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NORTHEASTERN SECTION • AMERICAN CHEMICAL SOCIETY
NESACS

THE NUCLEUS

December 2007 *Vol. LXXXVI, No. 4*

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Medicinal Chemistry Symposium
Signal Transduction Targets and Drug Discovery

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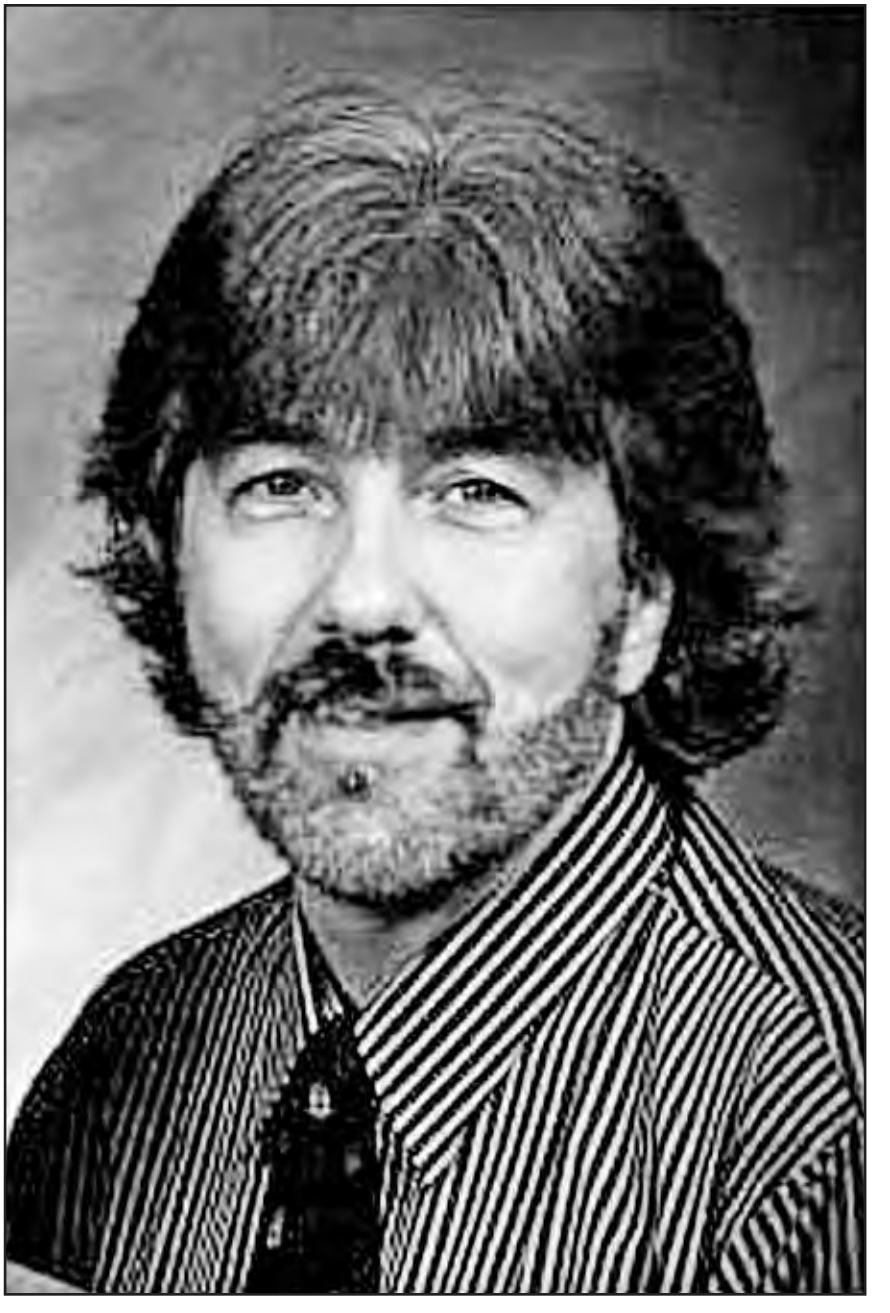

Why the "Northeastern Section?"

by M.S.Simon, Section Archivist

Periodically we have to justify the name of our Section for the benefit of newer members, some of whom think the name is misleading, seeing that we only cover eastern Massachusetts and the State of New Hampshire. The map on our centennial logo also raises the question. As usual, when New England is concerned, history plays a part and it's logic that gets lost in the dust.

Prior to the formation of the American Chemical Society in 1876, chemistry was alive and well in the Boston area, notably at Harvard and M.I.T., but also in other local colleges, high schools and industry. The American Academy of Arts and Sciences had been founded in 1780 and its *Proceedings* was one outlet for publications by the local chemists. Our forechemists might have been a stuffy lot, for they initially had little use for those latecomers in New York.

