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CENTER FOR MEDICINAL CANNABIS RESEARCH

2022 CMCR SYMPOSIUM
MEDICINAL CANNABIS AND
CANNABINOID-BASED MEDICINE:
Progress, Policy, and Partnership

Virtual Symposium: **April 21st and 22nd, 2022, 8AM-12PM PDT**
Poster Session: **April 21, 2022, 12pm - 1PM PDT**
Registration information: **CMCRsymposium.ucsd.edu**

Welcome

The University of California Center for Medicinal Cannabis Research (CMCR) is delighted to welcome you to the 2022 CMCR Symposium on 'Medicinal Cannabis and Cannabinoid-Based Medicine: Progress, Policy, and Partnership.' Our two-day, virtual conference will provide in-depth discussion with leaders in the fields of basic and clinical science discovery and therapeutics, the changing landscape of the cannabis industry, and the outlook of the regulatory environment impacting this research. As cannabis, cannabinoids, and the endocannabinoid system continue to increase their footprint on scientific and societal landscape, this annual symposium will continue to facilitate a meaningful dialogue between academic researchers and other important stakeholders, including business leaders involved with the production and commercialization of cannabis products; state and national policymakers and regulators; public and private funding agencies; clinicians and consumers. And in that spirit, we are thrilled to launch the 2022 CMCR Symposium with the presentation of the CMCR Pioneer in Medicinal Cannabis Research Award to Dr. Daniele Piomelli and the CMCR Award for Advancing Cannabis and Cannabinoids as Therapeutics to Dr. Donald Abrams. Their contributions will set the stage for presentations of bench-to-bedside research in the cannabis space and explorations of how we can work together with the cannabis industry, cannabis consumers, policymakers and funding agencies to improve our ability to apply scientific methodologies to answer the very questions about cannabis that the public is asking and that science is leading us to. We are pleased that you can join us.

Igor Grant, MD
Director, CMCR

David J. Grelotti, MD
Scientific Chair, 2022 CMCR Symposium

About

Overview

Established in 2000, the UC Center for Medicinal Cannabis Research (CMCR) has been at the forefront of advancing science and policy relating to the potential clinical benefits, and limitations, of cannabis and cannabinoids as medicine. The CMCR has conducted key studies regarding the short-term benefits of cannabis for the treatment of neuropathic pain and spasticity, and currently has an active, on-going program of research. Over the years the Center has established close and productive relationships with key Federal and State agencies, has significantly impacted policy, and remains a national leader in the field.

Mission

The mission of the Center for Medicinal Cannabis Research (CMCR) is to accelerate high quality scientific studies intended to ascertain the medical safety and efficacy of cannabis and cannabinoid products and examine alternative forms of administration. More broadly, the CMCR is concerned with the health effects of cannabis. This includes advancing cannabinoid science via the awarding of grant funding, establishment of data and sample repositories, and facilitating assessment and laboratory harmonization. The Center aims to be a model resource for health policy planning by virtue of its close collaboration with federal, state, and academic entities, as well as to act as a conduit for educating medical professionals and the public regarding the responsible use of cannabis/cannabinoids as medicine.

Sponsors

The CMCR wishes to acknowledge the following for support of our work, including the objectives of this Symposium.

State of California
National Institutes of Health
Wholistic Research and Education Foundation
UC San Diego
Greenwich Biosciences
and our multiple individual supporters

8:00am - 8:05am

Welcome from the CMCR Director
Igor Grant, MD
Distinguished Professor of Psychiatry, UC San Diego
Director, Center for Medicinal Cannabis Research

8:05am - 8:40am

2022 CMCR Pioneer in Medicinal Cannabis Research Award
Presentation of Award and Keynote Address
This award honors leaders in cannabis and cannabinoid research conducting basic and translational research of cannabinoids, other constituents of cannabis, and the endocannabinoid system. The recipient's work has led to significant advancements in our understanding of the mechanism and physiological effects of cannabinoids and related compounds. For groundbreaking discoveries related to the endocannabinoid system, the 2022 CMCR Pioneer in Medicinal Cannabis Research Award is awarded to:

Daniele Piomelli, PhD, MD (hon)
Distinguished Professor, Anatomy & Neurobiology, UC Irvine School of Medicine,
Louise Turner Arnold Chair in Neurosciences, UC Irvine
Trekking on the Endocannabinoid Trail
The pioneering work of Dr. Piomelli brought clarity to the complexity of the endocannabinoid system and its relevance to health and disease. In addition to his scientific discoveries, the scientific community and our society in general have greatly benefited from his leadership.

8:40am - 9:15am

2022 CMCR Award for Advancing Cannabis and Cannabinoids as Therapeutics
Presentation of Award and Keynote Address
This award honors those whose work has led to significant changes in our knowledge of or an expansion to the therapeutic use of cannabis and cannabinoid-based medicines. Recipients come from a diverse array of backgrounds, including drug development, medicine, public policy, and advocacy. For advancing clinical trial work in integrative medicine, the 2022 CMCR Award for Advancing Cannabis and Cannabinoids as Therapeutics is awarded to:

Donald Abrams, MD
Professor of Clinical Medicine, UCSF
Conducting Clinical Cannabis Research Tribulations and Trials
The pioneering work of Dr. Abrams bridged anecdotal accounts of the benefits of medicinal cannabis with the best practices in clinical research and clinical medicine. As a result, Dr. Abrams expanded options to alleviate the suffering of those from complex medical conditions.

9:15am - 9:20am - **5-minute break**

Moderated panel discussion and Q&A
2022 CMCR Symposium Award Recipients and Previous Award Recipients

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9:20am - 9:55am
Moderator:

Igor Grant, MD
Distinguished Professor of Psychiatry, UC San Diego
Director, Center for Medicinal Cannabis Research

Panelists:
Daniele Piomelli, PhD, MD (hon)
2021 Recipient of the CMCR Pioneer in Medicinal Cannabis Research Award
Donald Abrams, MD
2021 Recipient of the CMCR Award for Advancing Cannabis and Cannabinoids as Therapeutics
Raphael Mechoulam, PhD
2019 Recipient of the CMCR Pioneer in Medicinal Cannabis Research Award
Geoffrey Guy, MD
2019 Recipient of the CMCR Award for Advancing Cannabis and Cannabinoids as Therapeutics

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9:55am - 10:00am - **5-minute break**

CMCR Special Lecture

10:00am - 10:20am
Raphael Mechoulam, PhD

Professor of Medicinal Chemistry, Hebrew University of Jerusalem
Endogenous Anandamide-like Compounds

10:20am - 10:30am

Q&A with Dr. Mechoulam, PhD
Moderator:

Igor Grant, MD
Distinguished Professor of Psychiatry, UC San Diego
Director, Center for Medicinal Cannabis Research

Moderated panel discussion and Q&A:
Update on Federal Activities Affecting Cannabis Research

10:30am -11:50am

Moderator:

    Steve Gust, PhD
    Advisor to Center for Medicinal Cannabis Research

Panelists:
The invited federal stakeholders will discuss future directions in regulatory policy related to medicinal cannabis, funding for medicinal cannabis research, and access to cannabis and cannabanoids for research purposes.

