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NESACS

THE NUCLEUS

September 2005 *Vol. LXXXIV, No. 1*

September Meeting

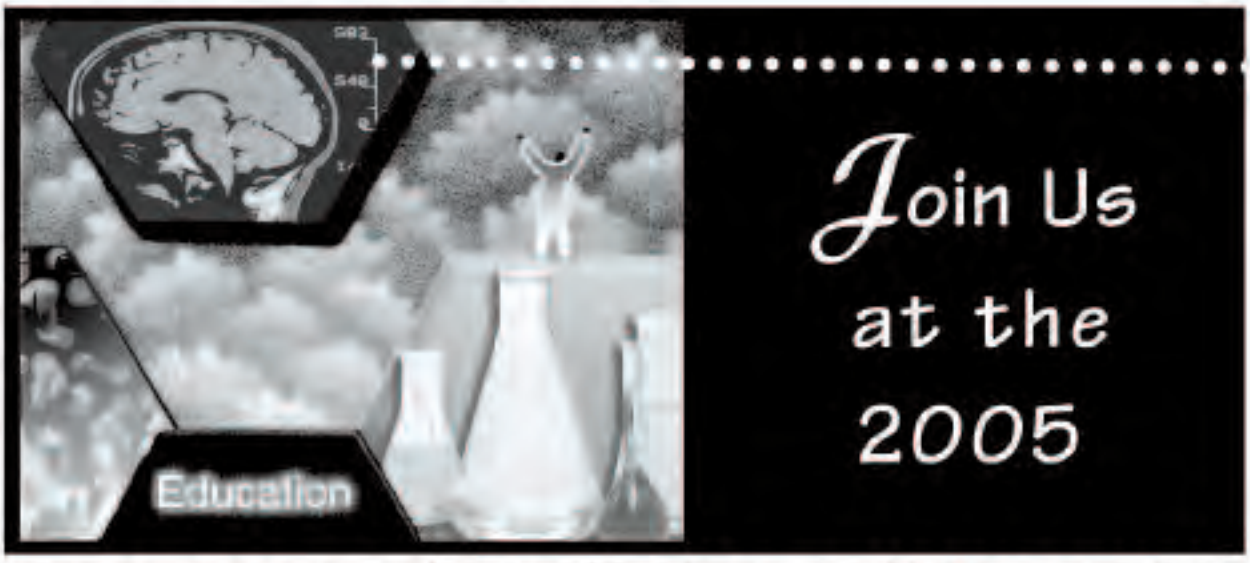
Medicinal Chemistry Symposium

2005 Norris Award

Award to Prof. Mort Hoffman

Biodiesel Alternative Fuels

An article by Martin Freier



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Contents

Cover: *At the Sans Souci Palace, Potsdam: (l-r) Bottom row: Amritanshu Sinha (M.I.T.), Elizabeth O'Day (Boston College), Elizabeth Vogel (M.I.T.), Pia Lopez (M.I.T.), Sarah Chobot (Boston University);*
Second row: Rukman De Silva (Dartmouth College), Tanja Schaffer (University of Regensburg), Xiaoguang Lei (Boston University), Daniel Kennedy (University of New Hampshire);
Third row: William Neeley (M.I.T.), Timothy Gay (Boston University), Jörg Thielemann (University of Potsdam);
Last row: Alexander Taylor (Harvard University), Ivan Korendovych (Tufts University).
See article on page 10 of Summer issue. (Photo: Mort Hoffman)

Deadlines: *November Issue: September 14, 2005*
December Issue: October 14, 2005

THE NUCLEUS

The Nucleus is distributed to the members of the Northeastern Section of the American Chemical Society, to the secretaries of the Local Sections, and to editors of all local A.C.S. Section publications. Forms close for advertising on the 1st of the month of the preceding issue. Text must be received by the editor six weeks before the date of issue.

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Call for Nominations

Gustavus John Esselen Award for Chemistry in the Public Interest

The Northeastern Section (NESACS) is inviting nominations for its prestigious Gustavus John Esselen Award for Chemistry in the Public Interest. This award is given annually to a chemical scientist, whose scientific and technical work has contributed to the public well-being and has thereby communicated the positive values of the chemical profession. The significance of this work should have become apparent within the five years preceding nomination. The recipient shall be a living resident of the United States or Canada at the time of the nomination.

There is no limitation to the field of chemistry. The selection committee focuses on the general public recognition of the work, as well as its scientific/technical significance.

The Award consists of a bronze medal and the sum of $5,000. Travel expenses incidental to the conferring of the award will be reimbursed. The award will be presented at the April 6, 2006 meeting of the Section. The recipient is expected to deliver an address related to the work for which the honor is conferred.