In 1876, the Americn Chemical Society was founded and chartered in New York. It was restricted by law so that only New York citizens could be its Directors and all of its business had to be done within New York State . Thus, in spite of its name, it represented only 200 to 300 mostly New York chemists. during the period of 1876 to 1890. However, by the latter date interest in the American Chemical Society was dropping off, membership was down to 238, and the decision was taken to become a national organization. A 1890 meeting in Newport, RI hosted by Harvard chemists Wolcott Gibbs and Josiah Cooke, at which formation of local sections was encouraged, followed by a conference in Washington in 1891, revisions of the Constitution and By-Laws in 1892 and a law passed in 1895 by the State of New York which removed residence restrictions, permitted the organization to indeed become a national chemical society.

Did our Boston area predecessors jump at the chance to join? They did not. In fact, at the tenth National Meeting of the ACS, located in Boston and Cambridge, there was no interest in forming a local section.

Time went on, Local sections were formed in Rhode Island, New York, Cincinnati, Washington,DC, Lehigh Valley, New Orleans, Chicago, Nebraska, North Carolina and Columbus. By the time the 1898 National Meeting was approaching, again to be held in Boston, the local folk had a change of heart. It is probable that Arthur Amos Noyes of M.I.T. was the gray eminence behind the decision to form the local section. He was certainly one of the leading chemists here and already had been highly active in the ACS. He was elected the first president of this local section upon its founding. The Section received its charter in 1898 as the eleventh local section of ACS.

And what about the naming of the section? Noyes appointed a By-Law Committee which voted that the territory of the section be the states of Massachusetts, New Hampshire, Vermont and Maine.. The Executive Committee proposed several names for the section: *Massachusetts Section , North Eastern Section*. (*Boston Section* was dropped early on) The membership went its own way and voted for the name we have, *Northeastern Sectio*n.

With an area of 60,000 square miles there was no way for chemists from the outlying areas to come to Boston for monthly meetings. In 1911 a Connecticut Valley Section was formed with a geographic radius of 30 miles from Hartford. The Maine Section was formed in 1912, removing all of Maine. Four years later founding the Green Mountain Section removed Vermont. In 1939 the Connecticut Valley Section added Hampden County and three counties from Massachusetts, Berkshire, Franklin and Hampshire. And in 1947 Worcester County became the Cenrtral Massachusetts Section.

While the Northeastern Section lost square miles, it grew in population and today remains one of the largest local sections of the American Chemical Society. What's in a name?

A more complete history of the Section may be found in the following references in the February 1998 Centennial Issue of the Nucleus.:

"Pre-Northeastern Section Professional Activities of Chemists" by David L.Adams

"Founding of the Northeastern Section, ACS" by Myron S. Simon

"The First Seventy-Five Years" by Edwards R Atkinson

"The Last Quarter Century" by Myron S. Simon, assisted by Phyllis A. Brauner, Arno Heyn, Arthur Obermayer and Edward R. Atkinson

"The Northeastern Section and the Nuclear Test Ban" by Myron S. Simon ◇

NEW NESACS WEBSITE !

The NESACS Board of Publications (BOP) is pleased to announce that we have a completely redesigned and improved website, thanks to the efforts of our webmaster, David Cunningham, who is also a BOP member, and Roy Hagen, a highly effective web consultant. You'll find that the present site provides both more local information and more convenient access to that information. The address is still www.nesacs.org <http://www.nesacs.org/>.

We'll welcome your comments and suggestions, both for the material now covered and for new features you'd like to see. How can we best serve your needs? Please address your thoughts to _webmaster(at)nesacs.org.

At the same time we call your attention to the new ACS website, www.acs.org <http://www.acs.org/>, which features a global navigation system with quick links to such destinations as ACS journals, programs, research, education, and new developments in our field. ACS encourages feedback to WebPresence(at)acs.org. ◇

The Northeastern Section of the American Chemical Society, Inc.

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http://www.NESACS.org
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Cover: *Dr. Tomi Sawyer, Chief Scientific Officer and Senior VP of Drug Discovery, Aileron Therapeutics, Cambridge, MA. Dr. Sawyer is the evening speaker at the this months Symposium on Signal Transduction Targets and Drug Discovery sponsored by the NESACS Medicinal Chemistry Group. Photo courtesy of Dr. Sawyer*

Deadlines: *February 2008 Issue: December 10, 2007*
March 2008 Issue: January 14, 2008

THE NUCLEUS

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Call for Nominations

James Flack Norris Award for Outstanding Achievement in the Teaching of Chemistry

Nominations are invited for the 2008 James Flack Norris Award for Outstanding Achievement in the Teaching of Chemistry. The Norris Award, one of the oldest awards given by a Section of the American Chemical Society, is presented annually by the Northeastern Section. The Award consists of a certificate and an honorarium of $3,000.

