell function. This study emphasizes that this new class of dual receptor agonists represents a new approach in the treatment of type 2 diabetes, wherein targeting weight loss, insulin resistance, and β -cell function collaborates to achieve greater reductions in HbA1c than seen previously with compounds that have single receptor specificity.”

From December 2020, Mirmira chose “Prevalence of Nonalcoholic Fatty Liver Disease (NAFLD) in Patients with Type 1 Diabetes Mellitus: A Systematic Review and Meta-Analysis,” by de Vries M., et al. “The systematic review and meta-analysis of de Vries and colleagues have attempted to address this issue and to explore associated characteristics with NAFLD,” he says. “The most notable finding of this study was that the pooled prevalence of NAFLD in patients with type 1 diabetes was 19.3% (range 0%-64.7%), increasing to 22% in adults. The study examined the entire spectrum of age among type 1 diabetes patients, and therefore provides an estimate of prevalence that suggests NAFLD is at least as prevalent in these patients as in the general population, but possibly higher. Moreover, the longer lifetime exposure of disease in individuals with type 1 diabetes and the increasing prevalence of obesity and insulin resistance in this group suggests that risk of NAFLD may increase in the coming years. The study emphasizes the need to standardize diagnostic criteria for NAFLD and to consider its occurrence in patients with type 1 diabetes.”

Dannecker C. et al.’s, “Low-Density Lipoprotein Cholesterol Is Associated with Insulin Secretion” from the May issue of JCEM was Mirmira’s final pick. “Despite their known benefits, the use of statins has been associated with the increased incidence of type 2 diabetes, particularly in vulnerable patients (such as the elderly, overweight/obese, and those with metabolic syndrome),” he says. “The exact mechanism(s) by which statins increase

the risk for type 2 diabetes has remained unclear. It has been proposed that low LDL cholesterol might be associated with reduced β -cell function and enhanced α -cell function. To clarify if and how LDL might be associated with insulin secretion, insulin clearance, and possibly glucagon secretion, Dannecker et al. interrogated a database from Southern Germany in which 3,039 non-diabetic individuals participated between 1993 and 2017. The findings from this study are suggestive of a positive effect of LDL cholesterol on insulin secretion, and that type 2 diabetes risk from statin use might result from the lowering of LDL cholesterol.”

Ursula B. Kaiser, MD, senior physician, Brigham and Women’s Hospital and professor of medicine, Harvard Medical School in Massachusetts, selected “Prediction of Adult Height by Machine Learning Technique,” by Smoish M., et al., from the July issue of JCEM. “This paper uses artificial intelligence and machine learning to predict the adult height of an individual,” Kaiser explains. “While growth charts are used to show if children are growing appropriately, based on an optimally growing healthy population, they are not typically used to predict final adult height. There are existing methods to predict adult height, but these are predictive at later, peri-pubertal ages and require X-rays to assess skeletal maturation. In this study, using artificial intelligence and machine learning, adult height of an individual could be predicted based on their childhood growth measurements up to age six years. The most important features for prediction were sex and height at age 3.4 – 6.0 years.”

“This paper was particularly interesting to me,” she continues, “because it is a harbinger of the increasing role and potential benefits that artificial intelligence/machine-learning will have in medicine/endocrinology. In addition, the paper has implications for both pediatric and adult endocrinologists. Moreover, the paper highlighted sex differences in growth and height, the mechanisms of which remain poorly understood. The ability to predict an individual’s adult height by the age of six years provides a theoretical window of opportunity to influence final adult height. While this may be a potential medical or health benefit in some cases, it also raises important ethical issues for consideration.” EN

“The study by Thomas, et al. is a post-hoc analysis comparing tirzepatide to dulaglutide (a GLP-1 receptor agonist), in which the authors focused on the effects of these drugs on biomarkers of insulin resistance and β -cell function. **This study emphasizes that this new class of dual receptor agonists represents a new approach in the treatment of type 2 diabetes, wherein targeting weight loss, insulin resistance, and β -cell function collaborates to achieve greater reductions in HbA1c than seen previously with compounds that have single receptor specificity.”**

— RAGHU G. MIRMIRA, MD, PhD, PROFESSOR OF MEDICINE; VICE CHAIR FOR RESEARCH, DIRECTOR, TRANSLATIONAL RESEARCH CENTER, UNIVERSITY OF CHICAGO, CHICAGO, ILLINOIS

An impassioned and vocal member of the Endocrine Society, Ricardo Correa, MD, EdD, talks to *Endocrine News* about his research, outreach to potential Latinx endocrine scientists, the importance of addressing health disparities, and how a trip to the endocrinologist when he was a teenager changed his entire life!



Ricardo Correa, MD,
EdD, FACP, FAPCR, FACMQ

For the Love of Hormones

A Life's Journey to Endocrinology

When he was only six years old, Ricardo Correa, MD, EdD, FACP, FAPCR, FACMQ, told his mother that not only did he want to become a doctor, but a doctor that somehow makes a contribution to the whole world.

Then at age 13, he saw an endocrinologist and as he told *Endocrine News* in 2016, that visit changed his entire life. "The hormonal world started to become something more important in my daily life and my love for medicine developed and intensified," he wrote. "By the age of 15, I started reading about cellular biology and I figured out that hormones, in any of their forms, are how our body communicates."

That eager little boy from Panama did grow up and become an endocrinologist; Correa is the program director of the endocrinology, diabetes and metabolism fellowship and director for diversity in graduate medical education at the University of Arizona College of Medicine. He also is staff clinician and researcher at Phoenix V.A.M.C. and serves as faculty for the Mayo School of Medicine, Mayo Clinic-Arizona, and Creighton University.

If you think simply entering adulthood dampened Correa's enthusiasm that so possessed him as a boy growing up in Central America, then you have obviously never met Ricardo Correa! After having

been a FLARE intern on the Endocrine Society's Trainee and Career Development Core Committee in 2016, Correa went on to serve on the Publications Core Committee for a three-year term, is currently part of the Adrenal and Pituitary Special Interest Group, and serves on the Clinical Endocrine Education Committee.

Correa talks to *Endocrine News* about his life's journey that has been inspired by his passion for endocrinology, his own research, and his ideas for bringing more Latinx scientists to the bench.

Endocrine News: How did the journey that brought you here today begin? Specifically, how did you choose endocrinology.

Ricardo Correa: Since I was a kid — six years old, according to my mom — I wanted to become a physician so I could change the lives of others. When I was 13, I visited a pediatric endocrinologist and fell in love with hormones. In the conversation with that doctor, I found that there was a connection between cells that I wanted to study, and that hormones are more than just simple signals but a conversation between two different types of cellular structures.

My decision was made. I continued my pathway with that goal in mind to become an endocrinologist. I entered medical school and from my first semester, I showed an interest in biochemistry and

how to better understand the molecular structure of hormones and how it can be modified. I was lucky that my mentor/advisor in medical school was also my biochemistry professor who was an endocrinologist. With him, I learned how to translate issues that occur in the lab to the clinical area. Finally, after finishing medical school, I continued my career with the goal of helping people with endocrine conditions. Because there were no endocrine fellowships in Panama, I came to the U.S. to train.

It was not an easy pathway due to multiple factors including the language barrier, but I left my home and came to America to follow my dream. I finished internal medicine at the University of Miami/Jackson Memorial Hospital and then entered the National Institutes of Health (NIH) to complete my endocrinology, diabetes, and metabolism fellowship. At the NIH (for me, the perfect place to train), I developed a special interest in neuroendocrine and adrenal problems and devoted my third year in that area. My mentors at the NIH guided me on how to approach complex patients and how to perform clinical research. As someone coming from a country where there was not a lot of clinical research, I was impressed by how research and endocrine medicine were related. For me, endocrinology is the perfect combination between science and medicine.

After finishing at the NIH, I went to Brown University where I started working on healthcare disparities in endocrinology, mainly with the Latinx community and diabetes. I was able to work in an underserved clinic and establish a peer support



Correa is pictured here at ENDO 2019 in New Orleans with (l to r): Kelvin Tran, MD; Gauri Behari, MD; Karyne Vinales, MD; Ghada Elshimy, MD; and John Matchette, PA, PhD. This team from the University of Arizona worked on research detailing adult-onset hypophosphatasia, among many other rare endocrine conditions.

“

The Latinx Community has contributed a lot to this country. From being on the frontlines in many jobs to being scientists and physicians who are making significant changes in the way we deliver healthcare to patients. I am proud of my heritage and proud of the things that we are developing. My hope is that more Latinos join us in our effort to grow our endocrine physician-scientist community.”

program to help the community. From there, I moved to the University of Arizona College of Medicine-Phoenix and the Phoenix VAMC to continue my career. I am now the program director for the fellowship. I love training the next generation of endocrinologists and sharing my passion for hormones with others. During this time and because of my passion fostering underrepresented minorities in medicine, I was named the director for diversity on graduate medical education.

I now have a job that combines my clinical passion with my research interest and my educational activities. On top of that, I can also change a little bit of my community by working on health equity in the Phoenix Valley.

EN: What is the main area of research of your lab?

