

Zach Klein's new documentary:

Raphael Mechoulam is 'The Scientist'

By Fred Gardner

Many of us who get interested in cannabis as medicine get *very* interested and want to learn more about how it works. One of the first facts you pick up is that the chemical structure of THC was worked out and published in 1964 by Israeli pharmacologists Raphael Mechoulam and Yechiel Gaoni.

Less well known is the sweep of Mechoulam's career. He has been conducting and guiding cannabinoid research all these years, the central figure in a vibrant worldwide entourage.

Zach Klein's beautifully filmed documentary *The Scientist* reviews Mechoulam's role in discovering and elucidating the endocannabinoid system, and proposing clinical applications.

Klein, 46, is one of those people who get *very* interested in cannabis. His 2009 documentary *Prescribed Grass* told the story of Tikun Olam, Israel's pioneering medical cannabis collective (a group Klein helped organize).

In *The Scientist* Klein plays the curious Everyman who questions Mechoulam about cannabis and how it works in the body. (Klein's face is handsomer and more expressive than Everyman's.) The interviews are conducted in the pleasant Jerusalem apartment where Raphi and Dahlia Mechoulam have lived since 1966, and in Mechoulam's lab at Hebrew University, and in his car as the scientist drives to and from work, and at a meeting of the International Cannabinoid Research Society (a group Mechoulam helped organize).

Klein occasionally carries a potted can-



FIVE KILOS OF HASHISH in Raphael Mechoulam's briefcase drew inquisitive looks and comments as he transported it from a Jerusalem

"A scientist should try to find topics of importance."

In response to Klein's first question, Mechoulam observes (in the mildest, sweetest tone of voice) that cannabinoid medicine "is not being used as much as it should be in the clinic. It is of great promise in the clinic [meaning 'in the treatment of patients']. Maybe this film can push it forward a bit."

Klein asks why, at the start of his career, Mechoulam chose to study the active compound(s) in cannabis.

Mechoulam replies, "Well, a scientist should try to find topics of importance..."

"Doing research in a small country with a very limited budget, my philosophy was that one should try to find out topics that

police station to his lab in 1963. The ride took 15 or 20 minutes, Mechoulam tells Zach Klein in *The Scientist*. Graphic by Ivan Art.

worth following."

In 1962 Mechoulam applied for a grant from the US National Institutes of Health. "But NIH wrote me back," he tells Klein, paraphrasing: "The topic you're interested in, namely the constituents of *Cannabis sativa*, is not a relevant topic for the U.S. It's not used in the U.S. When you have something more relevant, ask us for a grant."

About a year later, Mechoulam got a phone call from a high-ranking NIH pharmacologist who was interested in cannabis. "All of a sudden they had a change of mind. So I asked them what happened. Well, apparently someone high up — an important person, maybe a senator — had called NIH and asked, 'What does Cannabis do?'"

"It seems that his son had been caught smoking pot. He wanted to know if marijuana destroyed his mind. They didn't know anything about marijuana..."

"So the pharmacologist came over and asked if I was still working on it and I said yes, we had just discovered the active compound and we had a large amount — about 10 grams of THC."

"I was supported financially by the National Institutes of Health. And they never, never interfered with my research."

"So he said, 'Please give us the 10 grams and we'll do a lot of pharmacology in the U.S.'" Mechoulam complied. "So he got the world's supply of THC, took it to the U.S. — actually, he probably smuggled it because I don't think he had a license to take it to the U.S. But then of course nobody was looking for THC, it was not a known compound. So he took it to NIH and for the next couple of years most of the research on THC in the U.S. was done with materials supplied by us — those grams that they took."

"And for many years — nearly 45 years — I was supported financially by the National Institutes of Health. And they never, never interfered with my research."

"All those that took the THC were affected. But, surprisingly, they were affected differently."

