



ICRS NEWS

founded in 1991

Letter from the President

Dear ICRS Members,

The 16th ICRS meeting in Tihany is of course fast approaching, but before discussing this I wanted to comment on an important development that has taken place since our previous meeting in Clearwater. This concerns our Society website. A huge amount of work has gone into improving this over the last few months. As a result, the web site now looks really good and is so much more interactive than before! You can keep yourself updated not only with Society matters but also with the most interesting recent publications. There is a direct link to reviews on the most important topics in the cannabinoid field and a useful tool for young researchers who are considering applying for a cannabinoid research post. Up to now the Forum has been visited less than we would have expected, so I urge all of you to make use of it as it permits interactive exchanges of ideas among ICRS members. As part of our web site revamp, we mounted a competition to find a new logo for the Society. The winner was Natalia Realini, a Ph.D. student from Tiziana Rubino's lab, who created a very nice design in which the plant is the starting point for the discovery of the endocannabinoid system and its therapeutic applications. The logo will be presented at the meeting.

This year we received 232 abstracts, all closely examined by the Program Committee. The number of submissions was a little bit less than for past conferences but this is most probably due to the occurrence, at roughly the same time, of the FENS meeting in Vienna and the IUPHAR meeting in Beijing. At both these other conferences, a session on cannabinoids has been organized. In Vienna, the topic is "Targeting the endocannabinoid system in neurological and psychiatric disorders and pain." In Beijing, the cannabinoid session is entitled "The role of the endocannabinoid system," thereby confirming the ever growing interest in plant, synthetic and endogenous cannabinoids and their therapeutic



D a n i e l a P a r o l a r o

applications. Thus, the international relevance of our research continues to be confirmed strongly by scientists worldwide.

In Tihany, following the initiative started last year, we will have a Young Investigator Award sponsored by Sanofi-Aventis for a researcher less than 40 years of age. The lecture and ceremony will take place on the third day. The competition was very close and it was very difficult to make a choice between several candidates with excellent curricula! Dr. Miklos Palkovits, who has dedicated his life's work to neuroanatomy, neuroendocrinology and central autonomic regulatory mechanisms of pain, thermoregulation, cardiovascular function and food intake, will present the Kang Tsou Memorial lecture on the second day.

Newsletter
of the
International
Cannabinoid
Research Society

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The timetable of the meeting also includes a session on lipidology, organized and presented by Rao Rapaka (first day), that will focus our attention on this new and interesting signalling pathway that regulates several biological and pathological conditions in a complex manner.

Finally, our scrutiny of submitted abstracts revealed an increased amount of cannabinoid research relating to the nervous system and concerning either the link between cannabinoids and neuropsychiatric disorders (8 oral plus 10 posters) or the regulation of nervous function (5 oral plus 6 posters). Peripheral effects have received much more attention than previously (8 oral plus 16 poster), as has the immune system (7 oral and 2 posters). Clinical studies (6 oral plus 6 posters), neuroprotection (9 oral and 16 poster), pain and inflammation (5 oral plus 14 posters), receptor structure and signal transduction (10 oral and 19 posters), and the biosynthesis and inactivation of cannabinoids (6 oral plus 13 posters) are all well represented, indicating a continued growth of interest in these areas.

The meeting program will include two sessions each devoted to the discussion of a controversial hot topic. In the first of these sessions, we will be asking the question “Are there CB2 receptors in the brain?” and in the second we will be focusing on “Cannabidiol pharmacology.” During these sessions, we will organize interactive, informed discussions on these hot topics. That the brain expresses CB2 receptors is an indication that the regulation of endocannabinoid tone in the CNS is probably even more complex than we had previously thought and it is likely that the session on cannabidiol pharmacology will include a discussion of potential therapeutic applications for this non-psychotropic plant cannabinoid.

As you can imagine, you will be very busy. Even so, there will be the opportunity for a few moments of relaxation as Tibor has organized a boat excursion on Lake Balaton. As usual, we need your enthusiasm and participation to keep our meeting the most important annual occasion for scientists working in the cannabinoid field.