RC: I have created a research team with one of my colleagues, Karyne L. Vinales, MD, that focuses on several areas of endocrinology. We have one research project that involved the adrenal gland, including new drugs for hyperaldosteronism, the consequences of long-term mild autonomous cortisolism, among others. We have also been working on transgender health and the cardiovascular outcomes of hormone-reaffirming

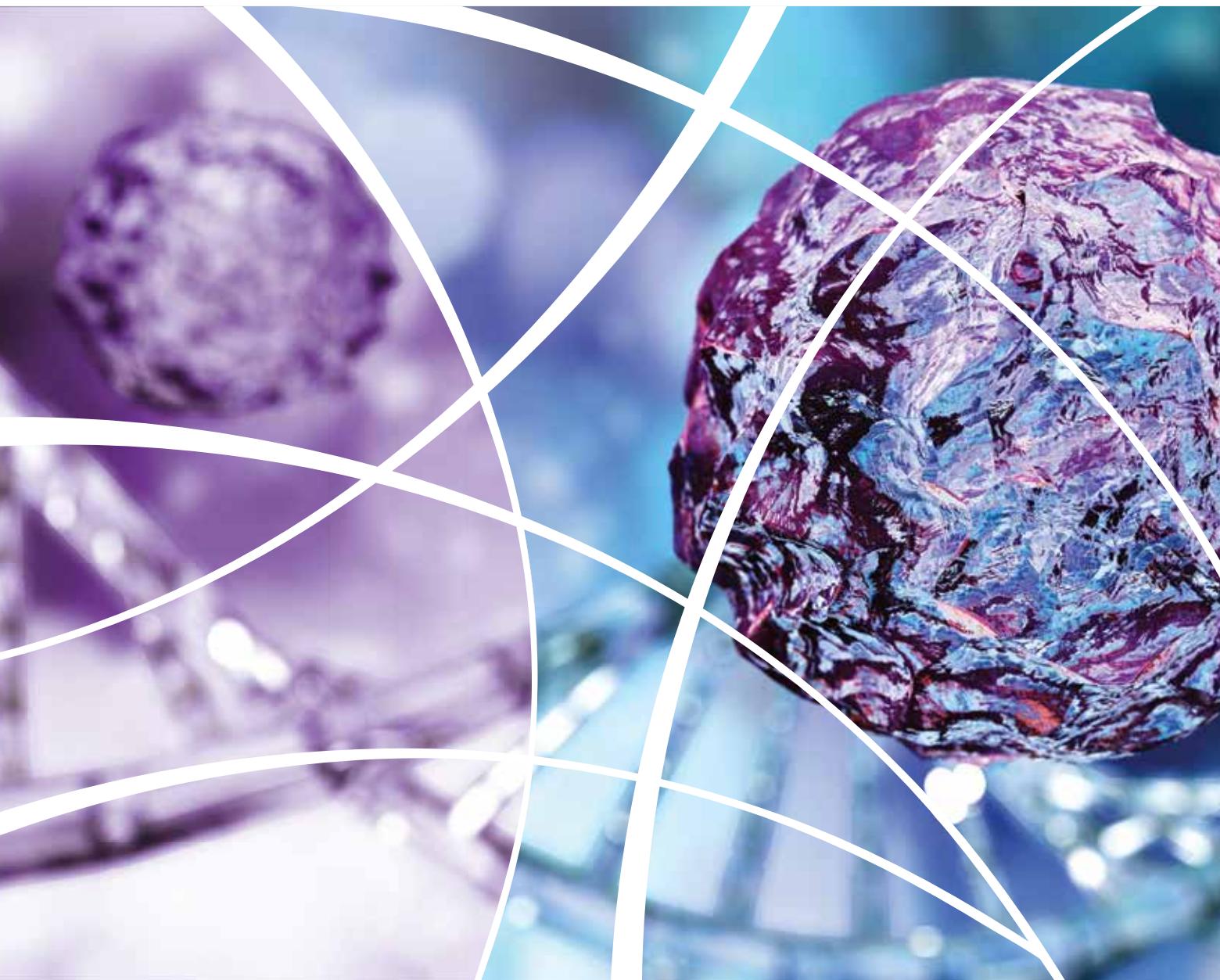
therapy (HRT). In addition to studying the relationship between HRT and cancer, our team also works closely on healthcare disparities of underserved populations, especially in Latinx communities (e.g., the implementation of a peer support program to decrease diabetes in the Latinx population). This focus reflects our interest of creating a structure with students, residents, and fellows that can support our endeavors.

EN: What can institutions/organizations do to foster interest in scientific careers among Hispanics?

RC: Institutions should focus on mentoring more Hispanics in science. If there are more Latinx scientists, then new people will come. We need to see scientists who look like us and we will enhance diversity. Currently, we see very few Latinx endocrine scientists. I understand that sometimes other issues like immigration status can affect the pursuit of a physician-scientist's career, but we need to figure out how everyone can pursue their dreams and apply for grants regardless of whether they're on visa or not. I would like for institutions to care more about producing strong research regarding health disparities. This, alone, would bring in more Latinx patients as subjects in clinical trials. At this time, there is reluctance due to prior episodes in medicine and the only way of changing it is if more principal investigators are from the same culture and can explain the processes and the procedures to the patient in their native language.

Finally, I would like to say that the Latinx Community has contributed a lot to this country. From being on the frontlines in many jobs to being scientists and physicians who are making significant changes in the way we deliver healthcare to patients. I am proud of my heritage and proud of the things that we are developing. My hope is that more Latinos join us in our effort to grow our endocrine physician-scientist community.

Correa wrote in *Endocrine News* in 2016 that he chose endocrinology because he wanted to excel at research while also being a clinician and educator, adding that “there is no other area of medicine that can combine these three skills in such a perfect way.” EN



ENDO2022

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ENDOCRINE.ORG/ABSTRACTS



2021:

a progress report



Endocrine research remains at the forefront of medical breakthroughs, which has led to cutting-edge treatment options, therapies, and products.

From remarkable new treatments for acromegaly, thyroid eye disease, hypoglycemia, and diabetes to new devices aimed at glucose monitoring in adults and children, a mail-in semen analysis kit, and much more, *Endocrine News* takes a closer look at some of these new innovations announced throughout 2021.

Another year down. Another year where pretty much everything was still impacted by the COVID-19 pandemic, but another year where endocrine researchers and clinicians continued to remain at the forefront of medical research, which has resulted in a variety of breakthroughs that not only address new treatment options, therapies, and products, but health disparities and equity as well.

WRITTEN AND COMPILED BY
DEREK BAGLEY

A New Treatment for Hypoparathyroidism

In January, the U.S. Food and Drug Administration (FDA) granted Orphan Drug Designation (ODD) to AZP-3601, Amolyt Pharma's clinical candidate for the treatment of hypoparathyroidism.

AZP-3601 is a therapeutic peptide designed to target a specific configuration of the parathyroid hormone (PTH) receptor to safely produce sustained levels of calcium in the blood and thereby manage the symptoms of hypoparathyroidism. The selective action of AZP-3601 through this distinct configuration of the PTH receptor is also intended to limit urine calcium excretion by stimulating calcium reabsorption by the kidney, consequently preventing chronic kidney disease. In addition, the receptor profile and short half-life of AZP-3601 are expected to preserve bone integrity, an important benefit since the majority of patients with hypoparathyroidism are middle-aged women often at increased risk of osteoporosis.

"We believe the FDA's granting of Orphan Drug Designation to AZP-3601 reflects the agency's recognition that new and more effective treatment options are needed for this serious endocrine disorder," says Endocrine Society member Thierry Abribat, PhD, chief executive officer of Amolyt Pharma. "We are pleased to have

recently dosed the first subject in our Phase 1 clinical trial, and we are committed to executing an efficient development program to diligently bring this promising therapeutic to patients."

Positive Data for Acromegaly Treatment

During ENDO 2021, Chiasma announced positive clinical data from its MPOWERED™ Phase 3 trial of MYCAPSSA.

The data showed that MYCAPSSA improved clinical symptoms and other patient-reported outcomes compared to long-acting injectable somatostatin receptor ligands (iSRLs) in patients with acromegaly. In addition, MYCAPSSA met the pre-specified, non-inferiority margin compared to long-acting iSRLs in maintenance of biochemical response.

"The new encouraging data from all five late-breaking poster presentations further expand our understanding of oral octreotide capsules' potential positive impact for patients with acromegaly who would otherwise need monthly, frequently burdensome SRLs injections," says Society member Maria Fleseriu, MD, lead investigator of the MPOWERED study, professor of medicine and neurological surgery, director of the Pituitary Center at Oregon Health and Science University in Portland, Oregon, and immediate past president of the Pituitary Society. "As a practicing endocrinologist, I believe that these data provide valuable insights to physicians on the potential benefit of a twice daily oral drug versus long-acting injections for most patients."

New Severe Hypoglycemia Treatment for People with Diabetes

Zealand Pharma in March announced that the FDA approved Zeglogogue® (dasiglucagon) injection for the treatment of severe hypoglycemia in pediatric and adult patients with diabetes aged 6 years and older.

The FDA approval was based on efficacy results from three randomized, double-blind, placebo-controlled multicenter Phase 3 studies of Zeglogogue in children aged 6 to 17 years and in adults with type 1 diabetes. The primary efficacy endpoint for all three studies was time to plasma glucose recovery (treatment success), defined as an increase in blood glucose of



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Glycemic control has been much harder to achieve in children due to unpredictable factors common in this age group, including physical growth and development, hormonal changes, and active lifestyles. **In fact, young adults around the age of 15 have the highest reported A1C in the T1D Exchange Registry, which includes data on over 31,000 individuals with type 1 diabetes and demonstrates the unique challenges in younger populations.”**

— ROBERT VIGERSKY, MD, CHIEF MEDICAL OFFICER, MEDTRONIC; PAST-PRESIDENT, ENDOCRINE SOCIETY



glucose recovery of only 10 minutes following Zeg掬ogue administration compared to 30 to 45 minutes for placebo. In the main Phase 3 adult trial, 99% of patients recovered within 15 minutes.

In these studies, the most common adverse events reported ($\geq 2\%$) were nausea, vomiting, headache, diarrhea, and injection site pain in adults; and nausea, vomiting, headache, and injection site pain in pediatrics.

Racial, Gender, and Socioeconomic Factors Could Impede Proper Diabetes Care

Researchers at the Perelman School of Medicine at the University of Pennsylvania found significant disparities in the use of sodium-glucose cotransporter 2 (SGLT2) inhibitors, a class of drugs proven to treat type 2 diabetes, with usage remaining low with Black, Asian, and lower-income groups despite an increase in overall usage for patients with type 2 diabetes. The study is published in *JAMA Network Open*.