Nominations shall include the names of two co-sponsors, a biography of the nominee, a description of the work which has been recognized as communicating the positive values of the chemical profession, along with copies of pertinent articles and popular news and feature articles indicative of public interest. Joint nominations are acceptable. Further information is available at www.nesacs.org.

Nominations Are Due October 15, 2005.

Award recipients will be notified by February 1, 2006.

Nominations *shall be directed to: Dr. William Klemperer, c/o Karen Piper 19 Mill Rd., Harvard, MA 01451.*

Inquiries *may be made to William Klemperer, Tel. (617) 495-4094; e-mail: klemperer@chemistry.harvard.edu or Karen Piper: Tel. (978) 456-8622* ◇

2005 James Flack Norris Award to Professor Morton Z. Hoffman

Professor Morton Z. Hoffman, Professor of Chemistry at Boston University, has been selected as the recipient of the 2005 James Flack Norris Award for Outstanding Achievement in the Teaching of Chemistry. The award will be presented on Thursday, November 17, 2005. The award is made annually by the Northeastern Section of the American Chemical Society to recognize an individual whose dedication and excellence in the teaching of chemistry have had wide-ranging effects on the profession.

Hoffman received his B.S. degree from Hunter College of the City University of New York in 1955, and an M.S. (1957) and Ph.D. degree (1960) from the University of Michigan. Following postdoctoralwork at the University of Sheffield in England, Hoffman joined the faculty at BU in 1961. He was promoted to Associate Professor with tenure in 1967, and to Full Professor in 1971. Mort has served as Associate Chair for Undergraduate Affairs and as Co-Advisor to the award-winning ACS Student Affiliates Chapter at Boston University. In recent years, he has been increasingly involved in developing innovative teaching techniques for the general chemistry course. These have included pioneering work on using peer-led team learning in large classes. He has been the recipient of BU's Metcalf Cup and Prize for Excellence in Teaching, and was the Founding Director of the Center for Teaching Excellence in the College of Arts and Sciences.

Mort Hoffman has been extraordinarily active with the American Chemical Society for over forty years. He is currently chair of the Division of Chemical Education. He was instrumental in strengthening undergraduate attendance at National Meetings, and has long been committed to facilitating chemical education events at Regional Meetings. Recently, he has been active in conveying the vitality of modern chemistry to teachers at all levels both nationally and internationally. Mort has also served the Northeastern Section of the ACS with great distinction, serving on a wide array of committees. He was Chair of the section in 2002, and is a recipient of the section's Henry Hill

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Monthly Meeting

The 862nd Meeting of the Northeastern Section of the American Chemical Society organized by the Medicinal Chemistry Section of NESACS

Symposium: ***Ion Channel Drug Discovery***

September 8th, 2005
Cambridge Marriott Hotel (617-494-6600)

1:00-4:00 Symposium

Mark Varney *Moderator* (VP of Drug Discovery, ***Sepracor Inc***)
Introduction

Speakers (in order of appearance)

Nancy Barta (Associate Research Fellow, ***Pfizer***)
The Role of α2-δ Calcium Channel Subunits in the Biological Activity of Pregabalin

Francesco Belardetti (Director of Ion Channel Research, *Neuromed*)
Discovery of Calcium Channel Blockers by Sequential Use of Fluorescence-Based Screens, Automated and Manual Patch-Clamp

Valentin Gribkoff (VP of Biology, ***Scion Pharmaceuticals***)
Discovery and Characterization of Openers of Neuronal and Smooth Muscle Potassium Channels

Mark Suto (VP of Chemistry, ***Icagen***)
Approaches to Ion Channel Modulators

4:00-5:00 Networking Cocktail Party

Cocktail Party reservations should be made no later than noon, Thursday, Sept. 1, 2005. Please call or fax Marilou Cashman at (800) 872-2054 or e-mail at MCash0953@aol.com. Reservations not cancelled at least 24 hours in advance must be paid. Members and Non-members $10, Retirees and Students, $5.
THE PUBLIC IS INVITED
Anyone who needs handicap services/transportation, please call Marilou Cash - man a few days in advance so that suitable arrangements can be made.
DIRECTIONS: **From the South:** Take 1-95 North to 1-93 North. Take 1-93 north to Exit 26 and follow the signs to Storrow Drive. Get onto Storrow Drive for approximately 1/4 mile. There will be a LEFT exit for Government Center/Kendall Square. Take that exit and at the bottom of the exit take a right. This will put you onto the Longfellow Bridge. Go over the Longfellow Bridge which will turn into Broadway. After the first set of lights, the hotel will be on the left. **From the West:** Take 1-90 East (Mass Pike) to Exit 18 (Brighton/Cambridge). Bear right towards Cambridge, Once off the exit, go straight and this will put you over the River Street Bridge onto River Street. Follow River Street, which turns into Prospect Street, for 4 blocks and turn right onto Broadway, Go through five lights and the hotel will be on the right.

2005 Norris Award

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Award for Outstanding Service.