Trelaine Ito, MS
Deputy Appropriations Director and Legislative Assistant
Office of U.S. Senator Brian Schatz (D-HI)
Congressional Actions Related to Cannabis Affecting Research

David Shurtleff, PhD
National Center on Complementary and Integrative Health (NCCIH), NIH
Cannabinoid Research at NIH

Cassandra Taylor, PhD
Chemist, Botanical Review Team
Office of Pharmaceutical Quality, Center for Drug Evaluation and Research, FDA
FDA Role in Regulation of Cannabis

Richard (Rik) Kline, PhD
Chief, Chemistry and Pharmaceutics Branch, NIDA
Role of the NIDA Drug Supply Program in providing cannabis products for research

Reflections on the Session and Introduction to the Poster Session

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11:50am - 11:55am

Igor Grant, MD
Distinguished Professor of Psychiatry, UC San Diego
Director, Center for Medicinal Cannabis Research

David J. Grelotti, MD
Associate Professor of Psychiatry, UC San Diego
Scientific Chair, 2022 CMCR Symposium

11:55am - 12:00pm - **5-minute break**

12:00pm - 1:00pm

2022 Poster Session
Breakout Rooms

CMCR Special Lectures
Neuroprotective Effects of Cannabinoids: Evidence from PTSD

8:00am - 8:15am
Leah Mayo, PhD
Assistant Professor, Centre for Social and Affective Neuroscience, Linköping University
Protective Effects of Elevated Anandamide During Stress Exposure

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8:15am - 8:30am
Christine Rabinak, PhD
Associate Professor, Department of Pharmacy Practice, Wayne State University
Cannabinoid Modulation of Corticolimbic Activation to Threat

8:30am - 8:45am
Marcel Bonn-Miller, PhD
Assistant Professor, Department of Psychiatry, University of Pennsylvania
Smoked Cannabis and PTSD

8:45am - 8:55am
Q&A with Dr. Mayo, Dr. Rabinak and Dr. Bonn-Miller
Moderator:
> **Arpi Minassian, PhD**
> Clinical Professor of Psychiatry, Chief, Psychiatry Embedded Services

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8:55am - 9:00am - **5-minute break**

CMCR Special Lectures
Cannabinoids and COVID-19

9:00am - 9:15am
Michelle Sexton, ND
Adjunct Assistant Professor of Anesthesiology, UC San Diego
Cannabis and COVID-19 Infection

9:15am - 9:30am
José Alexandre S. Crippa, MD, PhD
Professor of Neuroscience and Behavior, Ribeirão Preto School of Medicine, University of São Paulo
Cannabidiol (CBD) and COVID-19

9:30am - 9:40am
Q&A with Dr. Sexton and Dr. Crippa
Moderator:
> **Ajay Bharti, MD**

CMCR Special Lecture
FAAH inhibitor in the Treatment of Cannabis Use Disorder

9:40am - 9:55am

Deepak D'Souza, MD
Professor of Psychiatry, Yale University School of Medicine
Blunting Cannabis Use Disorder by Targeting the Endocannabinoid System

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9:55am - 10:00am

Q&A with Dr. D'Souza
Moderator:
> **Giordano De Guglielmo, PharmD, PhD**
> Assistant Professor, UC San Diego

10:00am - 10:05am - **5-minute break**

Moderated panel discussion and Q&A:
Promoting Industry and University Partnership to Enhance Cannabis Research

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10:05am - 10:55am

Moderator:
> **Igor Grant, MD**
> Distinguished Professor of Psychiatry, UC San Diego
> Director, Center for Medicinal Cannabis Research

Panelists:
Panelists will be invited to discuss partnerships between universities and the cannabis industry, providing models and exploring synergies.

Mahmoud ElSohly, PhD
Professor of Pharmaceutics and Drug Delivery, School of Pharmacy, University of Mississippi (UM),
Director of the National Institute on Drug Abuse (NIDA) Marijuana Project

Josh Hoerner, PhD
General Manager of Purisys LLC, Vice President and Head of Noramco R&D
Purisys LLC, Noramco LLC

Mark A. Ware BA MBBS MRCP MSc ICD.D
Chief Medical Officer, Canopy Growth Corporation

10:55am - 11:00am - **5-minute break**

Moderated panel discussion and Q&A:
Early Experience of Federally Licensed Growers

11:00am - 11:45am

Moderator:

Tom Marcotte, PhD
Professor of Psychiatry, UC San Diego
Co-Director, Center for Medicinal Cannabis Research

Panelists:
Representatives from DEA-licensed cannabis growers will discuss their early experience and future goals to produce cannabis and cannabinoid-based products for research.

Justin Abril
Chief Operating Officer, Royal Emerald Pharmaceuticals
Steve Groff, MD
Founder and Chief Medical Officer, Groff North America, LLC
George Hodgin, MBA
Founder and Chief Executive Officer, Biopharmaceutical Research Company (BRC)
Sue Sisley, MD
President of Scottsdale Research Institute/Field to Healed Foundation

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11:45am - 12:00pm

Closing Remarks from the CMCR Director
Igor Grant, MD
Distinguished Professor of Psychiatry, UC San Diego
Director, Center for Medicinal Cannabis Research

Daniele Piomelli, PhD, MD (hon)
Distinguished Professor
UC Irvine

THE CENTER FOR MEDICINAL CANNABIS RESEARCH
at the University of California San Diego

presents this award for
Pioneer in Medicinal Cannabis Research Award to:

Daniele Piomelli, PhD, MD (h.c.)

For groundbreaking discoveries related to the endocannabinoid system.

The pioneering work of Dr. Piomelli brought clarity to the complexity of the endocannabinoid system and its relevance to health and disease. In addition to his scientific discoveries, the scientific community and our society in general have greatly benefited from his leadership.

April 21, 2022

Dr. Piomelli studied pharmacology and neuroscience with James Schwartz and Eric Kandel at Columbia University (1983-1988), and with Paul Greengard at the Rockefeller University (1988-1990). In 2000, Kandel and Greengard were awarded the Nobel Prize for contributions to physiology and medicine. After working at the INSERM in Paris and at the Neurosciences Institute in San Diego, with Nobel Laureate Gerald Edelman, Daniele joined the University of California, Irvine, where he is now Louise Turner Arnold Chair in Neurosciences and Distinguished Professor of Anatomy and Neurobiology. Daniele is an author of 415 peer-reviewed articles in journals such as Nature, Science, Nature Medicine, PNAS and Nature Neuroscience, three full-length books, and 34 patents. He founded the department of drug discovery and development at the Italian Institute of Technology in Genoa (Italy), which he directed from 2007 to 2016, and three biopharmaceutical start-ups based on discoveries made in his lab. Since 2018, Daniele serves as Editor-in-Chief of Cannabis and Cannabinoid Research, the only peer-reviewed journal dedicated to the study of cannabis, its derivatives, and their endogenous counterparts in the human body. He directs the NIDA Center of Excellence ICAL (Impact of Cannabinoids Across the Lifespan) and UCI's Center for the Study of Cannabis.

Donald I. Abrams, MD
Professor Emeritus of Medicine
UC San Francisco

THE CENTER FOR MEDICINAL CANNABIS RESEARCH
at the University of California San Diego

presents this award for
Advancing Cannabis and Cannabinoids as Therapeutics to:

Donald Abrams, MD

For advancing clinical trial work in integrative medicine.

The pioneering work of Dr. Abrams bridged anecdotal accounts of the benefits of medicinal cannabis with the best practices in clinical research and clinical medicine. As a result, Dr. Abrams expanded options to alleviate the suffering of those from complex medical conditions.

April 21, 2022

Donald I. Abrams, MD is Professor Emeritus of Medicine at the University of California San Francisco. He received an A.B. in Molecular Biology from Brown University and his MD from the Stanford University School of Medicine. After completing an Internal Medicine residency at the Kaiser Foundation Hospital in San Francisco, he became a fellow in Hematology/Oncology at the University of California San Francisco in 1980 as the AIDS epidemic was emerging. He was one the original clinician/investigators to recognize and define many early AIDS-related conditions at San Francisco General Hospital where he also served as chief of Hematology-Oncology for 14 years. Long interested in clinical trials of complementary and alternative medicine interventions for HIV/AIDS and cancer, he received funding from the National Institute on Drug Abuse to conduct a study of the short-term safety of cannabinoids in HIV infection in 1997. Subsequently he received grants from the University of California Center for Medicinal Cannabis Research to complete a placebo-controlled trial of cannabis in patients with HIV-related peripheral neuropathy as well as a study evaluating vaporization as a smokeless delivery system. He conducted NIH-funded trials investigating the pharmacokinetic interaction between cannabis and opioid analgesics in chronic pain and cannabis in patients with sickle cell pain. He was a member of the National Academies of Sciences, Engineering and Medicine's committee that published The Health Effects of Cannabis and Cannabinoids: Current State of Evidence and Recommendations for Research in January 2017.

