



Institute of
Cannabis Research
COLORADO STATE UNIVERSITY PUEBLO



ANNUAL REPORT

2020



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LETTER FROM THE DIRECTOR

The fourth year of the Institute of Cannabis Research (ICR) has been one of change from the start. Even as I am writing this introduction to the Institute's Annual Report, Colorado, the nation, and world, are grappling with the COVID-19 pandemic. Like other institutions and organizations, the pandemic has resulted in changes to plans and normal operations; yet, despite these external challenges, this year has still been one of growth and acceleration for the ICR.

With the passage of HB19-1311, one of the most significant changes to come to the ICR this year was the formation of a Governing Board. This Board was constituted in the fall with the first meeting in October of 2019. Among the responsibilities of the Board include budgetary oversight, helping to shape the mission and vision of the ICR, and review of new Cannabis Degree and Certificate programs at colleges and universities in the state. More information about the Governing Board and its members can be found in this report.

Each spring since the ICR was created in 2016, the Institute has hosted a research conference to provide a forum for researchers from around the globe to share the latest results from their wide-ranging cannabis research. This year, our conference was scheduled to occur April 4-6, before it had to be postponed. The conference was shaping up to be an exceptional event and was marked by a substantial increase in interest by presenters—with two internationally renowned keynote speakers, a strong number of registered attendees, and increased interest by exhibitors. We were poised to pilot a pre-conference program that included tours of local facilities, professional development opportunities, and social activities. COVID-19 had other plans for us and for the world; the ICR Conference 2020 has been rescheduled for August 11-12, 2020 and will be held in a virtual format.

At its heart, the ICR exists to facilitate cannabis research and the dissemination of research results. You will find a short description of the wide-ranging cannabis research supported this year as part of this annual report. I encourage you to explore the report in detail to see what type of research is in progress. Unfortunately, the global pandemic has had an impact here as well, with suspension of research activities due to the ongoing public health crisis. We are hopeful that conditions will improve to the point researchers can resume this important work soon.

Other noteworthy activities from this year include the formation of the grassroots ICR Hemp Farmers Association and launch of the Journal of Cannabis Research. The first issue of the Journal was published in June of 2019 (after last year's Annual Report had been published), but I am excited to report that under the leadership of the Editor-in-Chief, Dr. David Gorelick, and in partnership with Springer Nature Publishing, the number of cannabis research articles and interest in the Journal has grown dramatically. Though there have been many changes it has been a very robust and exciting year with so many activities, and only a few can be highlighted in this introduction.

I hope you will explore this past year of ICR within the pages of this report. And if you have questions, please never hesitate to contact us. The ICR is a simple email or phone call away.

Chad Kinney, Ph.D.

Director, Institute of Cannabis Research



MEET THE ICR STAFF

DR. CHAD KINNEY

Director, ICR

Dr. Kinney joined the ICR as Director in July of 2018. Dr. Kinney's background is in Analytical and Environmental Chemistry. Many of the same analytical techniques employed in analytical and environmental chemistry are being employed in the development of extraction methods for phytochemicals by his research group. As Director of the ICR, Dr. Kinney provides leadership and management of the Institute's activities; supervises the exceptional ICR staff, collaborates with the new ICR Governing Board, facilitates cannabis related research supported by the ICR, liaises with external organizations, regional stakeholders, and government personnel/lawmakers; and facilitates the ICR's research, annual conference, and Journal of Cannabis Research.



NICOLE QUARTIERO

Assistant Director, ICR

Director of the Office of Research and Sponsored Programs

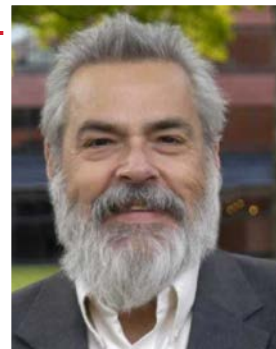
Nicole is a seasoned Research Administrator and works alongside the ICR Director to oversee the fiscal and administrative operations of the ICR. Nicole participates in the strategic planning, process development, collaboration building and day-to-day oversight of the ICR and its diverse functions. She serves as one of the main point of contacts for the Institute, its Governing Board and staff while striving to offer superior administration, organization and customer service.



DR. JOHN WILLIAMSON

Senior Director of Research

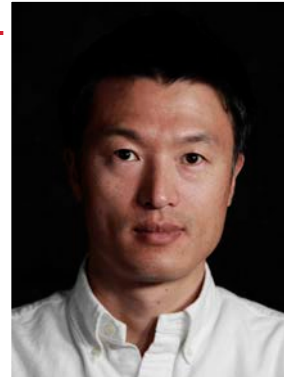
Dr. Williamson joined the ICR serving as Senior Director of Research. Dr. Williamson serves as the ICR's strategic development advisor pursuing research partnerships, collaborations, and external funding opportunities. John received his Ph.D. in medicinal chemistry and natural products chemistry from the University of Iowa. He served as a tenured professor of medicinal chemistry at the University of Mississippi for 25 years overseeing a drug discovery and development research program in infectious diseases, authoring 100+ peer-reviewed publications and receiving more than \$25M in extramural research funding. As a consultant, John has worked for a variety of governmental agencies, private industry, Time-Warner's Health magazine, and dozens of universities across the country.



SANG PARK

Senior Scientist
Resident Liaison

With extensive research experience in plant biology and genetics, Dr. Sang-Hyuck Park provides leadership with multi-tier ICR cannabis research projects. This research primarily involves cannabis genetics and chemistry and more recently, he has been focused on uncovering genetic regulations underlying agronomically important traits including cannabinoid/terpene biosynthesis. In addition, Dr. Park serves as a liaison with other entities to facilitate expanding existing knowledge on cannabis and translating this knowledge into applications that benefit society. This year, Dr. Park founded the ICR Hemp Farmers Association (IHFA) and serves as co-chair of the 4th ICR conference program committee.



XIAO CUI

Data Analyst

Xiao Cui has extensive experience in project management and proficiency in SAS, R, Minitab, SQL, and Tableau. Ms. Cui's role at the ICR is to perform experimental design and statistical analysis to facilitate the ICR research. She has co-authored publications related to cannabis public health impacts and harm reduction. Ms. Cui audits and monitors the fiscal data for the ICR, and generates financial reports and dashboards to stakeholders. She also manages the ICR website and email blasting. As a member of the ICR conference committee, she is involved in the planning of the annual conference, managing the abstract submission and registration portal, as well as creating and analyzing post-conference surveys.



WENDY FAIRCHILD

Administrative Assistant

Wendy accepted a larger role to support the growing needs of the ICR in an office management capacity. She continues to work with the team on reports, contracts, travel arrangements, planning and oversight of the annual conference, daily purchasing and accounting needs, directing incoming inquiries, and proof-reading and editing materials. Wendy regularly serves as the first contact for the ICR, and maintains a professional and enthusiastic rapport with current students, new student inquiries, professional contacts and the general public. She is beginning her ninth year working for her alma mater, CSU Pueblo.