Nominees must have served with special distinction as teachers of chemistry at any level: secondary school, college, and/or graduate school. Since 1951, awardees have included eminent and less widely-known but equally effective teachers at all levels.

The awardee for 2007 was Professor Diane M. Bunce of the Department of Chemistry of the Catholic University of America

Nominations should focus on the candidate's contributions to and effectiveness in teaching chemistry. The nominee's curriculum vitae should be included. Seconding letters are also an important part of a nominating packet. These may show the impact of the nominee's teaching in inspiring colleagues and students toward an active life in chemistry and/or related sciences, or may attest to the influence of the nominee's other activities in chemical education, such as textbooks, journal articles, or other professional activity at the local or national level. The committee looks for impact of the candidate's activities at the National and International level.

The nomination materials should consist of a primary nomination letter, supporting letters, the candidates curriculum vitae. Reprints or other publications should NOT be included. Ther material should not exceed thrity pages.

Please direct questions about the content of a nomination to the Chairperson of the Norris Award Committee. For 2008 the Committee Chairperson is Professor Barry Snider, Department of Chemistry, Brandeis University. email: snider(at)Brandeis.edu .

Send nomination packets electronically in Adobe PDF format to Ms. Marilou Cashman, Administrative Secretary of NESACS. email: mcash0953(at)aol.com.

The deadline for nominations is **April 15, 2008.** ◇

Call for Nominations

Philip L. Levins Memorial Prize

Nominations for the Philip L. Levins Memorial Prize for outstanding performance by a graduate student on the way to a career in chemical science should be sent to the Administrative Secretary of NESACS, 23 Cottage St., Natick, MA 01760 by **March 1, 2008**.

The graduate student's research should be in the area of organic analytical chemistry and may include other areas of organic analytical chemistry such as environmental analysis, biochemical analysis, or polymer analysis.

Nominations may be made by a faculty member, or the student may submit an application. A biographical sketch, transcripts of graduate and undergraduate grades, a description of present research activity and three references must be included. The nomination should be specific concerning the contribution the student has made to the research and publications (if any) with multiple authors.

The award will be presented at the May 2008 Section Meeting. ◇

For late breaking news, job postings and the latest meeting and event information please visit us at

WWW.NESACS.ORG

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Abbott Laboratories
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Merck
National ACS
Novartis
Pfizer
Sepracor
Vertex Pharmaceuticals

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2008 Nucleus Editorial Deadlines

Issue	Deadline
February 08	10-Dec-07
March 08	14-Jan-08
April 08	11-Feb-08
May 08	11-Mar-08
Summer 08	16-Jun-08
September 08	14-Jul-08
October 08	11-Aug-08
November 08	15-Sep-08
December 08	13-Oct-08
January 09	10-Nov-08
February 09	11-Dec-08

Submissions should be sent by email to Michael.filosa(at)zink.com ◇

Monthly Meeting

The 883rd Meeting of the Northeastern Section of the American Chemical Society
Jointly with the Medicinal Chemistry Group

Symposium
Signal Transduction Targets and Drug Discovery

Organized by the Medicinal Chemistry Division
Northeastern Section, American Chemical Society

Wednesday – December 12th, 2007

Holiday Inn, 15 Middlesex Canal Park Road, Woburn, MA

Program

3:00 pm Refreshments

3:15 pm Welcome
Raj (SB) Rajur, Program Chair, CreaGen Biosciences, Inc. Woburn, MA

3:20 pm Introductory Remarks
Norton Peet, International R&D consultant, North Andover, MA

3:30 pm ***Discovery of MP-529: A Selective Inhibitor of Aurora 2 Kinase in Development for the Treatment of Cancer.***
Hariprasad Vankayalapati, Director of Medicinal Chemistry, SuperGen Inc., 2401 S, Foot Hill Drive, Salt Lake City, Utah 84109.

4:15 pm ***Applications of Parallel Synthesis in Hit-to-Lead***
Adrian D Hobson, Group Leader, Hit-to-Lead Medicinal Chemistry, Abbott Bioresearch Center, Worcester, MA

5:00 pm ***The Discovery of Motesanib (AMG 706), a Multi-Kinase Angiogensis Inhibitor for Treatment of Human Cancers: From Crystal to Clinic***
Vinod F. Patel, Director of Medicinal Chemistry, Amgen Inc., Cambridge, MA

5:45 pm Social Hour

6:30 pm Dinner

7:45 pm ***Exploring Chemical Space in Protein-Protein Interaction Drug Discovery: Bridging Nature to Breakthrough Medicines***
Tomi Sawyer, Chief Scientific Officer and Senior VP of drug discovery, Aileron Therapeutics, Cambridge, MA

Dinner reservations should be made **no later than noon, Thursday, December 6, 2007**. Please call or fax Marilou Cashman at 800-872-2054 or e-mail at Mcash0953(at)aol.com. Reservations not cancelled at least 24 hours in advance must be paid. Members, $28.00; Non-members $30.00; Retirees, $18.00; Students, $10.00. Payment is made at the door by cash or check (no credit cards). Anyone who needs handicapped services/transportation, please call a few days in advance so that suitable arranÏÏgements can be made.