Raphael Mechoulam, PhD
Professor of Medicinal Chemistry
Hebrew University, Medical Faculty, Institute for Drug Research
Ein Kerem campus, Jerusalem

Dr. Mechoulam was born in Sofia, Bulgaria in 1930. RM went to an American Grade School in Sofia for 4 years until it was closed by the pro-German government. Dr. Mechoulam immigrated to Israel in 1949. He studied biochemistry at the Hebrew University in Jerusalem (M.Sc.) and the Weizmann Institute in Rehovot (Ph.D.) He spent a year in New York, at the Rockefeller Institute and returned to the Weizmann Institute in 1960. He worked on the chemistry of various natural products. In 1966 he moved to the Hebrew University, where he became a full professor in 1972. From 1979 to 1982 he was Rector (Academic Head) of the Hebrew University. His work has been mostly on the chemistry of natural products, the best known being on cannabinoids. In collaboration with numerous colleagues in Israel and abroad he has also published in pharmacology and on clinical trials. He has published about 470 scientific papers and has received numerous national and international prizes, including the Israel Prize – the most prestigious Israeli Prize – as well as a prize from the US National Institutes of Health. He is a member of the Israel Academy of Sciences. He married Dalia (born Borovitch) in 1955 and they have 3 children, Roy, a professor of mathematics at the Technion in Haifa, Hadas, an M.D. ophtalmologist and Dafna, an M.D. pediatric neurologist.

Geoffrey Guy, MBBS LRCP MRCS LMSSA Dip Pharm Med BSc DSc

With over 30 years of experience in medical research and global drug development, Dr. Geoffrey Guy is the founder of GW Pharmaceuticals and has served as its Chairman since 1998. Dr. Guy holds a BSc. in pharmacology from the University of London, an MBBS at St. Bartholomew's Hospital, an MRCS Eng. and LRCP London, an LMSSA Society of Apothecaries and a Diploma of Pharmaceutical Medicine from the Royal Colleges of Physicians. Geoffrey founded the drug delivery company Ethical Holdings plc in 1985 (now called Amarin Corporation plc). As Chairman and Chief Executive, he led the company to its NASDAQ listing in 1993. He also founded Phytopharm plc in 1989, of which he was Chairman until 1997. Geoffrey has been the physician in charge of over 200 clinical studies, including those determining the first dose of clinical trial drugs in man; pharmacokinetics, pharmacodynamics, dose-ranging and controlled clinical trials; and large-scale, multi-centred studies and clinical surveys. He is also an author on numerous scientific publications and has contributed to six books.Geoffrey was appointed as Visiting Professor in the School of Science and Medicine at the University of Buckingham in July 2011. He received the Deloitte Director of the Year Award in Pharmaceuticals and Healthcare in 2011, was appointed Visiting Professor at the University of Westminster in 2016 and was awarded an honorary DSc from the University of Reading in 2016.

Igor Grant, MD, FRCP(C)
Distinguished Professor of Psychiatry
Director Center for Medicinal Cannabis Research
UC San Diego

Igor Grant, MD, FRCP(C) is Mary Gilman Marston Distinguished Professor of the Department of Psychiatry at the University of California, San Diego School of Medicine. Since 2000, Dr. Grant has been Director of the State of California funded Center for Medicinal Cannabis Research (CMCR). He is also the Director of the HIV Neurobehavioral Research Program (HNRP), which encompasses a broad range of interdisciplinary HIV studies including the California NeuroAIDS Tissue Network (CNTN), the HIV Neurobehavioral Research Center (HNRC), and the CNS HIV Antiretroviral Therapy Effects Research (CHARTER). Dr. Grant is the founding Editor of the Journal of the International Neuropsychological Society and founding co-editor of the journal AIDS and Behavior.

Justin Abril
Chief Operating Officer
Royal Emerald Pharmaceuticals

Justin Abril is a 10-year veteran of law enforcement at the local, state and federal levels. He started his career in 2009 when he became the youngest Federal Police Officer for the Marine Corps Civilian Law Enforcement Program at Camp Pendleton. During this time, Mr. Abril held positions in both field training and first line supervision, overseeing the day-to-day operations of over 60 military and federal law enforcement personnel. Mr. Abril joined Royal Emerald Pharmaceuticals in 2019 as Chief Compliance Officer and developed, implemented, and assessed an effective compliance program to ensure all local, state, and federal laws were followed. Mr. Abril is now a Director and Chief Operating Officer for the company. "My experiences as a first responder to military and civilian populations gives me a clear perspective of the trauma that we all face and the problems that result. I'm excited to work at Royal Emerald Pharmaceuticals and confident that our research and development of pharmaceuticals will provide help to veterans and first responders who are experiencing the aftereffects of their exposure to traumatic incidents."

JH Atkinson, MD
Professor of Psychiatry (Emeritus)
Co-Director, Center for Medicinal Cannabis Research
UC San Diego

JH Atkinson, MD, is Professor of Psychiatry (Emeritus) at the University of California, San Diego. Since 2000 he has been a Co-Director of the Center for Medicinal Cannabis Research (CMCR). His research interests involving pharmacological and cognitive behavioral treatment of chronic pain, and neuropsychiatry aspects of HIV,

have produced over 250 peer-reviewed publications.

Ajay Bharti, MD
Associate Professor of Medicine
UC San Diego

Ajay Bharti, MD, is a board-certified infectious disease specialist who cares for patients with all types of infections or diseases caused by viruses, bacteria, fungi and parasites. He is part of the COVID-19 Telemedicine Clinic, which offers video visits and telephone consults for patients with mild to moderate COVID-19.He also treats people with hepatitis viruses, tuberculosis, influenza, and HIV/AIDS, as well as infections of the sinuses, heart, brain, lungs, gastrointestinal system, urinary tract, pelvic organs and bones. Dr. Bharti also has expertise in tropical infectious diseases. An associate professor of medicine at UC San Diego School of Medicine, Dr. Bharti instructs medical students, residents and fellows. His research interests include correlates of HIV and malaria co-infection and neurocognitive functioning in HIV-infected individuals. His research projects have received funding from the National Institutes of Health (NIH)/ National Institute of Allergy and Infectious Diseases (NIAID) and NIH/National Institute of Mental Health (NIMH). Currently, Dr. Bharti is leading a NIH/ National Institute on Drug Abuse (NIDA)-funded study examining the impact of HCV therapy on central nervous system outcomes.Dr. Bharti has coauthored many articles and his work has appeared in journals such as Journal of Acquired Immune Deficiency Syndromes and The American Journal of Tropical Medicine and Hygiene, among others. He completed infectious diseases fellowships at University of Texas Medical Branch and UC San Diego School of Medicine and an internal medicine residency at The Mercy Hospital of Pittsburgh. Dr. Bharti earned his medical degree from Jawaharlal Institute of Postgraduate Medical Education & Research in India. He is board certified in internal medicine and infectious disease. Dr. Bharti is a member of numerous professional organizations, including the American Society of Tropical Medicine & Hygiene, the American College of Physicians, the International Society for Neurovirology, the International AIDS Society and the Medical Council of India.

Marcel Bonn-Miller, PhD
VP, Human and Animal Research
Canopy Growth Corporation

Dr. Bonn-Miller earned a BA in psychology and PhD in clinical psychology from the University of Vermont. Dr. Bonn-Miller began his career at the Department of Veterans Affairs, where he held national positions at the Center of Excellence for Substance Abuse Treatment and Education and National Center for PTSD. After almost a decade within the VA, Dr. Bonn-Miller left to take a position at Zynerba Pharmaceuticals where he served as Director of Cannabinoid Research. After 3 years of work with Zynerba Pharmaceuticals, Dr. Bonn-Miller joined Canopy Growth Corporation where he currently

serves as Vice President, Human and Animal Research. Widely considered one of the early and leading research pioneers in the field of cannabis and mental health, Dr. Bonn-Miller has conducted seminal work on the interrelations between cannabis and a range of health conditions, including pain, anxiety, HIV, PTSD, and sleep disorders. Dr. Bonn-Miller brings a unique and diverse perspective to cannabinoid therapeutics, having worked within medical center and academic settings for over a decade and with industry for the past 6 years. He serves on the editorial boards of several scientific journals, has published over 150 peer-reviewed empirical publications on cannabis.

