Cannabis Scientist

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The Power of the List

Celebrating the people who make cannabis science great (again)





n this issue, we present The Cannabis Scientist Power List 2020 (page 13) – our index of the most influential people in cannabis analysis and R&D.

The List was developed in two stages. In stage one, we invited readers to nominate those who they felt deserved recognition. In stage two, a jury of noted cannabis scientists (who prefer to remain anonymous) selected their top picks from the slate of nominees; their rankings were combined to provide the final Power List.

We make no claims that this is a definitive list – there can be no such thing. You may not all agree with who is on the list – let alone the order of the two Top 20s. So why make a list at all? In the immortal words of Kool and the Gang, it's a celebration! We want to shout from the rooftops about the diversity, innovation and talent found within your ranks – whether big names or unsung heroes.

And who are our chosen few? We eschewed bland bios and instead invited our Power Listers to tell you about themselves in their own words – and we've been bowled over by their wit, wisdom and passion for the field. We only have room for a tiny taster in print, and I urge you to visit thecannabiscientist.com to read the full profiles.

To whet your appetite, here are a few favorite quotes:

"Do what you yourself consider scientifically important. Try to disregard (politely) what others believe that you should do to advance your scientific field." – Raphael Mechoulam

"I'm motivated by the absolutely amazing people I meet in the cannabis industry, as well as the medical cannabis patients that benefit from legal cannabis as a medicine. Their spirit, enthusiasm and strength motivate me daily." – Scott Kuzdzal

"I hope, in the future, cannabis and cannabinoid-related public policy, education, and patient care will be guided by evidence; dialogue will be driven by data, not by politics or personal belief." – Ziva Cooper

"It is much easier to build successful start-ups if you are focused on something that can change the world. From pharmaceuticals to food to a cleaner environment, cannabis cannot be ignored." – Kevin McKernan

To all those who participated, our sincere thanks. To those who made the List, our hearty congratulations. And to our readers: enjoy!

I'd love to hear your thoughts – good or bad – on the Power List at charlotte.barker@texerepublishing.com.

Charlotte Barker *Editor*

Cherle Kerlen



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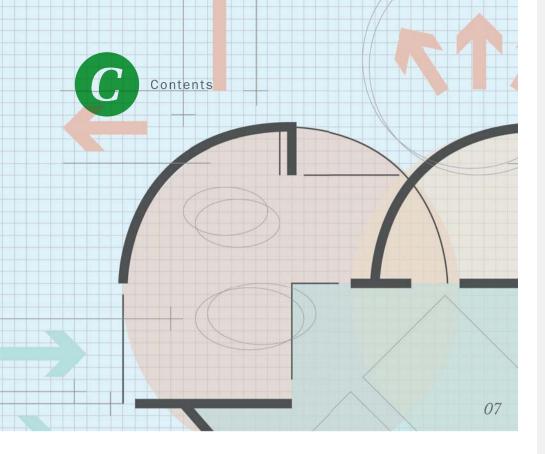
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- Andrew Fornadel and Bob 10 Clifford call for the industry to take action on heavy metal contamination



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Cannabis Scientist

ISSUE 10 - FEBRUARY 2020

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Distribution: The Cannabis Scientist, is published quarterly by Texere Publishing Inc, 175 Varick St, New York, NY 10014. Single copy sales \$15 (plus postage, cost available on request info@texerepublishing.com). Non-qualified annual subscription cost is available on request.

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A Secret Weapon?

Cannabigerol defeats multidrug-resistant bacteria in mice

Drug-resistant infections are a major threat to global health, raising the real possibility of a return to the pre-antibiotic age, when everyday infections could be lifethreatening. With 750,000 people already dying from drug-resistant infections every year, it's no surprise that researchers are racing to discover new antibiotics that can target these "superbugs."

Scientist have long been aware that cannabis (like many other plants) contains compounds that can kill bacteria on contact, but a new study suggests that one such compound – cannabigerol (CBG) – can fight drug-resistant infections inside a living organism.

In the as-yet unpublished study, researchers from Canada's McMaster University carried out a series of experiments to prove that CBG can kill multidrug-resistant *Staphylococcus auroras* (MRSA) bacteria both in the petri dish and in live mice (1). Mice treated with CBG showed similar reductions in MRSA counts as those treated with vancomycin, often the "last resort" antibiotic for drug-



resistant infections.

CBG was effective at killing not only regular bacterial cells, but also the specialized "persister" cells that have the greatest resistance to antibiotics and often survive treatment, causing recurrent infections. CBG was also able to prevent and disrupt MRSA "biofilms" that can form on skin or medical implants, even at low concentrations.

The results reported are preliminary and have not yet been subjected to peer review,

but if the findings are borne out in further studies, cannabinoids could represent an exciting new source of potential antibiotics. The authors agree, concluding "Our findings position cannabinoids as promising leads for antibacterial development that warrant further study and optimization."

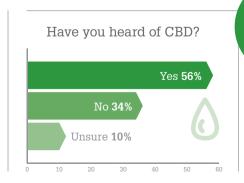
Reference

 MA Farha et al., "Uncovering the hidden antibiotic potential of Cannabis" (2020). Available at: https://bit.ly/2GvahzV.

INFOGRAPHIC



A new survey offers insights into perceptions, availability and consumption of CBD across Europe



of users reported that their ailment had improved when using CBD.



84%

of CBD users reported replacing an over-the-counter medication with CBD.

Cannabis Scientist



BITESIZE BREAKTHROUGHS FIVE PAPERS THAT PIQUED OUR INTEREST...

Dampening dyskinesia

Investigational drug HU-308, which acts on CB2 receptors in the brain, lessened involuntary movements (dyskinesia) – a common side effect of drug treatment for Parkinson's disease – in a mouse model (1).

Testing times

We already know that over one-fifth of CBD products for health and wellness contain THC not listed on the label (2). A new study now reports that two out of six participants tested positive for THC after vaping CBDpredominant cannabis just once – a combination that could spell trouble for users undergoing drug testing (3).

Losing sleep

Cannabinoids might not be the answer chronic pain sufferers have been waiting for. Even though recent studies found a positive effect of medical cannabis on sleep, a new report suggests that frequent use may result in tolerance and worse sleep overall (4).