The 2005 Norris Award Committee is: Howard Mayne (University of New Hampshire, Chair); Marietta Schwartz (University of Massachusetts, Boston); Don Smith (University of Massachusetts, Dartmouth); Barry Snider (Brandeis University); Jerry Mohrig (Carleton College); Mary Virginia Orna (College of New Rochelle); John Moore (University of Wisconsin, Editor of the *Journal of Chemical Educatio* ◇

Abstracts

Mark Varney, VP of Drug Discovery, Sepracor Inc, joined Sepracor in 2004 as Vice President of Drug Discovery. Formerly of Bionomics, Merck, SIBIA Neurosciences and Servier, Dr Varney has extensive experience in drug discovery focused in the areas of psychiatric and neurological disorders. Dr Varney has been involved in several ion channel discovery efforts that include voltage-gated Ca^{2+} channels, and ligand-gated ion channels from the nicotinic, glutamate and GABA-A receptor families.

Introductory Remarks
Ion channels represent an important class of targets for pharmaceutical intervention in a broad range of disease areas, generating over $12 billion in revenues in 2002. Examples of currently marketed drugs that exert their effects through ion channel modulation include calcium channel blockers, such as Norvasc and verapamil, sodium channel blockers, such as Lamictal and lidocaine, and potassium channel blockers, such as Glipizide. In addition, ligand-gated ion channel modulators are also effective pharmaceutics, which include GABA-A receptor modulators such as Ambien and Lunesta, used to treat insomnia, and benzodiazepines such as Xanax used to treat anxiety, and memantine, an NMDA receptor modulator that improves cognition.

Recent technological developments in cell-based assays and high-throughput electrophysiology now allow ion channels to be targeted in a similar manner to GPCRs, taking advantage of high-throughput screening, and lead optimization. In this symposium, speakers from industry involved in the discovery of drug candidates will discuss key components of ion channel discovery programs.

Nancy Barta, Associate Research Fellow, *Pfizer*, received her Bachelor's degree in chemistry from the University of Nebraska (1989), her Ph. D. from Michigan State University under the direction of Dr. John R. Stille, (1994) and did post doctoral research

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at the University of Michigan with Dr. William Pearson. Dr. Barta then began her career in the pharmaceutical industry in Process Research at Merck in Rahway, New Jersey. In 1998, Dr. Barta transitioned to Medicinal Chemistry at Pfizer Global Research & Development taking a position in Neuroscience Chemistry. Dr. Barta has worked in the neurodegeneration arena investigating FKBP 12 ligands and neurite outgrowth, and in psychotherapeutics with norepinepherine reuptake inhibitors and calcium sensitive ion channels.

The Role of a2-δ Calcium Channel Subunits in the Biological Activity of Pregabalin

α2-δ protein combines with α,β and γ subunits to form the complex that comprises voltage sensitive calcium channels (VSCCs). Electrophysiological studies with recombinant VSCCs demonstrate that the α2-δ subunit both increases cell membrane expression of functioning VSCCs and enhances conductance of calcium current through the channel pore. Biochemical studies revealed that α2-δ is the major component responsible for specific binding of pregabalin to pig brain membranes. Binding of pregabalin to α2-δ modulates calcium currents. This reduction in calcium flux attenuates evoked release of neurotransmitters such as glutamate. Structure activity relationship studies of compounds related to pregabalin and studies with transgenic mice have been carried out to better understand the role that pregabalin's α2-δ binding plays in its observed biological activity.

Dr. Francesco Belardetti, Director of Ion Channel Research, Neuromed, joined Neuromed in 2001, bringing to the company diverse research experience in both academic and industry settings, including more than three years as Principal Scientist for Glaxo Wellcome in Verona, Italy. He earned his MD from Milan' s Università Statale and his PhD from Scuola Normale Superiore, Pisa. After post-doctoral work at Columbia University with E.Kandel, he was recruited by A.G. Gilman at the Dept. of Pharmacology, UT Southwestern, Dallas, where he led an independent laboratory in the study of ion channel regulation by signal transduction pathways.

Discovery of Calcium Channel Blockers by Sequential Use of Fluorescence-Based Screens, Automated and Manual Patch-Clamp

Neuromed is a privately held biophar-

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Nominations

Richards Medal Award

Nominations are invited for the 2006 Theodore William Richards Medal Award for conspicuous achievement in any area of chemistry. The Northeastern Section of the American Chemical Society awards the Richards Medal, honoring America's first chemistry Nobel laureate and initially presented in 1932, every two years.

The medal was last presented to Prof. John Ross of Stanford University. The next presentation will be made in March 2006.