José Alexandre S. Crippa, MD, PhD
Professor
University of São Paulo (USP), Ribeirão Preto,
São Paulo, Brazil

Prof. Dr. José A Crippa is currently a Full Professor and was the Head (2017-2019) of the Department of Neurosciences and Behavior, Faculty of Medicine, University of São Paulo (USP), Ribeirão Preto, São Paulo, Brazil. He is also a Cannabinoid Pharma Consultant with Global Experience in Pharmaceutical Drug Development. Dr Crippa was a Honorary Visiting Lecturer at the Institute of Psychiatry, King's College London, UK (2009-2012). He is now the Co-Director of the Brazilian Cannabinoid Research Center. He is co-inventor of licensed patents and has served as a consultant to several large corporate and academic research programs internationally. He is a member and one of the founders of the National Institute for Translational Medicine (NITM) consortium. He was also invited by Uruguay's Presidential Office to join an international committee for the evaluation of documents regulating their legalization of marijuana and is currently a member of the international advisory board of The Australian Centre for Cannabinoid Clinical and Research Excellence (ACRE). I've been recognized by ExpertScape as the 1st top-rated expert in Cannabidiol in the world during the years 2011-2021. Dr Crippa accepted the International Association of Cannabinoid Medicines' (IACM) award for major contributions to cannabinoid clinical research in Berlin 2019.

Deepak D'Souza, MD
Professor
Yale University School of Medicine

Deepak Cyril D'Souza, MD is a Professor of Psychiatry, Yale University School of Medicine and a staff psychiatrist at VA Connecticut Healthcare System (VACHS). He received his medical degree from John's National Academy of Health Sciences, Bangalore, India in 1986 and completed his psychiatric residency at State University of New York Downstate in 1992 followed by a postdoctoral fellowship in Psychopharmacology and Neurosciences at Yale University School of Medicine. He joined the faculty in the Dept. of Psychiatry at Yale and VA Connecticut Healthcare System. He is an active clinician, teacher and researcher, with almost 25 years of experience. He directs the Neuropsychiatry Program at VA Connecticut, the clinical service that cares

for veterans with serious mental illnesses. He is actively involved in teaching residents. In recognition of his contributions as a teacher, he received the Yale Psychiatry resident's teaching award in 2008. He also directs the VA Schizophrenia Research Fellowship program which has contributed to the development of several promising researchers. He directs the Schizophrenia Neuropharmacology Research Group at Yale (SNRGY). His research includes three approaches. First, he has been using psychopharmacological probes such as ketamine, amphetamine, THC to evaluate the contributions of various neurotransmitter systems to the pathophysiology of psychosis, cognitive deficits, and reward processing. Second, he conducts clinical phase 1 to phase 4 trials in schizophrenia, MDD and cannabis dependence to develop new treatments. Finally, he is using neuroreceptor imaging (PET and previously SPECT) to study schizophrenia and cannabis dependence. His research is funded by the U.S. National Institute of Drug Abuse, the National Institute of Mental Health, the National Institute of Alcoholism and Alcohol Abuse, VA R&D and several foundations. His work has been published in the highest impact Psychiatry journals including Molecular Psychiatry, Biological Psychiatry, American Journal of Psychiatry and Neuropsychopharmacology. He is recognized as a leading expert on the relationship between cannabinoids and psychosis.

Giordano de Guglielmo, PharmD, PhD
Assistant Professor
UC San Diego

Dr. de Guglielmo has been working in the field of drug addiction for 15 years. He has contributed to the development of unique experimental methodologies to investigate the neurobiological basis of drug dependence and identify novel effective pharmacotherapies for alcohol, nicotine, cocaine and opioid addiction. Recently he has identified and characterized a neuronal ensemble in the brain that controls alcohol drinking in dependent subjects. He is currently an Assistant Professor in the Department of Psychiatry at UCSD. His present scientific work is focused on interactions between neurocircuits that modulate pain and addiction. In 2019, Dr. de Guglielmo has received a CMCR Pilot Grant to investigate the effects of CBD treatment on alcohol dependence. Dr. de Guglielmo has published over 50 research papers in high-quality journals, including Nature Communications, PNAS, Biological Psychiatry, Neuropsychopharmacology, and Journal of Neuroscience.

Mahmoud A. ElSohly, PhD
Research Professor, National Center for Natural Products Research
Professor of Pharmaceutics and Drug Delivery, School of Pharmacy,
University of Mississippi (UM)
Director of the National Institute on Drug Abuse (NIDA) Marijuana Project

Dr. ElSohly has been at UM since 1975 and in 1985 he started a private laboratory ElSohly Labs, Inc. (ELI) in Oxford, MS, which is an analytical laboratory specializing in providing drug testing services to the industry and also a product development laboratory with a successful SBIR and STTR funding. In 2002 ELI received the National Tibbetts

Award for outstanding contributions to the SBIR Program. Dr. ElSohly is board certified by the American Board of Forensic Examiners and the American Board of Forensic Medicine, and ELI is certified by (DHHS) and the College of American Pathologists since 1988. Dr. ElSohly has been active in NIH funding over the years with over 1.5 million dollars/year. He authored or coauthored over 400 peer-reviewed publications and over 30 patents. In 2011 Dr. ElSohly received the University of Pittsburgh's Legacy Laureate Award, in 2013 the UM Research and Creative Achievement Award and the (ICRS), Life time Achievement Award, and in 2016 the Alexander O. Gettler Award from the (AAFS).

David J. Grelotti, MD
Associate Professor of Psychiatry, UC San Diego
Scientific Chair, 2022 CMCR Symposium

Dr. Grelotti is an Associate Professor of Psychiatry and the Medical Director of the Center for Medicinal Cannabis Research (CMCR) at the University of California San Diego. An adult and child psychiatrist, he graduated from medical school at the Johns Hopkins University School of Medicine and completed residency and fellowship training at Harvard Medical School. With colleagues at the CMCR, he is conducting studies of cannabis, cannabinoids, and the endocannabinoid system in a variety of health conditions and on driving.

Steve Groff, MD
Founder, Chief Medical Officer
Groff North America, LLC

Steve served his community for nearly 20 years as an Orthopedic Surgeon. During his career in medicine, he served as President of KDV Orthopedics and led a large multi-organization merger to form OSS, a vital healthcare entity in South Central Pennsylvania. He served three terms as President of OSS Health System and was founding Chairman of the ambulatory surgical center. Following a successful career in medicine, Steve founded Wyndridge Farm in 2014 which serves as a restaurant, wedding and corporate event venue, and beverage manufacturer in York County, PA. Since Q4 2018, Steve has founded three new companies: Groff North America, Groff Health, and Groff NA Hemplex. "Groff North America serves as a comprehensive hemp-cannabis refinery, extraction, purification, and formulation facility. Our diverse team of experts leads the way in research and production of raw materials from all aspects of the cannabis plant." – Steve Groff, M.D.

Steve Gust, PhD
Advisor to Center for Medicinal Cannabis Research

Dr. Gust is currently an advisor to CMCR. He has recently retired from the National Institute on Drug Abuse where he had over 30 years of experience developing and managing research programs on drug abuse and addiction, including over 20 years of managing the USG cannabis research and production programs. He has developed an extensive knowledge of the regulatory requirements for conducting research on cannabis and its constituents, including experience with the DEA and FDA. He also chaired the NIDA Cannabis Science Interest group and represented the Institute to many governmental and non-governmental organizations.

George Hodgin, MBA
CEO and Founder
Biopharmaceutical Research Company (BRC)

George Hodgin is the Founder and CEO of Biopharmaceutical Research Company (BRC), a US-based specialty pharmaceutical cannabis company. BRC does not violate federal law and is licensed by the US DEA to produce, research, analyze, import and distribute cannabis products. BRC is one of the first federally licensed cannabis companies working within the US DEA and FDA frameworks for pharmaceutical drug development. He is a former Navy SEAL officer and alumnus of the Stanford University Graduate School of Business. He was commissioned as an officer in the Navy in 2009, after earning a BA in Economics and Mandarin from the University of North Carolina at Chapel Hill, where he was a Morehead-Cain scholar. George led SEALs in combat in counter-terrorism operations in Afghanistan and Southeast Asia. His hobbies include fly-fishing and hiking with his family and dog. He and his wife and two sons live in Carmel Valley, California.