Breaking connections

Endocannabinoid 2-AG reduces

connections in the brain that cause stress and anxiety, a new study found. A strong circuit between the amygdala and frontal cortex is linked to anxiety disorders – so pharmacologic treatments to increase levels of 2-AG could regulate anxiety symptoms and avoid reliance on medical marijuana (5).

Clouding the issue

An analysis of 240 news articles published between January 2015 and June 2019 showed that treatments involving cannabis and opioids received a disproportionate degree of press coverage, at the expense of best practice non-drug treatments (6).

References

- P Rentsch et al., Neurobiol Dis, 134, 104646 (2019).
- 2. MO Bonn-Miller et al., JAMA, 318, 1708-1709.
- 3. TR Spindle et al., J Anal Toxicol, bkz080 (2019).
- SR Sznitman et al., BMJ Support Palliat Care, [Epub ahead of print] (2020).
- DJ Marcus et al., Neuron, [Epub ahead of print] (2020).
- 6. H Devan, N Z Med J, 133, 92 (2020).

Don't Go Breaking My Heart

Does cannabis use damage cardiac function?

Concerned by the dearth of information available on how cannabis affects cardiovascular function, researchers at Queen Mary University of London reviewed cardiac MRIs from thousands of UK patients, to look for differences between the hearts of cannabis users and non-users (1).

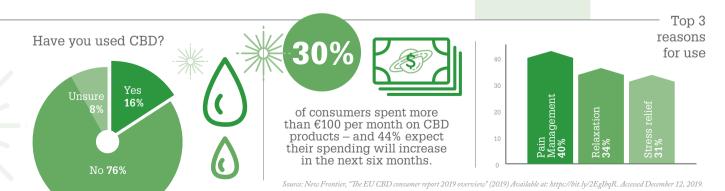
They retrospectively evaluated scans from 3,407 participants in the UK Biobank population study. Of these, 3,255 reported rarely or never using cannabis, 105 reported previous weekly or daily use, and 47 reported ongoing weekly or daily cannabis use.

> The researchers found that current users were more likely to have enlarged left ventricles (the main pumping chamber of the heart) and early signs of impaired heart function – even after accounting for factors such as age and cigarette smoking. They conclude that further research is required to understand the long-term implications of cannabis use on the cardiovascular system.

Reference

R17

 MY Khanji et al., JACC Cardiovasc Imaging, 19, 31009 (2019).



Is There a Doctor in the House?

Clinicians must take center stage in the future of medical cannabis research

By Simon Erridge, Honorary Research Fellow, Department of Surgery and Cancer, Imperial College London and Business Development Director, Sapphire Medical Clinics, and Mikael H Sodergren, Managing Director & Academic Lead, Sapphire Medical Clinics, Research Director, EMMAC Life Sciences, Consultant Hepatopancreatobiliary Surgeon and Honorary Senior Clinical Lecturer, Imperial College London, UK.

The cannabis plant has been noted for its medicinal properties for approximately 8,000 years and was first reported in a modern medical journal by WH O'Shaughnessy in an 1840 paper for the Boston Medical and Surgical Journal that described the use of hemp resin in convulsive disorders. Medical use of cannabis continued well into the 1900s before socio-political changes led to its prohibition. Recent changes to attitudes and laws surrounding the use of cannabis has since brought the medicinal potential of the plant back to the attention of patients, doctors, researchers and policymakers. There is huge demand from patients and their families, particularly those who have received significant benefit from cannabis administered off-prescription, to widen access to medical cannabis for a range of ailments.

However, it is difficult for clinicians to prescribe medical cannabis with confidence. Research into the therapeutic properties of the plant has been restricted by its reputation and scheduling as a drug of misuse and we are yet to fully understand how cannabis can be best used in the clinic. Since Raphael Mechoulam isolated THC – the main psychoactive component of cannabis – in 1964, over 100 cannabinoids have been identified from the cannabis plant. This is in addition to the hundreds of terpenes, flavonoids, stilbenoids, amino acids, fatty acids, alkaloids, hydrocarbons, carbohydrates, and phenols present within unprocessed flower products, many of which have their own touted medical properties. This diversity presents a number of therapeutic opportunities, but has made it difficult to conduct the randomized controlled trials upon which clinicians are accustomed to forming their evidence base.

The Cannabis genus is composed of two well-recognized species (Cannabis sativa and Cannabis indica) and their hybrids. Different cultivars of each species have been developed by growers aiming to adapt the chemical composition and attain specific end-user effects. This presents yet more challenges to interpreting the results of medical cannabis studies. Although inferences can be made according to chemical profile, the results of clinical studies with unprocessed flower or whole plant extract cannot be precisely extrapolated to other products. Until recently, clinical research has also been limited by the lack of adherence to good manufacturing practice, making it

difficult to standardize the chemical and therapeutic properties even within the same study. If you are unable to provide standardized medication concentrations, your results are unlikely to supply convincing evidence of benefits or harms.

The challenges of conducting research with unprocessed flower and/or whole plant extracts have encouraged many researchers to focus on cannabinoid isolates, most commonly THC and CBD. This has given us a clearer understanding of the impact of individual compounds in conditions such as treatment-resistant childhood epilepsy syndromes and chemotherapy-induced nausea and vomiting. However, the use of isolated cannabinoids does not necessarily represent the full therapeutic potential of the plant and certainly does not reflect common prescribing practices in mature markets, such as Germany and Canada, where 43 and 41 percent of medical cannabis prescriptions, respectively, are for unprocessed flower.

With so many complicating factors to consider, how can we conduct high-quality clinical trials of medical cannabis products? First, individuals and regulatory bodies must recognize that medical cannabis is not one medicine. Both academics and prescribing clinicians should be involved in the development of trials. Experienced

Experts from across the world share a single strongly held opinion _or key idea

In My

View

medical cannabis prescribers can help identify specific cultivars for further examination within traditional frameworks set out by experienced clinical trialists. Though many in the cannabis industry refute the calls for randomized controlled data, preferring observational studies, it is important to recognize that performing randomized controlled trials in medical cannabis is in no way impossible, just more challenging. To this end, Sapphire Medical Clinics has developed a clinical trials hub to broaden patients' access to appropriate studies - both to further our knowledge and to improve access to medications that may not be available to patients outside the context of a clinical trial.