A nomination package consists of a brief curriculum vitae, a list of up to twenty citations for key publications, and a clear and concise nomination letter outlining the nominee's "conspicuous achievements in chemistry ." These materials ***must*** be submitted electronically in a single Adobe® PDF format file to:

Dr. Charles Kolb
Aerodyne Research, Inc.
Billerica, MA 01821-3976
kolb@aerodyne.com

Nominations must be received by **November 1, 2005.** Nominators are responsible to confirm receipt of their e-mail nomination package.

For additional information contact: Chuck Kolb, phone: 978-663-9500, ext. 290; fax: 495-663-4918; email: kolb@aerodyne.com ◇

The 9th Andrew H. Weinberg Memorial Lecture

This annual event functions to highlight achievements and focus on the development of new strategies for the treatment of cancer patients.

Reality Testing: Are We Leaving the Age of Alchemy in Oncology Yet?

Stephen H. Friend, M.D., Ph.D.
President, Rosetta Inpharmatics
Executive Vice President, Advanced Technologies and Oncology, Merck & Co., Inc.

Monday, September 26, 2005, 4:00 pm

The Smith Family Room, Dana 1620
Dana-Farber Cancer Institute
44 Binney Street, Boston, MA 02115

Sponsored by the Andrew H. Weinberg Endowment at Dana Farber, Team Andrew, the Jimmy Fund Walk, and in part by the Medicinal Chemistry Group, Northeastern Section of the American Chemical Societ

For more information, please call 617-632-3971 ◇

Grants-in-Aid to Undergraduates

to Attend the 231st ACS National Meeting in Atlanta, Georgia March 26 – March 30, 2006

The Northeastern Section of the American Chemical Society (NESACS) will provide *Grants-in Aid* of $250 to each of four undergraduates to attend the 231st ACS National Meeting in Atlanta, Georgia and to present a paper at the Undergraduate Research Poster Session in the Division of Chemical Education. The institutions of the successful applicants are expected to match the award.

Eligibility: Applications will be accepted from students at colleges and universities within the Northeastern Section. The undergraduate student must be a chemistry, biochemistry, chemical engineering, or molecular biology major in good standing with at least junior status, and must be currently engaged in under graduate research.

Application: Application forms are available from departmental offices and the NESACS office. In addition, application forms may be obtained from the NESACS Web site at http://www.nesacs.org. The deadline for ***receipt*** of completed applications by Professor Ruth Tanner, the Chair of the Selection Committee, is October 21, 2005. Completed applications are to be sent to:

Professor Ruth Tanner
University of Massachusetts Lowell
Department of Chemistry, Olney Hall
1 University Avenue, Lowell, MA 01854-5047
Phone: (978) 934-3662 Fax: (978) 934-3013
e-mail: Ruth_Tanner@uml.edu

Notification: Applicants will be notified of the results by e-mail on October 28, 2005.
The deadline for electronic submission of abstracts to the American Chemical Society in Washington, D.C. is November 5, 2005. ◇

Abstract

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maceutical company committed to developing small organic calcium channel drugs for the treatment of human diseases such as pain, anxiety, epilepsy and cardiovascular diseases. Pipeline programs are focused on validated therapeutic targets including the N-type and T-type calcium channels. As part of these programs, Neuromed has developed a unique high-throughput fluorescent assay for Low-Voltage Activated (T-type) calcium channels. Unlike other T-type fluorescent assays that require the co-expression of secondary ion channels to alleviate calcium channel inactivation, Neuromed's assay achieves similar results using a combination of specific osmotic conditions and a pore-forming peptide to hyperpolarize the cell membrane. The recent introduction of practical planar electrodes that are routinely capable of achieving gigaohm-seals followed by stable, low-noise whole-cell recordings from a variety of suspended cells can substantially increase screening efficiency without sacrificing quality of the data. Neuromed currently employs PatchXpress 7000A for safety pharmacology (hERG block screening). Finally, manual patch-clamp still plays an important role whenever suspended cells are unavailable and/or for small scale studies. We will present data showing how these assays are used in combination to identify high affinity and selective blockers of T-type calcium channels, which may lead to the development of drugs for the treatment of epilepsy and cardiovascular disease.

Valentin Gribkoff, VP of Biology, *Scion Pharmaceuticals*, received his Ph.D. in Physiological Psychology and Neuroscience from the University of California Riverside in 1983, after which he took an appointment as an NIH Post-Doctoral Fellow in the Department of Physiology at the Tulane University School of Medicine. He began his industrial career in 1987 as a Post-Doc at then Bristol Myers Company (now Bristol-Myers-Squibb) and rose through the ranks to become a

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Biodiesel Alternative Fuels Offer Promise for Achieving Energy Independence

By Martin Freier

In the past few decades, chemists and scientists have been concentrating a great deal of their efforts in solving the energy crisis. But for one reason or another, they have not been able to create a near term, cost effective, environmentally friendly alternative. For a number of years, atomic energy was touted as the way to achieve industrial energy independence. More recently, powering our vehicles by means of batteries and fuel cell hydrogen technology have been proposed. Oddly enough, the much less sophisticated biodiesel fuel has been largely ignored until now. In fact, this technology based on vegetable oil or various animal fats offers something the other technologies do not — simplicity and an approach for immediate implementation with little impact on existing infrastructures.