The hashish from which Mechoulam isolated THC and CBD in the early '60s had been obtained from the police in Jerusalem. Bringing it back to his lab on a bus, Mechoulam drew inquisitive looks and remarks from fellow passengers puzzled by "this very unusual smell." His reminiscence is brought to life in *The Scientist* by the formidable Swiss-based cartoonist Ivan Art.

Mechoulam shows Klein (and us) a glass column like the one he and Gaoni used all those years ago to separate out "10 or 12 compounds" from their hashish. Of those compounds, only one was found to be active. (Activity was defined as having a sedating effect on monkeys).

That one active compound, Mechoulam explains, "now named delta-9 tetrahydrocannabinol — THC — causes, essentially, all the hashish-type cannabis type effects."

With basic safety having been established in the medical literature going back centuries and confirmed at the monkey colony, the logical next step was an experiment with humans.

"We had a few of our friends take 10 milligrams of pure THC on a piece of cake my wife prepared," Mechoulam recalls. "And five took only the cake without the THC, and we compared the effects."

"None of us had ever used cannabis before. As a matter of fact very few people had used cannabis at that time in Israel."

"All those that took the THC were affected," Mechoulam tells Klein. "But surpris-



ingly, they were affected *differently*. Some said, 'Well, we just feel kind of strange, in a different world. We want to sit back and enjoy.'

"Another one said 'Nothing happens' — but he didn't stop talking all the time. A third one said, 'Well, nothing's happened. But every 15, 20 seconds he would burst out laughing.'

One of the participants experienced anxiety. Mechoulam says. "She felt, I believe, that her psychological guards... are breaking down and all of a sudden she was open to everybody. So she really got into an anxiety state."

Mechoulam observes, "These effects are well-known today. People are *differently*

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nabis plant — a signature prop, like Charlie Chaplin's cane.

Although Mechoulam's manner is gentle and undemanding, he is making a strong plea in *The Scientist*: cannabis-based medicines should be made available to patients. He does not point an angry finger at any agency or entity that has impeded progress — he shrugs in bemused disappointment.

are not being pursued by the major groups throughout the world. We cannot compete with them... We should try to find — by studying the literature, by thinking about important projects — we should follow research pathways that were not being followed by major groups. Nobody was working on cannabinoid chemistry. So we thought at that time that this was a project



EARLY HUMAN EXPERIMENT conducted by Mechoulam involved "a delicious cake" baked by his wife Dahlia with portions containing 10 milligrams of THC (and an unspiked cake for control purposes). Five of the Mechoulams' friends ingested THC in a social setting, and their responses were carefully observed. These responses ran the now familiar gamut ranging from pleasant social disinhibition to unpleasant anxiety. Illustrations by Ivan Art.



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affected. In some cases we definitely see anxiety attacks. Most do not [experience anxiety]. Most just feel kind of a little bit disoriented. Just maybe a little bit sedated. Maybe a little bit open to discussion and socially open to whatever is being discussed.”

Note Mechoulam’s use of “maybe” and “I believe.” He abjures strong assertions and tends towards understatement, as if his knowledge is provisional.

“It’s not just he discovered THC... but he continued to have such a vision for the next step and the next step and the next step.”

—Mahmoud ElSohly

Promoting research

Klein filmed Mechoulam attending a meeting of the International Cannabinoid Research Society in Freiburg, Germany, in the summer of 2012. “I feel that Dahlia has to be next to me if I want to survive on a trip,” he comments over footage of them boarding a plane.

Among Mechoulam’s colleagues interviewed in *The Scientist* is Mahmoud ElSohly, famous for growing the marijuana that the U.S. National Institute on Drug Abuse (NIDA) provides to researchers. ElSohly tells Klein that Mechoulam has never rested on his laurels, is always seeking to advance research. “It’s not just he discovered THC... but he continued to have such a vision for the next step and the next step and the next step.”

In addition to the ICRS, Mechoulam was a charter member of the more clinically oriented International Association for Cannabinoid Medicines. “Meetings are useful in many ways,” he tells Klein. “People learn what other people are doing and going to do... People from different aspects of a topic talk to each other and maybe something new comes out.”