Josh Hoerner, PhD
General Manager of Purisys LLC, Vice President and Head of Noramco R&D
Purisys LLC, Noramco LLC

Josh Hoerner is the General Manager of Purisys, LLC (a subsidiary of Noramco LLC) and heads all operations for the business unit. Josh also serves as the Vice President and Head of Noramco R&D. During his tenure at Noramco over the last 9 years, Josh has held a variety of technical and business roles, significantly expanding Noramco's product portfolio and modernizing its key manufacturing technologies. Josh co-led the formation of Purisys LLC, which is a market leader in small volume customer synthesis as well as being a specialized pharmaceutical cannabinoid and psychedelic manufacturer. Prior to working at Noramco, Josh served as a Principal Scientist at Merck & Co., where

he was responsible for integrated product development and lifecycle management strategy of Boceprevir, Zontivity, and Liptruzet. Josh holds a B.S. in Chemistry from Hobart College and Ph.D. in Chemistry from the University of Massachusetts Amherst.

Trelaine Ito, MS
Deputy Appropriations Director and Legislative Assistant
Office of U.S. Senator Brian Schatz (D-HI)

Trelaine Ito is the Deputy Appropriations Director and Legislative Assistant for U.S. Senator Brian Schatz (D-HI). He is the policy lead on judiciary issues, focusing on drug reform, criminal justice and prison reform, and civil rights. Senator Schatz has been a champion of streamlining the research approval process for marijuana research, as well as ensuring access to medical marijuana for veterans in states where it is legal. Trelaine is also the policy lead on the education and census portfolios. He received his master's in Justice, Law and Society with a concentration in Social Thought and Jurisprudence from American University; and his bachelor's in Ethics, Society, and Law, and Politics and Government from Pacific University. Trelaine currently serves as the co-chair of GLASS, the Senate LGBTQ+ staff association.

Richard (Rik) Kline, PhD
Chief, Chemistry and Pharmaceutics Branch, NIDA
Role of the NIDA Drug Supply Program in providing cannabis products for research

Tom Marcotte, PhD
Professor of Psychiatry
Co-Director
Center for Medicinal Cannabis Research, UC San Diego

Dr. Marcotte is Professor of Psychiatry at the University of California, San Diego, and Co-Director of the Center for Medicinal Cannabis Research at UC San Diego (www.cmcr.ucsd.edu), which has conducted clinical trials of cannabis for almost 20 years, and has an active, ongoing portfolio exploring the effects of cannabinoids (plant-based, synthetic) in various medical/psychiatric conditions. He is the principal investigator (PI) on studies of the effects of acute cannabis use, and cannabis and alcohol use, on driving performance, and has also been the PI on numerous HIV studies evaluating the impact of HIV-associated neurocognitive disorders on real-world functioning, including driving. He serves on a number of impaired-driving task forces, and previously was on the editorial boards of Neuropsychology and the Journal of the International Neuropsychological Society. He is currently the PI on a study addressing cannabis for the treatment of pain, and has previously been co-investigator on cannabis studies examining pain, and spasticity in multiple sclerosis.

Leah Mayo, PhD
Assistant Professor
Center for Social and Affective Neuroscience, Linköping University

Leah Mayo received her PhD in Neurobiology from the University of Chicago in 2015. She completed her postdoctoral fellowship at the Center for Social and Affective Neuroscience at Linköping University in Sweden, where she then established her independent research group in 2020. A primary focus of her work has been exploring the role of the endocannabinoid system in stress- and fear-related behaviors in humans, in an effort to identify novel pharmacotherapeutic strategies for stress-related disorders such as post-traumatic stress disorder and substance use disorders. She has recently received early career awards from the European Behavioral Pharmacology Society and the Society Social for Social Neuroscience, as well as recognition from the Society for Biological Psychiatry (Somerfeld-Ziskind Research Award) and the Brain and Behavior Foundation (NARSAD Young Investigator Award). Her research is currently funded by an establishment grant from the Swedish Research Council.

Arpi Minassian, PhD
Clinical Professor of Psychiatry
Chief, Psychiatry Embedded Services

Dr. Minassian's research program is focused upon understanding the relationship between biology and behavior in mental illness, medical illness, and substance abuse. Much of her research has implemented physiological and cognitive paradigms to understand brain dysfunction in psychiatric populations such as bipolar disorder, schizophrenia, PTSD, and substance addiction as well as neuromedical conditions such as HIV. The methodologies she has helped develop and implement can be translated to animals, an application which accelerates our understanding of biological mechanisms. She serves as Principal Investigator on an NIH-funded R01 grant where she and her colleagues are studying the effects of cannabis use on cognition and endocannabinoids in people with HIV. She is also a co-investigator on a number of NIH-funded studies of cognitive deficits in bipolar disorder, HIV, and substance use. Dr. Minassian is a clinical psychologist and an attending clinician in the UC San Diego Health System. Her clinical area of expertise is consultation-liaison and she oversees psychological services at the Burn Center, the Pulmonary Rehabilitation Program, and others. She is co-Chair of the department's Diversity Committee and also serves on university- and hospital-wide diversity focus groups.

Christine A. Rabinak, PhD
Associate Professor
Wayne State University

Dr Rabinak is an Associate Professor in the Departments of Pharmacy Practice, Psychiatry & Behavioral Neurosciences, Pharmaceutical Sciences, the Translational Neuroscience Program, and the Merrill Palmer Skillman Institute and the Director of the Translational Neuropsychopharmacology Lab (www.tnp2lab.org) at Wayne State University. My research objectives are built on the state-of-the-science formulation that posttraumatic stress disorder (PTSD) is driven partly by ineffective fear extinction, and that treatments can be more effective if fear extinction and/or its retention are facilitated. We are currently investigating the endocannabinoid system in the brain as a potential pharmacological target for improving the learning that goes on in therapy and perhaps increasing efficacy and durability of exposure therapy in treating PTSD (e.g. shortening treatment while strengthening and prolonging gains).

Michelle Sexton, ND
Medical Staff Professional, Center for Integrative Medicine
UC San Diego

Dr. Sexton is a Naturopathic Doctor, graduated from Bastyr University in Seattle, WA. She completed pre- and post-doctoral fellowships at the University of Washington, formally studying the endocannabinoid system. Her NIH-funded pre-doctoral and postdoctoral research investigated cannabis use and cannabinoid impact on neuroinflammation and neurodegeneration. She has continued research into health effects of cannabis at UCSD as Assistant Adjunct Professor in the Department of Anesthesiology. She is currently affiliated with the Center for Integrative Medicine at UCSD. Dr. Sexton's clinical practice, research and teaching focus on the endocannabinoid system and roles in integrative medicine across the lifespan. Dr. Sexton has presented her research internationally and published 24 papers in peer-reviewed journals. She is a member of the International Cannabinoid Research Society, the International Association of Cannabinoid Medicine the California Naturopathic Doctors Association, and the American Association of Naturopathic Doctors. She maintains a private medical practice in San Diego, CA. When not caring for patients or pursuing research activities, you can find her in the garden, paying music, playing with grandchildren, swimming or riding her bike to the beach for a surf session!

David Shurtleff, PhD
National Center on Complementary and Integrative Health (NCCIH), NIH
Cannabis and cannabinoid research at NIH

David Shurtleff, Ph.D., is Deputy Director of the National Center for

Complementary and Integrative Health (NCCIH) at the National Institutes of Health (NIH), the leading Federal agency for research on integrative and complementary health practices. Dr. Shurtleff is also the Acting Scientific Director and Acting Chief for both the Clinical Investigations Branch and the Pain and Integrative Neuroscience Branch, Division of Intramural Research. He served as Acting Director of NCCIH from October 2017 to November 2018.

Sue Sisley, MD
President of Scottsdale Research Institute/Field to Healed Foundation

Dr. Sisley is President of Scottsdale Research Institute & best know serving as Principal Investigator for the only FDA-approved randomized controlled trial in the world examining safety/efficacy of smoked marijuana flower in combat veterans with severe post traumatic stress disorder PTSD. Sue is striving to put crucial medically-active plants thru entire FDA drug development process to eventually be on the market to treat chronic pain, opioid dependence and PTSD as a safer alternative to synthetic pharmaceuticals. Scottsdale Research Institute in conjunction with their 501(c)(3) arm Field to Healed Foundation is already hard at work on implementing their next FDA approved controlled trials which now include PSILOCYBIN MUSHROOMS, and partnering with farmers to source natural plants/fungi from their fields and learn how to harness their potential as therapeutic tools.