Scientists, who are not directly working on the energy problem, must find it difficult to comprehend why, with all the technology and tools available in this day and age, the energy problem is so intractable. Some people go so far as to suggest that there must be some kind of a conspiracy going on between the auto industry, oil companies, OPEC, and even the governments. A more sober analysis, however, would show that science has been trying very hard indeed.

As for the various governments and corporations, they have come forth with all kinds of funds on research and development and various incentives. Some of the results so far have been impressive - we can point to atomic plants, wind farms, battery-powered and hydrogen-powered automobiles and solar-heated homes just to name a few. The reason these energy alternatives are not more prevalent in the market place today, has more to do with the absence of a viable economic implementation plan on a global scale that would satisfy consumers' and industrial daily needs than with any other factors.

Historically, chemists have been able to develop chemical alternatives to deal with many of the most intractable problems, but in the case of energy, which is so multidimensional in nature, the ultimate result thus far has not been as promising as initially expected. Unlike other problems (such as dealing with medicines and space travel), in the case of energy for the consumers and the industrial base, there are just too many other obstacles to overcome that have nothing to do with chemistry - things like infrastructure, the complexities of international and global markets, the economics of supply and demand, finite natural resources, the engines that run our vehicles on the road, boilers for heating offices and factories, just to name a few.

Let us consider for a moment the problem in fueling our automobiles, trucks, buses, trains, and jet planes. What we are dealing here are the relatively inefficient, but cost-effective engine designs that have been with us for a long time. These engines were designed and developed by various companies many years ago, other than by the automakers themselves who for the most part are preoccupied with styling, assembly, marketing, sales, and the labor unions. More efficient engine designs are already available but they are not yet cost-effective. Given adequate time and research

Martin Freier is a consultant specializing in technical management, technical, and training strategies. He holds a BS in Chemistry from Brooklyn College and an MS degree in Engineering and Management Science from Worcester Polytechnic Institute. He is a member of the ACS, Northeastern Section.

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funds, we might be seeing them introduced in the newer models that will reach the global market soon. Unfortunately, we cannot afford the wait.

In reality, if it were up to the automakers, they would have preferred to build diesel-powered rather than gasoline-powered automobiles. Diesel engines summon for us contradicting images of the smooth BMWs or the noisy and polluting trucks and buses. As such, they are more expensive and profitable than the traditional gasoline engine-powered vehicles. Oddly enough, they are also more fuel-efficient. Some diesel engines achieve as much as 50 miles per gallon. If profit were the only primary motive, it would have made perfect sense for the automakers to move in that direction. By converting to diesel engines oil consumption could have been reduced by as much as 1/3 and would have brought in more money to the ailing auto industry.

Nevertheless, the diesel approach is not considered viable because today's diesel engine pollution levels of various kinds are unacceptable to the public and the EPA, even if it could be the answer to our energy problem. Therefore, cleaner diesel engines should really be our number one near term priority. But new diesel engine technology is in fact already a very high priority. The auto industry is anticipating the new 2007 diesel engine technology as a potential panacea.

While engineers and scientist are working to design "cleaner" diesel engines, chemists are moving forward in developing biodiesel, a product designed for diesel engine users, in particular, for the heavier transportation industry (consisting of buses, locomotives, tractors, etc.) and heating industry (oil burners). Hopefully, a scientist will stumble on the solution that will bring on a revolution in energy.

According to Michele Rubino, an executive with World Energy Alternatives, Ltd., a supplier of biodiesel blends and biodiesel fuels, with headquarters in Chelsea, Massachusetts, the company he works for develops, produces, markets, and distributes pure biodiesel and the various blends of that product. World Energy Alternatives uses various subcontractors to help in the various aspects of development and production and dealers with the sale and distribution.

"The chemistry of biodiesel production is relatively simple, " said Steve Howell, an energy consultant with Mark-IV Consulting and technical director of the National Biodiesel Board (The NBB is a Jefferson City, Mo based national trade association representing the biodiesel industry as the coordinating body for research and development in the USA).

Biodiesel fuels are mono-alkyl esters and there are three basic methods to produce them from natural oils (such as soybean oil) and fats: (1) transesterification of the oil with alcohol, (2) esterification of the oil with methanol, (3) conversion of the oil to fatty acids and then to alkyl esters with acid catalysis

The majority of the mono-alkyl esters are produced today via transesterification (base-catalyzed reaction) because it is the most economic for the following reasons: (1)low temperature (150degrees F) and pressure (20 psi) processing, (2)high conversion (98%) with minimal side reactions and reaction time, (3)direct conversion to methyl ester with no intermediate steps, and (4) exotic materials of construction are not necessary.