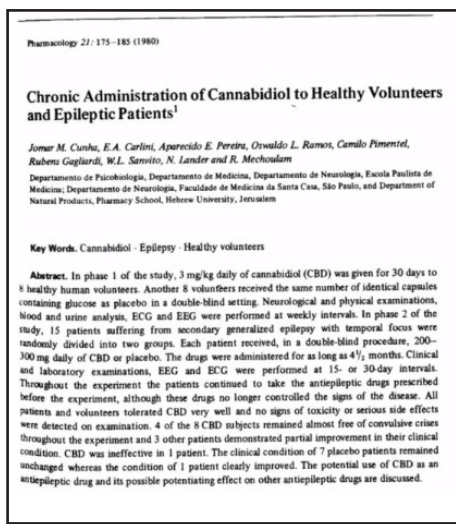
“So the field kind of told us: ‘Try it on epilepsy.’”

Ideas also come from a respectful reading of centuries-old texts. “Mechoulam recalls his role in advancing a Brazilian study of CBD as a treatment for epilepsy, telling Klein (and us) of “an Arab story from the 15th century and it says that one of the Arab leaders had epilepsy. A physician came over and gave him cannabis and it cured him. But he had to take it for his entire life.

“So the field kind of told us: ‘Try it on epilepsy.’”

In other words, from Mechoulam’s POV, it was not his original insight that cannabinoids would have anti-seizure effects, it was a logical conclusion from reading his scientific ancestors. What a modest way to describe his role! And how revealing about insight itself!

The Brazilian study, Mechoulam goes on, was conducted after “we first tried it on



CBD REDUCING EPILEPTIC SEIZURES was reported in the journal *Pharmacology* in 1980, but resulted in no follow-up research with an eye towards drug development.

animals and it worked. Trials took place in Sao Paolo. They had about 10 people who had epilepsy that could not be affected by the known drugs. We started giving them high doses of cannabidiol —200 mg per day...

“We were happy to note that indeed they had no seizures while they were taking cannabidiol. And it was published. And nothing happened afterwards. So far, 34 years later, this is the only publication of cannabidiol in humans against epilepsy.”



MORENO AND ROSA MECHOULAM

“I was very well aware...”

Raphael Mechoulam was born November 5, 1930 in Sofia, Bulgaria, where his father was a physician in private practice and also head of the Jewish Hospital. “I was a child during the war,” Mechoulam tells Klein. “So I was very well aware of what was going on.”

When severe anti-Jewish laws were enacted, Mechoulam says, the family moved to a series of small villages where a doctor was needed and respected. “But at some point somebody decided that my father should be taken to a concentration camp,” Mechoulam says. Dr. Mechoulam was released, apparently in appreciation for his heroic usefulness after a fire destroyed the camp.

“Luckily,” Mechoulam goes on, “the Bulgarian Jews were not killed. The conditions were bad enough, but Bulgarian Jews were not killed. My uncle saved them...” And with a twinkling eye, Raphael Mechoulam tells Klein how his uncle [Dr. Bonko Levy] saved the Jews of Bulgaria from the Nazis’ extermination camps. We won’t spoil it. You’ve got to watch this lovely movie for yourself.



and they talk to each other and maybe something new comes out.

Like most Bulgarian Jews, the Mechoulams emigrated to Israel after World War Two. After a stint as a land surveyor, Mechoulam spent three years in the army, which had him doing research on insecticides. He got his PhD degree from Hebrew University “on the topic of natural products related to biological problems.”

After doing post-doctoral research at the Rockefeller Institute in Manhattan, Mechoulam took a position at the Weizmann Institute in Rehovot, which is where he and Gaoni isolated the compounds in hashish. Mechoulam joined the Hebrew University faculty in 1966.