ONGOING

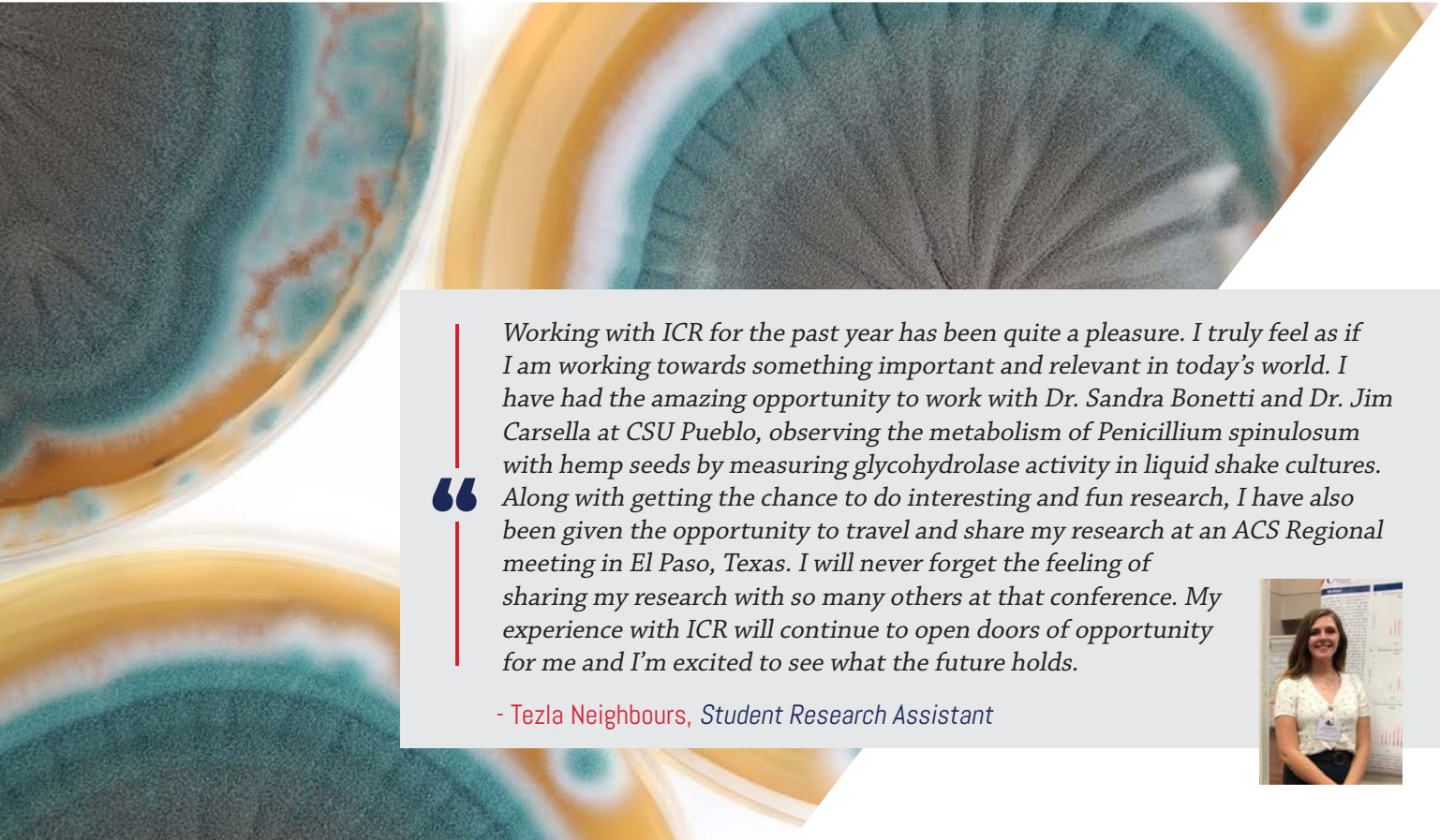
RESEARCH STUDIES

Interactions of *Penicillium Spinulosum* with Hemp and Non-psychoactive Hemp Compounds



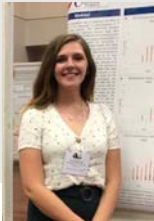
PI.: Sandra Bonetti
Co-Investigator: James Carsella
Student Researcher: Tezla Neighbours

Fungal growth and contamination of hemp plants and derived-products is a serious health and economic concern to both consumers and producers. Our scientific studies are focused on (1) determining how hemp products affect the growth of fungi and (2) how fungi, in the course of metabolizing hemp, alter the chemical composition of valuable hemp products including cannabidiol or CBD. Immunocompromised individuals, such as cancer patients, are especially susceptible to systemic fungal infections that may be acquired through ingestion of contaminated products. In order to address this problem, our research examines how the chemicals in hemp induce fungal growth. Hemp research is compelling because the market for hemp-derived products is a largely expanding market. According to the Hemp Business Journal, in 2017, in the US alone, sales of hemp products were approximately 820 million dollars and this figure is expected to more than double by 2021.



“Working with ICR for the past year has been quite a pleasure. I truly feel as if I am working towards something important and relevant in today’s world. I have had the amazing opportunity to work with Dr. Sandra Bonetti and Dr. Jim Carsella at CSU Pueblo, observing the metabolism of *Penicillium spinulosum* with hemp seeds by measuring glycohydrolase activity in liquid shake cultures. Along with getting the chance to do interesting and fun research, I have also been given the opportunity to travel and share my research at an ACS Regional meeting in El Paso, Texas. I will never forget the feeling of sharing my research with so many others at that conference. My experience with ICR will continue to open doors of opportunity for me and I’m excited to see what the future holds.

- Tezla Neighbours, Student Research Assistant



An Ongoing Investigation into the Effects of Medicinal Cannabis on Seizures in Adults with Medically Refractory Epilepsy



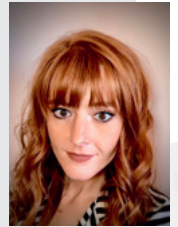
PI.: Dr. Barbara Brett-Green

This observational study examines the effects of medicinal cannabis use on seizures and behavior in adults with medically refractory epilepsy who elect to use cannabidiol (CBD) as an adjunctive treatment.

Participants are followed for one month prior to adding CBD to their treatment regime and for five months after. No cannabis is provided to the participants. Support for the participants medicinal cannabis use is provided by Realm of Caring. Participants wear a wireless physiological recording device that measures electrodermal activity, blood pulse volume, motion/acceleration, and temperature. This data is processed to produce seizure reports. Three times during the course of this study, participants fill out questionnaires assessing quality of life, seizure severity, anxiety/depression, and adverse events. They also provide urine samples that are processed for cannabinoid levels. Preliminary analysis of behavioral data indicates there is a statistically significant decrease in anxiety with CBD use and a trend towards decreased depression. Additional analyses are underway.



As an undergraduate student, I assisted Dr. Brett in her epilepsy research by compiling peer reviewed research and preparing material for presentations, such as the Annual Institute of Cannabis Research Conferences. I also had the opportunity to attend the Rocky Mountain Psychological Association Meeting in Denver.



Corissa Cibulka,
Student Research Assistant



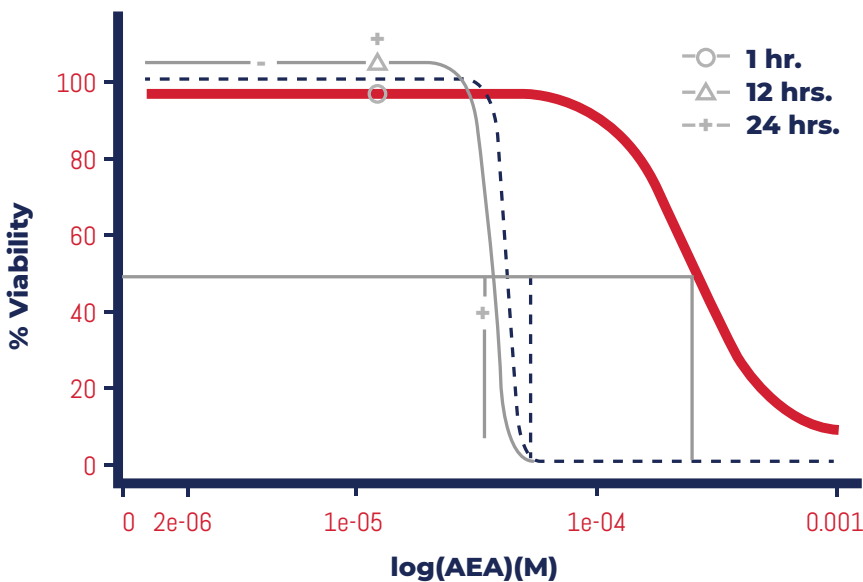
Anti-Cancer Potential of Fermented Dietary Hempseed (*Cannabis Sativa L.*) Metabolites and the Role of CB Receptors in Human Colon Cancer Cell CACO2 Viability, Proliferation, and Energy Metabolism



PI.: Dr. Annette Gabaldón

We began this project with two objectives using basic research methodologies to investigate cultured human colorectal carcinoma cell (Caco-2) viability, proliferation, and metabolic responses to treatment with fermented hempseed metabolites (Study 1) and to treatment with cannabinoid receptor ligands (Study 2). Fermentation metabolites can have profound influences on human health and there is much interest in identifying novel metabolites with anti-cancer activity. We know nothing about hempseed fermentation metabolites and their bioactive properties. Secondly, the role that the endocannabinoid system may play in cellular health and disease is not well understood. Both studies are in progress. One interesting finding so far is that the endocannabinoid, anandamide (AEA), is highly toxic to cancer cells at very high concentrations. Thus, AEA may be a useful therapeutic for cancer treatment.