“Study after study, including large, randomized trials, have demonstrated a cardio-protective and kidney-protective effect of this class of medications,” says the study’s lead author, Lauren Eberly, MD, MPH, a cardiology fellow at the University of Pennsylvania. “We know there are already higher rates of heart failure and kidney disease among Black patients. What is concerning is that this is a therapy we know prevents death from those conditions and prevents progression from those conditions, and yet, we found that Black patients are less likely to get this therapy, as well as female patients and those with lower socioeconomic status.”

cgm evolution

Time in Range Improves in Patients Using the Medtronic MiniMed™ 780G

Medtronic in June announced real-world clinical outcomes for 4,120 individuals on its MiniMed™ 780G system, a small subset of those on the system across nine countries in Europe. Data showed an average overall time in range of 76.2% and



an overnight Time in Range of 83%. From an experience perspective, users remained in Advanced Hybrid Closed Loop (AHCL) mode, also referred to as the SmartGuard™ algorithm, for an average of 94% of the time, and an overall reduction in interactions required with the system demonstrated a more seamless experience than previous insulin pump systems.

"It is extremely encouraging to see Medtronic advancing both clinical outcomes as well as the user experience through their latest MiniMed 780G system. It is clear that learning from the launch of the world's first hybrid closed loop informed the design of this next-generation system," says Society member Chantal Mathieu, MD, PhD, an endocrinologist at University Hospitals Leuven-KULeuven, Belgium. "We know that no two individuals with type 1 diabetes are the same, and that life gets in the way of managing diabetes perfectly. I am confident in this system's ability to do what a person with diabetes may not be able to do on their own by helping them minimize highs and lows, and ultimately live their lives less burdened by their diabetes."

The advanced SmartGuard algorithm in the MiniMed 780G system automates and personalizes the delivery of basal insulin by adjusting every five minutes, 24 hours a day. The latest system also includes an advanced algorithm that automatically corrects highs every five minutes through autocorrection dosing, in addition to protecting against lows. Autocorrection dosing is designed to correct highs that may result from not logging a meal, logging a meal late, or underestimating the carbohydrate content of the meal.

The MiniMed 780G system is currently approved for the treatment of type 1 diabetes in people aged 7 to 80 years. The system enables the personalization of glucose goals with an adjustable target setting as low as 100 mg/dL — lower than any other insulin pump system. The MiniMed 780G system is currently being reviewed by the Food and Drug Administration (FDA) for approval in the U.S.

Can CGM Use Impact Diverse Populations?

Dexcom presented two new studies during the 14th International Conference on Advanced Technologies & Treatments for Diabetes, focusing on clinical outcomes of CGM use in broader and more diverse populations and new data from Dexcom's G7 CGM.

The MOBILE study, published in the *Journal of the American Medical Association*, found that people with type 2 diabetes who use basal insulin benefited from the use of CGM. With the publication of the MOBILE data, Dexcom has demonstrated significant outcomes driven by its CGM technology in randomized controlled trials across the full spectrum of insulin use in people with diabetes.

Key clinical benefits of Dexcom CGM use in this population included:

- ▶ Increased time in range
- ▶ Significant A1c reduction
- ▶ More patients reaching A1c goals
- ▶ A profound decrease in hyperglycemia

The randomized clinical trial was led by HealthPartners Institute's International Diabetes Center and coordinated by The Jaeb Center for Health Research in Tampa, Fla.

"The clinical benefits of Dexcom CGM were seen across all patient demographics regardless of age, education, numeracy, or socioeconomic status," says Society member David Price, MD, vice president of medical affairs at Dexcom. "The MOBILE study

design also affirms our ability to meet the needs of the diverse communities we serve.”

MOBILE Study Findings

- ▶ The group of patients using Dexcom CGM spent an average of 3.8 hours more each day within the optimal range of blood glucose levels (70-180 mg/dL), 3.6 hours less each day in the very high glucose range (>250 mg/dL), and with a reduction in CGM measured hypoglycemia in the CGM group compared to the finger-stick glucose monitoring group
- ▶ 63% of patients using CGM to guide therapy adjustments had an HbA1c less than 8% compared to only 39% of patients using finger-stick glucose reading
- ▶ The group using CGM to guide therapy and lifestyle adjustments also had significantly lower HbA1c levels (9.1 to 8.0%) than the group of patients using traditional finger-stick glucose monitoring (9.0 to 8.4%); this was an adjusted difference in mean change in HbA1c of -0.4%, 95% CI -0.8% to -0.1%, P=0.02
- ▶ Adherence and satisfaction were also high among the CGM group

Dexcom also presented new data on its next generation interoperable CGM, Dexcom G7, drawn from clinical trials supporting the company's efforts toward a CE Mark submission and U.S. pre-pivotal work. The data represents the latest G7 technology, demonstrating the consistent performance of the sensor across the spectrum of glucose readings and duration of wear.

In this study, researchers examined data from October 2015 to June 2019 from more than 900,000 diverse, commercially insured patients with type 2 diabetes and found that the cumulative percentage of patients treated with SGLT2 inhibitors increased from 3.8% to 11.9%. However, the analyses showed that Black, Asian, and female patients had lower rates of SGLT2 inhibitor use, as well as patients whose median household income was less than \$50,000. The study also found that usage rates remained low for patients with heart failure, cardiovascular disease, and chronic kidney disease.

The study found that having a visit with an endocrinologist in the last 12 months was one of the strongest factors associated with SGLT2 inhibitor use, acknowledging that the demonstrated clinical benefit may not be common knowledge yet for many non-specialist providers treating patients with diabetes. Additionally, marginalized patient groups likely have barriers to accessing specialty care. Eberly and her fellow researchers encourage the development of strategies to increase the comfort of all providers, especially primary care and cardiology providers, with prescribing this class of drugs.

“If left unaddressed, these inequities in utilization will continue to widen well-documented disparities in cardiovascular and kidney outcomes in the U.S.,” Eberly says.



“ The pandemic taught us the importance of connected devices in managing chronic conditions remotely, and we continue to see the benefit from the latest advances in digital health.

Continuous glucose monitoring is one of the most significant health tech innovations in the last decade, and I see the life-changing benefits firsthand from my patients every day.”

— KURT MIDYETT, MD, PEDIATRIC ENDOCRINOLOGIST, MEDICAL DIRECTOR, MIDWEST PEDIATRIC SPECIALISTS, OVERLAND PARK, KAN.

TEPEZZA Improves TED Outcomes

Horizon Therapeutics in April published pooled data from the TEPEZZA® (teprotumumab-trbw) Phase 2 and Phase 3 clinical trials in *The Lancet Diabetes & Endocrinology*. The data further reinforce that TEPEZZA significantly improves proptosis and diplopia for patients with thyroid eye disease (TED) in different subgroups, with most maintaining a long-term response. TEPEZZA is a fully human monoclonal antibody (mAb) and a targeted inhibitor of the insulin-like growth factor-1 receptor (IGF-1R).

“This integrated analysis comprises one of the largest controlled study populations reported to date in people living with thyroid eye disease, which allowed us to evaluate a variety of patient subgroups, including those whose symptoms were considered more severe,” says Society member George Kahaly, MD, PhD, professor of medicine and endocrinology and metabolism at Johannes Gutenberg University Medical Center in Mainz, Germany, and primary author of the paper. “Of most importance, the data clearly show that TEPEZZA mitigates varying levels of disease severity, including proptosis and diplopia, which are the most progressive and difficult findings to treat, and that improvements continue for the long term.”

In this report, treatment study outcomes and follow-up off-treatment data were integrated from two 24-week multicenter, double-masked, placebo-controlled clinical trials where patients were randomized to receive TEPEZZA (n=84) or placebo (n=87) once every three weeks for a total of eight infusions. The final treatment study visit was at week 24, which was three weeks after the final infusion. Responses were also evaluated at seven weeks and 51 weeks after the final dose. Responses were analyzed for proptosis and diplopia, as well as a post-hoc analysis of a combined outcome measure: the “ophthalmic composite outcome.”

The composite outcome is calculated as the percentage of patients with clinical improvement in one eye in at least two of the following: 1) proptosis, 2) diplopia, 3) eyelid swelling, 4) lid aperture, 5) globe motility, and 6) Clinical Activity Score, without deterioration of at least two of these outcomes in either eye.

New Study Findings

- ▶ There was no evidence for acute disease rebound (increase in percentage of patients no longer meeting proptosis, diplopia or ophthalmic composite outcome) seven weeks after the last dose of TEPEZZA.
- ▶ Proptosis (87%; 62/71), diplopia (66%; 38/58), and ophthalmic composite outcome (92%; 66/72) responses were observed seven weeks after the last dose of TEPEZZA.
- ▶ A post-hoc analysis of the composite ophthalmic outcome

CAN PROBIOTIC INTERVENTIONS IMPROVE TYPE 2 DIABETES MANAGEMENT?

A new study from the American Diabetes Association's (ADA) 81st (Virtual) Scientific Sessions appears to show Pendulum Glucose Control increases circulating butyrate and ursodeoxycholic acid (UDCA), a secondary bile acid in people with type 2 diabetes, and supports the mechanism for improvement in glucose control.



"This study, part of an ongoing series, is adding to the body of knowledge on the microbiome and its role in metabolic disease including type 2 diabetes," says Society member Orville Kolterman, MD, chief medical officer at Pendulum Therapeutics and principal investigator of the study.

"This data builds upon the research Pendulum Therapeutics presented at ADA's 79th Scientific Sessions two years ago. Our initial presentation showcased the efficacy of Pendulum's proprietary microbiome symbiotic formulation (Pendulum Glucose Control) and its ability to improve glucose control in patients with type 2 diabetes. This newest data will further inform the development of a portfolio of products that target the microbiome as a pathway to augment the dietary management of impaired glucose metabolism and other metabolic diseases."

indicated that 81% (68/84) of TEPEZZA patients versus 44% (38/87) of placebo patients were responders at Week 24.

- ▶ Proptosis (67%; 38/57), diplopia (69%; 33/48), and composite outcome response (83%; 48/58) were observed 51 weeks after the last dose of TEPEZZA for those who had long-term off-treatment data available.