Receptor and agonist

The Scientist is subtitled *Are we missing something?* —which is the last sentence in a book Mechoulam compiled, *Cannabinoids as Therapeutic Agents* (1986). Klein asks Mechoulam to explain what he had in mind. “Plant cannabinoids,” Mechoulam says, “had been evaluated in the test tube, they had been evaluated in animals and to a certain extent in human patients. But nothing was known at that time about the mechanism.”

“Receptors are made for compounds that we produce, not because there is a plant out there.”

In 1988 the finding of a cannabinoid receptor in rat brain by Allyn Howlett and colleagues at the St. Louis University School of Medicine was characterized by Mechoulam as “a major, major discovery—the first indication that THC acts on a receptor.”

Undoubtedly, Mechoulam points out, “Receptors are made for compounds that we produce, not because there is a plant out there.” So the next challenge for scientists was to find the body’s own endogenous cannabinoids.

“In my lab there were three collaborators who contributed a lot in this research,” Mechoulam tells Klein, as he enters a room where two of those collaborators —Lumír Hanuš and Aviva Breuer— are still at the bench.

Hanuš explains that he came from Czechoslovakia 23 years ago “just for one year, and got a little bit overextended.” Already working with Mechoulam as of 1991 was Bill Devane, who played a key role in Allyn Howlett’s lab when the receptor was identified.

“We initially worked on brains of pigs,” Mechoulam says of the search for the endogenous cannabinoid. “It is generally accepted that the organs of pigs and the organs of humans are somewhat closely related. And probably pigs and humans are also somehow closely related. Well, I’m not sure that the pigs will be very happy to be related to humans, but that’s something else.

“So we wanted to work on pig brains and pig brains are not so easy to get in Jerusalem.” A butcher was found in Tel Aviv who supplied the brains readily at first, but began charging as he realized that his new customers had an ongoing need for the material.

“Each time when we came to buy it again, the price was higher,” Hanuš recalls. “At the end it was very expensive.”

Devane explains how he would take a thin slice of the brain material “and put it over a silica sand column and separate a

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and pig brains are not so easy to get in Jerusalem.



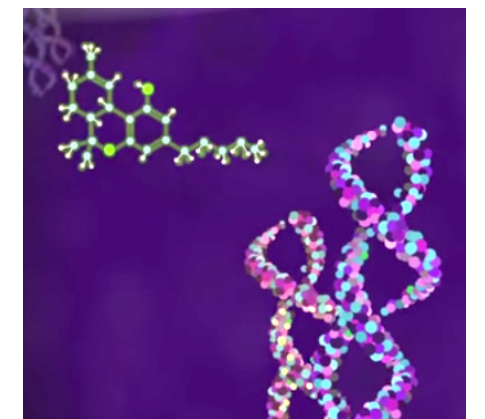
AVIVA BREUER, part of the team that isolated anandamide.



LUMÍR HANUŠ (LEFT) joined the search for the endogenous cannabinoid(s) in 1991. At right is Ester Fridé, who worked with Mechoulam.



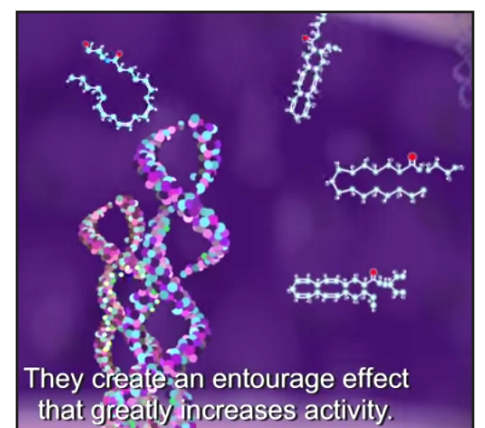
WILLIAM A. DEVANE proposed the name “ananda”—the Sanskrit word for bliss— for the endogenous cannabinoid.



DELTA-9 THC MOLECULE (left) will fit into a cannabinoid receptor pocket (structure at right). The receptor was first identified in Allyn Howlett’s lab at the University of St. Louis School of Medicine. Illustrations by Ehud Graph from *The Scientist*.