With best regards,



D a n i e l a

New Cannabinoids/Endocannabinoids in the NIDA Drug Supply

In addition to a wide range of classical cannabinoids (unlabeled and radiolabeled), the NIDA Drug Supply Inventory also has endocannabinoids, CB1 and CB2 cannabinoid antagonists (inverse agonists), and a FAAH inhibitor. A number of these compounds are also tritium labeled. The more popular compounds are unlabeled and tritium labelled anandamide, CP 55,940, SR141716, and SR144528. Unlabeled 2-arachidonylglycerol (2-AG) is available, now in larger quantities due to an improved synthesis. Tritium labeled 2-AG (in the glyceryl or arachidonyl moieties) are current targets of investigation. More recently added items include HU 210, noladin, N-arachidonylalanine, N-arachidonylglycine, and p-mentha-2,8-dien-1-ol. The most recent addition is URB 597.

For ordering or additional information contact Hari Singh at: hsingh@ngmsmtp.nida.nih.gov
or Kevin Gormley at: kgormley@ngmsmtp.nida.nih.gov.

Mechoulam Invested as Doctor *Honoris Causa*

By Javier Fernandez - Ruiz

Professor Raphael Mechoulam from the Department of Medicinal Chemistry and Natural Products at Hebrew University of Jerusalem received the doctorate *honoris causa* from Complutense University during a ceremony held in Madrid on January 27. The award was proposed by a number of professors and researchers from Complutense including José A. Ramos, Miguel Navarro, Manuel Guzmán and me, because of Raphi's professional and personal merits.

Based on an ancient university tradition, we dressed in special academic robes for the ceremony. It was a very emotional moment for us all when Raphi received from the University "Rector" all symbols of this doctorate, including a ring, a science book, a pair of white gloves and an academic cap called a "birrete." José Antonio Ramos said in his tribute speech, "Raphael has come back home by receiving this honour," in reference to the Spanish-Jewish origins of the Mechoulam family.



Travel Grants Available for International Young Investigators

The National Institute on Drug Abuse (NIDA) will be sponsoring an all-day satellite mini-convention at this year's Society for Neuroscience (SfN) meeting on Friday October 13, 2006 in Atlanta, GA. The "Frontiers in Addiction Research" mini-convention will hold four symposia and a poster session for early career investigators (graduate students, postdoctoral fellows and junior faculty). The symposia are: The Role of Hypothalamic Peptides in Addiction and Obesity; Social Neuroscience; Scanning the Genome for Addiction and other Complex Disease Genes, and Neural Cell Adhesion and Synapse Formation.

In order to have as diverse a group of poster presenters as possible, NIDA and the ICRS will co-sponsor three international (non-U.S.) early career investigators with travel awards of \$1000 each. If you are interested presenting, please contact the ICRS office at: ICRS@cannabinoidsociety.org for more details.

Cannabinoid Meetings of Interest from 2005



2nd Annual European Workshop on Cannabinoid Research

By Daniela Parolaro

The second edition of the European workshop on cannabinoid research took place in Busto Arsizio (Varese) Italy on April 29 and 30, 2005. Organized by Daniela Parolaro and Tiziana Rubino of the University of Insubria, it drew more than 150 researchers from a variety of European countries. The workshop consisted of four sessions:

- 1) Pharmacology and Cannabinoid Signalling;
- 2) Cannabinoids and Drug of Abuse;
- 3) Cannabinoids in Neuroprotection and Neurodegenerative Disorders; and
- 4) Cannabinoids and Peripheral Functions.

The opening lecture in the Pharmacology and Cannabinoid Signalling session by Raphael Mechoulam proposed an intriguing and new parallel between the immune and the endocannabinoid systems, suggesting that the central task of the endocannabinoid system could be a protective one against brain trauma, cancer proliferation and several neurological diseases. Like the immune system, the endocannabinoids may cause damage if they are erroneously generated, such that in some cases enhancement of neurological damage has been noted. Roger Pertwee presented some interesting data on new naturally occurring compounds that behave as neutral CB1 receptor antagonists and antagonize WIN55212 and anandamide in a highly potent manner. Vincenzo Di Marzo presented a comprehensive update of the regulation of the endocannabinoid levels, showing how the pharmacological manipulation of the enzymes involved in endocannabinoids synthesis/degradation can be used in basic and clinical research. The properties and distribution of monoglycerol lipase were fully examined by Christopher Fowler, who suggested the generation of selective compounds to probe the function of 2-AG in the brain. Bela Szabo opened the second part of the first session with electrophysiological characterization of endocannabinoids as retrograde modulators of synaptic transmission in the cerebellum. Tiziana Rubino presented some interesting data on the role of the ERK pathway in the neuroadaptive mechanisms underlying cannabinoid tolerance. Finally, Gerard Le Fur highlighted the efficacy of rimonabant therapy in the management of patients with cardiovascular risks, in addition to its effects on nicotine addiction and obesity.