Positive Results for Novel Therapy that Addresses Type 1 Diabetes Causes

Precigen ActoBio in June announced positive topline results for the ongoing Phase 1b/2a clinical study investigating AG019 ActoBiotics™ for the treatment of recent-onset type 1 diabetes. Results from the primary analysis were presented at the Federation of Clinical Immunology Societies (FOCIS) 2021 Virtual Annual Meeting by Society member Kevan Herold, MD, professor of immunobiology and of medicine at Yale University.

AG019 is formulated as an oral capsule of engineered *Lactococcus lactis* specifically modified to deliver autoantigen human

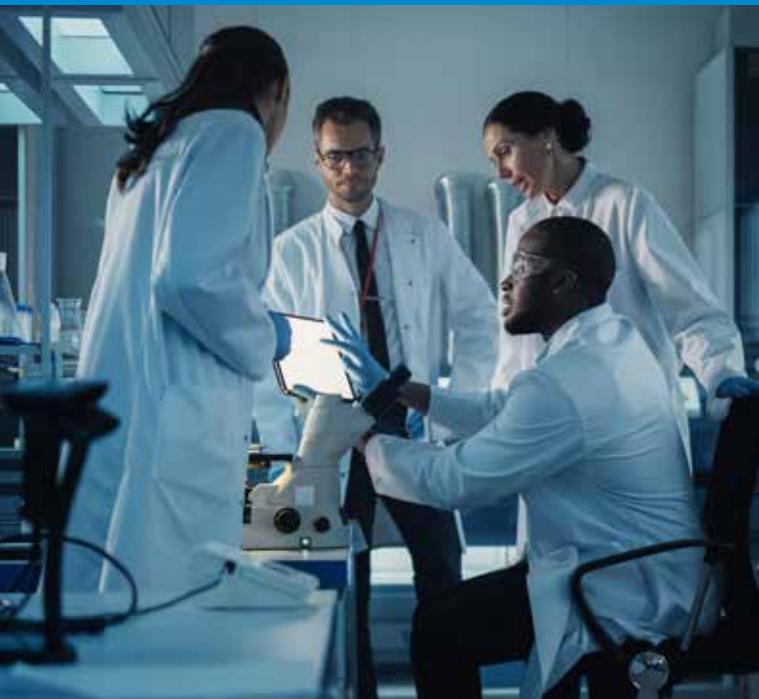


2021: a progress report

proinsulin (hPINS) and the tolerance-enhancing cytokine human interleukin-10 (hIL-10) to the mucosal lining of the gastrointestinal tissues. Administration of AG019 is designed to induce specific regulatory T cells (Tregs) that could reduce or eliminate the destruction of insulin-producing cells, potentially stabilizing or improving insulin production.

The Phase 1b open-label portion of the study evaluates the safety and tolerability of AG019 as a monotherapy in adult (age 18-42) and adolescent (age 12-17) patients. The primary endpoint for assessing safety and tolerability is treatment-emerging adverse events (TEAEs) reported up to six months post treatment initiation. The Phase 2a double-blind portion of the study investigates the safety and tolerability of AG019, in combination with an investigational anti-CD3 monoclonal antibody, teplizumab (PRV-031).

The primary endpoint of both the Phase 1b AG019 monotherapy and the Phase 2a AG019 combination therapy was met. AG019 was well tolerated and safe when administered to adults and adolescents either as monotherapy or in combination with teplizumab. No serious adverse events (SAEs) were reported and no AG019 treatment discontinuation occurred due to TEAEs. No severe TEAEs were reported in patients treated with AG019 monotherapy. The TEAEs reported for both the mono- and combination therapy were mostly mild and sometimes

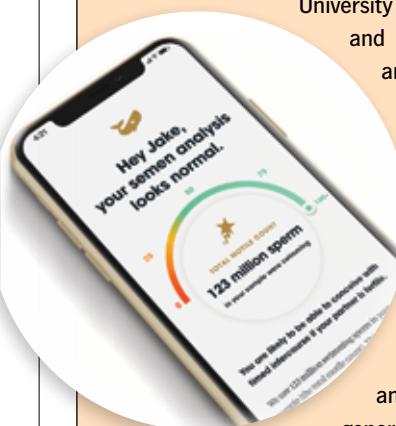


MALE FERTILITY TEST KIT VIA MAIL

The journal *Fertility and Sterility* published a paper on the development and validation of the Fellow kit, for mail-in semen analysis.

The study was led by James Smith, director of Male Reproductive Health in the Urology Department at University of California San Francisco, a team of clinicians from the University of Southern California, Yale, and Hackensack Medical Center, and in partnership with the male reproductive sciences company, Fellow Health.

After comparing hundreds of semen samples in a clinical trial, researchers found the mail-in Fellow test provided the same accuracy as semen samples analyzed within 1 hour of generation.



UCSF was the first health system in the U.S. to offer the Fellow kit. "This mail-in system offers men easy access to high quality semen analysis from the comfort of their homes," Smith says, adding "the at-home option is valuable as people forgo doctor office visits to limit their exposure to COVID-19." EN

moderate severity. The TEAEs reported in the combination cohorts are in line with the safety profile reported for teplizumab and no unexpected TEAEs were identified. In addition, pharmacokinetic analyses demonstrated localized intestinal delivery of AG019 and no systemic exposure of hPINS, hIL-10 and of AG019 bacteria in the blood of the patients, confirming the safety profile of AG019.

"The primary analysis shows that AG019 can be administered safely, either as a monotherapy or in combination with teplizumab and provides an opportunity for chronic treatment of type 1 diabetes," Herold says. "The stabilization of C-peptide in the monotherapy with a single eight-week treatment cycle of AG019 is encouraging in addition to the synergistic effect observed between AG019 and teplizumab. There may be an opportunity for sustained treatment effect following prolonged AG019 treatment."

Spinal Cord Stimulation Therapy to Treat Chronic Pain Associated with PDN Approved

In July, Nevro, a spinal cord stimulation company announced receipt of FDA approval of its Senza® System for the treatment of chronic pain associated with painful diabetic neuropathy (PDN). This approval is specific to Nevro's unique 10 kHz stimulation.

Study participants demonstrated significantly improved and sustained outcomes with 10 kHz Spinal Cord Stimulation (SCS), including substantial, sustained pain relief and improved health-related quality of life. The six-month results for the SENZA-PDN randomized controlled trial (RCT) were published in *JAMA Neurology* in April 2021, and the 12-month follow-up results and six-month crossover patient data were presented at the American Diabetes Association 81st Scientific Sessions in June.

MEDICAL DEVICE COMPANIES PARTNER TO MONITOR CHRONIC DISEASES

Withings and One Drop teamed up to connect One Drop's predictive health platform with Withings' smart medical devices for blood pressure and weight management. Together, the companies want to bring connected health solutions to employers worldwide to make more informed decisions and live healthier lives.

Through this partnership, members enrolled in the One Drop employer program can qualify to receive a Withings Body smart scale or a Withings BPM Connect smart blood pressure monitor in addition to the One Drop glucose meter. Withings devices integrate directly with the One Drop app, allowing members to seamlessly measure and monitor weight and blood pressure alongside glucose, A1C, food, medications, and physical activity. Members also receive health forecasts powered by nearly 28 billion health data points, one-on-one coaching from certified health professionals, and evidence-based behavioral interventions for chronic disease prevention and management. EN

"Diabetic neuropathy is one of the most prevalent and debilitating chronic complication of diabetes, and for years, PDN patients have struggled with a lack of effective treatment options when conventional medications fail or are not tolerated," says Frances Broyles, MD, medical director of diabetes/endocrinology and nutrition at Swedish Health Services in Seattle, Wash. "The ability to now offer Nevro's proven 10 kHz Therapy, which may enable discontinuation of long-term drug therapy and eliminate unwanted drug side effects, is a welcome addition as a treatment option for my PDN patients dealing with this challenging condition. My personal practice experience with the Nevro 10 kHz Therapy was nothing short of life changing for the patient."

FDA Approves First Interchangeable Biosimilar Insulin

The FDA in July approved the first interchangeable biosimilar insulin product, indicated to improve glycemic control in adults and pediatric patients with type 1 diabetes and in adults with type 2 diabetes. The FDA granted approval for insulin glargine-yfgn to Mylan Pharmaceuticals Inc., who is marketing the product as Semglee.

Semglee (insulin glargine-yfgn) is both biosimilar to and interchangeable with its reference product Lantus (insulin glargine), a long-acting insulin analog. Semglee is the first biosimilar product to get the "interchangeable" designation in the U.S. for the treatment of diabetes. Approval of these insulin products can provide patients with additional safe, high-quality, and potentially cost-effective options for treating diabetes.

An interchangeable biosimilar product may be substituted for the reference product without the intervention of the prescriber. The substitution may occur at the pharmacy, a practice commonly called "pharmacy-level substitution" — much like how generic drugs are substituted for brand-name drugs, subject to state pharmacy laws, which vary by state.

"Biosimilar and interchangeable biosimilar insulin products have the potential to lower costs for patients. Hopefully, this approval will help drive prices down for insulin in the long term. Access to affordable care, and particularly affordable insulin, is a priority in diabetes care," says Society member Rita Kalyani, MD, associate

thyroid treatment progress

Potential DTC Therapy Under Review by the FDA

In August, Exelixis, Inc., announced that the FDA accepted the company's supplemental New Drug Application (sNDA) for CABOMETYX® (cabozantinib) as a treatment for patients 12 years and older with differentiated thyroid cancer (DTC) who have progressed following prior therapy and are radioactive iodine-refractory (if radioactive iodine is appropriate). The FDA granted Priority Review designation and assigned a Prescription Drug User Fee Act (PDUFA) target action date of December 4, 2021.