In transesterification, we have a fat or oil reacting with methanol, in the presence of a catalyst to produce glycerin and the fatty acid methyl ester. The methanol is charged in excess to assist in quick conversion and recovered for reuse. The catalyst is usually sodium or potassium hydroxide, which has already been mixed with the methanol.

The great thing about this transesterification process is that some of the methanol can be recovered and that glycerin (that is used in pharmaceuticals and other applications) is also a by-product. In this process, the glycerin needs to be removed to assure that it does not get converted to formaldehyde or acetaldehyde when burned; both of which would pose a health hazard. It is particularly interesting that

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the oil to be used is typically derived from the soybean, a high protein legume of which 80% is animal feed and the remaining 20% will serve as the oil in the biodiesel synthesis. However, any oil, animal fat, lard, or any other recovered cooking oil, can also be used, provided that filtration to remove the degradation products is part of the process.

When I asked Howell how much of the present diesel fuel requirements could be replaced by biodiesel, he responded, "Because of limited feedstocks for biodiesel production capacity, right now our strategy is not to replace existing diesel fuel. Instead, we would like to make various blends of the pure biodiesel with the existing diesel oil."

The rationale here is to leave the two technologies independent of each other and to provide a fuel blend that will be compatible with today's and tomorrow's diesel engine technology. The actual blending of the two fuels could be accomplished at the terminal or someplace downstream.

Some of the readers here may wonder whether or not biodiesel is the only natural alternative. Why not use raw un-reacted oil or fat in the diesel tank?

To assure the consumers that standards of quality are adequate, biodiesel is fully registered with the US EPA and that means that it has passed tier 1 and tier 2 emissions tests. Also an ASTM Specification D 6751 has been developed. A B 20 (20 percent biodiesel and 80 diesel blend) specification is in progress. The D 6751 specification is being modified to address stability concerns and compatibility with 2007/2010 diesel technology.

As for using fat or oil in the diesel engine, instead of biodiesel, the current diesel engines require that the fuel viscosity be comparable to diesel oil, which is about 2 or 3, while soybean oil has a viscosity of 40. In addition, the problem is glycerin is a by-product, which if not removed, would produce the hazardous formaldehyde or acetaldehyde emissions when burned.

When I asked Rubino what he sees as the greatest challenge the biodiesel industry faces, he responded, "The greatest challenge is to develop cleaner diesel engine technologies and better quality diesel fuels," Rubino said. "And that could take years."

In the meantime, it already makes sense for companies such World Energy Alternatives to actively produce the various blends of biodiesel and existing diesel oil, since the two oils are miscible and the resulting price difference is now hardly noticeable. World Energy Alternatives' most popular product is the B 20 biodiesel.

"Another major challenge would be to build the infrastructure for producing an adequate supply of biodiesel oil. " Rubino added.

According to Howell, at this time the infrastructure (i.e., oil and fat supply) is there to keep up with the current demand for biodiesel. In addition to passenger vehicles, biodiesel has applications in various other market segments, including heating oil, electrical generators, transit, fleets, farming equipment, marine vessels and boats, and buses. As of 2004, 25 to 30 million gallons/year of pure biodiesel is being produced. The actual installed capacity is 220 million gallons/year. Another 240 Million gallons/year of biodiesel capacity will be added in 12-18 months. The potential biodiesel from existing feedstock sources is as high 1 billion gallons/year. Howell anticipates that demand should substantially increase in the next 12 to 18 months as oil prices keep increasing and consumers realize that with the tax credits, biodiesel may actually become cheaper in some parts of the country. The US Department of Energy goal is to have non-petroleum sources like biodiesel represent 5 percent of the total yearly diesel requirements.

It appears to me that if there is adequate demand for the biodiesel, more concentrated blends could be developed and there could even be a much more aggressive move towards 100% pure biodiesel, which is more environmentally friendly. Capacities could be added by shifting current diesel refineries towards biodiesel and more energy independence in the United States. Whether or not this shift towards biodiesel will happen could largely depend on the actual pricing structure of the current diesel and economies of scale pricing break for the biodiesel.

Although I have not discussed the home heating market thus far, the immediate potential application in this market is even more than in the transportation market. R. H. Lindsay an executive with Mass Energy (a non-profit organization that both advocates and acts in the marketplace on behalf of consumers and the environment) is using the pure biodiesel (100%) from World Alternatives to provide a mixture of 10% biodiesel and 90% diesel (Bio-Heat). He anticipates that the trend towards biodiesel fuel will pick up when consumers become aware that biodiesel is actually lower in sulphur content and cheaper than diesel as the diesel prices keeps rising while the consumers are realizing a tax credit to offset any difference in price.