AEA TREATMENT FOR 1, 12, & 24 H





Applications of Industrial Hemp at CSU Pueblo



PI.: Dr. Brian Vanden Heuvel

Co-Investigators: Dr. Leonardo Valencia Bedoya, Dr. Yaneth Correa-Martinez, Dr. Richard Farrer, Dr. Chad Kinney, Dr. Sang Park

This project, entitled “Applications of Industrial Hemp at CSU Pueblo,” enables an inter-departmental, multi-faculty collaborative workflow that builds on 18 months of previous achievements by the PI and CO-PIs and established infrastructure through previous ICR funding. We believe that it is time to extend our work to applied projects.

Specifically, this grant proposal asks: 1) Can industrial hemp be used as a remediation tool for metals and metalloids from soil and municipal sewage sludge?, 2) Can cannabinoid extraction methods developed in previous ICR projects be scaled up to industrial volumes?, 3) Can waste products from industrial hemp production (stems/leaves) be a reliable source of important biopolymers?, and 4) Can the recently sequenced genomes for industrial hemp be a framework for continued research into what genes are turned on and off during different growth stages, affecting important traits like disease resistance, drought tolerance, yield, specific concentrations of cannabinoids or other secondary chemicals?

Data Analytics in Cannabis Research



PI.: Dr. Kuangyuan Huang

Co-Investigators: Dr. Yoanna Long

We are working on two interrelated projects. First, based on our previous findings on the importance of providing online social support to cannabis rehabbers, who might experience difficulties in acquiring support in face-to-face settings, we developed a mobile app to assist people undergoing cannabis rehabilitation. This mobile app allows cannabis rehabbers to search and acquire information essential for their rehabilitation. It also tracks and reports rehabbers’ recovery milestones. Additionally, it connects people to other like-minded rehabbers to allow them to exchange encouragements and best practices.

The second project is to continue with our previous efforts in analyzing a large amount of online social support messages; 29,301 online discussion threads, containing 184,668 message postings have been collected and analyzed. The goal of this investigation is to identify ways of promoting online social supportive interactions.

The result of this project has been published at an international conference HCII (Human Computer Interaction Internal) 2020. This project has engaged multiple undergraduate students that have made significant contributions to this research project.



ONGOING RESEARCH STUDIES, *Continued*

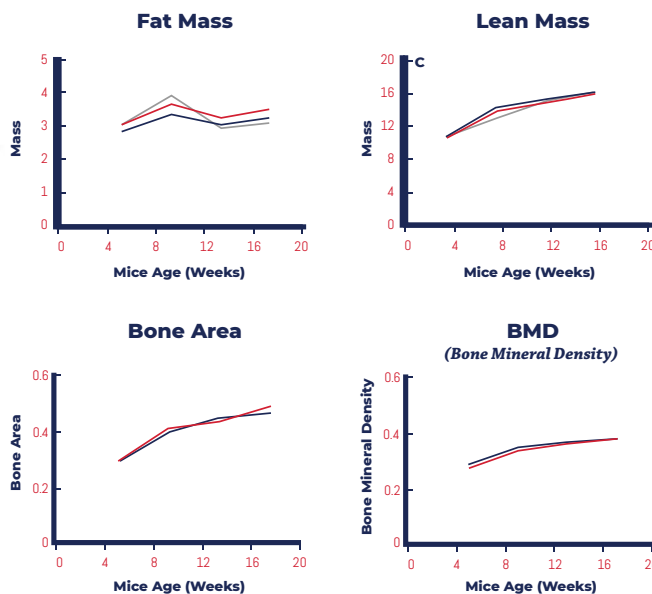


Effects of Dietary Hempseed (*Cannabis sativa* L.) on Growth Patterns, Body Composition, Bone Mineral Density, and Gut Microbiota Diversity in Female C57BL/6 Mice

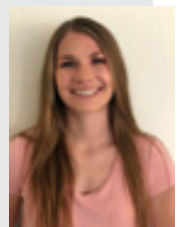


PI.: Dr. Annette Gabaldón

Hempseed is a nutrient-dense food and contains phytochemicals which have the potential to alter body composition during developmental growth. Our preliminary results suggest there is no remarkable influence of the hempseed diet on body composition in young growing mice. Data up to the midpoint of the study are shown, for mice fed the control (0% hempseed, HS), 5% HS, and 15% HS diets. Fecal analysis of microbial diversity is in progress and may reveal a dietary influence.



“ My experience at Colorado State University Pueblo as an undergraduate research assistant doing research through the Institute of Cannabis Research (ICR) has provided myself, as well as other students, with the amazing opportunity and flexibility to examine research topics of their choosing. Participating in this research program helped me gain a more thorough understanding of general biological processes and instrument technology, as well as allowing me to delve into the world of dietary supplementation using hempseed for potential human consumption or agricultural use. Under the guidance of Dr. Gabaldón, the aim of this research was to determine if dietary supplementation with hempseed would influence growth patterns and body morphometric parameters, such as lean mass, fat mass, bone mineral density, and total tissue mass. I am very fortunate to have been a member of the research team at CSU Pueblo, and I strongly recommend undertaking a project of your own during your journey toward obtaining a degree.



Hailey Streff,
Student Research Assistant



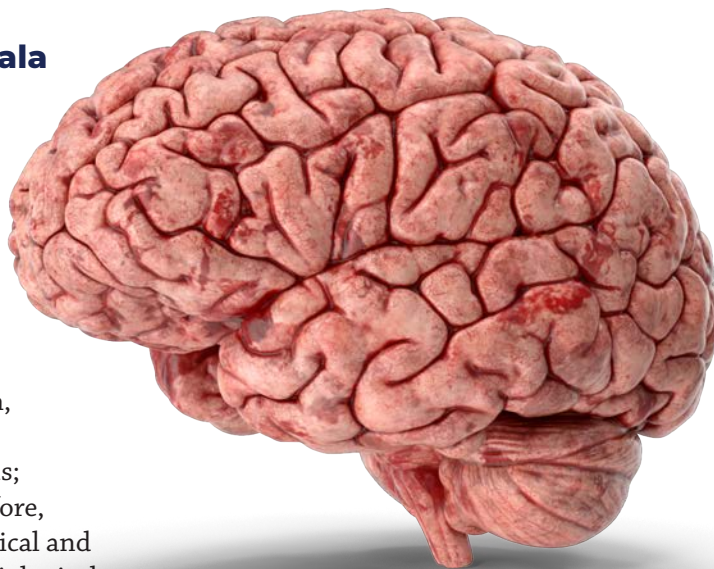
Sexually Demorphic Effects of Cannabinoids on Cognitive and Reflexive Learning and Memory-Dependent Neuronal Network Activity in Mouse Hippocampus and Amygdala



PI.: Dr. Jeff Smith
Co-PI.: Amy Uhernik

Between 12 and 15% of Americans take antidepressant medicines for problems that range from depression, to Post Traumatic Stress Disorder and Alzheimer's disease.

Unfortunately, side effects include increased anxiety, other neurological problems, gastrointestinal difficulties, weight gain, and sleep difficulties. Cannabis-derived medicines have been purported as alternatives to antidepressants for these problems; however, very little research is available to support this. Therefore, our laboratory is focusing on comparatively evaluating anatomical and physiological targets of these drugs, which support the neurobiological mechanisms that underlie such disorders. Our approaches include pre-clinical animal behavior, electrophysiological, and molecular methods aimed at showing how the effects of the anti-depressant, Citalopram, compares to cannabidiol in affecting discrete neural circuitry and function that is fundamental to the expression of these disorders.