The sNDA is based on the results of COSMIC-311, a Phase 3 pivotal trial evaluating CABOMETYX versus placebo in patients with radioactive iodine-refractory DTC who progressed after up to two prior vascular endothelial growth factor receptor (VEGFR)-targeted therapies. At a planned interim analysis, CABOMETYX met one of the trial's primary endpoints, demonstrating a significant improvement in progression-free survival versus placebo.

In February 2021, the FDA granted Breakthrough Therapy Designation to CABOMETYX as a potential treatment for patients with DTC that has progressed following prior therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate) based on these results. Detailed study findings were presented at the 2021 American Society of Clinical Oncology Annual Meeting and were published by *The Lancet Oncology* in July.

Dosage Flexibility of Liquid Hypothyroidism Treatment Introduced for Patients and Clinicians

Americans diagnosed with hypothyroidism and their clinical providers now have access to greater dosage flexibility within levothyroxine therapy, with three new dosage strengths of levothyroxine sodium oral solution now available to treat hypothyroidism. IBSA Pharma markets the drug as Tirosint®-SOL.

The unique new dosing options — 37.5, 44, and 62.5 micrograms — are a first in the U.S. market and offer clinicians precision and flexibility when treating patients. The three new doses add to Tirosint-SOL's existing 12 options and create a new industry standard of 15 strengths of levothyroxine therapy, the widest range of any therapy for hypothyroidism that is approved by the U.S. Food and Drug Administration (FDA).

Recently published research has demonstrated that dissatisfaction is common among adults treated for hypothyroidism. While the causes of patient dissatisfaction are complex, the common practice of frequent dose titration of thyroid hormone treatment (more than two dose changes per year) has been associated with significantly lower levels of patient satisfaction with hypothyroidism therapy.



Tirosint-SOL's extensive dosing options provide clinicians with more choices, enabling them to adapt levothyroxine therapy to individual needs and better treat the full spectrum of hypothyroid patients. Increased dosage flexibility may also

eliminate or reduce the need to change patients' doses.

"The addition of 37.5, 44, and 62.5 microgram dosages represents a much-needed advance in levothyroxine therapy, which is the standard of care for treating hypothyroidism," says Charles Carter, PharmD, interim chair and associate professor of clinical research, Campbell University College of Pharmacy and Health Sciences. "Up to this time, clinicians have often instructed parents, caregivers, and patients to split levothyroxine tablets to create these doses, which can result in significant dosing errors and inconvenience. Levothyroxine is a narrow therapeutic index drug with potentially deleterious clinical outcomes if administered in sub- or supratherapeutic doses. The splitting of tablets by patients can result in inconsistent levels of levothyroxine therapy, which should be a concern to clinicians and the patients they care for."

Tirosint-SOL is indicated to treat hypothyroid patients regardless of age. Patients can administer it by pouring the contents of the monodose ampule directly into the mouth, using a spoon or mixing it in water. A data matrix was recently added to the monodose ampule to facilitate its use in hospitals, where more complex cases of hypothyroidism are often initially treated.

NEW TEST MORE ACCURATELY PREDICTS COVID-19 MORTALITY IN PATIENTS WITH AND WITHOUT DIABETES

In November, Precision Diabetes, Inc., presented data demonstrating that the 1,5-anhydroglucitol blood test (GlycoMark®) is more accurate than commonly used diabetes tests in predicting mortality in hospitalized COVID-19 patients with and without diabetes. The study, "1,5-anhydroglucitol is an Independent Predictor of Mortality in Patients with COVID-19," was presented at the American Heart Association 2021 Scientific Sessions conference.

The study was conducted at Sinai Hospital in Baltimore, Md., and showed that the GlycoMark® test had 76% mortality accuracy (AUC) compared to the accuracy for HbA1c and fasting glucose of 51% and 60%, respectively. The accuracy of GlycoMark was higher in patients without diabetes (79%) than in patients with diabetes (73%). An algorithm, which included age, BMI, and GlycoMark had an accuracy for prediction of mortality of 89%.

"GlycoMark may have utility in triaging



COVID-19 patients in the hospital setting at higher risk of severity and mortality," says Paul Gurbel, MD, a cardiologist at the LifeBridge Health Cardiovascular Institute and lead investigator of the trial. "This may be especially important in COVID-19 non-diabetic patients who may develop new-onset diabetes, which brings higher risks of severe disease and death." EN



professor at Johns Hopkins School of Medicine in Baltimore. “From a patient perspective, this can help increase access to less expensive alternatives from the pharmacy. However, there will be some individuals that still prefer the brand insulin and there will need to be more education going forward that these two products are, in fact, interchangeable.”

The approval of this new biosimilar is in line with the Endocrine Society’s Position Statement from January, “Increasing Insulin Affordability.” Before Semglee, there were only two biosimilars available, made by Eli Lilly (Basaglar) and Sanofi (Admelog), two of the three insulin manufacturers. “For biosimilars to have an impact on the price of insulin, availability must extend beyond current manufacturers and new companies must be willing to undertake a costly development and strict review process,” the Position Statement authors write.

FDA Approves Abbott's Freestyle Libre 2 iOS App

Abbott announced in August that the FDA cleared the FreeStyle Libre 2 iOS application for use with compatible iPhone,

providing a comprehensive digital offering for its FreeStyle Libre 2 integrated continuous glucose monitoring (iCGM) system.

Approved for adults and children (4 years and older) with diabetes, the new FreeStyle Libre 2 app creates a seamless experience for users and healthcare professionals.



The app enables users to get glucose readings directly on their iPhones without the use of a reader. A key benefit of the app is the ability for caregivers to remotely monitor their loved one's glucose readings and get real-time alarms via the LibreLinkUp app.

According to a Gallup poll, one in five Americans currently tracks health statistics using a mobile app. The FreeStyle Libre 2 app will offer personalized, up-to-the-minute glucose data for people with diabetes who are using FreeStyle Libre 2 glucose sensors. By scanning the sensor with the FreeStyle Libre 2 app, users will get their current glucose reading and trend arrow which can help them determine how food, exercise, and other lifestyle factors impact diabetes management.

“The pandemic taught us the importance of connected devices in managing chronic conditions remotely, and we continue to see the benefit from the latest advances in digital health,” says Society member Kurt Midyett, MD, pediatric endocrinologist and medical director at Midwest Pediatric Specialists, Overland Park, Kan. “Continuous glucose monitoring is one of the most significant health tech innovations in the last decade, and I see the life-changing benefits firsthand from my patients every day. As a doctor, it’s invaluable to receive my patients’ glucose data remotely via systems like LibreView – enabling more meaningful conversations with my patients, and ultimately, improving treatment decisions and their long-term health.”

Children on Medtronic's MiniMed 780G Achieve Time in Range

In October, Medtronic announced one-year, real-world clinical data on 3,211 pediatric and adolescent patients with type 1 diabetes 15 years old and younger using the MiniMed™ 780G system with the Guardian™ Sensor 3. Data on this subset of patients on the system in Europe showed an average time in range of 74% — surpassing clinical consensus guidelines and closely mirroring time in range for adults at 77%. Overnight time in range of 82% also mirrored that of adults (82%).

From an experience perspective, younger users remained in Advanced Hybrid Closed Loop (AHCL) mode, also referred to as the SmartGuard™ algorithm, for an average of 93% of the time, similar to the 92% observed in users older than 15 years. When the pediatric group set a blood glucose target of 110mg/dL and an Active Insulin Time (AIT) of two hours, they achieved an average Time in Range of 77% and a Glucose Management Indicator (GMI) of 6.7%. With these settings, they only spent 2.7% of their time <70 mg/dL.

The real-world performance analysis aggregates information from children 15 years old and younger whose caregivers agreed to allow Medtronic to use anonymized data that was automatically uploaded their data to CareLink™ Personal from August 27, 2020 to July 22, 2021. A large majority of pediatric users included in the analysis are achieving glycemic goals recommended by major diabetes professional organizations, including:

- ▶ 75.3% of pediatric users had a glucose management indicator (GMI) less than 7%, which mirrors the average A1C level that would be expected based on mean glucose.
- ▶ 69.6% of pediatric users had a time in range above 70%.

DISCLAIMER: INCLUSION OR DISCUSSION OF ANY PRODUCT, PHARMACEUTICAL, OR SERVICE DOES NOT SUGGEST AN ENDORSEMENT BY ENDOCRINE NEWS OR THE ENDOCRINE SOCIETY.

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Biosimilar and interchangeable biosimilar insulin products have the potential to lower costs for patients. Hopefully, this approval will help drive prices down for insulin in the long term. **Access to affordable care, and particularly affordable insulin, is a priority in diabetes care.”**

— RITA KALYANI, MD, ASSOCIATE PROFESSOR, JOHNS HOPKINS SCHOOL OF MEDICINE, BALTIMORE, MARYLAND

- ▶ 67.5% of pediatric users achieved both, a GMI less than 7% and a time in range above 70%.

A sub-analysis of patients 15 years old and younger with at least 10 days of CGM data both pre- and post-AHCL initiation (n=661) showed substantial improvements across both time in range and GMI — even among those who were relatively well controlled at baseline. This group saw a 12% increase in time in range, to 74% on average — equivalent to an additional 2.8 hours/day in the target range. From a user experience perspective, results also showed patients were able to stay in AHCL mode 93% of the time once it was initiated.

“These results are extremely encouraging. Glycemic control has been much harder to achieve in children due to unpredictable factors common in this age group, including physical growth and development, hormonal changes, and active lifestyles. In fact, young adults around the age of 15 have the highest reported A1C in the T1D Exchange Registry, which includes data on over 31,000 individuals with type 1 diabetes and demonstrates the unique challenges in younger populations. Because the algorithm in the MiniMed 780G system adjusts basal and correction insulin doses in near real-time every 5 minutes thereby providing near real-time course correction, it helps make up for underestimated carbohydrate counting and occasional late or missed meal doses,” says Robert Vigersky, MD, chief medical officer of the Diabetes business at Medtronic and past president of the Endocrine Society. “The Medtronic AHCL algorithm offers advanced protection and permits unprecedented personalization in insulin delivery by offering a wide range of Active Insulin Time

settings and three different glucose targets. These improvements reinforce that the MiniMed 780G system is a better alternative than previous therapy these patients were on, even for those who were relatively well-controlled.”