Sapphire Medical Clinics is well placed to recruit trial participants, having been

set up to provide a second opinion service to doctors to assess whether a patient may benefit from a trial of cannabisbased medicine. Our doctors are guided by clinical evidence through a rigorous clinical governance framework and provide thorough post-treatment monitoring.

Though they provide the highest level of evidence in investigating medical cannabis, clinical trials are often expensive and timeconsuming. While we wait for this data, it is important that regulators look to other methodologies to investigate the effects of medical cannabis. One way to do this is to collect large-scale observational data. This is the premise behind the formation of the UK Medical Cannabis Registry (www.ukmedicalcannabisregistry.com). Established by a group at Sapphire Medical Clinics, the registry seeks to capture essential data, including prescribed formulations, adverse events, and patientreported outcome measures across a range of conditions. Open to both NHS and private prescribers, the registry will be important in providing data to national regulators to help inform their guidelines in the future. Clinicians have been an integral part of these efforts; for example, helping to identify clinically important outcome measures to study chronic diseases.

Traditional pharmaceuticals run through pre-defined stages of in vivo studies, clinical trials and post-marketing research. In medical cannabis, all three are now running concurrently. As such, physicians will play an important role in dictating the future direction of medical cannabis research.



Heavy Metal Measurement Made Light

Heavy metal contaminants pose a risk to health – the cannabis industry must react accordingly



By Andrew Fornadel, Marketing Manager, and Bob Clifford, General Manager of Marketing, Shimadzu Scientific Instruments, Columbia, Maryland, USA.

The legal, cultural, and societal acceptance of cannabis as a therapeutic or recreational drug has exploded in recent years. Concurrently, concern regarding the presence of contaminants - notably pesticides, residual solvents, mycotoxins, and heavy metals - in commercial cannabis products has increased. Heavy metals can interfere with metabolic functions by mimicking metals that are vital enzyme components, ultimately inhibiting their normal function. The result of chronic heavy metal ingestion is damage to a variety of vital organs, including nervous system and kidneys. Moreover, heavy metals can be mutagenic, causing damage to DNA, and leading to a cascade of further problems such as tumor growth.

For cannabis, standards organizations, such as ASTM International, are in the process of developing consensus methods for assessing contaminants, including heavy metals, in cannabis. We should expect the number of metals covered by such methods and regulations will only continue to grow and target concentration levels will continue to decline. The metals of immediate concern have been arsenic, cadmium, lead, and mercury; however, in some jurisdictions, this has expanded to include others, such as barium, chromium, selenium, and silver. The nonuniformity of regulations between states and between countries has proven to be a particular challenge. In the US, these challenges will continue until there are federal guidelines akin to those for pharmaceuticals (FDA) or food products (USDA). The cannabis testing industry will likely contribute to the basis for the inevitable federal guidelines through participation and contribution to voluntary consensus standards development through organizations such as ASTM International and AOAC International.

Most laboratories assess the metal composition of cannabis products by digesting samples in an acidic matrix and conducting analysis with inductively coupled plasma mass spectrometry (ICP-MS). This technique has high sensitivity - in the parts per trillion range for most elements. ICP-MS also affords the advantage of rapid sample throughput, with typical analysis times of around 2-3 minutes per sample. Advances in instrument hardware and software have also made modern ICP-MS instruments much more user-friendly than their predecessors, meaning they can be operated by a much wider panel of users than previously possible.

Testing currently focuses on the end product to be supplied, whether that be cannabis flower, extracts (waxes or oils, for example), or cannabis edibles. However, it is possible that testing will expand to include sources of contamination outside the product itself. Several recent studies have demonstrated the sputtering and vaporization of heavy metals from heating filaments in vaporizers and socalled "vape-pens" (1). In this case, the cannabis product itself is free from metal contamination, but the user exposes themselves to metals by using the vaporizer; this scenario is analogous to drinking clean water delivered to the tap by lead-contaminated plumbing.

Metal analysis will form a necessary component of more comprehensive testing of cannabis product purity and safety. As legalization efforts continue, the methods for detecting metals and other contaminants will likely include a greater number of target compounds at increasingly stringent detection limits. Nevertheless, as methods become increasingly harmonized between states, countries, and standards organizations, the challenges the cannabis industry faces should narrow.

To tackle the myriad challenges with metal testing in cannabis, it behooves the industry, including testing laboratories, instrument vendors, and regulatory agencies to understand the issues of metal contamination and to unify on validated methods for sampling, sample preparation, and sample analysis. Some of this work is being done and exchanged at conferences and symposia focused on cannabis, which are excellent venues to share the growing body of knowledge. Additionally, committees within ASTM International are beginning to codify standard test methods, which will likely form a framework for future federal regulation. It is incumbent upon the entire industry to advance our scientific understanding of cannabis as its chemistry, various uses, and legitimacy continue to grow.

Reference

 P Olmedo et al., "Metal concentrations in e-Cigarette liquid and aerosol samples: the contributions of metallic coils", Environ Health Perspect, 2, 027010 (2019). DOI: 10.1289/ EHP2175

Application Note

Rugged Isocratic LC-UV Method for the Analysis of 16 Cannabinoids in Hemp and Cannabis Samples

With the mounting interest in hemp and cannabis products for medicinal and recreational use around the world, the need for suitable analytical methods to identify and determine the concentration of cannabinoids is essential for ensuring consumer safety. Traditional analyses for measuring the potency of cannabinoids in cannabis and hemp samples have focused mainly on 5 primary analytes: THC, THC-A, CBD, CBD-A, and CBN. As the industry continues to expand and evolve, more attention is being directed toward additional, although less prevalent, cannabinoids that have been shown to exhibit physiological effects. This application note outlines a simple and robust method for the detection and quantitation of 16 cannabinoids in hemp and cannabis samples using an isocratic HPLC method coupled with UV detection. Baseline

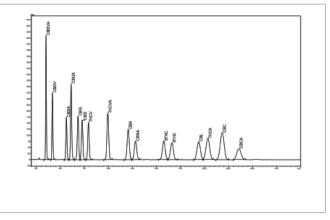


Figure 1. Chromatogram of the highest calibration standard (62.5 μ g/mL).

separation of all 16 cannabinoids, including the critical pair $\Delta 9$ -THC and $\Delta 8$ -THC, was successfully achieved using a Selectra[®] C18 column. Examples of hemp flower and oil samples analyzed using the analytical method are also presented.

