Lab Now Testing For Pathogens, Cannabinoids; High-CBD Strain Becoming Available to Patients

By Fred Gardner

Two plant strains relatively rich in cannabidiol (CBD) have been identified by an analytic-chemistry lab recently established to serve the medical cannabis industry in California.

CBD is a cannabinoid with intriguing medical potential that gets bred out of cannabis when the breeder’s goal is high THC content (as it has been in California for generations). It has long been assumed that available strains contained less than 0.1 percent CBD.

The availability of cannabis that is approximately 5 percent CBD by weight will enable doctors and patients to test its effectiveness in treating various conditions.

High-CBD cannabis might prove palatable to many people who dislike the effects of high-THC cannabis.

Because CBD is not psychoactive, high-CBD strains bred to be low in THC might prove palatable to many people who dislike the effects of (currently available) marijuana.

Such high-CBD strains might enable patients who need large doses of canna- bis to ingest pharmacologic doses of the medical potential that gets bred out of cannabis when the breeder’s goal is high THC content (as it has been in California for generations). It has long been assumed that available strains contained less than 0.1 percent CBD. Learning how to use the sophisticated test- ing apparatus and refining their proce- dures under the tutelage of a sympathetic univer-sity-connected chemist.

Lampach, who put up the original funding, operates the gas chromatog- raph-mass spectrometer (GC/MS) and flame ionization detector (GC/FID).

DeMoura is liaison to the dispensaries, many of whose operators are eager to take part in the testing program.

Software customized by Kind Com- puter Services will enable the lab to handle 100 or more samples per day. It will be up and running by July.

The lab has been refining its proce- dures by testing eight to 10 samples a day provided by Oakland’s Harborside Health Center and Sebastopol’s Peace in Medicine dispensary. Harborside propri- etor Steve DeAngelo has backed the project from its inception. “If you’re call- ing for regulation, you’ve got to get ready for inspection by public health au- thorities,” DeAngelo says.

Another backer, Morpheus of the Cornerstone Research Collective in Los Angeles, says, “This is a wonderful ex- periment that is taking place in Califor- nia—but nobody has to keep an eye on what’s being provided to patients.”

Promoting quality control is a mis- sion shared by the “Clean Green” or- ganic certification program, the Medi- cal Cannabis Safety Council and other industry groups. (see stories on page 23-24). As longtime activist Michele Nelson puts it, “the whole industry is in a tran- sition towards professionalism.”

The Steep Hill lab has found levels of mold, notably Aspergillus Fumigatus, that bear witness to unsanitary produc- tion methods. Almost 3% of samples tested this spring were found to contain Aspergillus and the pounds from which they came were returned to vendors by the dispensary.

Some people will have to clean up their acts, DeAngelo says. “It can’t be the whole family and friends sitting around all with the dogs in the living room. We’re putting out the message, ‘Clean up your trim areas, clean up your growing storage areas, do not have cannabis cur- ing in an area that’s exposed to animals. Set a clean room and put on different clothes when you go in. Wear gloves. Wash your hands. In other words, re- member that your product is medicine and treat it as medicine.”

Input from the lab has already resulted in growers improving their operations, according to Rick Pfrommer, Harborside-Harbour

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CBD: a Treatment for Breast Cancer?

By O’Shaughnessy’s News Service

When California Pacific Medical Center took a half-page ad in the San Francisco Chronicle to announce a pub- lic forum on October 7, 2008, it may have been the first time in history that a hospital pitched its cannabinoid research program to prospective patients. “From Water Bottles to Marijuana Derivatives,” the text called out, “Latest Discoveries about Breast Cancer.”

The ad convinced about 100 women and a few men to skip the second Obama-McCain debate on TV and attend the CPMC forum.

William Goodson, MD, gave a brief talk addressing his listeners to avoid car- cinogens in the environment—a diffi- cult task, given the quality of our air and water. Goodson singled out Bisphenol A, a hormone-disrupting chemical that can leach out of plastic in water bottles, baby bottles, and the lining of “tin” cans. Glass makes the safest container, he said.

Bisphenol A can leach out of plastic in water bottles, which cancer cells escape from a primary tumor and seed secondary tumors at different sites in the body. He also pointed out that “the orchestra conductor” of this process.