"How many homes are actually using your Bio-Heat product," I asked Lindsay.

"About 70 homes."

"Can you accommodate more homes?"

" Certainly. We could service several thousand homes; however, we do have some limitations in selling Bio-Heat. But it has nothing to do with the availability of that product. We have customers waiting to join us and we can get the product."

It turns out that Lindsay's major impediment is to convince the dealers to take on this Bio-Heat product for wider distribution. Part of the dealer 's task is to do the actual blending of the fuel components.

In conclusion, while biodiesel does not currently solve our energy problem, by the very the nature of the new undertaking, chemists are sending a clear message to the world that this new chemical product deserves our attention as part of our strategy to achieve energy independence in the not too distant future. ◇

AstraZeneca Pharmaceuticals proudly announces the 2005 Excellence in Chemistry Awardees:

Professor Dean Toste
University of California, Berkeley

Professor Phil Baran
Scripps Research Institute

The **21st Annual Awards Symposium** will be held at the AstraZeneca Brandywine Auditorium
1800 Concord Pike, Wilmington, Delaware

Thursday, October 27, 2005, from 1:00 – 5:00 pm

Distinguished Lecturer:
Professor Scott Denmark
University of Illinois

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Sponsored by the AstraZeneca Chemistry Department, these awards are presented to promising young faculty who are affiliated with universities in the United States and Canada, recognizing outstanding research in synthetic, mechanistic, or bioorganic chemistry. Each awardee receives a $50,000 unrestricted research grant.

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Abstract

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Senior Principal Scientist in Neuroscience Drug Discovery over the course of 17 years. He was involved in a variety of projects within CNS Drug Discovery, including BMY-21502 for Cognition and BMS-204352 (Maxipost) for Stroke. In 2004 he joined Scion Pharmaceuticals as the Vice-President for Ion Channel Biology. Dr. Gribkoff has authored over 71 peer-reviewed papers, a number of book chapters and several issued U.S. patents.

Discovery and Characterization of Openers of Neuronal and Smooth Muscle Potassium Channels

The many known families of potassium (K^+) channels are important regulators of excitability in neurons and other excitable cells, including smooth muscle. In neurons, K^+ channels contribute to the regulation of neuronal excitability in a number of ways, including their contribution to the resting membrane potential, to the duration and patterning of action potentials, and the regulation of neurotransmitter release. In smooth muscle, K^+ channels regulate membrane potential, ultimately acting as a brake on contraction by regulating the entry of calcium (Ca^{2+}). In these and other tissues, K^+ channels are themselves regulated by numerous biochemical pathways, including phosphorylation-mediated changes in open probability induced by factors such as nitric oxide, and activation by second messengers such as calcium and phosphatidylinositol 4,5-bisphosphate (PIP2). The central role of many of these channels in controlling cellular excitability has led to their identification as targets for the development of therapeutics in a number of areas.

While compounds capable of inhibiting current flow through K^+ channels ('blockers') have long been known (and are easy to find in the case of hERG, or $K_V11.1$ blockers), openers or activators of K^+ channels, compounds that would augment the regulatory function of specific K^+ channel species, were limited until recently to the K_{ATP} channels. This presentation will focus on the recent discovery, characterization and potential utility of openers of 3 types of K^+ channel; the large-conductance Ca^{2+}-activated (maxi-K or BK, Slo) K^+ channel ($K_{Ca}1.1$), the neuronal KCNQ channels ($K_V7.2$-7.5), and the recently discovered sub-family of Slo-like sodium-dependent K^+ channels such as Slack (Slo2; $K_{Ca}4.1$). There appears to be a high degree of overlap between some classes of openers of these channels, suggesting common structural determinants for activity that may reflect common mechanisms for endogenous regulation. Openers of these channels could have utility in conditions characterized by neuronal or smooth muscle hyperactivity, including epilepsy, pain, stroke and smooth muscle disorders such as overactive bladder, hypertension and irritable bowel syndrome.

Mark Suto, VP of Chemistry, *Icagen*, has over twenty years of pharmaceutical and biotechnology industry experience in medicinal and computational chemistry, drug discovery and preclinical development. He has a strong track record of building and managing research teams, designing and implementing product-focused R&D programs, and integrating technologies critical to the drug discovery process. Prior to joining Icagen, Dr. Suto was Executive Vice President and Chief Scientific Officer of Neurion Pharmaceuticals, Inc. Prior to Neurion, Dr. Suto held senior management positions at Deltagen Research Laboratories, DuPont Pharmaceuticals, and CombiChem, Inc. He was also Senior Director, Medicinal Chemistry/Technology Management and Licensing at Signal Pharmaceuticals, Inc. Dr. Suto began his career at Parke-Davis Pharmaceutical Research. He has developed an international scientific reputation in chemistry through his authorship of over 100 research publications, book chapters, abstracts and presentations and is an inventor on over 30 patents. He is a member of several editorial boards and was Editor-in-Chief of Current Medicinal Chemistry, Anti-Inflammatory and Anti-Allergy Agents. Dr. Suto earned his Ph.D. in Medicinal