View the full application note here! https://bit.ly/2trFS2w







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WHO ARE THE MOST INFLUENTIAL PEOPLE IN CANNABIS SCIENCE?

That's the question we posed to ourselves – and then to you – earlier this year, with open nominations followed by evaluation from our expert judging panel.

Here, we celebrate the answer– highlighting the Top 20 scientists in two categories: cannabis analysis and cannabis research.

ANALYTICAL GURUS

20. GARY K. WARD

CHIEF COMPLIANCE OFFICER AND PRINCIPAL LABORATORY SCIENTIST, PACLAB ANALYTICS, HILLSBORO, OREGON, USA

Activities: Currently retired and serving as a laboratory consultant and an experienced third-party assessor certified by the US EPA. Consulting to PacLab Analytics cannabis testing laboratories in Oregon and California and providing regulatory comments to the California BCC as a member of CCIA.

19. ALDWIN ANTEROLA

ASSOCIATE PROFESSOR, SOUTHERN ILLINOIS UNIVERSITY, CARBONDALE, USA

Research: Biosynthesis of natural products, including terpenophenolic compounds, such as the phytocannabinoids, and other medically important secondary metabolites. Developing standards and methods for cannabis testing through different organizations, such as the ASTM and AOAC.



<u>SCIENCE, PHYLOS</u> <u>BIOSCIENCE, PORTLAND,</u> <u>OREGON, USA</u>

Motivation: Until genomic science companies like Phylos entered the picture, cannabis was deeply understudied compared to other crops – and we haven't even begun to scratch the surface of its potential. Through the application of genomic and molecular biology tools, we're discovering the connection between traits and the genes that control them at an unprecedented pace. This dramatically speeds up our ability to develop hemp varieties that will perform well in the hands of farmers and growers in diverse regions.

16. JACK HENION

CO-FOUNDER AND CSO (RETIRED), ADVION, ITHACA, NEW YORK, USA AND EMERITUS PROFESSOR OF ANALYTICAL TOXICOLOGY, NEW YORK STATE COLLEGE OF VETERINARY MEDICINE, CORNELL UNIVERSITY, NEW YORK, USA

Starting out in cannabis science: I attended the first Cannabis Science Conference, and was concerned about the limited scientific analytical methods being employed – it reminded me of where the pharmaceutical industry was back in the 1980s. I have a passion for the appropriate employment of highly selective and sensitive analytical techniques, and I wanted to contribute what I had learned in the pharmaceutical industry to the cannabis analytical community.

17. ROBERT CLIFFORD GENERAL MANAGER, SHIMADZU

<u>SCIENTIFIC INSTRUMENTS,</u> COLUMBIA, MARYLAND, USA

Where is cannabis analysis heading? We're now seeing an expansion of the cannabis industry to the academic arena, with universities offering new degree programs to fulfill the growing demand for jobs. In addition, I expect to see an increase in research on the almost infinite number of cannabinoids and terpene combinations possible. Having been previously employed at Campbell Soup and the FDA, I've always been very aware of the importance of what we consume. Cannabis is no different, with the same focus on quality and safety.



15. KAITLIN URSO

ENVIRONMENTAL CONSULTANT, COLORADO DEPARTMENT OF PUBLIC HEALTH AND ENVIRONMENT, DENVER, USA

Starting out in cannabis science: I studied mechanical engineering because I loved math and science but later found that my passions didn't align with my degree. Now, I apply the technical problem-solving skills I developed from my degree to protecting Colorado's environment – a job I love! *Most exciting project:* Helping the marijuana industry quantify and reduce their air quality impacts.



14. MARKUS ROGGEN FOUNDER AND CEO, COMPLEX BIOTECH DISCOVERY VENTURES, VANCOUVER, CANADA

Challenges facing the field: Right now, the industry is testing for around 10 cannabinoids and 50 terpenes. We can buy maybe 16 different cannabinoids as reference standards. But in my lab we are tracking over 800 molecules that come from the plant or its production processes. Getting a handle on all those molecules is the biggest challenge for cannabis analysis.

13. JULIA BRAMANTE

LEAD SCIENTIST, MARIJUANA REFERENCE LABORATORY, COLORADO DEPARTMENT OF PUBLIC HEALTH AND ENVIRONMENT, CHAIR OF THE ACS CANNABIS CHEMISTRY SUBDIVISION AND CHAIR OF THE AOAC CANNABIS ANALYTICAL SCIENCE PROGRAM MICROBIAL CONTAMINANTS WORKING GROUP, DENVER, USA

Inspiration: Because the field of cannabis analysis is relatively young, it provides the opportunity to conduct robust method development and validation using standard methodologies in conjunction with innovative technologies.

12. SCOTT KUZDZAL

<u>VP OF MARKETING, SHIMADZU</u> <u>SCIENTIFIC INSTRUMENTS,</u> BALTIMORE, MARYLAND, USA

Motivation: The absolutely amazing people I meet in the cannabis industry, as well as

the medical cannabis patients that benefit from legal cannabis as a medicine. Their spirit, enthusiasm and strength motivate me daily.





11. JEFFREY RABER

<u>CO-FOUNDER AND CEO, THE WERC</u> SHOP, LOS ANGELES, CALIFORNIA, USA

Career highlight: Being invited by Health Canada to lecture their regulators about cannabis testing and help shape their emerging adult-use market regulations. *Where is the field heading?* Analysis will become more complex and more specifically geared towards hunting for new molecules. Work will be aimed towards characterizing currently unknown compounds and elucidating the structure of rare and minor constituents of the plant.





8. JULIE KOWALSKI

INDEPENDENT CONSULTANT, SPOKANE, WASHINGTON, USA

Challenges facing the field: The biggest roadblocks aren't technical. We are all learning, exploring and striving to build better methods – that is the fun part. But our efforts are hampered by the economic pressure felt by many labs, combined with regulations that are ambiguous at best, and, at worst, nonsensical.