In the section on Cannabinoids and Drug Abuse, Walter Fratta examined the potential therapeutic application of cannabinoid antagonists in the treatment of addiction. Daniela Parolaro described the biochemical and behavioural interaction between cannabinoids and opioids, presenting data supporting therapeutic utility in the field of pain management. Silvana Gaetani, in place of Vincenzo Cuomo, reported that developmental exposure to cannabinoids, at doses devoid of overt signs of toxicity and that do not affect gestational and reproductive parameters, may provoke long-term neurological disturbances.

In the section on neuroprotection, Javier Fernandez-Ruiz presented evidence that the endocannabinoid signalling system in the basal ganglia might serve as a novel target for the development of specific pharmacotherapies in the treatment of motor-related disorders, whereas Julian Romero characterized the adaptation of the endocannabinoid system under neuroinflammatory conditions. Beat Lutz provided ↗

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strong evidence that direct endocannabinoid-mediated control of glutamatergic neurotransmission exists in the hippocampus and Mariaelvina Sala presented data that supported a neuroprotective role of both CB1 and VR1 cannabinoid and vanilloid receptors. The talk by Barbara Costa gave details of their new data, showing efficacy of SR141716A in an experimental model of neuropathic pain. Geoffrey Guy presented recent data on the efficacy and tolerability of Sativex in symptomatic multiple sclerosis and chronic pain patients. The topic of cannabinoid and cancer was presented by Maurizio Bifulco, which showed the ability of CB1 receptor agonists as antitumoral agents, as they inhibit growth, angiogenesis and metastasis. Mauro Maccarrone pointed towards a key role for endocannabinoids in the hormone-cytokine network that regulate human reproduction in both females and males. The relevance of the endocannabinoid system in a number of gastrointestinal diseases was examined by Angelo Izzo, raising the possibility of its pharmacological modulation in the treatment irritable bowel syndrome, ulcerative colitis and other gastrointestinal disorders. The oral presentations were closed with the lecture of Michael Randall, which examined the cardiovascular actions of cannabinoids. The poster session consisted of 60 interesting presentations, mainly by young researchers, and was a great success. Daniela closed the scientific meeting with a discussion of potential future venues for the upcoming, third annual conference, including Nottingham England and other European countries.

The social dinner for the invited speakers was friendly and a pleasure not only for taste, but also for furthering collaborative relationships among the people. We also discovered a musician among us when Maurizio Bifulco treated us all to Italian music at the piano.