Rheological Characteristics of Hemp-based Filament Composites for 3D Printing Abstract



PI.: Dr. Neb Jaksic
Co-Investigator: Dr. Mel Druelinger

This research aims to investigate flow characteristics of various hemp-based composites used in 3D printing. We purchased and installed a research grade rheometer (LCR 7002 Capillary Rheometer System) shown in Figure 1. We also received some training on this rheometer. In addition, we added an objective of 100x to our Primotech MAT microscope. We also installed the Zeiss microscope software (ZEN blue edition) for image processing of photos obtained by the microscope camera.

We produced 300 3D printed hemp-plastic pins for the ICR 2020 conference (shown in Figure 2). The experimental portion of the research was halted by COVID-19 university/state measures. So, we changed the focus of the research to include a literature search of automation practices in hemp growing, from seeding and harvesting to applications. We are looking for process bottlenecks that may be overcome by automation.



Figure 1: Dynisco LCR 7002 Rheometer



Figure 2: 2020 ICR Conference Pin



Cannabis Use Survey Instrument Development and Implementation



PI.: Dr. Karen Yescavage

Individuals may be self-medicating with cannabis in an attempt to manage stress and psychological pain, defined as anxiety, depression, anger, or other negative emotions. Researchers debate whether THC in particular has any medicinal value, especially with respect to psychological pain management. A review of the empirical literature yields varying results on the efficacy of cannabis to alleviate anxiety. While some research has found high THC levels to be associated with heightening anxiety, other research finds CBD to be associated with alleviating anxiety. We are conducting an online survey of adults regarding their perceived efficacy of cannabis (both THC and CBD) to manage psychological pain as well as to assess any adverse reactions that may be compounding the problem from which they seek relief. We are especially interested in veterans' self-reported use of cannabis to attempt to regulate negative emotions such as anger and frustration.

Exploring Factors to Mitigate Customer's Perceived Risk of CBD Oil Usage



PI.: Dr. Laee Choi

Customers are often hesitant to buy and use products they aren't familiar with and might perceive risks with these products, especially if they are innovative new products such as those derived from cannabis oil (CBD, etc). These products can be seen as having a higher risk factor than general products that are more familiar due to lack of both direct and indirect experiences with these cannabis-derived products. This study investigates if organizational approval (e.g., FDA certificate) and manufacturer's reputation mitigate customers' perceived risks, and in turn lead customers to buy cannabis-derived products with more confidence. This question is answered through this research project using analysis of the data collected from U.S. customers.



RESEARCH SPOTLIGHT

Exploring the Potential Health Benefits of Dietary Hempseed

(Research in Dr. Annette Gabaldón's Biology Lab)

Research Team:

Derrick Williams, *Biology-M.S.*

Whitney Lujan, *Biology-M.S.*

Kayana Casias, *Biology Graduate Student*

Hailey Streff, *Biology Graduate Student*

With support of the ICR, we have been exploring the potential health benefits of dietary hempseed. Hempseed is increasingly being used as a dietary aide for humans because of its rich macronutrient and phytochemical composition. The pressed seed cake is also commonly supplemented into agricultural animal feed. However, we still know very little about the physiological influences of dietary hempseed. Like other edible seeds, there is potential for widespread bioactive properties.

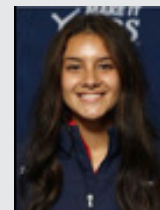
In our first ICR study, we performed microbiology studies to determine if probiotic bacteria could ferment and grow in a media containing whole hempseed as the only carbon source. We chose two strains of probiotic bacteria that are commonly found in the human large intestine, and which are capable of producing fermentation metabolites with known anti-cancer activity. We discovered that whole hempseed supports probiotic growth (i.e. it can serve as a dietary “prebiotic”), and that short chain fatty acids with anti-cancer activity can be generated through fermentation. The significance to human health is the potential for protection against colon cancer. This research was conducted by M.S. biology graduate student, Mrs. Whitney Lujan, and undergraduates.

In a second ongoing ICR study, we are performing cell culture studies to explore the anti-cancer activity of hempseed fermentation metabolites. Cancerous human colon epithelial cells were selected as the model system. We chose colon epithelial cells because the colon is the site of direct action of the probiotic bacteria. The colon lining is protected against cancer by the probiotic bacteria. For example, butyric acid, produced through fermentation of plant fibers, is an energy source for healthy cells but is toxic to cancerous cells, thus helping to prevent proliferation and cancer spread. Cultured cells will be treated with the fermentation media and tested for cytotoxicity, viability and proliferation (growth). Here, we are using a more complex probiotic combination obtained through fecal slurries, to ensure diversity of the probiotic bacteria naturally found in the colon. This research is being conducted by M.S. biology graduate student, Ms. Kayana Casias, undergraduates, and Mr. Derrick Williams.

A third major ICR supported study investigated the influence of dietary hempseed on growth parameters and gut microbial diversity using the C57BL/6 female mouse as an animal model. We obtained young mice at 5 weeks of age and separated them into three diet groups (Control, 0% Hempseed; 5% Hempseed; and 15% Hempseed). The mice were fed their respective diets for 25 weeks while we recorded food intake, body weight, and body composition (via DEXA scanning), at regular intervals. The hempseed diet did not have a remarkable influence on growth parameters. Feed efficiency (gram body weight gain per gram food eaten) decreased with aging and was not altered by the hempseed diet. The gut microbial diversity studies will be undertaken this year along with other measurements on collected tissue samples. This research was conducted by Mr. Derrick Williams, M.S., and M.S. biology graduate student, Ms. Hailey Streff.



This has been my first year in the biology master's program at CSU Pueblo and I have had the wonderful opportunity of being able to grow and develop my research through the ICR grant. I do my research under Dr. Gabaldón and plan to observe the effects of hempseed fermentation metabolites on human colorectal carcinoma (Caco-2) cells. Through this experience, I have gained critical thinking skills, the ability to search the literature, and the opportunity to further expand my research project. Thanks to the ICR grant, I can continue to grow as both a student and a scientist through my research.



- Kayana Casias, *Student Research Assistant*



RESEARCH PARTNERSHIPS

How Does Cannabidiol Modulate Learning and Memory in Humans?



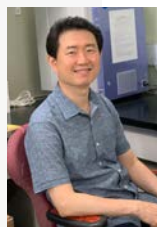
PI.: Dr. Moussa M. Diawara

Co-Investigator: Dr. Jeff Smith, Amy Uhernik

Partner: Dr. Libby Stuyt, Colorado Mental Health Institute at Pueblo

Cannabidiol (CBD) is a form of cannabinoid that lacks the psychoactive (high) effect associated with Tetrahydrocannabinol (THC), the primary cannabinoid found in cannabis. Research findings point to CBD as a possible memory-enhancing agent that could be used to treat cognitive disorders of learning and memory (L&M) whereas treatment of PTSD might not be an appropriate, or neurodegenerative disease of L&M like Alzheimer's. We hypothesize that CBD is a modulator of human L&M. Our broad objective is to examine the potential effect of CBD on human L&M in relatively large scale surveys and in isolation from other confounding factors (i.e., other drugs being specifically combined with CBD or particular preexisting medical conditions). We specifically aim to determine whether CBD, when administered alone to healthy human subjects is a modulator of human L&M, and aim to determine whether particular demographic factors present in the general population (e.g., starting age of cannabis use, race, gender, smoking, mental health status, SSRI (or other drug use) will affect the modulatory effect of CBD on L&M.