“Marijuana derivatives” referred to “Soma A+” plants grown indoors in California –but somebody has to keep an eye on what’s being provided to patients.”

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CBD for Breast Cancer

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McAllister: We’re about to publish the results of the work we’ve done in vitro, combining THC and CBD against glioblastoma multiforme, an aggressive form of brain cancer. We found a synergistic increase in the ability of the compounds to induce apoptosis—programmed cell death. That finding is going to be presented at the ICRS [International Cannabinoid Research Society] meeting. I was quite surprised at how well the combination worked. Now we’re trying to get the funding to do the experiment in vivo.

I proposed to look at many different combinations. I started with THC and CBD because they’re the most abundant. We found that in two out of three aggressive brain-cancer cell lines that we looked at, when you added CBD at a lower concentration than THC, we saw a synergism in terms of its ability to induce cell death.

O’S: What was the most effective ratio of THC to CBD?

McAllister: About fourfold less CBD than THC. This occurred in more than one cell line. And we have discovered a molecular mechanism that may explain why if you add THC and CBD together, they might synergize.

O’S: Could you explain the mechanism?

McAllister: There is a family of signaling proteins called mitogen-activated kinases (MAPK). These proteins control cell growth and survival. Depending on how they function, they can either stimulate cell growth or, if you stimulate them for too long in cancer cells, you can cause the cells to undergo programmed cell death, which is a desirable property in a cancer drug. We found that when you add either compound at lower concentrations alone you produce either no effect or marginal effects on certain MAPK. But when you combine them, you get a pretty dramatic change that leads to increased cell death and reductions in proliferation.

This ties in a little to Guzman’s work. [A 1998 paper by Manuel Guzman and colleagues documented anti-cancer effects of THC and inspired McAllister to test other cannabinoids for similar effects.] He showed that modulation of MAPK was essential for THC’s ability to increase cell death. So we’re carrying on with that story and looking at the different components and seeing which can help. Which fits in with the theory that the endogenous cannabinoids have an “entourage effect.” One compound is not the whole story.

We really want to follow up in vivo now. We have access to actual primary brain tumors from patients—not just cell lines that have been passed for a long time. The problem with cell lines can be that when you passage them for years and treat them with semi-artificial high-serum and all the things that you do in cultures their genetic profile can change so that they’re not the same as the original primary tumor.

But now we have techniques where you can actually take the tumor out of the patient and keep it under conditions where years down the road it would have the same genetic profile as the original tumor. Which gives you a real model to test the efficacy of whatever treatment you’re testing.

The in vivo work we’ve done so far looks promising in regard to CBD being able to inhibit metastasis. And now we’re going to combine it with THC. It makes sense to combine cancer treatments with multiple types of treatments that target different pathways. That’s a classical approach with cancer treatments.

O’S: At the forum you said you had begun using a mouse model.

McAllister: We use a mouse model of aggressive breast cancer. We treat the mice every day with a very respectable concentration—5 milligrams per kilogram [of body weight]. We inject it—systemic administration. These mice get a primary tumor in the breast and just like the common human progression, after a certain amount of time it metastasizes to the lung. We find that if we treat it with the drug, you get significantly less metastasis to the lung.

O’S: Are you still on track to have clinical trials in less than two years?

McAllister: STI pharmaceuticals is talking to clinics in the UK that do these kind of trials. They’re looking at the data. Yes. We’re definitely getting closer.

O’S: Who has the IND [license to conduct the trial] in the UK?

McAllister: STI pharmaceuticals. That’s where we’re thinking the trial will be.

O’S: Women in California will be disappointed.

McAllister: We’re going to try and do a parallel trial here as well. I don’t think it will be a problem.

O’S: What will that trial look like?

McAllister: I need to collect data for about another six months to a year and talk with physicians in order to propose a trial design. I have questions with regard to dosing. In the model we’ve been working with, the mice have a functional immune system. Vincenzo Di Marzo’s group did a study using a human cell line with a compromised immune system. I’ve read reports of CBD modulating the immune system, which raised some concerns. I want to try a couple of different dosing schedules. Do we want to give these patients systemic dose every three days? Every four days? Would oral administration be effective? It is difficult to truly extrapolate between mice and humans but we need more detailed in vivo data before we can proceed.