9. ROBERT MARTIN JR

CO-FOUNDER AND CEO, CW ANALYTICAL, OAKLAND, CALIFORNIA, USA

Motivation: To be a contributor in an emerging market like this is both provocative and wonderfully exciting. It makes for a very stimulating time intellectually, commercially, and socially.

7. SWETHA KAUL

VICE PRESIDENT, BOARD OF DIRECTORS, CALIFORNIA CANNABIS INDUSTRY ASSOCIATION, USA

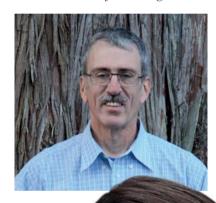
Motivation: Raising standards and bringing legitimacy to a new industry, and paving the way for social equity and small businesses. I am extremely datadriven and believe that information based on sound methods and good science will drive the best decisions. Lesson learned: Regardless of the industry or type of company, it is important to treat people with respect and integrity, and foster diversity of people, ideas and experiences. Where is the field heading? Along the path of standardization. The process often takes decades in other industries but I believe the timeline will be accelerated in the cannabis industry.

10. KEITH ALLEN

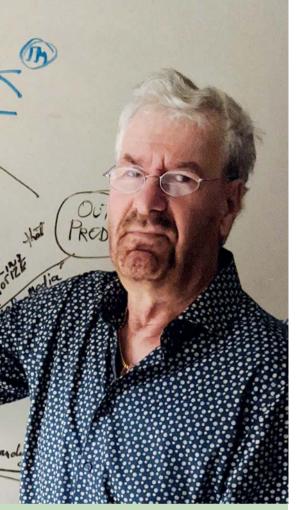
<u>DIRECTOR OF</u> <u>BIOINFORMATICS, FRONT</u> <u>RANGE BIOSCIENCES,</u> AFAYETTE, COLORADO, USA

Starting out in cannabis science: I came to the field as a refugee from the "Big Ag" consolidations, just as people were starting to apply the tools of modern genomics and breeding in this crop that science has ignored for so long.

Lesson learned: The ability to jump between fields at just the right time!







5. JOHN ABRAMS

CHAIRMAN AND CSO, THE CLINICAL ENDOCANNABINOID SYSTEM CONSORTIUM (CESC), SAN DIEGO, CALIFORNIA, USA; SCIENTIFIC DIRECTOR OF THE EMERALD CONFERENCE; ACTING CSO, ORION GMP SOLUTIONS, ROCHESTER HILLS, MICHIGAN, USA

Motivation: Finding out how cannabis chemotypes influence the overall user experience. *Career highlight:* Pursuing fundamental discovery research in the fields of immunology for over 30 years, and now over the past decade in cannabis science. *Most exciting project:* Integrating cannabis chemotype data with user brainwave EEG response patterns and attempting to establish correlations with underlying human genetics.



6. CHRISTOPHER HUDALLA

FOUNDER AND CSO, PROVERDE LABS, MILFORD, MASSACHUSETTS, USA

Motivation: The knowledge gap in the cannabis industry, resulting from decades of prohibition, provides tremendous opportunities for scientists and researchers to study cannabis as plant, as an agricultural crop, and as medicine for the body and mind.





4. KEVIN MCKERNAN FOUNDER AND CSO, MEDICINAL GENOMICS, BEVERLY, MASSACHUSETTS, USA

Motivation: It is much easier to build successful start-ups if you are focused on something that can change the world. From pharmaceuticals to food to a cleaner environment, cannabis cannot be ignored.

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3. REGGIE GAUDINO

<u>VP R&D, FRONT RANGE</u> BIOSCIENCES, LAFAYETTE, <u>COLORADO, USA</u>

Most exciting project: Every project is exciting because we have so much to learn and there is so much "low hanging fruit." Where is the field heading? Methods that allow characterization of sample content with fewer preparation/extraction steps will be needed to meet high-throughput demands. But we also need more detailed analysis. Eight cannabinoids and a handful of terpenes isn't enough. The more we know, the better we'll be able to make use of this highly versatile plant.



Nominator comment: "A visionary."



1. DONALD LAND

PROFESSOR OF CHEMISTRY, FORENSIC SCIENCE, AND BIOTECHNOLOGY, UNIVERSITY OF CALIFORNIA, DAVIS; CHIEF SCIENTIFIC CONSULTANT, STEEP HILL; CONSULTANT, FRONT RANGE BIOSCIENCES; EXPERT WITNESS IN CONTROLLED SUBSTANCES, CALIFORNIA, USA

Starting out in cannabis science: In 2010, I was hired as a consultant and co-founded Halent Laboratories, an early cannabis

testing lab. Prior to that, I had taught similar methods for controlled substance determination in forensics. We merged with Steep Hill (first to market in the cannabis testing space) in 2013.

Proud moment: Helping a mother procure high CBD, low THC tincture – at that time almost impossible to find – to decrease her two-year-old's seizure frequency from dozens per day to one every few months.

Motivation: Helping people. Educating people. Using evidencebased information to inform a more just society.

2. SUSAN AUDINO

ISO ASSESSOR AND INSTRUCTOR, SCIENTIFIC ADVISOR AT AOAC INTERNATIONAL CASP, AND CHEMISTRY LABORATORY CONSULTANT AT S.A. AUDINO & ASSOCIATES, LLC, WILMINGTON, DELAWARE, USA

Luckiest break: Surrounding myself with bright and energetic people who share their knowledge and expertise. Respect and admiration within the professional circle are the greatest foundations for success.

Challenges facing the field: Experience. Efficiency. Confidence. Experience in building and qualifying test methods, understanding that efficiency is not always about the shortest run-time, and global confidence in the test results. I remain hopeful that this very young industry will continue to transcend the challenges.



Nominator comment: "On a mission to help cannabis labs clean up their act!"

R&D TRAILBLAZERS

20. HEATHER BRADSHAW

PROFESSOR OF PSYCHOLOGICAL AND BRAIN SCIENCES AND DIRECTOR OF SCIENCE, TECHNOLOGY, AND RESEARCH SCHOLARS, INDIANA UNIVERSITY, BLOOMINGTON, USA

Proud moment: Every time I watch my students have a flash of insight in the lab or communicate their discoveries with the world. Having someone greet me at a conference with "Wow, your student gave a great talk" – that's something I cherish.