Identification And Characterization of Hemp Components That Control Abnormal Proliferation of Human Rheumatoid Arthritis Fibroblast-like Synoviocytes And Triple-negative Breast Cancer Cells

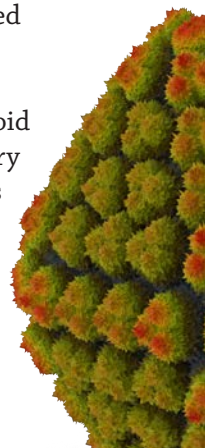


PI.: Dr. KyungHo Lee, Konkuk University, South Korea (Partner)

Co-Investigator: Dr. Sang-Hyuck Park, CSU Pueblo

Research Scientist: Ms. YoonGyeong Lee, Konkuk University, South Korea

Both Rheumatoid arthritis (RA) and triple-negative breast cancer (TNBC) are characterized by abnormal proliferation and an association with an affected immune response. Abnormal proliferation and inflammation disrupt endoplasmic reticulum (ER) homeostasis and induce the unfolded protein response (UPR). The UPR is associated with the pathogenesis of various human diseases including autoimmune diseases, neurodegenerative disease, and diverse cancers. Therefore, the UPR could be served as a favorable therapeutic target for the treatment of RA and cancer. Previously, we have shown that hempseed oil and DHA, one of the polyunsaturated fatty acids, showed the anti-rheumatoid and anti-cancer effects in association with the UPR pathway. Therefore, it is highly possible to find hemp components that control abnormal proliferation of rheumatoid arthritis fibroblast-like synoviocytes (RA-FLSs) and cancer cells under inflammatory conditions. Therefore, in this research, we propose to identify hemp components that control abnormal proliferation of human RA-FLSs and TNBC cells and investigate underlying mechanisms, focused on the UPR.



Formation of Cannabinoids in Glandular Trichomes of *Cannabis*



PI.: Dr. Eunsoo Kim, Konkuk University, South Korea (Partner)

Co-Investigator: Dr. Sang-Hyuck Park, ICR

This study will provide a base for a future thrust relating to a selection of hemp varieties. According to the morphological aspect, three types of glandular trichomes in *Cannabis sativa* are recognized: bulbous, capitate-sessile, and capitate-stalked trichomes. Capitate-stalked trichomes have garnered research interest, whereas the other two types of trichomes have scarcely been investigated during the past twenty years.

Our goal is to determine the functional activities of the three types of glandular trichomes related to the biosynthesis of cannabinoids. First, we will examine and compare the external features, distribution, and densities of these glandular trichomes using digital microscopy and scanning electron microscopy. Second, we will analyze secretory cavity contents of individual glandular trichomes removed through microcapillary procedures from hundreds of trichomes of each type using gas chromatography. Third, we will examine localization and distribution of available antibody probe for CBD in chemically fixed and embedded tissues using transmission electron microscopy.



Capturing Archaeal Biochemistry to Build Bigger Botanical Biomass in Cannabis

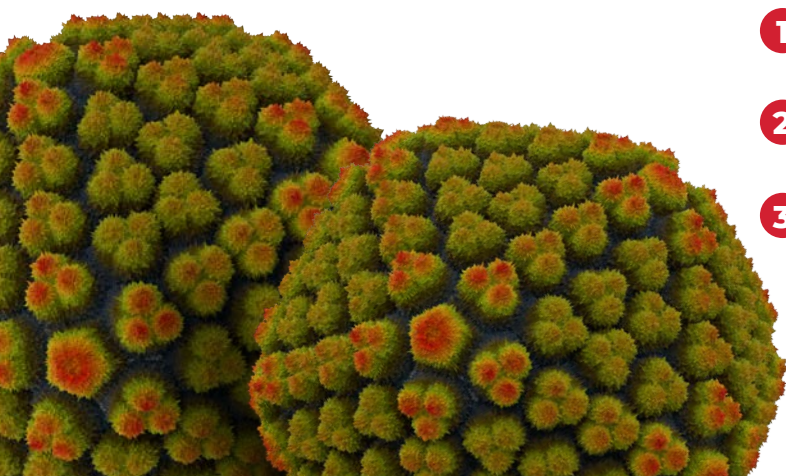


PI.: Dr. Nate Bickford

Partner: Rebecca Roston and Nicole Baun, University of Nebraska, Lincoln

Oxidative stress is a byproduct of harsh environmental conditions and can limit efficient growth throughout the three kingdoms of life. Ultra-reactive side-products of an oxygen-based metabolism can damage critical cellular components and force programmed cell death. In plants, the cell's redox status is intimately tied to interpreting environmental cues. Our preliminary data recently showed that a small antioxidant compound from anaerobic methane-producing archaea (CoX) appears to be a superio natural antioxidant with the potential to change a plant cell's redox status and increase growth by 250%. It remains unclear if these high yields will be sustained in an ecosystem setting. A convenient complex ecosystem for testing this question is aquaponics because it is a complete and yet contained ecosystem that is scalable for agricultural purposes. Thus, in this proposal we address the question, "Can the CoX archaeal redox system be used to increase cannabis yield in an aquaponics setting?" We investigate this through the following three objectives:

- 1 ▶ Build a collaborative bridge between Colorado State University Pueblo and the University of Nebraska Kearney.
- 2 ▶ Determine the concentration of CoX conferring cannabis enhancement in the aquaponics environment.
- 3 ▶ Determine the effects of CoX supplementation on aquaponics and cannabis health.



RESEARCH

PROGRESS SUMMARY

PROJECT	EXPERIMENTAL DESIGN	DATA COLLECTION	DATA ANALYSIS	NO. OF STUDENTS
An Ongoing Investigation into the Effects of Medicinal Cannabis on Seizures in Adults with Medically Refractory Epilepsy*	100%	95%	10%	6
Anti-cancer Potential of Fermented Dietary Hempseed Metabolites and the Role of CB Receptors in Human Colon Cancer Cell Caco2 Viability	100%	50%	50%	4
Applications of Industrial Hemp (Phytoremediation, Cannabinoid Recovery, and Biopolymers)*	100%	70%	50%	5
Cannabis Use Survey Instrument Development and Implementation	100%	0%	0%	8
Capturing Archaeal Biochemistry to Build Bigger Botanical Biomass in Cannabis	100%	40%	20%	3
Effects of Dietary Hempseed on Growth Pattern, Body Composition, Bone Mineral Density, and Gut Microbiota in Mice*	100%	100%	100%	3
Exploring Factors to Mitigate Customers Perceived Risk of CBD Oil Usage	100%	100%	80%	0
Formation of Cannabinoids in Glandular Trichomes of Cannabis*	40%	20%	20%	0
How Does CBD Modulate Learning and Memory in Humans?	80%	30%	20%	1
Identification and Characterization of Hemp Components that Control Abnormal Proliferation of Human Rheumatoid Arthritis Fibroblast-like Systems	100%	100%	100%	0
Interactions of Penicillium Spinulosum with Hemo and Nonpsychoactive Hemp Compounds	70%	30%	30%	1
Rheological Characteristics of Hemp-based Filament Composites for 3D Printing*	95%	25%	0%	1
Sexually Dimorphic Effects of Cannabinoids on Cognitive and Reflexive Learning and Memory-Dependent Neuronal Network Activity in Mouse Hippocampus	100%	30%	20%	8
Social Network Data to Support Cannabis Rehabilitation	70%	70%	70%	2
Understanding Genomic Constituents of Cannabis and Genetic Regulation Underlying Cannabinoid Production	80%	70%	70%	3

*Multi-year Project



INTERNATIONAL COLLABORATIONS

iSAMS Conference and attendees including ICR Director Dr. Chad Kinney and ICR Sr. Scientist Dr. Sang Park



In the last year the ICR has engaged in the development of collaborations with international partners, with particular success from partnerships with universities and organizations in South Korea. In 2019 and 2020, the Institute of Cannabis Research (ICR) has signed four memorandum of understanding (MOU) contracts with academic and research institutes in South Korea - Konkuk University, the Korea Hemp Institute (KHI), the Medicinal Association of Pharmacopuncture Association (MAPI), and the Chuncheon Bioindustry Foundation (CBF) to facilitate Cannabis research cooperation between the parties. The aim of the MOU was to establish the innovative joint-research collaborations by exchanging research resources, experts, and knowledge. As a