ANANDAMIDE MOLECULE (left) in the vicinity of a CB1 receptor pocket, into which it will fit.



They create an entourage effect that greatly increases activity.

“MINOR” CANNABINOIDS and other compounds in the vicinity of the receptor influence how it gets activated: the “entourage effect.”

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ROGER PERTWEE, professor of Pharmacology at the University of Aberdeen, confirmed that anandamide produced by the body behaved like plant-produced THC.

few fractions and test them [radioactively tagged] for how they bound to the receptor. And I thought, 'Oh, it won't take long.'

But when Hanuš's year at the lab came to an end, the endogenous cannabinoid still hadn't been isolated. "So we asked Professor Mechoulam to extend," Hanuš tells Klein.

Other scientists were seeking to identify the endogenous cannabinoid. Devane says Mechoulam "thought we might be scooped by some other lab." But he kept Devane and Hanuš on the project and in 1992 they isolated a small amount of compound they identified as arachidonoyl ethanolamide.

"It was only like a few droplets in the end of a little test tube," Devane remembers.

"It was only like a few droplets in the end of a little test tube," Devane remembers.

The steps to confirm that the newly discovered compound did indeed have the properties that define a cannabinoid were carried out by University of Aberdeen pharmacologist Roger Pertwee.

Devane, who had studied Eastern philosophy, proposed that the newly identified cannabinoid should be named for the Sanskrit word for bliss, *ananda*. "Although some people do not agree with me," Mechoulam tells Klein, "in Hebrew there are not too many names for happiness. For sorrow you can find a lot of names, but... not for extreme happiness."

Because the compound was an ethanol amide, and *amide* fit nicely behind the Sanskrit root, the endogenous cannabinoid was dubbed "anandamide" — a name that says something about its effect and its chemical structure.

Isolation and structure of a brain constituent that binds to the cannabinoid receptor
WA Devane, L Hanuš, A Breuer, RG Pertwee... - Science, 1992 - ... Isolation and Structure of a Brain Constituent That Binds to the Cannabinoid Receptor ... The structure of anandamide was established ...
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The 1992 paper by Devane et al announcing the "Isolation and Structure of a Brain Constituent that Binds to the Cannabinoid Receptor" had been cited 4,342 times as of 2014. "They don't cite it any more," Mechoulam tells Klein, uncomplainingly, "because it's considered such a well-known thing, an obvious thing... They mention that anandamide does A and B and C."



VINCENZO DIMARZO: Raphe basically spoke to me about this entourage idea and he made a very nice comparison between a politician going alone or as head of a delegation.

I was convinced that one should only test pure compounds with one target, whereas it's the combination of the compounds sometimes that can do the trick.



HEATHER BRADSHAW: A cannabinoid field was starting to really come online and there was this big connection with endogenous cannabinoids and exogenous cannabinoids and pain. My PhD was in female reproductive pain. Now we're actually understanding some of the mechanisms of why women basically have taken cannabis for thousands of years for reproductive pain.

An entourage of investigators

In addition to directing research in his own lab, Mechoulam — all these years — has been disseminating ideas and encouragement worldwide. *The Scientist* includes a montage of ICRS investigators acknowledging Mechoulam's guidance — a small cross-section of the many he has helped. It was Mechoulam who inspired Ethan Russo and Vincenzo DiMarzo to think in terms of entourage effects — compounds acting in concert — instead of single molecules. It was Mechoulam who urged Itai Bab to explore the role of endogenous cannabinoids in bone, and Ester Fride to study their role in the birthing process and breastfeeding.

Mechoulam notes matter of factly that nowadays "a huge number of researchers are involved in investigating this system from many aspects... A very serious group of researchers has recently published a paper saying that the endocannabinoid system is involved in essentially all human diseases."

"Hashish for Children?"

Klein reminds Mechoulam, "In 1995 you had an idea of testing THC on children."