19. JONATHAN PAGE CSO, AURORA CANNABIS, EDMONTON, CANADA

Career highlight: The publication of the cannabis genome sequence in 2011 with my University of Toronto collaborators Tim Hughes and Harm van Bakel. The paper has become a landmark in cannabis science and I like to think it propelled cannabis forward as an organism worthy of serious study, right at a crucial time.



18. GABRIELLA GOBBI <u>PROFESSOR, MCGILL</u> <u>UNIVERSITY, MONTREAL</u>, <u>CANADA</u>

The next 10 years: I hope that in the next decade we will identify the therapeutic properties of cannabinoids and stop thinking that cannabis is the remedy for all kinds of diseases. I also hope the next generation of adolescents will be aware of the negative mental health consequences of cannabis.

16. SAGNIK BHATTACHARYYA <u>PROFESSOR OF</u> <u>TRANSLATIONAL</u> <u>NEUROSCIENCE &</u> <u>PSYCHIATRY, KING'S</u> <u>COLLEGE LONDON,</u> <u>AND CONSULTANT</u> <u>PSYCHIATRIST,</u> <u>SOUTH LONDON</u> <u>& MAUDSLEY NHS</u> FOUNDATION TRUST, UK

17. M-J MILLOY

CANOPY GROWTH PROFESSOR OF CANNABIS SCIENCE, ASSISTANT PROFESSOR, DEPARTMENT OF MEDICINE, UNIVERSITY OF BRITISH COLUMBIA, CANADA

Scientific heroes: As one of the first scientists to hold a named professorship in cannabis science, my heroes include

pioneers like Donald Abrams and Mark Ware. Despite the barriers of prohibition, they persisted in trying to better understand the effect of cannabinoids on health; I hope all of us lucky enough to work in the era of legal cannabis honor them by striving to produce high-quality, rigorous and useful research.

Read more about M-J's work on page 26.

Career highlight: Cannabis use has

long been associated with harmful effects on mental health and cognition, and even 15 years ago the idea that compounds from the same plant could be used to treat some of those same mental health conditions was not taken seriously. I feel incredibly lucky to have been involved in some of the human studies that paved the way for the ongoing clinical trials of CBD for various neuropsychiatric indications.

14. ANDREA HOHMANN GILL CHAIR OF NEUROSCIENCE AND PROFESSOR, DEPARTMENT OF PSYCHOLOGICAL & BRAIN SCIENCES, INDIANA UNIVERSITY, BLOOMINGTON, USA

Career highlight: The discovery that cannabinoids act at a neural level to suppress pain. I was alone in the laboratory one night with only an anesthetized rat for company when I saw, for the first time, that a cannabinoid turned off the firing of a neuron in the spinal cord that coded information about pain.

15. JEFFREY CHEN

EXECUTIVE DIRECTOR, CANNABIS RESEARCH INITIATIVE, UNIVERSITY OF CALIFORNIA LOS ANGELES, USA *Unanswered question:* The entourage effect – is it always the case that whole plant extracts are more efficacious or have fewer side effects than individual components?

12. DANIELA VERGARA

DIRECTOR AND FOUNDER, AGRICULTURAL GENOMICS FOUNDATION AND RESEARCH ASSOCIATE, UNIVERSITY OF COLORADO, BOULDER, USA

Motivation: That there is always something new to learn, and something I can improve on. But for my research in particular, curiosity motivates me. What's going to happen? What am I going to find? I want to know now!

What's next? So many things! Front Range Biosciences is now funding my research, and that has opened the door to many cool projects. Breeding, genetics, hemp – they are all possible avenues.

Čannabis Scientist

13. MARY ABOOD

<u>PROFESSOR, TEMPLE</u> <u>UNIVERSITY, PHILADELPHIA,</u> <u>PENNSYLVANIA, USA</u>

Proud moment: Being selected by my colleagues for the 2015 Mechoulam award, bestowed by the International Cannabinoid Research Society to a scientist who is deemed to have made outstanding contributions to the field and moved the discipline forward.

11. DAVID NUTT

EDMOND J SAFRA CHAIR IN NEUROPSYCHOPHARMACOLOGY, DIRECTOR OF THE NEUROPSYCHOPHARMACOLOGY UNIT, DIVISION OF BRAIN SCIENCES, IMPERIAL COLLEGE, LONDON, UK

Research: Drugs that affect the brain and conditions such as addiction, anxiety, and sleep. Member of the Committee on Safety of Medicines, and past President of the European College of Neuropsychopharmacology.



10. ZIVA COOPER

ASSOCIATE PROFESSOR AND RESEARCH DIRECTOR, UCLA CANNABIS RESEARCH INITIATIVE, JANE & TERRY SEMEL INSTITUTE FOR NEUROSCIENCE & HUMAN BEHAVIOR, DEPARTMENT OF PSYCHIATRY AND BIOBEHAVIORAL SCIENCES, UNIVERSITY OF CALIFORNIA LOS ANGELES, USA

Career highlight: Working with 16 colleagues with diverse areas of expertise on the National Academies of Sciences consensus report on the health effects of cannabis and cannabinoids, published in 2017. Lifelong friendships were made and a landmark, datadriven publication of cannabis' health effects was produced.

9. IAIN MCGREGOR

DIRECTOR, THE LAMBERT INITIATIVE FOR CANNABINOID THERAPEUTICS, UNIVERSITY OF SYDNEY, AUSTRALIA

> Motivation: Scientific curiosity – cannabinoid science is the most exciting frontier in modern pharmacology.





8. GEOFFREY GUY

CHAIRMAN AND FOUNDER, GW PHARMACEUTICALS, CAMBRIDGE, UK

Research: Creator of approved cannabinoid medicines Sativex and Epidiolex and leader of innovation and new product discovery at GW Pharmaceuticals. Physician in charge of over 300 clinical studies including first dose in man, pharmacokinetics, pharmacodynamics, dose-ranging, controlled clinical trials and large-scale multi-centered studies and clinical surveys.