As always, this piece could go on and on and fill not just the pages of this issue, but probably several more. Advancements in endocrinology continue to be made, even as this issue goes to press. Can’t wait to see what’s next. EN



— BAGLEY IS THE SENIOR EDITOR OF ENDOCRINE NEWS. IN THE NOVEMBER ISSUE, HE WROTE ABOUT THE COMPLEXITIES SURROUNDING INSULIN PRICING.



David A. Katz, PhD

Q&A: Is It Time for a New Approach to Treating Cushing's Syndrome?

David A. Katz, PhD, CEO of Sparrow Pharmaceuticals, launched the company to specifically target the therapies bigger companies were ignoring. He talks to *Endocrine News* about these new therapies and how they could possibly change the way people with Cushing's syndrome, autonomous cortisol syndrome, and other disorders are treated.

BY ERIC SEABORG

For many endocrine researchers, their career path typically takes them to a lab at an academic institution or a research facility. However, there is another path for those scientists who possess an entrepreneurial spirit – industry.

To encourage its members who want to pursue the entrepreneurial route, the Endocrine Society has created the Entrepreneurship Special Interest Group (SIG), that provides an online community where members can meet and connect with other likeminded endocrinologists to discuss and share ideas, best practices, and more.

One of the benefits of these SIGs is a series of webinars and other networking events where experts in the field share their knowledge and expertise. One recent Entrepreneurship SIG event was entitled “Pitching Your Idea Effectively” hosted by David Katz, PhD, chief scientific officer and founder, Sparrow Pharmaceuticals, Portland, Oregon, and Christopher Adams, MD, professor of medicine and research chair at the Mayo Clinic, in Rochester, Minn., and president of Emmyon, Inc.

However, going into the business realm in no way means that these researchers abandon their duties in the laboratory. In fact, prior to founding Sparrow, Katz was a pharmaceutical R&D leader at Abbott and AbbVie, where he led clinical development and drug discovery teams. Dedicated to mentorship of the next generation of life sciences entrepreneurs, Katz is currently an entrepreneur-in-residence at Oregon Health & Science University and has held post-doctoral fellowships in immunology at both the Universities of Chicago and Michigan; earned MPhil and

“ Excess corticosteroids play a central role in devastating diseases such as Cushing’s syndrome and autonomous cortisol syndrome (ACS), but treatment has been suboptimal. We identified a new approach that we felt larger companies have neglected.”

— DAVID A. KATZ, PHD, CHIEF SCIENTIFIC OFFICER/FOUNDER, SPARROW PHARMACEUTICALS, PORTLAND, OREGON

PhD degrees in molecular biophysics and biochemistry from Yale University; and is an alumnus of Pomona College (BA, chemistry).

With more than 50 peer-reviewed scientific papers to his name, Katz has recently turned his attention to potential new treatments for Cushing’s syndrome and related disorders since many of the current therapies are not always effective. *Endocrine News* speaks with Katz, who believes that drugs now in clinical trials could change current therapeutic paradigms by taking new approaches to inhibiting corticosteroid regulation and action.

Endocrine News: What is your background as it relates to your work at Sparrow Pharmaceuticals?

David A. Katz: I was a leader in personalized medicine, drug discovery, and clinical development at Abbott and AbbVie. I used what I learned from that experience to start Sparrow.

EN: Why did you found Sparrow? What was the perceived need you want to meet?

DAK: Large pharmaceutical companies have de-prioritized many early-stage investigational drugs with strong clinical

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In Cushing's, if we find that SPI-62 substantially reduces symptoms and that the degree of HSD-1 inhibition correlates well with clinical improvement, a new standard-of-care could be to monitor SPI-62 effect with the urinary HSD-1 ratio. **That's readily obtained from spot urine samples, which means no more 24-hour collections!**

— DAVID A. KATZ, PhD, CHIEF SCIENTIFIC OFFICER/FOUNDER,
SPARROW PHARMACEUTICALS, PORTLAND, OREGON



potential. It's good for patients that companies like Sparrow exist to bring those forward to the market. Excess corticosteroids play a central role in devastating diseases such as Cushing's syndrome and autonomous cortisol syndrome (ACS), but treatment has been suboptimal. We identified a new approach that we felt larger companies have neglected.

EN: What is that new approach and how might it help solve the puzzle of treating Cushing's syndrome and ACS?

DAK: SPI-62 is a small molecule that inhibits 11 β -hydroxysteroid dehydrogenase type 1 (HSD-1), an intracellular enzyme that converts inactive cortisone to active cortisol. HSD-1 is expressed in a number of tissues (including liver, adipose, bone, brain, skin, muscle, and eye) in which hypercortisolism causes wide-ranging symptoms in patients with Cushing's or ACS, such as hyperglycemia; dyslipidemia; hypertension; osteopenia; affect; cognition and sleep disorders; impaired wound healing; sarcopenia; and glaucoma.

The therapeutic hypothesis for SPI-62 in Cushing's and ACS is that HSD-1 forms most of the excess intracellular cortisol that can bind to intracellular glucocorticoid and mineralocorticoid receptors and thereby cause symptoms. HSD-1 inhibition by SPI-62 diminishes that intracellular cortisol and so has the potential to diminish symptoms. Several lines of evidence support the potential of this approach:

- ▶ Patients with Cushing's and unusually low HSD-1 activity showed no hypercortisolism-related symptoms despite very high 24-hour urinary free cortisol (UFC) results.
- ▶ A pilot open-label trial of another HSD-1 inhibitor, mainly in patients with ACS, showed positive trends on glycemic control and body habitus.
- ▶ SPI-62 showed efficacy on glycemic and lipid control in patients with type 2 diabetes in a Phase 2 clinical trial.

EN: What new scientific insights are leading Sparrow Pharmaceuticals to develop therapies targeted at intracellular corticosteroid regulation?

DAK: A key insight is that most of the intracellular cortisol that can bind intracellular receptors is made by HSD-1; only a small portion comes from the circulation. Pharmacologists think a lot about the free fraction of drugs — the portion not bound to plasma proteins — because that's the amount available to tissues. We apply that thinking to cortisol and cortisone. Cortisol is about 95% protein-bound in circulation. Even though total cortisol is higher than total cortisone, the relationship is reversed for the free fraction because cortisone is much less protein bound.

More cortisone enters cells, where HSD-1 converts it to cortisol. We and others have published evidence that in the liver, about 90% of intracellular cortisol is made by HSD-1. That proportion might be even higher in patients with Cushing's or ACS, in whom HSD-1 is overexpressed compared to the general population.

EN: How might inhibiting HSD-1 improve outcomes for patients with Cushing's or ACS?

DAK: By blocking formation of most of the excess cortisol that has access to intracellular receptors, SPI-62 has potential to attenuate most of the symptoms associated with hypercortisolism in Cushing's and ACS. That's certainly the case in rodents — both HSD-1 gene knockout and HSD-1 inhibitors (including SPI-62) prevent or reverse multiple negative effects of exogenously administered corticosteroids including hyperglycemia, dyslipidemia, hypertension, osteopenia, skin atrophy, sarcopenia, glaucoma, anxiety, and cognitive deficits. There's also the natural experiment of patients with Cushing's and unusually low HSD-1 activity, who were asymptomatic despite very high UFC.

SPI-62 was associated with reduced hemoglobin A1c, glucose, cholesterol, and triglycerides levels in patients with diabetes. In patients with Cushing's or ACS, it might show larger effects because cortisol is the primary etiology of their hyperglycemia and dyslipidemia, rather than one factor out of many. But we're basically at equipoise regarding the relative benefit of HSD-1 inhibition across the domains of Cushing's and ACS symptoms. We'll cast a wide net in Phase 2 trials with the aim to figure that out. I'm quite interested to assess whether SPI-62 shows benefits on the affect, cognition, and sleep symptoms that patients with Cushing's

FEVER PITCH: HOW TO SELL YOUR OWN IDEAS

As part of the Endocrine Society's Entrepreneurship

Special Interest Group, David



Katz, PhD, and Christopher Adams, MD, professor of medicine and research chair at Mayo Clinic, in Rochester, Minn., and president of Emmyon, Inc., shared their pointers for effective pitch meetings in a webinar entitled "Pitching Your Idea Effectively."

Below are a few highlights:

- ▶ Every presentation is a pitch.
- ▶ Target the audience.
- ▶ There is more than one pitch for the same audience.
- ▶ Curate content carefully.
- ▶ Use an efficient palette of fonts, colors, and visual motifs.
- ▶ Vary the format of consecutive slides.
- ▶ Include repetitive visual elements on single slides.
- ▶ Eschew graphics that don't contribute to your message.
- ▶ Avoid slide transitions, animations, and builds.
- ▶ Plant questions you are ready to answer.
- ▶ Look at your audience when you speak.
- ▶ Practice your presentation.

Endocrine Society members can watch the entire webinar on Community Connect! [Log in using your [endocrine.org credentials](#).] EN

“ Pharmacologists think a lot about the free fraction of drugs — the portion not bound to plasma proteins — because that's the amount available to tissues. We apply that thinking to cortisol and cortisone.”

— DAVID A. KATZ, PHD, CHIEF SCIENTIFIC OFFICER/FOUNDER, SPARROW PHARMACEUTICALS, PORTLAND, OREGON

and ACS notice, but which haven't been studied extensively.

EN: Is there something about corticosteroid excess that most endocrinologists don't understand? What is the new research that is leading to new treatments?

DAK: UFC to monitor Cushing's patients could be an incorrect approach. UFC is a biomarker for circulating cortisol, while most of the cortisol with access to intracellular receptors is made by HSD-1. There's evidence in the literature that UFC normalization doesn't correlate well with clinical outcomes in patients with Cushing's. It doesn't have that essential feature of a surrogate biomarker.