It had long been known, Mechoulam responds, that cannabis reduces the nausea brought on by anti-cancer drugs. Children given these drugs "vomit and want to vomit — nausea — they're really in a bad shape. And they cry all the time and their parents are in a bad shape. Luckily, most little children can be cured of the cancer. But the treatment is absolutely difficult."



Finito, that was it.



ALLYN HOWLETT: We've got a lot of research going on because we know now that there are CB1 and CB2 receptors in those types of cells that either help degrade the bone or help rebuild the bone.

In this day and age women are living beyond menopause and men well into old age. We're going to think about how to preserve those bones so they can last another 40 years after menopause.

Mechoulam arranged for a clinical trial led by pediatric oncologist Ava Abramov. "Obviously children cannot smoke. We had children that were not even one year old. She dropped THC in olive oil under the tongue two or three times a day, small doses, during the anti-cancer treatment.

After a week she told me 'I'm not going ahead with that. I know exactly who is getting the THC. I know exactly who is not getting it.'

"In the beginning we wanted to do a double-blind study. Some of the children got the THC, some other children got only the olive oil. After a week she told me 'I'm not going ahead with that. I know exactly who is getting the THC. I know exactly who is not getting it.'

"There was a complete separation. Those that didn't get it continued to vomit. So she went ahead doing an open study. She gave THC — pure THC — under the tongue about 400 times [during the course of a child's treatment]. And at the end we had complete — complete — block of vomiting, a complete block of nausea by a small amount of THC. We did not cause any psychoactivity, nothing.

So here we had a complete therapeutic effect and we published that, and again, essentially nothing happened. Finito, that was it. It's still not being used in children."

Klein repeats the conventional challenge: "And you think it's a good idea to use it for children?"

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Professor Manuel Guzmán
Spain

MANUEL GUZMAN: We know that cannabinoids can exert anti-tumor actions in animals. Not only in brain tumors but in many different types of tumors. We know that cannabinoids act not only by inducing cell death but by inducing cell death through that specific mechanism called apoptosis. We know that cannabinoids can tackle other processes of cancer cell growth, such as angiogenesis, metastasis, cell cycle, etc.

We did a trial with nine volunteers that had a very malignant form of brain cancer, glioblastoma multiforme. And we observed some positive effects of cannabis on survival of the patients and also on tumor growth, based on magnetic resonance imaging and also based on the measurement of biomarkers of tumor progression."



MARY ABOOD: For several years I was researching a motor neuron disease, Amyotrophic Lateral Sclerosis and was able to show that THC was actually protective in the mouse model of ALS. The mice that were given THC lived a little longer."



AARON LICHTMAN: "We're trying to discover how the world works. In our case, how cannabinoids work and how the brain works."



ITAI BAB explained to Klein that mineralized bone is continually broken down by osteoclasts (resorption) while osteoblasts continually form new bone tissue. He and Mechoulam developed semi-synthetic versions of oleoyl serine, an "endocannabinoid-like" fatty acyl amide present in bone. One, HU-671 (the HU is for Hebrew University), was found to increase bone density in a mouse model by decreasing resorption and stimulating bone formation. Bab died in October 2014.



ANDREAS ZIMMER breeds the genetically modified mice used by cannabinoid researchers. Mechoulam wants to see studies involving human patients. "Mice are nice animals," he tells Klein, "but they're definitely not humans."



JAVIER FERNANDEZ-RUIZ has found that cannabinoids may benefit Huntington's and Parkinson's Disease patients.

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Mechoulam has no misgivings. “Well, I believe it’s an excellent idea because we help those children that suffer. But I have no influence on oncologists.” He shrugs and smiles ruefully.

Cut to Allyn Howlett re-enforcing the point, ardent: “If there is a cancer patient who’s got pain and that pain is not being controlled well by other types of drugs, they’re on cancer chemotherapy, they’re vomiting, I think it’s *unethical* to withhold a drug from them that can be very useful to help them in their pain management and in their ability to cope with their disease.”