6th Annual Meeting of the Spanish Cannabinoid Research Society

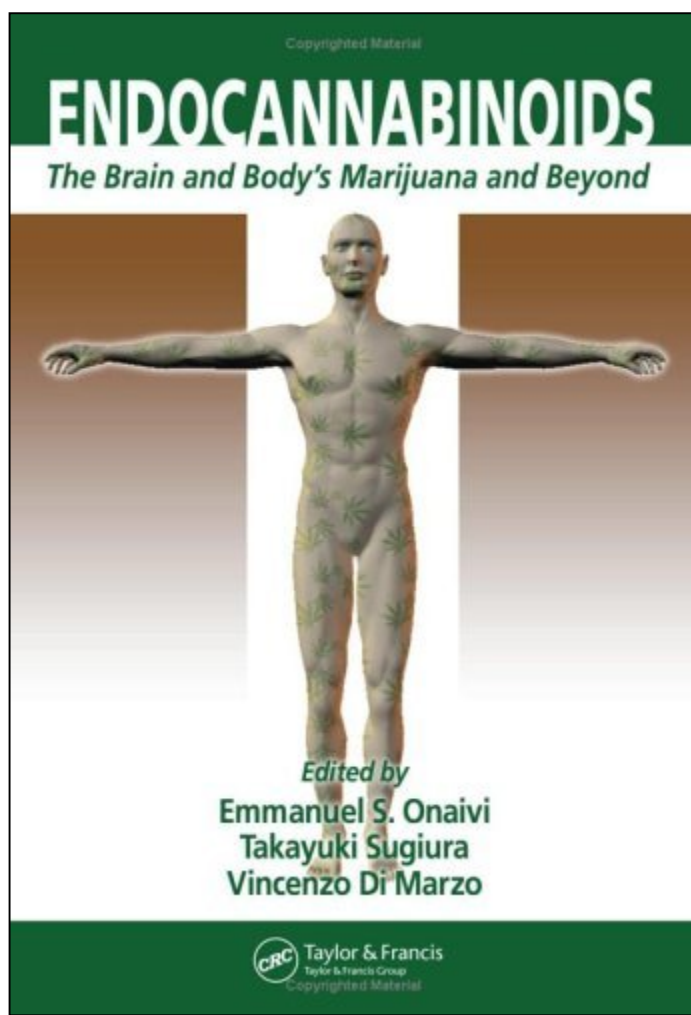
By Javier Fernández-Ruiz



The Spanish “cannabinologists” met November 25-27, 2005 in Barcelona for the sixth annual meeting of the Spanish Cannabinoid Research Society (SEIC) that first started to meet regularly in 2000 in Madrid. The choice of Barcelona was not casual, but rather was a response to the desire to be close to hospitals in this, and other, Catalan cities that started (in November 2005) to evaluate the potential of the cannabis-based medicine Sativex in treating various disorders. During the meeting, we had the opportunity to garner the details of the Catalan clinical trials in a round table with the people responsible for these trials, as well as to discuss ongoing drug development activities with representatives of GW Pharmaceuticals and Sanofi-Aventis. The information was very interesting for all in attendance. So, too, was the second round table, for which were gathered together some of the most prestigious psychiatrists in Spain in the field of cannabis abuse. Attention focused on the possible relationships between cannabis abuse and psychiatric disorders, with special emphasis on schizophrenia, including self-medication with marijuana for this disorder.

Profesor Ester Fríde was our guest this year for the opening lecture. Ester provided an excellent presentation entitled “Impaired function of the endogenous cannabinoid system as the first animal model for “non-organic failure-to thrive” in infants.” She described, in detail, her previous studies on the effects of CB₁ receptor blockade in feeding and survival of rat newborns. She then moved on to talk about her present data, also obtained with neonatal animals, and to her proposals for developing an animal model for “non-organic failure-to thrive” based on manipulations of endocannabinoid activity. Together with Ester’s lecture, there were 35 oral presentations, most of them presented by young predoctoral students in the field of cannabinoid research from different laboratories in Spain. It is impossible for me to give due justice to the original content, relevance and scientific quality of these presentations in this brief note and so instead I am citing the Web address from where the abstract book of the meeting can be downloaded: www.ucm.es/info/seic-web/libro2005.pdf. Of course, the abstracts are written in Spanish, except the one prepared by Ester Fríde, but even so, I expect that you will be able to identify those that of particular interest to you. Importantly, for next year’s meeting that will take place in Toledo, again in November, it has been agreed that the abstracts will also be presented in English so as to make this event more visible to the international scientific community.

Book Review - By Brian F. Thomas



Endocannabinoids: The Brain and Body's Marijuana and Beyond

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Amazon.Com Fun Statistic:

Provides the reader with
1,869 words per US Dollar

This comprehensive hardcover describes the major advances in our understanding of endogenous cannabinoid lipid molecules, or endocannabinoids, their receptors, and the physiological systems involved in their synthesis, chemical messaging and degradation. It begins with a most interesting perspective on early research and discovery with cannabinoids, as experienced by Dr. Raphael Mechoulam. The volume includes chapters from over 20 preeminent research groups to then continue the discussion of the remarkable breakthroughs in our appreciation of one of the most prevalent signaling and receptor systems in the human brain and body. The scope of the text covers the molecular biology and phylogenetics of the cannabinoid receptor, as well as endocannabinoid pharmacology physiology and pathology in the central nervous system and periphery. The breadth of the discussions parallels the system's extensive distribution and the broad roles the endocannabinoids play in the function of the brain and most organ systems. Gastrointestinal, cardiovascular, endocrine and immunological activities of endocannabinoids are described, as are the role endocannabinoids play in cancer, reproduction and development. Also included is an in depth discussion of molecular modeling and computational chemistry studies of the structure of arachidonylethanolamide and other endocannabinoids, which further illustrates the complexities inherent in lipid signaling and termination processes. This substantial compilation of research findings finishes with a perspective on endocannabinoids as potential therapeutic agents. It is an impressive list of authors that have contributed to this interesting subject matter, and the information that it contains will certainly be a valuable reference for those working with cannabinoids, endocannabinoids and other lipid messenger molecules.