There's a urinary assay to quantitate hepatic HSD-1 activity and inhibition thereof. In the liver, 5- and 3-steroid reductases metabolize cortisol and cortisone to tetrahydro metabolites that are rapidly excreted in urine. The ratio of cortisol (HSD-1 product) to cortisone (HSD-1 substrate) metabolites reflects the intrahepatocellular levels. The urinary HSD-1 ratio is elevated about 45% in patients with Cushing's and about 15% in patients with ACS compared with controls. That is consistent with HSD-1 induction by hypercortisolism. The ratio was about 65% lower in asymptomatic patients with Cushing's compared with a historical patient cohort. In healthy adults and in patients

with diabetes, SPI-62 reduced the ratio by 90%. Upcoming clinical trials in Cushing's and ACS are aimed at assessing SPI-62 effect on HSD-1 activity and exploring how well changes in urinary HSD-1 ratios correlate with clinical outcomes.

EN: What do you see as the future of endocrinology as it relates to understanding the role of corticosteroids?

DAK: The potential of SPI-62, which of course has to be demonstrated through clinical trials, includes a focus shift in Cushing's from circulating to intracellular cortisol as well as improved recognition of ACS as a prevalent form of hypercortisolism.

In Cushing's, if we find that SPI-62 substantially reduces symptoms and that the degree of HSD-1 inhibition correlates well with clinical improvement, a new standard-of-care could be to monitor SPI-62 effect with the urinary HSD-1 ratio. That's readily obtained from spot urine samples, which means no more 24-hour collections! We hypothesize that under HSD-1 inhibition, the residual intracellular cortisol from the circulating pool might be a sufficient buffer to prevent adrenal insufficiency, potentially obviating the monitoring and dose titration that are needed with today's drugs.

ACS might be the most under-recognized condition in endocrinology. Most people don't undergo the imaging studies that could reveal an adrenal tumor; some tumors might not be documented on studies ordered for unrelated reasons; and most patients with tumors don't receive endocrinological follow-up. It's possible that as few as 3% of patients with ACS have been diagnosed. That's shocking for a condition associated with so much cardiometabolic and bone morbidity; negative effects on affect, cognition, sleep, muscle, and skin; and excess mortality. If SPI-62 development for ACS is successful, availability of a targeted medication for the disease will hopefully raise awareness and improve the diagnosis rate.

EN: What's the status of the therapeutics you are developing?

DAK: Phase 2 trials of SPI-62 are planned to start by the end of 2021 for Cushing's and a few months thereafter for ACS. **EN**



ExCEL

EXCELLENCE IN CLINICAL ENDOCRINOLOGY LEADERSHIP

SUPPORTING NEW LEADERS IN CLINICAL CARE

PHYSICIAN LEADERSHIP IS THE FUTURE OF HEALTHCARE

The Excellence in Clinical Endocrinology Leadership (ExCEL) program offers comprehensive leadership training and mentorship to early career physicians of communities underrepresented in medicine and science. Whether you are just beginning as an endocrine fellow or navigating the next steps in your career beyond fellowship, the ExCEL program will help you build leadership skills, explore opportunities for advancement, and expand your network of peers and colleagues.

ExCEL PROGRAM COMPONENTS

LEADERSHIP SKILLS BUILDING:

ExCEL awardees will participate in developing key leadership competencies and management training through a multi-day Clinical Endocrine Career and Leadership Workshop.

BUILDING PARTNERSHIPS AND EXPANDING NETWORKS:

ExCEL's mentoring network will connect fellows with a core team of mentors, provide quarterly virtual check-ins, and deliver continued training through seminars intended to continue skills development and community building.

LEADERSHIP SKILLS IN PRACTICE:

We will assist ExCEL awardees in enhancing their professional credentials through opportunities to volunteer within the Endocrine Society, travel awards to attend and network at the annual meeting, ENDO, and enhance speaking abilities and near-peer mentoring through a Visiting Physician Faculty series.

We are accepting applications for 2022 program until December 10, 2021.
PLEASE VISIT [ENDOCRINE.ORG/EXCEL](https://endo.org/excel) TO APPLY.

2021 Advocacy Year in Review

The Endocrine Society advocates on behalf of our members, the patients they treat, and the science they research. Though our work in 2021 remained virtual, we successfully advocated for our policy priorities and raised the visibility of the value of endocrinology and endocrine research.

Let's look back at some of our wins from this year.

- ▶ We joined with LGBTQ+ youth and reproductive health organizations to intervene in the UK case Bell v. Tavistock and provided the UK Court of Appeal with information about the standard of transgender healthcare, our clinical



practice guidelines, and consent of minors. The Court ruled in our favor, allowing minors with gender dysphoria to provide consent to puberty delaying medication.

- ▶ We called on Congress to pass legislation that would lower the cost of insulin. We issued a position statement in January that launched discussions and our recommendations were incorporated into President Biden's request. We worked with members of Congress, including the bipartisan Diabetes Caucus, and met with representatives and senators throughout the year to share our recommendations. During



our Clinical Hill Day, we made insulin affordability a key message and launched an online advocacy campaign where our members could contact their senators and representatives about insulin affordability. We also led an effort with other provider groups to call on congressional leadership to address insulin pricing immediately, and shared stories from across the country about lack of access to affordable insulin with members of Congress. As a result of our advocacy, drug pricing provisions specifically calling out insulin were included in the massive social policy legislation known as Build Back Better.

- ▶ We successfully advocated for funding increases of over \$2 billion for the National Institutes of Health (NIH) that were incorporated into both the House and Senate versions of fiscal year 2022 funding legislation. Although the legislation has not been finalized as of this writing, we successfully educated many congressional offices about the importance of endocrine research, and we will continue to advocate for finalized legislation in December.
- ▶ We worked with senators Joe Manchin (D-WV), Kevin Cramer (R-ND), and Jeanne Shaheen (D-NH) to urge the Senate Appropriations Committee to include language in its FY 2022 appropriations bill encouraging HHS to review the data collected on audio-only services to expand



access to healthcare for patients in rural and underserved communities. We launched an online campaign urging other senators to support this issue and 18 senators joined the Manchin-Cramer-Shaheen effort. The final Senate Appropriations Bill included our audio-only report language.

- ▶ We were selected to have a seat at the high-level roundtable for the EU's chemicals strategy for sustainability. Our

“Endocrine Society advocacy leads to real results and benefits our member researchers, clinicians, and the people they treat. Our success this year would not have been possible without our members’ participation. Taking action in an online campaign, amplifying our message on Twitter, or meeting with your member of Congress really does make a difference. We appreciate your work this year and look forward to continued success in 2022.

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objective was to ensure that revisions to legislation as part of implementation of the chemical strategy reflected the latest science on endocrine-disrupting chemicals (EDCs). Our members have and will continue to provide input on reports and give direct advice to policy makers to inform legislative developments, including pending revisions of the REACH and CLP legislation.

- ▶ We responded to proposals to establish a new federal agency, known as the Advanced Research Projects Agency – Health (ARPA-H), and presented at two listening sessions hosted by the NIH and the White House Office on Science and Technology Programs (OSTP) where we shared our concerns and recommendations. We also shared our priorities for the new agency with Congress. We want to ensure that ARPA-H funds unique projects and does not compete with the NIH for funds. Our feedback was reflected in legislative language put forward by Rep. Anna Eshoo (D-CA), as well as the NIH summary report of the listening sessions.
- ▶ We conducted a virtual briefing with the Society for Women’s Health Research to discuss the importance of including sex as a biological variable (SABV) in research, provide an update on the NIH 2016 SABV policy and how the field has changed in the past five years, and offer recommendations for overcoming barriers to the inclusion of SABV in research, ensuring better healthcare for all.

▶ We worked with the newly formed House Caucus on Social Determinants of Health to discuss ways Congress can help close disparity gaps. We continue to keep caucus members informed about our work and meet with them to find ways Congress can address this important issue.

▶ We provided a contribution in response to a call by the UN Special Rapporteur on toxics and human rights and submitted a response to an NIH Request for Information to inform the development of new diversity, equity, and inclusion (DEI) initiatives at the NIH. Our priorities are to ensure that policy makers are aware of the disproportionate effects of EDCs on marginalized or disadvantaged communities, and that NIH policies are updated to ensure that diverse input is taken into consideration e.g., during grant reviews. The UN report on the Right to Science in the Context of Toxic Substances cited our contributions and echoed some of our key messages.

As you can see, Endocrine Society advocacy leads to real results and benefits our member researchers, clinicians, and the people they treat. Our success this year would not have been possible without our members’ participation. Taking action in an online campaign, amplifying our message on Twitter, or meeting with your member of Congress really does make a difference. We appreciate your work this year and look forward to continued success in 2022.

Medicare Releases Physician Fee Schedule Final Rule for 2022

The Center for Medicare and Medicaid Services (CMS) released its final rule for the Medicare Physician Fee Schedule (MPFS) for calendar year 2022. Earlier this year, the Endocrine Society provided detailed comments on the

proposed rule. While we still have serious concerns, several of our recommendations to benefit endocrinologists were incorporated into the final rule. For 2022, CMS finalized a conversion factor of \$33.5983, which is a decrease of \$1.2948 from the 2021 conversion

factor of \$34.8931. This reduction is largely the result of the expiration of the 3.75% conversion factor increase for 2021, which Congress approved in late 2020. Congress approved this cut to avoid a large reimbursement decrease during the public health emergency (PHE). Congress has the authority to mitigate this cut and the Society has been working closely with congressional offices to address this issue before the end of the year.

CMS also finalized other policies in the final rule important to the Society. CMS proposed to implement the clinical labor pricing inputs used to calculate the direct PE of services. We were pleased that CMS listened to our recommendation to phase in these new inputs over a four-year period, mitigating the immediate financial impact in 2022. The Society was pleased that CMS will continue to allow for services on their temporary telehealth list to remain until the end of 2023. We were also glad that CMS broadened its definition of “home” pertaining to delivery to telehealth services. The Society urged CMS to continue covering audio-only evaluation and management

services after the PHE concludes. Unfortunately, CMS did not change this policy putting audio-only coverage at risk at the end of the PHE. The PHE is expected to continue through at least the fall of 2022, and we will continue to advocate for audio-only to be made permanent. Finally, CMS did finalize its policy to make virtual check-in available permanently.