Cassandra Taylor, PhD
Chemist, Botanical Review Team, Office of Pharmaceutical Quality,
Center for Drug Evaluation and Research, FDA

Cassandra Taylor, Ph.D. is a Chemist at U.S. Food and Drug Administration within the Center for Drug Evaluation and Research (CDER) and is a member of the Botanical Review Team (BRT) residing within the Office of Pharmaceutical Quality (OPQ) and serves as an expert resource on all botanical issues. Dr. Taylor received her B.S. in Chemistry from St. Francis University (2005), and her Ph.D. in Analytical Chemistry from the University of Maryland (2014). Dr. Taylor has evaluated over 100 botanical drug submissions across CDER's clinical divisions, with a focus on reviewing cannabis submissions. She serves as a cannabis subject matter expert (SME) for CDER and across FDA, concentrating on the botanical and quality aspects of cannabis. Dr. Taylor is the technical lead on the draft FDA guidance for industry titled "Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research." She leads and coordinates the internal CDER Cannabis working group and leads many cannabis initiatives within CDER and FDA. Dr. Taylor is an active SME in the FDA cross-agency cannabis working group, Cannabis Products Committee (CPC). She collaborates with colleagues across FDA to help close substantial knowledge gaps about the science, safety, and quality of cannabis and cannabis-derived products.

Dr. Mark A. Ware BA MBBS MRCP MSc ICD.D
Chief Medical Officer
Canopy Growth Corporation

Since joining Canopy Growth in July 2018, Dr. Ware has advised the company on scientific and ethical aspects of Canopy Growth's global research efforts and is responsible for the Company's product safety program encompassing all R&D and commercial activities. Before joining Canopy Growth, Dr. Ware was a tenured associate professor in the Faculty of Medicine at McGill University. He obtained his medical degree at the University of the West Indies and secured his MSc in Epidemiology. He began evaluating the role of cannabis in pain management at McGill University in 1999. He was a co-founder of the non-profit Canadian Consortium for the Investigation of Cannabinoids and served as Executive Director from 2007 to 2018. He has advised the Canadian federal government on cannabis policy since 2001. In 2016, he served as the Federal Task Force's vice-chair on the Legalization and Regulation of Cannabis in Canada. In 2021, Dr. Ware completed the ICD-Rotman Directors Education Program (DEP), given to business leaders committed to the highest standard of directorship, while contributing to best-in-class governance education, thought leadership, and peer-to-peer networking.

Orally Administered *N*-Oleol Alanine Pretreatment Blocks Acute Morphine Withdrawl-Induced Conditioned Place Aversion and Attenuates Somatic Withdrawal Following Chronic Opiate Exposure in Rats

Samantha M Ayoub[1], Erin M. Rock[1], Reem Smoum[2], Cheryl L. Limebeer[1], Marieka DeVeuno[1], Raphael Mechoulam[2], Linda A. Parker[2.]

1. Department of Psychology and Collaborative Neuroscience Program, University of Guelph, Guelph, ON Canada
2. Institute of Drug Research, Medical Faculty, Hebrew University of Jerusalem, Jerusalem, Israel

Introduction: The endogenous N-acyl amino acid N-Oleoyl glycine (OlGly) reduces affective and somatic behaviours produced by withdrawal from acutely administered morphine in rats when delivered by intraperitoneal (i.p.) injection. However, OlGly is rapidly inactivated by amidases, limiting its therapeutic potential in clinical models. A methylated version of OlGly, named N-Oleoyl alanine (OlAla; HU595), was synthesized to increase the stability of this compound. Like OlGly, i.p. OlAla reduces naloxone-precipitated acute morphine withdrawal behavioral responses through similar neural mechanisms (CB_1R and PPARα), but can do so over a longer duration of time. Additionally, OlAla reduces several signs of somatic withdrawal behavior following treatment with chronic opiates, whereas OlGly is ineffective. Treatment with OlAla also blocks naloxone-precipitated elevations of heroin self-administration, and reverses some of the changes in brain and gut endocannabinoidome and gut microbiota induced by naloxone. Taken together, these data are consistent with the hypothesis that OlAla is a more stable compound, and suggests OlAla may be a more effective therapeutic option for treatment. To increase the translational appeal of using OlAla in clinical drug applications, the current experiments aimed to test whether oral OlAla pretreatment could also alter the behavioral effects of opiate withdrawal in rats.

Methods: In Experiment 1, place conditioning was used to determine if orally (intragastric gavage, i.g.) administered OlAla (5 mg/kg and 20 mg/kg) or its vehicle would reduce the establishment of an acute naloxone-precipitated morphine withdrawal induced conditioned place aversion. In Experiment 2, somatic withdrawal observations were conducted following chronic steady state heroin exposure (via minipumps) in rats pretreated with oral OlAla (5 mg/kg – 80 mg/kg, i.g.)

Results: In Experiment 1, pretreatment with oral 20 mg/kg OlAla, but not 5 mg/kg OlAla, blocked the establishment of a morphine withdrawal-induced conditioned place aversion. In Experiment 2, pretreatment with oral 5 mg/kg OlAla, but not other doses tested, reduced heroin withdrawal-induced abdominal contractions ($p < 0.01$) and diarrhea ($p < 0.001$).

Conclusions: This study demonstrated a dose-specific reduction of withdrawal responses from chronic and acutely administered opiates by orally-administered OlAla, and suggests that oral OlAla could be effective in reducing opiate withdrawal in clinical populations. Given the dose-specific observations, we can speculate the loci of OlAla's effect on withdrawal behavior to be central for affective withdrawal, and peripheral for somatic withdrawal.

Cannabidiol Prevents Withdrawal Symptoms and Relapse to Nicotine Vapor in Rats

Caitlin Crook; McKenzie Pavlich; Giordano de Guglielmo, PhD; Marsida Kallupi, PhD

Rationale: Preclinical models of voluntary nicotine electronic cigarette have shown that 3 weeks of daily (1 h) nicotine vapor self-administration produce addiction-like behaviors, including somatic signs of withdrawal, anxiety-like behavior, and relapse-like behavior during abstinence. Cannabidiol (CBD) is known to modulate nicotinic receptor function. However, preclinical evaluation of its efficacy on nicotine vapor dependence is still lacking.

Objectives: The goal of this study was to test the preclinical efficacy of chronic CBD treatment by preventing nicotine vapor dependence, using measures of withdrawal, anxiety, and relapse.

Methods: Rats self-administered daily 0.5mg/ml of nicotine vapor in 1 h sessions via operant vapor chambers over 3 weeks. One group of rats received CBD injections (30 mg/kg/day) for 2 weeks, or its vehicle, starting after stable nicotine intake was achieved. The control group included rats that self-administered air vapor and received CBD or vehicle injections of sesame oil. Throughout the experiment, withdrawal, anxiety, and relapse induced by stress and cues associated to nicotine vapor were performed.

Results: CBD (30 mg/kg/day) prevented rats from exhibiting somatic signs of withdrawal and anxiety like behaviors during acute abstinence. In rats with a history of nicotine vapor self-administration, presentation of stress and stimuli predictive of drug availability reinstates drug seeking, triggering relapse. The animals that self-administered nicotine vapor and chronic treatment of CBD did not reinstate their behavior.

Conclusions: This preclinical study suggests that CBD treatment may be beneficial as a strategy to alleviate the withdrawal symptoms and relapse in animal models of nicotine vapor self-administration.

Effects of Chronic CBD Treatment on Alcohol Dependence

Giordano de Guglielmo, PharmD, PhD
University of California, San Diego, San Diego, CA

Cannabis contains distinct non-psychoactive, non-addictive elements that may offer medical benefits and may be more readily amenable to therapeutic use. Cannabidiol (CBD) is a major candidate that has recently received attention for its potential to decrease drug and alcohol use. The currently approved medications for alcohol use disorder (AUD) have limited efficacy and significant side effects and are used by only 10% of patients with AUD. The development of novel and more effective medications for the treatment of AUD is a pressing medical need. The development of novel medications for the treatment of AUD is a pressing medical need. Preclinical studies have shown that chronic CBD treatment attenuated alcohol drinking and prevented the reinstatement of alcohol seeking induced by environmental cues and stress. However, these studies were performed in nondependent animals.