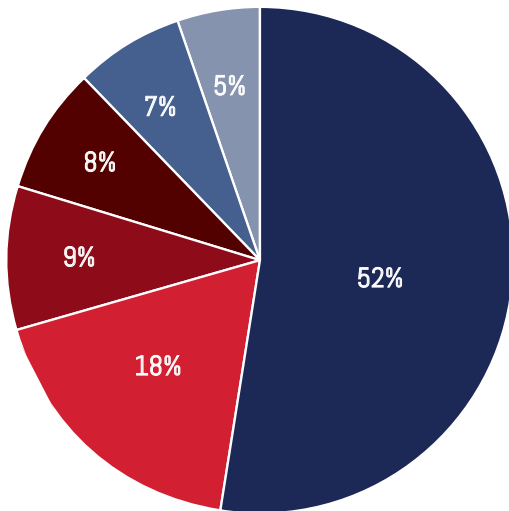
first effort, two visiting scientists, Dr. Eunsoo Kim and Ms. YoonGyeong Lee from Konkuk university joined the ICR research projects. More researchers from MAPI and CBF are expected to join the ICR in this upcoming fiscal year to initiate a new partnership project that will focus on the medical and industrial uses of CBD. The MOUs will facilitate closer collaboration between the parties, as we work towards achieving greater discoveries in medicinal Cannabis and increase social and medical contributions to both countries.

Memorandum of Understanding (MOU) ceremony between the Institute of Cannabis Research, CSU Pueblo and the Chuncheon Bioindustry Foundation, of South Korea (CBF).



FY20 BUDGET

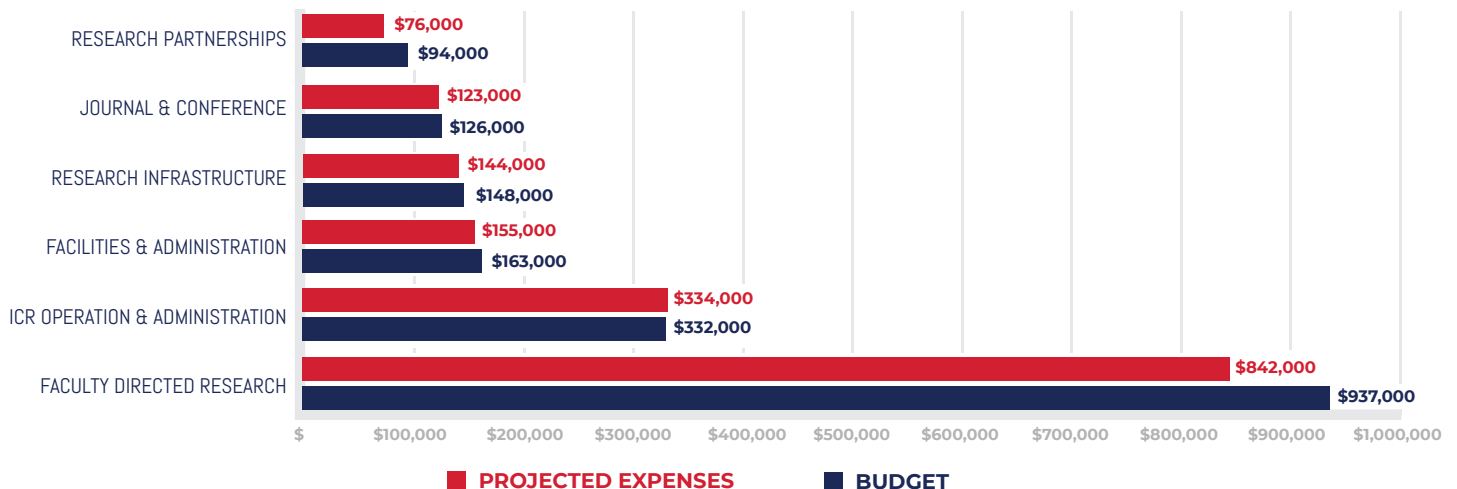
The annual budget for the ICR is used to implement the mission and vision of the Institute. The largest components of the annual budget are related to execution of cannabis research (direct research support, research staff, and research infrastructure), which makes up >65% of the FY20 budget. This year the ICR is projecting that at fiscal year end there will be some unobligated funds, which are primarily associated with Research. This is largely the result of the fact that all research activities had to be suspended in response to the statewide stay at home order that was implemented to protect public health. At the time this order was implemented more than 25% of the research year still remained. The ICR is projecting that about 15% of the monies budgeted for research will be unobligated at the end of the fiscal year. In addition to research support, the other large budget categories are related to the operation of the ICR (administrative staff and operating expenses) and activities associated with the dissemination of research results (the annual ICR Conference and the Journal of Cannabis Research)



FACULTY DIRECTED RESEARCH	\$937,000
ICR OPERATION & ADMINISTRATION	\$332,000
FACILITIES & ADMINISTRATION	\$163,000
RESEARCH INFRASTRUCTURE	\$148,000
JOURNAL & CONFERENCE	\$126,000
RESEARCH PARTNERSHIPS	\$94,000

TOTAL \$1,800,000

ICR FY 2020 BUDGET AND PROJECTED EXPENSES



COMMITTEES & BOARDS

In an effort to maximize impact and ensure proper governance the ICR has historically and continues to interact with a variety of Committees and Boards.

ICR Governing Board

The ICR Governing Board was formed in response to passage of HB19-1311 in spring 2019. The key roles of the Governing Board are to guide the mission and budget of the ICR. Other roles of the Governing Board include advising institutions of higher education developing cannabis related curricula and providing input to the Colorado Commission on Higher Education on new cannabis-related degrees and certificates, as well as lead efforts to secure resources to support the mission of the ICR. The Governing Board meets on a monthly basis, and information related to upcoming Board meetings can be found on the ICR Website. In addition to topics related to their key roles, the Board also considers topics such as research priorities for the ICR, a process for a statewide competition for research support, and the annual ICR Conference. The Governing Board was convened in the fall of 2019 and is comprised of:

The Chancellor of the Colorado State University System or their Designee:

Dr. Timothy Mottet, *President of Colorado State University Pueblo* (Designee)

The Executive Director of the Colorado Commission on Higher Education or their designee:

Mr. Scott McWhorter, *CEO Rocky Mountain Extraction Services* (Designee)

The President of the University of Colorado or their designee:

Ms. Ann Bennan, *Regulatory Compliance Associate University of Colorado Boulder* (initial designee);
Dr. Jon Reuter, *Assistant Vice Chancellor of Research Integrity & Compliance University of Colorado Boulder* (current designee)

The Executive Director of the Department of Public Health and Environment or their designee:

Ms. Mara Brosy-Wiwchar, *Legislative Liaison Department of Public Health and Environment* (Designee)

Three Scientists from relevant fields and employed at appropriate research-oriented institutions:

Dr. L. Cinnamon Bidwell (Board Chair), *University of Colorado Boulder*
Dr. Maureen Leehey, *University of Colorado Anschutz Medical Campus*
Dr. Suzanne A. Sisley, *Scottsdale Research Institute*

Four members associated with Cannabis-Related Industries within Colorado:

Dr. Malik Muhammad Hasan, *Neurologist and NuVue Pharma*
Mr. Sherard Marshon Rogers, *SRMG LLC*
Mr. Salvatore Pace, *SMP LLC*
Mr. John Desmond Lord, *CEO LivWell*



COMMITTEES & BOARDS, *Continued*

Steering Committee

The ICR Steering Committee has historically been involved in leading and guiding the ICR at CSU Pueblo. The initial legislation that led to the creation of the ICR in 2016 provided resources to support Cannabis Education and Research at Colorado State University Pueblo. The Steering Committee helped oversee the implementation of this mandate across the campus. The Committee has included representation from the campus Administration and Faculty invested in seeing the ICR be successful. With the passage of HB19-1311 in spring of 2019, the mandate for the ICR as well as the governance of the ICR changed. A Governing Board was created, and its members announced in fall of 2019. This shifted the role of the Steering Committee to being more advisory and ensuring good communication with stakeholders on the CSU Pueblo campus.