Throughout December, the Society will continue to strongly advocate for Congress to avert the Medicare cuts scheduled to take place next year. In addition to the MPFS conversion factor cut, there are two additional cuts scheduled to occur. Unfortunately, these cuts could result in almost a 10% cut in Medicare reimbursement on January 1, 2022. To avert these cuts, Congress must act, and the Society is urging Congress to prevent these cuts from taking place. We will launch an online grassroots advocacy campaign so that you can contact your members of Congress on this issue. Please stay tuned for more information at www.endocrine.org/advocacy.

Endocrine Society Advocates for Increased Immunization Rates

With flu season in full swing, the Endocrine Society encourages its members to help “Raise the Rates” and increase adult immunization rates among their patients.

Raise the Rates is an initiative led by the American College of Physicians (ACP) to help internists and other primary care providers in both understanding the immunization rates of their patients and making practice changes that promote immunizations.

The program provides QI educational and virtual coaching support from ACP Advance expert coaches to support increased adult immunization coverage as well as access to virtual learning community, tailored educational offerings, and the opportunity to earn more than 54 CME and ABIM MOC credits for participating program participants.

Patients with diabetes, even well-managed, are often at higher risk of developing serious flu complications which can result in hospitalization and death. According to the Centers for Disease Control, about 30% of adults hospitalized with flu reported to have diabetes during recent flu seasons. Furthermore, serious

flu complications can make chronic health problems like diabetes worse as they weaken the immune system and make it harder for a patient to control their blood sugar levels. Coupled with the disproportionate risk diabetes patients face with severe illness from COVID-19, it is especially important for people with diabetes to have their immunization shots up to date.

National Flu Immunization Week this year runs from December 5 through 11. To obtain additional information about the Endocrine Society’s efforts to raise immunization rates, please contact government affairs manager Grace Kranstover at gkranstover@endocrine.org. We encourage our members to have these conversations with their patients, especially during this time when peak flu season has just begun.



As the European Commission makes progress towards implementation of the Chemicals Strategy for Sustainability (CSS), the Endocrine Society continues to provide input to ensure that the strategy modernizes the European Union's approach to identification and regulation of endocrine-disrupting chemicals (EDCs).

Our members are providing feedback in several different ways, including as a member of the High-Level Roundtable for the Chemicals Strategy. On November 25, the members of the Roundtable met to approve a report outlining the group's discussions concerning enforcement and compliance of chemicals legislation. The report describes the requirements of a successful enforcement and compliance structure aligned with the CSS and identifies barriers in enforcement and compliance preventing achievement of the CSS goals. We contributed to the report by offering suggestions aimed at improving the dialogue between enforcement authorities and scientists, especially in areas where new science-based legislation and regulations are forthcoming, such as for EDCs.

Meanwhile, the European Commission collected broader public input via an Open Public Consultation on the Targeted Revision of the Regulation on Classification, Labelling and Packaging of Substances and Mixtures (CLP). The CLP regulation identifies chemical hazards among different classes of substances and prescribes labeling requirements to disclose information from manufacturers to consumers about potential hazards in products. Importantly, the Commission proposes that EDCs are considered a new hazard class that will need to be addressed in the CLP regulation. Our expert EU Task Force developed a response to the consultation focused on the need to establish clear categories for the classification of EDCs depending on the level of evidence available for each substance.

The Chemicals Strategy for Sustainability is an important component of the EU Green Deal and includes many proposed actions over the coming years to achieve a zero-pollution future. Endocrine Society members will be vital to ongoing discussions about how best to manage human health and ecological hazards from EDCs. To become involved in the Society's EDC advocacy, send a message to Joe Laakso, director of science policy at: jlaakso@endocrine.org. 

EU Chemicals Strategy Advances Endocrine Society EDC Priorities

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Our expert EU Task Force developed a response to the consultation focused on the need to establish clear categories for the classification of EDCs depending on the level of evidence available for each substance.

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Under The Hood

Proper ventilation in a lab setting is key to ensuring the safety of all personnel, making the fume hood one of the most important pieces of safety equipment in the lab.

COMPILED AND WRITTEN BY COURTNEY CARSON

Selecting the appropriate hood for your lab depends on many factors. The intended application will determine whether you can use a ductless fume hood or variable air velocity, features that can help improve the energy efficiency of this equipment. The chemicals that will be used in the hood will also determine what material the hood should be built from. Choosing the right fume

hood for your lab will help keep your lab staff safe when working with hazardous chemicals.

Endocrine News has rounded up some options for labs looking to increase safety measures, improve energy efficiency, and upgrade existing equipment.



◀ Protector Echo Filtered Fume Hoods

The Protector Echo Filtered Fume Hood is available in 4', 5', 6', and 8' widths. Featuring Neutrodine® Filtration Technology, this hood offers comprehensive molecular filtration. Optional gGuard® communication software offers real-time monitoring by a designated facility manager. From a remote location, data such as usage authorization, filter saturation detection, sash position, and temperature may be observed and managed. At this time, these hoods are only available only in the Americas.

www.labconco.com



► Endeavour™ Ductless Fume Hood

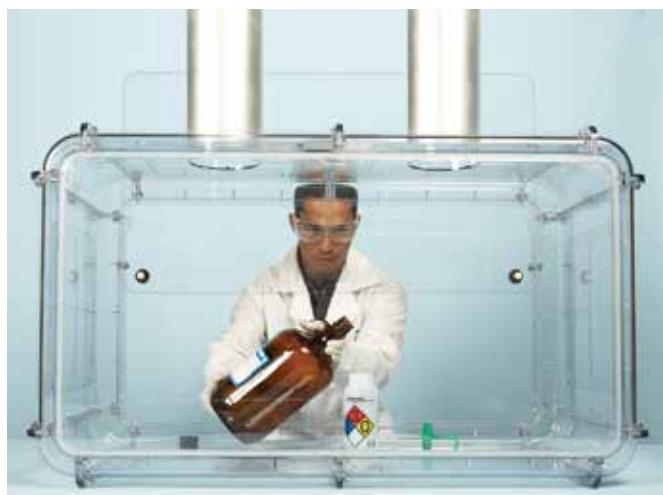
The AirSafe™ NXT provides touchscreen access to all functions of the Endeavour ductless fume hood. Automatic blower control, filter monitoring, alarm notifications, and energy use meter are just a few of the standard features provided by the AirSafe NXT automatic safety controller. The ChemMinder™ application acknowledgement system provides the end user with real-time data on approved chemical class. This hood includes a filter safety lockout to ensure correct filter replacement, while AirZone™ technology works to prevent fume hood roll and provide containment of gases and vapors.

www.aircleansystems.com

► UniFlow Specialty Fume Hoods

The UniFlow Specialty Fume Hoods feature UniFlow Superstructure non-metallic construction for total chemical resistance and durability. Unitized construction reduces weight for ease of installation, while the vertical raising viewing sash offers extended viewing height through clear tempered safety glass with corrosion resistant PVC framing. These hoods are designed to be energy efficient and can be equipped with service fixtures, electrical services, work surfaces, sinks, base cabinets, exhaust ducting, blowers, and filters to meet your lab's exact requirements.

www.hemcofumehoods.com



◀ Scienceware Clear View Fume Hood

Scienceware® Clear View fume hoods come equipped with a three-position sash offering 360° visibility while safely venting noxious or potentially hazardous fumes and dust. The clear polycarbonate construction means the hoods are durable while effective, and six-inch vent openings are located on top of each unit for easy hook-up to exhaust systems. The sash can be completely lowered or fixed at two height positions.

www.belart.com

► Purair Advanced Ductless Fume Hood

The Purair® Advanced Series ductless fume hoods offer a series of high-efficiency products designed to protect the user and the environment from hazardous vapors generated on the work surface. At the heart of the Purair ductless fume hood product line is the innovative Air Science® Multiplex™ Filtration Technology that creates a safe work environment over a wide range of applications. Improved clamping eliminates bypass leakage while high-capacity filters allow for more demanding applications.

www.airscience.com



Ensure the safety of all personnel working "under the hood" by equipping your lab with the latest supplies created to work best for your application. The options are endless which means the ideal option is available for your lab. EN

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FUTURE LEADERS ADVANCING RESEARCH IN ENDOCRINOLOGY

PROMOTING THE ADVANCEMENT OF EARLY CAREER INVESTIGATORS

FLARE prepares promising graduate students, postdoctoral fellows, clinical fellows, and junior faculty from underrepresented minority groups for leadership roles as independent biomedical researchers.

FLARE WORKSHOP

The FLARE Workshop is a two-day program that teaches the “business of research,” providing leadership training that addresses the unique challenges faced by early career researchers. It provides trainees and junior faculty with the skills they need to successfully market themselves for employment, transition into full-time research positions, and sustain and advance their careers.

WORKSHOP HIGHLIGHTS

- Create Your Own Individual Development Plan (IDP)
- Craft A Strong Grant Proposal
- Build Your Lab and Research Team
- Networking and Collaborations

OTHER FLARE COMPONENTS

The **FLARE Internship** provides a year of service on one of the Endocrine Society’s governance committees. Interns gain exposure to the Society’s leadership and help shape the Society’s programs.

The **FLARE Mentoring Network** offers a way to identify, connect with and build lasting relationships with accomplished scientists.

The **Early Career Reviewer Program** connects FLARE fellows interested in honing their skills as journal peer reviewers with seasoned reviewers and editorial board members to co-review journal articles.

100% of FLARE participants say they’d recommend this program to their peers and colleagues.

We are accepting applications for our 2022 workshop until December 10, 2021.

PLEASE APPLY ONLINE AT [ENDOCRINE.ORG/FLARE](https://endocrine.org/FLARE).

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