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7. VINCENZO DI MARZO

CANADA EXCELLENCE RESEARCH CHAIR ON THE MICROBIOME-ENDOCANNABINOIDOME AXIS IN METABOLIC HEALTH, UNIVERSITÉ LAVAL, QUEBEC, CANADA, AND ASSOCIATE RESEARCH DIRECTOR, INSTITUTE OF BIOMOLECULAR CHEMISTRY OF THE NATIONAL RESEARCH COUNCIL (ICB CNR) NAPLES, ITALY

Motivation: To understand how such a complex plant, and its many bioactive components, act pharmacologically and modulate so many aspects of mammalian cell, tissue, organ and organism physiology and pathology.



6. GEORGE KUNOS SCIENTIFIC DIRECTOR, NATIONAL INSTITUTE ON ALCOHOL ABUSE AND

ALCOHOLISM, NATIONAL INSTITUTES OF HEALTH, BETHESDA, MARYLAND, USA



Starting out in cannabis science: My first foray into cannabinoid research came in 1993 when my friend Raphael Mechoulam persuaded me to explore the role of the newly discovered endocannabinoid, anandamide, in cardiovascular regulation. I've been hooked ever since!

5. MELANIE KELLY

PROFESSOR OF PHARMACOLOGY, OPHTHALMOLOGY & VISUAL SCIENCES, ANESTHESIA, PERIOPERATIVE MEDICINE AND PAIN MANAGEMENT, DALHOUSIE UNIVERSITY, NOVA SCOTIA, CANADA

The next 10 years: This is an exciting time in endocannabinoid research due to the high level of public interest and the changed political landscape for cannabis. I strongly believe that the next decade will lead to a greater understanding of the body's endocannabinoid system and result in breakthrough new therapeutics.



4. DAVID (DEDI) MEIRI

ASSISTANT PROFESSOR, TECHNION ISRAEL INSTITUTE OF TECHNOLOGY, ISRAEL

Career highlight: When my group discovered three specific cannabinoids that kill leukemia cancer cells. Clinical trials are now starting based on our work.

Scientific hero: Raphael Mechoulam, one of the greatest Israeli scientists and the father of cannabis research from the 1960s until the present day. He deserves a Nobel prize for his achievements.

What's next? Our goal is to correlate the action of compounds in cannabis to the role of the endocannabinoid system in cancer and neurodegenerative diseases.







INTERNATIONAL CANNABINOID-BASED DRUG DISCOVERY & DEVELOPMENT (iCBD3) CONGRESS

ROTTERDAM, THE NETHERLANDS 4-5 March 2020

Pharmaceutical and biotech development of cannabinoid-based drugs has become an active and fertile ground for generating a new class of regulated therapeutics. The combination of advancing understanding of the biology of the endocannabinoid system and the production of natural and synthetic cannabinoid products is now being shown to have therapeutic value for myriad medical conditions.

The inaugural International Cannabinoid-Based Drug Discovery and Development (iCBD3) Congress, March 4-5 in Rotterdam, Netherlands will explore an array of drug targets, therapies, manufacturing processes, regulatory frameworks, clinical studies and market opportunities for cannabinoid-based pharmaceuticals.

Read the agenda to see who is on the speaker panel.

www.global-engage.com/event/cannabinoid-drug-discovery



MELANIE KELLY CSO, Panag Pharma SPEAKERS INCLUDE:



ALEXANDROS MAKRIYANNIS Director, Center For Drug Discovery, Northeastern University

www.global-engage.com



GEORGE KUNOS Senior Investigator, NIAA, NIH

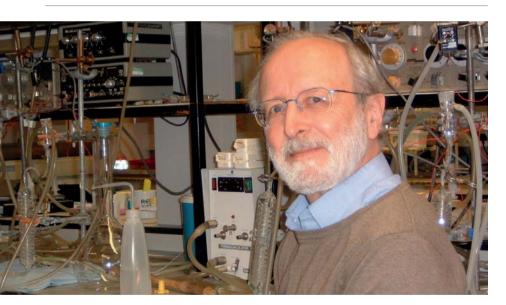
3. DANIELE PIOMELLI

PROFESSOR OF ANATOMY AND NEUROBIOLOGY AT UCI SCHOOL OF MEDICINE, AND DIRECTOR OF THE UCI CENTER FOR THE STUDY OF CANNABIS, IRVINE, CALIFORNIA, USA

Most exciting project: More than 20 years after its discovery, we know that the endogenous cannabinoid system plays highly important and pervasive roles in the brain as well as in the periphery of the body. But we still don't know how exogenous cannabinoids like THC can influence the activity of this system. My lab is now addressing this important question, with surprising results!



Nominator comment: "The most important cannabis researcher in the world today."



2. ROGER PERTWEE EMERITUS PROFESSOR, UNIVERSITY OF ABERDEEN, UK

Career highlight: My contribution to the discovery of (i) the endocannabinoid system and (ii) an allosteric site on the cannabinoid CB1 receptor. Other highlights include my contributions to

the discovery of THCV in cannabis and to the intriguing pharmacological characterization of numerous plant and synthetic cannabinoids.

Where is the field heading? Toward a much more complete understanding of the pharmacological actions and effects of plant, synthetic and endogenous cannabinoids, and ultimately more approved cannabinoid medicines.

1. RAPHAEL MECHOULAM

PROFESSOR OF MEDICINAL CHEMISTRY, MEDICAL FACULTY, HEBREW UNIVERSITY, JERUSALEM

Career highlight: I believe that my most important contribution has been the discovery of the endogenous cannabinoids, anandamide and 2-AG. *Unanswered question:* Although there is a large amount of published preclinical information on the action of the endogenous cannabinoids, we have almost no direct knowledge of their action in humans. We also lack clinical data on many of the actions of the plant cannabinoids.

Lessons learned: Do what you yourself consider scientifically important. Try to disregard (politely) what others believe that you should do to advance your scientific field.



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The AZURA Analytical system by KNAUER is dedicated for the analysis of six common cannabinoids of high medicinal interest. Cannabidiol (CBD), cannabidiolic acid (CBDA), cannabinol (CBN), Δ 8-tetrahydrocannabinol (Δ 8-THC), Δ 9-tetrahydrocannabinol (Δ 9-THC), and Δ 9-tetrahydrocannabinolic acid (Δ 9-THCA) can easily be quantified according to the monography of German Pharmacopeia. *Learn more at www.knauer.net*

Overcoming the Opioid Overdose Crisis

6

Sitting Down With... M-J Milloy, Research Scientist at the British Columbia Centre on Substance Use, and the Canopy Growth Professor of Cannabis Science, Department of Medicine, The University of British Columbia, Canada.