We used two different animal models to induce alcohol dependence in rats: the chronic intermittent ethanol vapor exposure (CIE) model and the recently developed

ethanol vapor self-administration model (EVSA). The new EVSA model highlights the volitional aspects of alcohol dependence. The effects of chronic CBD treatment were evaluated in ethanol dependent rats by measuring their levels of alcohol intake, withdrawal-induced anxiety and hyperalgesia, somatic withdrawal signs and alcohol seeking.

We found that chronic CBD treatment prevented the escalation of alcohol intake and reduced withdrawal-induced anxiety, hyperalgesia, somatic withdrawal signs and alcohol seeking in animals made dependent through CIE. The treatment was also effective in reducing alcohol consumption in animals made dependent by EVSA. Finally, the animals treated with CBD showed decreased alcohol-induced neurodegeneration compared to control rats.

These results extend to the current literature and indicate a profile of potential benefit of CBD for the treatment of alcohol dependence.

Short-term Residual Effects of Cannabis on Simulated Driving Performance

Kyle F. Mastropietro, BS; Anya Umlauf, MS; David J. Grelotti, MD;
Robert L. Fitzgerald, PhD; Igor Grant, MD; Thomas D. Marcotte, PhD
University of California, San Diego, San Diego, CA

Background: Between periods of use, some heavy cannabis consumers may display selective cognitive deficits ("residual effects"), particularly in memory and attention, which usually resolve within 30 days. Whether such deficits are seen in real-world behaviors, such as driving, is largely unexamined, with one study (Dahlgren et al., 2020; n = 44) finding that a subset of users with an earlier age of onset of regular use exhibited decrements in simulated driving performance during a short period of non-use, whereas another study found users performed better than non-users on a simulation (Brooks-Russell et al., 2021; n = 85). The current study sought to further examine whether non-acute, short-term residual effects of cannabis are seen in driving simulator performance during abstinence and are associated with use history or key demographic factors.

Methods: 191 healthy cannabis users with a wide range of use patterns completed a 25-minute drive on a high-fidelity driving simulator following at least 48 hours of abstinence. The simulation included both urban and rural driving segments, and common real-world traffic challenges (e.g., making a left turn across incoming traffic). The main outcome was the Composite Drive Score (CDS), a global measure of driving performance comprised of key variables, including standard deviation of lateral position (SDLP, i.e., swerving), a divided attention task during the drive, and car following abilities (Marcotte et al., 2022).

Results: Participants were abstinent for a mean of 5.35 days (SD = 5.87), with heavier use intensity over the previous six months predicting shorter abstinence periods (r = -.17, p = .035). CDS was unrelated to indicators of past cannabis use, including cannabis use intensity over the previous six months, days of abstinence, blood THC and related cannabinoid concentrations, and age of use onset, nor with demographic variables including gender, age, and level of education (all ps > .10). In addition, none

of the components comprising the CDS (e.g., SDLP and car following) were related to indicators of past use or any demographic variables (all ps > .10).

Conclusions: The current study, the largest study of its kind to date, did not find evidence of a relationship between chronic cannabis use and decrements in simulated driving performance during short periods of cannabis abstinence, suggesting that the short-term residual cognitive effects of cannabis might not translate directly to reductions in some overlearned behaviors, such as driving. Future studies would benefit from inclusion of a non-cannabis-using comparison group.

Exploring Avenues for Cannabis Plant Improvement: from Virus Disease Management to the Control of THC Production by Non-transgenic, Viral Vector-based Approaches

James Ng

Department of Microbiology and Plant Pathology, University of California, Riverside, USA

Hemp/cannabis plants can be infested by a host of phytophagous insects, including those that can stealthily feed on specific cell contents and tissues, i.e., sucking piercing insects in the order Hemiptera (e.g., aphids, whiteflies, and leafhoppers), and others whose feeding activities can result in disproportional decimation of whole cells and tissues, e.g., Acari (mites) and Thysanoptera (thrips). Insects can also inflict damages on the plants by transmitting specific viruses. However, as an underutilized crop that hitherto has received relatively less support in the form resources and attention compared to other agronomic crops, information on the viruses and other diseases and disease etiologies that negatively impact cannabis plant production have been limited. To date, a small but important number of viruses that infect cannabis plants have been identified and several of them are prevalent in California. Other known and yet to be identified viruses are expected to appear as the cultivation of cannabis plants increases throughout the State. Therefore, it is imperative to establish a rapid and robust early detection system as this is one of the best approaches towards managing the rapid spread of readily transmissible diseases. Nucleic acid amplification-based and immuno-based technologies such as PCR and ELISA, respectively, are efficient diagnostic tools for detecting known viruses, while shotgun and high throughput sequencing techniques are useful for identifying unknown viruses. We have experience working with a number of viruses known to infect cannabis and will highlight the results obtained using several different diagnostic methods.

Studies have found that some commercial hemp varieties selected for high levels of cannabidiol (CBD) production may contain illegal levels of *delta-9-tetrahydroxycannabinol* (THC). Administering CBD products adulterated with unknown levels of THC may result in inconsistent treatment outcomes and subject patients to unknown risks. Although THC can be eliminated from hemp/cannabis plants through conventional breeding and genetic engineering, these approaches are often time-consuming and hampered by labor-intensive procedures. We have developed the cloned infectious cDNA of lettuce chlorosis virus (LCV) (family *Closteroviridae*), a

whitefly transmitted virus isolated from lettuce plants in Southern California (https://doi.org/10.1016/j.virusres.2012.08.010).   Recently, LCV has also been found to infect hemp/cannabis plants (https://dx.doi.org/10.3390%2Fv11090802).   Using the infectious clone of LCV and that of other closely related viruses, we have gained valuable insights into the molecular biology and functions of these viruses. This knowledge is essential in supporting the development of a viral vector-based, transgenesis-free biotechnology platform for synthetic biology and RNA interference-driven applications aimed at benefitting plant growth and development – e.g., from understanding the biosynthesis mechanisms of CBD and other cannabinoids to modifying plant biology to enhance CBD and/or THC production. This poster provides a proof-of-concept example of how a viral vector-based approach can be used to effectively control THC production in hemp/cannabis plants or consistently reduce its levels to below the legal limits appropriate for use within the health system.

Cannabis Use May Attenuate Neurocognitive Performance Deficits Resulting from Methamphetamine Use Disorder

Jeffrey M. Rogers, BS[1]; Igor Grant, MD[2]; Maria Cecilia G. Marcondes[3], PhD, Erin E. Morgan[2], PhD, Mariana Cherner, PhD[2], Ronald J. Ellis MD, PhD[2,4], Scott L. Letendre, MD[2,5], Robert K. Heaton[2], PhD, Jennifer E. Iudicello, PhD[2]

[1]San Diego State University/University of California San Diego Joint Doctoral Program in Clinical Psychology, San Diego, CA
[2]Department of Psychiatry, University of California San Diego, San Diego, CA
[3]San Diego Biomedical Research Institute, San Diego, CA
[4]Department of Neurosciences, University of California San Diego, San Diego, CA
[5]Department of Medicine, University of California San Diego, San Diego, CA

Background: Methamphetamine and cannabis are two widely used substances with complex and possibly opposing effects on the central nervous system. While methamphetamine use has been associated with neurocognitive (NC) deficits, evidence of the NC effects of chronic cannabis use is mixed, and findings regarding their combined effects are inconclusive. We aimed to compare global and domain NC performance in people with lifetime cannabis or methamphetamine use disorder diagnoses, or both, relative to people without either of these diagnoses.
Methods: 423 (71.9% male) participants, stratified by lifetime cannabis (C-/C+) and methamphetamine (M-/M+) DSM-IV abuse/dependence were categorized into four study groups: C-M- (n=170), C+M- (n=59), C-M+, (n=78) and C+M+ (n=116), and completed a comprehensive neuropsychological, substance use, and psychiatric assessment. Global and domain NC performance (i.e., T-scores) and impairment (i.e., deficit scores) were examined using multiple linear regression and multiple logistic regression, respectively, controlling for relevant covariates that differed between the study groups and may impact cognition. Methamphetamine and cannabis use characteristics were also considered in similar models restricted to the M+ (n=194) and C+ (n=175) groups, respectively.
Results: Globally, C+M+ did not perform significantly better or worse than C-M- or