O’S: Who provides your CBD?

McAllister: NIH. They synthesize it.

O’S: You know that a high CBD strain has been located in California.

McAllister: I have a DEA license here and I’m working towards getting standardized plant extracts from Arno Hazenramp in the Netherlands to confirm that it’s always been my goal to work with extracts. But it’s not easy to find a place to give you extracts with quality control. To do an experiment in a sound, scientific manner you have to know exactly where the material’s coming from, and its make-up.

There’s so much to learn about how these components interact. It was just a few years ago that they found CB-2 agonists in terpenes. And there’s probably even more structures in the extracts that might modulate the activity, depending on whatever physiological effects you’re looking for.

O’S: How do the cannabinoids exert their anti-cancer effects?

McAllister: In the breast cancer model, CBD appears to target two major pathways, resulting in modulation of MAPK and an increase in production of reactive oxygen species. Both changes lead to damaging effects in cancer cells.

That’s different than

AGGRESSIVE BREAST CANCER CELLS lose ability to invade through an extracellular matrix. Cells left at untreated controls; right, cells treated with CBD. Invasive ability is an indication of the cells’ metastatic potential in the body. Photomicrographs by Sean McAllister

breast cancer because of the way the brain tumor model where the majority of the drug’s effect is inducing cell death. With breast cancer it looks like there are two primary pathways.

O’S: If and when high-CBD strains become available to cannabis users in California and people start using it for various reasons—with or without input from their doctors—is there a downside, a danger to that?

McAllister: Yes. I’ve actually seen this in my in vivo experiments. There’s definitely a specific dose-response occurring with CBD. If you’re too low or too high you won’t see an effect. You need to be within specific therapeutic window. If the treatment is not formulated and you don’t really know what dose you’re getting, you might not see any effect.

O’S: If somebody’s using high-CBD cannabis for, say, spasm, they could titrate and figure out an effective dose—two puffs, or three, or four…

McAllister: They probably could. One problem would be the placebo effect. You wouldn’t really know if the effect was due to the drug or the placebo effect on that person.

O’S: I’ve heard it suggested that the placebo effect itself might involve the endocannabinoid system.

McAllister: Why not? When it came to reduction of pain, the placebo effect involved the endorphin system—this system was discovered through research on opiates/opioid. So why couldn’t the placebo effect for spasticity involve the endocannabinoid system? It makes sense. And there’s nothing wrong with the placebo effect. But for cancer it’s going to be important to have the correct dosing schedule.

PhRMA Denial Campaign Continues. But…

Hormone Replacement Therapy

Link to Breast Cancer Confirmed

In July 2002 the Women’s Health Initiative reported that women taking Wyeth’s blockbuster HRT drug Prempro—a combination of estrogen and progestin—had a heightened incidence of breast cancer. Wyeth and their allies in the medical establishment challenged the WHI data, claiming that a drop in the rate at which women were getting mammograms led to fewer cancers being detected. But millions of women stopped taking Prempro, and when the data for 2003 was analyzed, the U.S. breast cancer rate, which had been rising for decades, was shown to have dropped 7%, from 210,000 new cases to fewer than 190,000. This excellent news was reported by researchers at the M.D. Anderson Cancer Center, and again Wyeth et al tried to downplay it.

Now the numbers through 2005 have been analyzed in The New En gland Journal of Medicine (“Breast Cancer after Use of Estrogen-plus Progesterin in Postmenopausal Women,” by Chlebowski et al). The conclusion: “The increased risk of breast cancer associated with estrogen-plus-proges tin therapy declined markedly soon after discontinuation of the therapy and was unrelated to a change in the use of mammography.”

Chlebowski estimates that HRT caused breast cancer in 200,000 women between 1992 and 2002.

“About 22 percent of women who get breast cancer die from it,” according to medical writer Virginia Hopkins, “so by extrapolation we can infer that some 44,000 women died during that decade due to taking synthetic HRT.”

HRT also increases the risk of breast cancer, stroke, heart disease and gallbladder disease and dementia. The role of breast cancer prob ably explains why Marin County has had an elevated breast cancer rate: it’s a function of more and “better” health care available to the affluent.

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