Tell us about your role as the University of British Columbia's inaugural Canopy Growth Professor of Cannabis Science. It's a privileged position: a professorship that supports research examining the potential of cannabis to address the opioid overdose crisis and other substance use disorders. The funding comes from arm's length gifts to the university from Canopy Growth - a licensed producer of cannabis - and the Government of BC's Ministry of Mental Health and Addictions. For a number of years, we've been focused on trying to better understand the opioidcannabis relationship. In particular, we hope to characterize the relationship between chronic pain, opioid use, and cannabis consumption. A large proportion of individuals in our society are living with chronic pain, and many are now dependent on high-risk opioid analgesics. This is a crucial factor behind the ongoing opioid overdose crisis.

How does that translate into your research?

Last year, we published the results of an observational study investigating the impact of cannabis use in over 800 participants with chronic pain and opioid use disorder, who were at high risk of overdose (1). The results revealed that people using cannabis at least once a day were significantly less likely to take illicit opioids on a daily basis. This study adds to a body of evidence suggesting that cannabis could have value for people living with substance use disorders. For example, participants administered CBD in a controlled trial had significantly lower rates of opioid cravings when presented with a visual cue (2). We're confident that our latest observational study provides valuable preliminary evidence, although we can't conclude a causal relationship just yet. However, given the urgency of the opioid crisis and the need to find better ways to provide care to these patients, we

cannot waste any time. More substantial trials are urgently needed.

What is the ultimate goal of this work? Unlike other molecules under clinical and therapeutic investigation, cannabis and cannabinoids are already "in the wild" in other words, people with substance use disorders are already using cannabis. In the first instance, I'm optimistic that our work will provide people living with substance use disorders, their care providers and families with some useful evidence to guide better self-medication. This is already a population that is tremendously stigmatized by society and often do not have strong relationships with the medical community. Ultimately, the aim is to provide the evidence doctors and patients need to determine whether cannabis could play a part in tackling what is the dominant public health crisis of our era.

Is cannabis a viable treatment for other conditions?

Recent reports by the National Academy of Science in the United States have added to the growing body of evidence that cannabis can be used as an analgesic; for years, survey after survey has reported that chronic pain is the most common target of self-medication and there are a number of hypothesized routes of action within the endocannabinoid system that could explain this phenomenon. Common sense suggests that there must be some analgesic action - how else can we explain the fact that a substantial proportion of chronic pain patients are able to reduce or eliminate opioids by adding cannabis to their regimen?

In addition to my research on pain and substance use disorders, I have also been supported by National Green BioMed Ltd., a local company seeking a license to produce medical cananbis, to study the potential therapeutic effects of cannabis for HIV patients, especially in the realm of HIV-associated pain. "The aim is to provide the evidence doctors and patients need to determine whether cannabis could play a part in tackling the dominant public health crisis of our era."

What's next on your agenda?

One important aspect of legalization in Canada was a series of reforms to the regulations surrounding the use of cannabis in scientific research studies; we're hopeful this will remove some of the "red tape" around studies on cannabis and clear the way for larger human trials. We will soon be recruiting patients for a series of controlled trials exploring the risks and benefits of cannabis use for those living with chronic pain or dependence.

References

- S Lake et al., "Frequency of cannabis and illicit opioid use among people who use drugs and report chronic pain: a longitudinal analysis", PLOS Medicine, 16, e1002967 (2019). DOI: 10.1371/journal.pmed.1002967
- YL Hurd et al., "Cannabidiol for the reduction of cue-induced craving and anxiety in drug-abstinent individuals with heroin use disorder: a double-blind randomized placebo-controlled trial", Am J Psychiatry, 176, 911–922 (2019). DOI: 10.1176/appi. ajp.2019.18101191

Cannabis and Hemp Rapidly expanding analytical fields



Agilent solutions are at the forefront of analytical screening efforts to accurately test medicinal and recreational cannabis, hemp, and cannabinoid products derived from these plants. States that have passed laws permitting usage of medicinal and recreational marijuana are now requiring rigorous testing to assure the safety and quality of retail products. State and forensic laboratories further need to authenticate hemp based on it potency.

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Pesticides and Mycotoxins

Potentially harmful pesticides may be present in cannabis crops and extracts. It is therefore crucial that analytical monitoring of pesticide levels in cannabis takes place in order to assure consumer safety and comply with regulatory standards.¹

Potency

Canada and U.S. states that have legalized the use of medicinal or recreational marijuana require cannabinoid quantitation for total potency and cannabidiol. In some U.S. States, other cannabinoids are also regulated. These include cannabinol(CBN) and cannabigerol(CGB). Hemp products must also be tested for total potency.2

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Heavy Metals

Contamination with heavy metals such as arsenic, lead, cadmium, and to human health. Cannabis products must therefore be rigorously tested to assure consumer safety. ^{3,4}

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Agilent

Agilent products and solutions are intended to be used for cannabis quality control and safety testing in laboratories where such use is permitted under state/country law. idues in Cannabis Smoke. Journal of Toxicology 378168, 2013 nnabinolds - A Complex Picture. Progress in the Chemistry of O b and Hg) Uptake by Plants through Phytoremediation. Internati

nabis: Microbes, Heavy Metals and Pesticides. Botany and Biotechnology 2017: 457-474

Terpenes

Terpenes contribute to the flavor and fragrance of cannabis. Terpenes have also been used as a means of more accurately identifying and characterzing cannabis cultivars.5,6



Microbial Testing

The presence of dangerous pathogens in cannabis poses a potential threat to consumers if those microbes synthesize toxigenic mycotoxins.



Residual Solvents

he plant may contain solvents used in the extraction process. Residual solvent testing is required to ensure these volatile chemicals do not exceed levels deemed to be harmful

Contact Agilent to learn more about our cannabis testing solutions. Visit: agilent.com/chem/cannabis