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Historical Note

J.Lawrence Oncley

J.Lawrence Oncley died July 14, 2004 in Harwich, MA at the age of 94. He was born in Wheaton, IL, attended high school and Southwestern College in Winfield, KS, and earned a Ph.D. in chemistry at the University of Wisconsin in 1932. He came to MIT, but began working with Edmund Cohn at Harvard Medical School on the physical properties of plasma proteins. He moved to Cohn's laboratory in 1936 and became a faculty member of HMS in 1939. His major contribution to the Cohn Laboratory effort during WW II was his isolation and purification of gamma globulin. After the war he also isolated and purified high and low density lipoproteins, HDL and LDL, the cholesterol bearing proteins.

Dr. Oncley was elected to the National Academy of Sciences in 1947, the youngest person to receive that honor at that time. He received his appointment as full professor at Harvard in 1950.

Biophysics and his role as father of the discipline, originated after a four week conference in 1958 was organized by the Biophysics Study Section of NIH and resulted in publication of a book edited by Dr. Oncley, editor in chief, entitled "Biophysical Science: A Study Program" The Biophysical Society was formed shortly thereafter, and he became its president in 1962-64.

In 1962 Dr. Oncley moved to the University of Michigan as Director of its new Biophysics Research Division and Professor of Chemistry and Biologic Chemistry. In 1976 he gave up the directorship, but continued his own research, and in 1980 was made Emeritus Professor. His last research paper was published when he was 93 years old.

Dr. Oncley had been married twice, to Genevieve Reese and, after her death in 1972, later to Lephia French, who died in 1995. Both were his college classmates. He fathered two daughters, had two stepchildren, seven grandchildren, five step grandchildren, and seven great grandchildren. MSS

Historical Notes to be continued

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Abstract

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Chemistry and his B.S. in Medicinal Chemistry at the State University of New York at Buffalo.

Approaches to Ion Channel Modulators

Icagen has established an integrated set of core technologies for the discovery of drugs that act upon ion channel targets. Our platform technologies, which we apply across all of our drug discovery programs, broadly cover the key disciplines of importance to ion channel drug discovery, including molecular biology, electrophysiology, high throughput screening, chemistry, bioanalytics and pharmacology. Our chemistry resources are focused on identifying compounds that potently and selectively modulate the targeted ion channel and that have drug-like characteristics. Our capabilities span the key disciplines of medicinal, combinatorial and computational chemistry. As part of this approach we have been able to generate an enriched library containing multiple classes of compounds with activity against the targeted ion channel for subsequent medicinal chemistry efforts. Examples of the application of this approach across several different ion channels will be discussed. ◇

Calendar

Check the NESACS Homepage for late additions: http://www.NESACS.org

Note also the Chemistry Department web pages for travel directions and updates.
These include:
http://chemserv.bc.edu/seminar.html
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Sep 7

Prof. Steven V. Ley (Univ. of Cambridge)
Wyeth Lecture
MIT, Room 6-120. 4 pm

Sep 13

Dr. Mitch Delong (Procter & Gamble)
The Discovery and SAR of 'Osteoprost' a Preclinical Candidate for the Treatment of Osteoporosis
UNH, Room L103 11:10 am

Sep 22

Prof. Sarah Larsen (Univ. of Iowa) [Nanotechnology]
UNH, Room L103 11:10 am

Sep 26

Stephen H. Friend, M.D., Ph.D. (Rosetta Inpharmatics)
Reality Testing: Are We Leaving the Age of Alchemy in Oncology Yet?
9th Andrew H. Weinberg Lecture
Dana-Farber Cancer Institute
The Smith Family Room, Dana 1620
44 Binney St, Boston. 4:00 pm.

Sep 27

Dr, Jeffrey Elton (COO, Novartis Institutes for BioMedical Research)
Pharmaceuticals: Good Medicine for Business!
Cambridge College presents the Carl F. Barron Distinguished Lecture Series
Cambridge Family YMCA Theatre,
820 Mass. Ave., Cambridge, 7:00 pm

Prof. Louis Brus (Columbia Univ.)
A. D. Little lectures in Physical Chem
MIT, Room 6-120 [Subject to change], 4:30 pm

Sep 28

Prof. Louis Brus (Columbia Univ.)
A. D. Little lectures in Physical Chem
MIT, Room 6-120 [Subject to change], 4:00 pm

Sep 29

Prof. Louis Brus (Columbia Univ.)
A. D. Little lectures in Physical Chem
MIT, Room 6-120 [Subject to change], 4:00 pm

Notices for the Nucleus Calendar should be sent to:

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