Can cannabis cure cancer?

Klein asks, “Can cannabis cure cancer?” Mechoulam answers: “We know that THC lowers the [nausea] effects of cancer treatment. But what you’re asking is ‘is it an anti-cancer drug?’ And the answer is, ‘I don’t know.’ And the reason for that is silly.

“It has been tested in the test tube. THC has been tested, cannabidiol, crude cannabis and yes, in many cases it blocks the development of cancer cells. Yes.”

Mechoulam notes the findings of Manuel Guzman, then restates his main theme:



MAURO MACCARRONE notes that in the *Divine Comedy*, the poet Dante Alighieri was in a “gloomy wood” (akin to the Black Forest where the ICRS was meeting), but drew inspiration from the Roman poet Virgil. Maccarrone compared Mechoulam’s influence on his fellow scientists to Virgil’s influence on Dante.

“Though we have done quite a lot in the field of cannabinoids and endocannabinoids, we have not done enough in clinical trials. This is something that has to be done. If this is not done we will certainly miss a lot and we will not be helping human patients. It should be done.”



A recurring dream

Klein asked Mechoulam, “Do you have a dream?” The answer was earthbound and poignant: “I have one dream that comes on and off in very different ways. I’m in a city that I don’t know, and I don’t know how to go back to the hotel I’m staying and I don’t remember the name of the hotel and I get into an anxiety and I wake up. And this has happened many times. I think it has to do with whatever happened in the Second World War when my parents told me ‘Remember these names and these addresses.’ Because if we disappear, you should go there. Which is, well, not very pleasant, which is quite a shock, probably, to a child. And of course we were very afraid that we’ll be separated, my parents and I. I was afraid.

I now remember more than I did over the many, many years that have passed since then. Older people, they start remembering things that happened in their childhood.”

Mechoulam describes a study in which cannabis “seems to be helping the symptoms of Alzheimer... Alzheimer at the moment is a huge, huge problem and there is very little that can be done for Alzheimer’s

patients. So maybe if it is well researched in the future, we should know how to help these patients... We are lucky that cannabis is not toxic.”

The Scientist ends with a clip from Mechoulam’s 2012 talk to the International Cannabinoid Research Society.

“We don’t know why we have different personalities.”

“And now I’d like to end with something that is really crazy speculation,” he says. “Each one of us has a different personality and we have no idea why. Why do we have different personalities? Part of it is the effect of the environment, okay. But part of it is genetic. And we don’t know why we have different personalities.”

Mechoulam elaborates to Klein: “One way of explaining it is there are several hundred endocannabinoid-like compounds—they are like anandamide in their chemical structure—present in the brain.

“And it’s quite possible that each one of

us has a slightly different level of these compounds. This is genetic. This is based on the different DNA of everybody. But



DNA doesn’t affect the personality —It is the compounds that are formed from DNA through RNA to proteins and peptides and secondary compounds. So it is quite possible that differences in the endocannabinoid system—the endocannabinoid-like system—can have something to do with the different personalities. Well, that’s a very complicated story, but it may work.”

Mechoulam tells his colleagues in Freiburg that a mathematician confirmed that different combinations and permutations of 200 fatty acids could account for 8 billion distinct personalities. “This is crazy speculation,” he repeats, “but at some point we’ll have to find the biochemical basis of why we are different.”



STROLLING IN THE BLACK FOREST, Mechoulam stopped to take photos with a small camera. “Many years ago I used to take extreme close-ups and the objects looked interesting,” he told Klein. “One can’t do everything... Unfortunately, I don’t have time for hobbies.”

Rik Musty —an ICRS prime mover

By John McPartland and Fred Gardner

The longtime executive director of the International Cannabinoid Research Society, Rik Musty, died July 26, at home in Wacouta, Minnesota, at the age of 72.