Community Liaison Board

The ICR Community Liaison Board (CLB), was started in 2018 and is made up of community members from the broader Pueblo area that represent a variety of stakeholder groups including public health and health care, education, law enforcement, and business sectors. This group serves to advise the ICR on the impacts of cannabis in the community, potential areas of research need, as well as perceptions related to the ICR and its activities. The CLB provides a collegial mechanism for information sharing between the ICR and regional stakeholders.

Scientific Research Advisory Board

The Science Research Advisory Board (SRAB) was created to enhance the ICR scientific research effectiveness, timeliness, and to suggest important research directions. Cannabis scientific research represents a dynamic and changing landscape and the SRAB is intended to assist the ICR in identifying and maintaining activities at the cutting edge of cannabis research. Board members provide regular input to the ICR Director regarding the direction of cannabis scientific research and possible research areas warranting attention by the ICR. The SRAB does not operate independently of the ICR or the ICR Director but serves as an advisory body. The SRAB provides input in the following areas:

- 1 ▶ Advise the ICR on high impact scientific research topics at the forefront of cannabis research.
- 2 ▶ Advise the ICR on potential funding streams, from private, state, and federal sources, to support cannabis scientific research broadly defined.
- 3 ▶ Advise the ICR on topics for sessions or panels at upcoming ICR Conferences to maintain the greatest benefit to the cannabis research community.
- 4 ▶ Advise the ICR on potential high impact collaborations with academic, private, state, and federal entities to enhance the scope of scientific research/products supported by the ICR.
- 5 ▶ Advise the ICR on strategies to maximize the impact and elevate the profile of the Journal of Cannabis Research and other publications.
- 6 ▶ Advise on other areas or topics as prompted from the ICR.

SRAB MEMBERSHIP

Robert Sievers, Ph.D
(CU Boulder Chemistry and Biochemistry and Environmental Studies Program)

Joseph DiVerdi, Ph.D
(CSU Fort Collins, Associate Professor of Chemistry)

Jeff P. Smith, Ph.D
(CSU Pueblo, Associate Professor of Biology; ICR Supported Researcher)

Joanna Zeiger, Ph.D
(Founder, Canna Research Group)

Alisha Holloway, Ph.D
(VP Research & Data Science at Phylos)

Kyle Hill
(Co-founder of Scientific Partnership to Educate, Advocate, and Research)

Sang-Hyuck Park, Ph.D
(ICR Senior Scientist / Research Liaison)



ICR Hemp Farmers Association (IHFA)

The ICR Hemp Farmers Association (IHFA) was founded in August of 2019 by an innovative collaboration with the Institute of Cannabis Research located at the Colorado State University Pueblo and farmers both locally and nationally.

The initiative is intended to provide an open platform that offers an opportunity for stakeholders to share knowledge and updates in regard to best hemp cultivation practices such as pest/weed management and harvest and extraction strategies. Additionally, the collaborative group provides unique opportunities for new hemp growers and industrial stakeholders to seek research and entrepreneurial partnerships. The IHFA is comprised of hemp research scientists, experienced hemp farmers, and entrepreneurs. The IHFA is open to anyone who is interested in growing hemp and who has an interest in hemp for industrial, medical or scientific purposes.

The chair of the IHFA along with advisory members (Dr. Sang Hyuck Park, Dr. Neb Jaksic, Kelly Bitner, and Alan Smith) are currently working on transforming the IHFA into a workshop format to effectively address the farmers season-specific inquiries raised during their cultivation practices. The workshop topics, presenters, and dates will be announced in the ICR website. For more information about the association or about the workshop series, please contact Dr. Sang Park via email at sanghyuck.park@csupueblo.edu.

Working with Sang-Hyuck Park, Chad Kinney, and Nicole Quartiero has been a real honor and the Academic/Scientific and public collaboration is a necessary step forward in establishing Hemp Farming and Processing as a viable, professional, and sustainable business model. This new industry needs all possible input and cooperative efforts to insure success and decrease failures and negative experiences for new growers. We have been most appreciative and grateful for the opportunity to work with ICR and their professional and knowledgeable leadership to further the knowledge base and collaboration among dedicated and committed farmers and processors to grow this fledgling industry into a science based opportunity for those who want to bring back jobs and provide quality products for the health and wellness sector. We hope to be able to participate in the future, and contribute to the success and growth of ICR and the Hemp Farmers Association. We feel this effort to put the research, science, and collaboration ahead of the marketing and sometimes unreliable and scattered information base is the right approach to maximize the success of Hemp as a unique opportunity due to the many diverse products and ingredients it can provide. We are in unusual and changing times with economic challenges and global uncertainty. From our experience we feel ICR, with its excellent vision and leadership, is uniquely positioned to contribute to the overall success of Cannabis Science and Business, and provide a valuable and needed hub for the investigation, incubation, and formulation of principles, ideas, research, and knowledge to further the orderly and organic growth of this incredible sector.

Wes and Susan Dye,
CFH.Ltd, Colorado Processing, LLC, and Sacred Giftz

As an experienced farmer growing hemp for the first time, ICR's Hemp Farmers Association has provided me opportunities to develop strong practical connections with others in the hemp industry, many who have gone through similar challenges, not only within southern Colorado, but across the United States and even internationally. The association has allowed me access to broader social networks within the industry than I might have discovered alone, has helped me to acquire substantial grounded knowledge from experienced producers, has introduced me to vendors providing oftentimes hard to find material inputs, has exposed me to a wide range of hemp processing technologies, and has been an ongoing source of social support. Every now and then we eat some really good food together too. Because the association is nested within the university, the association ideally provides an essential bridge between the theoretical and practical, across which we as producers can appreciate the benefits of scientific hemp research, and researchers can come to better understand those of us with our fingers deep in the soil.

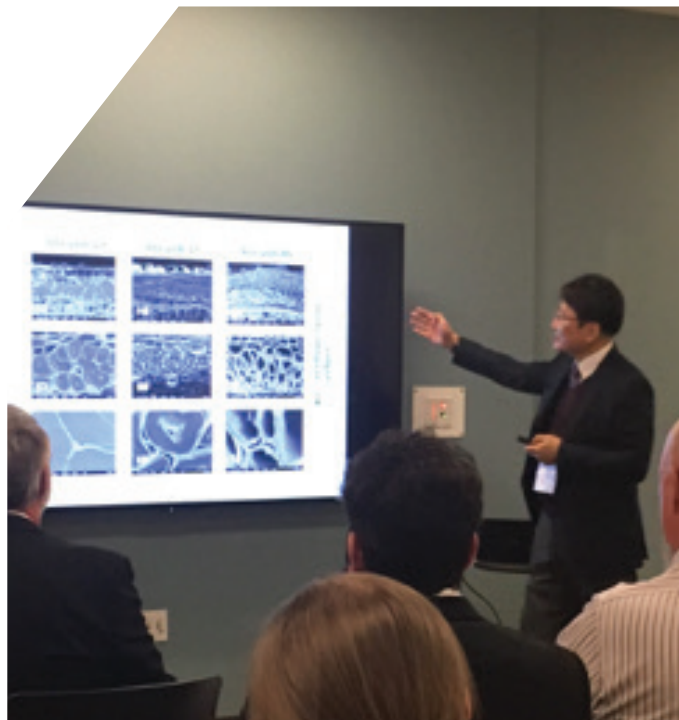
Alan Smith,
HoneyGold Farms and Adjunct Professor Univ. of Maryland Global Campus



2020 ICR CONFERENCE

The annual ICR Conference is a highlight of the activities supported through the ICR. Not only does the Conference provide the opportunity for ICR supported researchers and students to share the latest results of their research efforts, this is an event that brings the best minds in cannabis research to Colorado to share the results of their research activities. With the changing legal landscape of cannabis in the United States, many cannabis conferences and expos have emerged; however, few are geared toward wide-ranging research topics like the ICR Conference. Since the creation of the ICR in 2016, the ICR Conference has gained a reputation as a forum for collegial discussion and dissemination of cannabis research drawing participants from around the globe. As stated in the introductory note from the ICR Director, the ICR Conference 2021 has been postponed from April 4-6 to August 11-12, as a result of the COVID-19 crisis.