C+M-. C+M+ performed significantly better than C-M+ globally (M_{diff}=3.58) and on measures of executive function (M_{diff}=2.91), speed of information processing (M_{diff}=3.40), learning (M_{diff}=4.92), recall (M_{diff}=4.47), and working memory (M_{diff}=4.79). C+M- did not perform significantly worse than C-M- on NC domain measures. C+M+ also displayed lower odds of domain impairment than C-M+ for speed of information processing (OR=0.28), learning (OR=0.49), and recall (OR=0.42), as well as for global impairment (OR=0.27). C+M- displayed lower odds of executive impairment than C+M+ (OR=0.41), but C-M- did not display lower likelihoods of impairment than C+M+. C+M+ and C+M- differed significantly in their cannabis initiation age (M_{diff}=-2.0), cumulative density of use (M_{diff}=1.0), and age at first diagnosis (M_{diff}=-2.7). Between C+M+ and C+M-, younger age at first diagnosis may partially account for differences in learning and recall performance. Methamphetamine use characteristics did not appear to account for differences in NC performance or impairment between M+C+ and M+C-. Younger age at first diagnosis, younger age at first use, and greater cumulative density of methamphetamine use were associated with poorer NC performance.

Conclusions: While methamphetamine use has been shown to confer risk for NC decline, cannabis use does not appear to exacerbate this risk. Concurrent cannabis use may provide some protection against NC deficits precipitated by methamphetamine use disorder.

Gut Barrier Dysfunction Associated with Diet-Induced Obesity is Exacerbated in Mice With Conditional Deletion of Cannabinoid Receptor Subtype-1 in the Intestinal Epithelium

Mark B. Wiley, Nicholas V. DiPatrizio, Division of Biomedical Sciences, School of Medicine, University of California-Riverside, Riverside, CA, USA

Introduction: The gut barrier is essential for providing protection from pathogens that can enter our body from the digestive tract, and its function is dysregulated in several pathologies that include diet-induced obesity (DIO) and inflammatory bowel diseases (i.e., leaky gut). Studies from our lab and others suggest that the endocannabinoid (eCB) system in the gut is dysregulated in DIO and participates in gut barrier function; however, specific molecular mechanisms involved in these processes and whether the eCB system serves a protective or detrimental role in gut barrier integrity is unclear. We used our novel transgenic mouse that is conditionally deficient in CB1Rs in the intestinal epithelium to directly address these gaps in our understanding of roles that CB1Rs play in gut barrier function in health and disease. We tested the hypothesis that *signaling at cannabinoid receptor subtype-1 (CB_1R) in the intestinal epithelium provides protection from diet-induced gut barrier dysfunction*.

Methods: Mice conditionally deficient in CB1Rs in the intestinal epithelium (intCB$_1$-/-) and control mice (intCB$_1$+/+) were placed on a (*i*) low-fat/no-sucrose control diet or (*ii*) obesogenic high-fat/high-sucrose diet for 8 weeks. Levels of eCBs and related lipids in the large intestinal epithelium, and activity of their biosynthetic and degradative enzymes, were quantitated via LC/MS methods after completion of the study. Paracellular permeability was tested in vivo throughout development of DIO, and analysis of

changes in expression of genes for gut barrier components and inflammatory markers in the large intestinal epithelium was performed via NanoString analysis.

Results: When compared to lean mice, DIO mice had reduced levels of the eCB, 2-arachidonoyl-*sn-glycerol* (2-AG), and several other monoacylglycerol species in the large intestinal epithelium due to reduced activity of their biosynthetic enzymes. Furthermore, paracellular permeability in the large intestine was increased during development of DIO, an effect that was exacerbated in $intCB_1$-/- mice. Moreover, $intCB_1$-/- mice displayed a reduction in expression of genes for tight junction proteins in parallel with an increase in expression of inflammatory-related molecules in the large intestinal epithelium.

Conclusions: DIO is associated with downregulation of eCB production in the large intestine and a compromised gut barrier that is exacerbated in the absence of local CB_1Rs, which suggests that CB_1Rs in the intestinal epithelium serve a protective role in gut barrier function. These signaling pathways may be a target for cannabinoid-based therapeutics aimed at improving gut barrier function and inflammation in DIO. Future studies will examine the impact of cannabis exposure on gut barrier function in health and disease.

Cannabidiol (CBD) Reduced Arterial Blood Pressure and Body Mass and Improved Insulin Resistance During Metabolic Syndrome in OLETF Rats

Jessica N. Wilson, M.S.[1], Mark Mascal, Ph.D[2], Robert Fitzgerald, Ph.D[3], Nicholas DiPatrizio, Ph.D[4], Rudy M. Ortiz, Ph.D[1]

1. Department of Molecular and Cell Biology, School of Natural Sciences, University of California, Merced, CA, USA
2. Department of Chemistry, University of California Davis, 95616, Davis, CA, USA.
3. Department of Pathology, University of California, 10300 Campus Point Drive, Suite 150, San Diego, CA 92121, USA.
4. Department of Biomedical Sciences, University of California, 1126 Webber Hall 900 University Ave. Riverside, CA, 92521, USA.

Background: Cardiovascular disease (CVD) is the leading cause of death in the U.S. and a primary outcome of metabolic syndrome (MetS). MetS is diagnosed by the presentation of at least 3 of the 6 cluster conditions: 1) abdominal obesity, 2) atherogenic dyslipidemia, 3) elevated arterial pressure, 4) glucose intolerance ± insulin resistance, 5) pro-inflammatory state and 6) prothrombotic state. Pinpointing the root cause of these conditions individually is difficult but identification of treatments which potentially affect multiple conditions of MetS has greater potential to ameliorate later-onset CVD. The therapeutic potential of cannabidiol (CBD) is widely recognized for powerful anti-inflammatory and antioxidative properties, which have been shown to be cardioprotective. However, these effects have not been probed in the context of MetS.

Methods: A cohort of 14-week-old Otsuka Long-Evans Tokushima Fatty (OLETF) rats were administered 175mg/kg CBD extract by oral gavage for 5 weeks (CBD; n=8).

Animals were fed ad *libitum* and monitored alongside vehicle-treated OLETF (OLETF; n=8) and vehicle-treated Long-Evans Tokushima Otsuka (LETO) rats, the lean-strain controls (LETO; n=8). Rats were implanted with blood pressure monitors [DSI; HD-S10] at 12 weeks. An oral glucose tolerance test (oGTT) was performed after 5 weeks of treatment.

Results: CBD reduced arterial pressure within the first week of dosing (6 ± 1.4mmHg; 4.1%; $p<0.05$ vs. OLETF control) and, after 5 weeks, by 9.7 ± 1.7mmHg (6.5%; $p<0.05$ vs. OLETF) from baseline. CBD blunted body mass gain and reduced abdominal adiposity by 39% ($p<0.0001$) compared to untreated OLETF. Following 5 weeks of CBD, glucose absorption ($AUC_{glucose}$ 10 minutes after glucose bolus) was reduced 21% ($p<0.01$) and enhanced uptake (slope 60 minutes to 120 minutes after glucose bolus) by 160% ($p<0.05$). However, neither glucose response overall nor static fasting blood glucose were improved following 5 weeks of CBD treatment. On the other hand, Insulin response ($AUC_{insulin}$) was reduced 77% ($p<0.0001$) compared to OLETF, which ultimately resulted in the overall reduction of calculated insulin resistance index (IRI) of 79% ($p<0.0001$). Moreover, CBD treatment reduced fasting plasma insulin by 76% compared to OLETF ($p<0.001$). The noteworthy loss of adiposity by CBD likely contributed to the 59% ($p<0.0001$) reduction of circulating plasma leptin.

Conclusions: A chronic, high dose of CBD may ameliorate hypertension by improving multiple cluster factors of MetS, including insulin resistance, which are strongly associated with abdominal adiposity.