Rik was born in Minnesota, earned a BA from Carleton College in 1964, and a PhD in Psychology from McGill in 1968. He joined the University of Vermont faculty that year, and chaired the Department of Psychology from 1975 to 1987. He mentored 31 Masters and Doctoral students, and served on the committees of 20 additional theses and dissertations.

His cannabinoid research began in 1973, as a Visiting Professor in Sao Paulo Brazil, working with Karniol and Carlini. That fruitful collaboration continued through 2006, bolstered by sabbatical leaves to Brazil in 1981 and 2004. PubMed lists 25

posium on Cannabinoids (following an IUPHAR meeting) and edited a report published by the Australian government.

In 1990 Rik, Consroe, and Alex Makriyannis organized a symposium on Crete at which Rik proposed that cannabinoid researchers form a society to hold annual meetings. He had brought by-laws of a Vermont non-profit to expedite the launch of an International Cannabinoid Research Society. The 45 charter members include many still active in the society: Greg Chesher, Dale Deutsch, Mahmoud ElSohly, Javier Fernandez-Ruiz, Eliot Gardner, Allyn Howlett, Toby Jarbe, Thomas Lundqvist, Alex Makriyannis, Raphael Mechoulam, Roger Pertwee, Patti Reggio, and Herb Seltzman.

Consroe says that the creation of the ICRS loosened the vice-like grip of the US

then was executive director through 2010. Assisted by Diane Mahadeen Musty, he ran exceptionally collegial, increasingly well-attended meetings in memorable locations. The Society acknowledged his contribution through an ICRS Career Achievement Award presented at the Lund, Sweden meeting in 2010.

Rik was a quiet-spoken man with wide interests. Few people know his political career. Rik teamed with Bernie Sanders in 1982, which propelled both of them into office—Rik as Burlington City Councilman for Ward 1, and Bernie as Mayor. Rik served for four years on the city council; Bernie went on to run for higher office. In 1986 the two men taught a class at the University of Vermont on “The ‘60s.” (Video of their first 2-hour-long class has been made available by the archivists at Burlington’s Channel 17 / Town Meeting TV.)

Rik’s political skills were on display at the 1998 ICRS meeting in La Grand Motte, France. At the end of the NIDA presentations, Ed Rosenthal of High Times bluntly asked “Do any of you think your work is influenced by [NIDA Director] Alan Leshner’s bias?” There was a pause as the panelists looked at each other to see who would respond. After a few beats Rik said, “Science is always influenced by the culture in which it’s conducted.”

Earlier this year Rik forwarded (to FG) a warning posted on the US Food and Drug Administration website about products falsely labeled as to their cannabidiol content. He said he hoped that, “as the first

U.S. researcher to investigate CBD,” his request to the FDA for more information would be honored. Martin Lee of Project CBD recommended a lawyer to help Rik prod FDA, and was planning to publish whatever he could find out about FDA’s monitoring and testing of CBD products.

Rik’s Minnesota sense of humor was like Garrison Keillor’s. My [J. McP.] first appointment to meet Rik at his office in October 1993 was delayed by a freak Autumn snowstorm. My second visit in May 1994 also occurred in the midst of an unseasonable snowstorm that shut down Burlington. Rik smiled and asked me to limit my visits to normal winter months. He will be missed.



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publications. Musty also wrote a dozen book chapters—including two published in 1984 on the anti-anxiety effects of cannabidiol, A paper he coauthored (*Eur Neurol.* 38:44-8) encouraged the development of a cannabis-based medicine for the treatment of multiple sclerosis and has been cited more than 200 times.

In 1987, Rik, Greg Chesher, and Paul Consroe chaired the Melbourne Sym-

National Institute on Drug Abuse on conference content. NIDA is still the dominant funder of cannabinoid research and strongly influences the ICRS agenda—but not to the extent it once did, says Consroe.

The first ICRS symposium was held in Keystone, Colorado, in June, 1992, as a satellite meeting of the College on Problems of Drug Dependence.

Rik served as the first ICRS treasurer,