The ICR is continuing to look for ways to improve and enhance the conference. This year that has included taking steps to broaden the engagement of the cannabis research community in the development of the program, enhanced the cannabis research exhibition, as well as featuring a pre-conference program that includes professional development opportunities. These are all in addition to continuing other successful components of the conference including the Mechoulam Lecture, to be delivered by World Renowned Researcher Dr. Roger Pertwee from the University of Aberdeen, Scotland, and the Opening Plenary Address to kick off the conference, which will be delivered by Dr. Jeffrey Steiner, the Associate Director of the Global Hemp Innovation Center at Oregon State University.



JOURNAL OF CANNABIS RESEARCH



Journal of Cannabis Research

The Institute of Cannabis Research has partnered with publisher Springer Nature to launch the Journal of Cannabis Research (JCR) last year. The first issue was published in June, 2019. Launching a new journal is a

challenging process. It takes time to develop name recognition and a reputation for publishing quality research. Editor-in-Chief Dr. David Gorelick has done an exceptional job ensuring high standards for the published research that appears in JCR, which includes recruiting world-class section editors and editorial board, and tirelessly promoting the Journal. In 2019 ten manuscripts were published. Through the end of the first four and a half months of 2020 fourteen research articles have been published. Like the ICR itself and the ICR Conference, the Journal serves as a forum for researchers from across the spectrum of cannabis-related research to disseminate the results of their research to a global audience. The Journal is open access, which means that research articles published in JCR are accessible to the general public, industry stakeholders, and academic researchers alike. Please take the opportunity to view the wide-ranging research published in the Journal of Cannabis Research.



ICR DISSEMINATION ACTIVITIES

- 1 Montoya Z, Uhernik A, Smith J. Fear Memory Extinction is Enhanced and Generalized Fear is Reduced By Cannabidiol When Administered to Female Mice Before Fear Conditioning. 17th Annual Front Range Neuroscience Conference; 2019; Fort Collins, CO.
- 2 Uhernik A, Montoya Z, Turner C, Smith J. Fear Memory Extinction is Enhanced and Generalized Fear is Reduced By Cannabidiol When Administered to Female Mice Before Fear Conditioning. Society for Neuroscience; 2019; Chicago, IL.
- 3 Vigil J, Uhernik A, Smith J. HU-211-Sensitive, Cognitive Learning and Memory Processes Modulate GluN2B Surface Expression in the Mouse Brain. 17th Annual Front Range Neuroscience Conference; 2019; Fort Collins, CO.
- 4 Vigil J, Uhernik A, Smith J. HU-211-sensitive, Cognitive learning and Memory Processes Modulate GluN2B Surface Expression in the Mouse Brain. Society for Neuroscience; 2019; Chicago, IL.
- 5 Park S-H, Staples SK, Gostin EL, Smith JP, Vigil JJ, Seifried D, et al. Contrasting Roles of Cannabidiol as an Insecticide and Rescuing Agent for Ethanol-induced Death in the Tobacco Hornworm *Manduca sexta*. *Sci Rep.* 2019 19;9(1):10481.
- 6 Farrer R, Mendel G, Bedoya Valencia L, Correa-Martinez Y, Highfill B. Toward the Production of Novel Fibers Produced Using Biopolymers Extracted from Hemp Plants and/or Biomass. *ACS SWRM/RMRM*; 2019 Nov.
- 7 Neighbours T, Bonetti SJ, Carsella J. Investigation of Glycohydrolase Activities in *Penicillium Spinulosum* Liquid Shake Cultures Supplemented With Varying Amounts of Crushed Hemp Seeds. *SWRM/RMRM*, Southwestern and Rocky Mountain Combined Regional American Meeting of the American Chemical Society; 2019 Nov; El Paso, TX.
- 8 Streff HM, Williams DW, Blanton C, Gabaldón AM. Effects of Dietary Hempseed on Growth Patterns and Body Composition in Young Female C57BL6 Mice. *CSU Pueblo CSM Research Symposium*; 2019 Nov.
- 9 Kim ES. What is a Glandular Trichome in Cannabis, and What is a Major Function of Secretory Cavity? Presentation in preparation; 2020.
- 10 Long Y, Huang K, Cui X, Lichliter D, Zamora M. Mobile App: WeRehab. 2020.
- 11 Pauli CS, Conroy M, Vanden Heuvel BD, Park S-H. Cannabidiol Drugs Clinical Trial Outcomes and Adverse Effects. *Front Pharmacol.* 2020;11:63.
- 12 Regas T, Fullard A, Vanden Heuvel B, Kinney CA, Carsella J, Bickford N. The Potential of Hemp as a Remediation Tool for the Uptake of Heavy Metals and Metalloids. Presentation in preparation; 2020.
- 13 Vigil J, Uhernik A, Smith J. Comparison of Cannabidiol and Citalopram in targeting Fear Memory in Female Mice. To be Presented at the Institute of Cannabis Research 2020 Conference; 2020; Pueblo, CO.
- 14 Vigil J, Uhernik A, Smith J. HU-211-Sensitive, Cognitive Learning and Memory Processes Modulate GluN2B Surface Expression in the Mouse Brain. To be Presented at the Institute of Cannabis Research 2020 Conference; 2020; Pueblo, CO.
- 15 Jaskic N. State of Hemp Research in the Engineering Department at CSU Pueblo. South Korea – CSU Pueblo Meeting; 2020 Feb.
- 16 Seifried D, Ramos MF, Kinney CA. Pressurized Liquid Extraction: A Robust Extraction Method for Cannabinoid Analysis and In-extraction Chemical Modification of Acidic Cannabinoids. *ACS National Meeting*; 2020 Mar.
- 17 The Daily Sentinel, Park S-H. *GJSentinel.com* regarding Human endocannabinoid system. 2020.
- 18 The Durango Herald, Park S-H. Human Endocannabinoid System. 2020.
- 19 Park S-H. Defensive Role of Cannabidiol (CBD) against Pest Insect Tobacco Hornworm *Manduca sexta* Through Disrupting Exoskeleton Development. American Chemical Society (ACS) CANN Subdivision ElSohly Award Presentation; 2020 May.
- 20 Long Y, Huang K. WeRehab: Assisting Cannabis Rehabilitation Via Mobile Application. in *Proceedings of HCI INTERNATIONAL 2020. 22nd International Conference on. Human-Computer Interaction*; 2020 Jul.
- 21 Park S-H. Defensive Role of Cannabidiol (CBD) against Pest Insect Tobacco Hornworm *Manduca sexta* Through Disrupting Exoskeleton Development. The 30th Annual ICRS Symposium on the Cannabinoids, Presentation in preparation; 2020 Jul.
- 22 Choi L, Hwang J. Exploring Factors that Influence Adaption of Cannabis-Derived Products: An Application of Protection Motivation Theory. *Journal of Consumer Psychology*. Manuscript in preparation.
- 23 Huang K, Long Y, Cui X. Quit Together: Identifying Textual Factors that Promote Supportive Interactions in Online Cannabis Support Forums. Manuscript in preparation.
- 24 Montoya Z, Uhernik A, Smith J. Preconditioning Administration of Cannabidiol Enhances Extinction of Cognitive Memory in Female Mice. *Journal of Cannabis Research*. Manuscript in preparation.
- 25 Park S-H. Cannabis Contaminants Limit Pharmacological Use of Cannabidiol targeting *Frontiers in Pharmacology*. Manuscript in preparation.
- 26 Uhernik A, Montoya Z, Smith J. Expanded Analytical Approaches for Resolving Drug Effects with Fear Conditioning Experimentation. *Journal of Neuroscience Methods*. Manuscript in preparation.
- 27 Yescavage K, Cui X. Cannabis Legalization and Opioid-Related Deaths in Colorado, 1999–2018. Manuscript in preparation.





Photos by Wendy Fairchild