THE PUBLIC IS INVITED

Directions to the Holiday Inn:
http://www.ichotelsgroup.com/h/d/sl/1/en/hotel/bosms/transportation

Abstracts and Bios

Hariprasad Vankayalapati

Discovery of MP-529: A Selective Inhibitor of Aurora 2 Kinase in Development for the Treatment of Cancer.

One of the important targets for discovering new therapeutics for treating various cancer disease is represented by Aurora kinases, a family composed of three Ser/Thr protein kinases such as Aurora-A, B, and C. Aurora kinases play a crucial role in proper spindle formation at mitosis. Overexpression of Aurora-A leads to dysregulation of the centrosome cycle resulting in the formation of multipolar mitotic spindles. The resulting abnormal mitotic events lead to genomic instability which is an underlying process in tumorigenesis. Inhibition of the Aurora kinase activity in tumor cell lines typically leads to the accumulation of polyploidy cells, apoptosis, and block of proliferation. As a part of our oncology drug development program to identify small molecule kinase inhibitors, we have initially identified a very selective sub-nanomolar inhibitor of the pyrimido[4,5-*b*]indole class of Aurora A kinase using a *de novo* fragment-based design strategy by utilizing X-ray crystal structure of an Aurora-A kinase. To further validate the inhibitory effect of this initial lead molecule, it was subjected to several cell-based assays in which it exhibited activity in the mid- to high-micromolar range. These results suggest that the lead compound is effectively hitting the intended cellular target and that lead optimization will likely be required to produce greater cellular potency. Therefore, we have employed lead optimization and successfully synthesized several compounds that led to the identification of MP-529 potent and selective Aurora A kinase inhibitor that belong to pyrimido[4,5-*b*]indoles series. Based on its high Aurora-A selectivity and antiproliferative activity on different cancer cell lines, favorable

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Advantages of Preparing Submission-Ready Documents

Michelle Foster, Ph.D. and Mukund S, Chorghade, CTD Quality Consulting

The pharmaceutical and biotechnology industries in the Boston metropolitan area have been at the forefront of drug discovery. The efforts of many researchers have led to the discovery and development of numerous novel therapeutic agents for the treatment of a wide spectrum of diseases. Before the fruits of this labor can be tasted, submission of a New Drug Application (NDA) or a Biologics Licensing Application (BLA) to the regulatory agencies is an important landmark in the life of a company.

Imagine what it would be like to be nearing the filing of a marketing application with most of the reports for the filing nearly complete, having been prepared "submission-ready" throughout development. Sound unreal? With some planning and training, this could be a reality for your products. Preparation of submission-ready documents (SRDs) during preclinical and clinical development reduces preparation and review time, makes more efficient use of resources, expedites the process from "mind to market" and achieves shorter sustainable submission cycles, thereby reducing cost and stress to the organization.

Documents may be written during early development in an expandable/modular format that allows for submitting them in the clinical application, the Investigational Drug Application (IND) and then amending, modifying, and replacing them throughout development. As the product moves through the development stages, gaps are filled with new data and findings to meet marketing application demands. Regional differences, for example, differences between what is required for Europe and the U.S., may be addressed using a modular format, by having different subsections for different regions. Information that does not need to be submitted to regulatory agencies, which must be kept on file for GMP documentation, can be placed in appendices. The report can be quickly customized prior to submission with the relevant information.

Challenges in CMC Documentation

Preparation of Chemistry, Manufacturing, and Controls (CMC) documentation for regulatory submissions faces unique challenges not usually found in documentation required for other areas in nonclinical and clinical studies. Regulatory guidance is readily available for clinical study reports, for example, but format/content guidance is not as complete for all types of CMC documents. Preparation of CMC documentation is done by multiple departments, for example, Research and Development, Manufacturing, Validation, Quality Control, and Stability, within the company, as well as by contract manufacturing, and testing labs. Up front training of authors, with agreed-upon templates, ensures consistency of content and format between reports. It is important to get expert assistance in the IND stages in preparing reports in submission-ready format to avoid inefficiencies and delays in finalizing submission reports. Representative examples of reports for which training in preparing submission-ready documents can be provided are: characterization, formulation development, manufacturing development, method validation and process validation, justification of specifications, stability, stress studies and container-closure evaluation

Benefits of the CTD Format

The '**Common Technical Document**' or '**CTD**' is a set of specifications for an application dossier for the registration of medicines and designed to be used across Europe, Japan and the United States. It was developed by the European Medicines Agency (EMEA, Europe), the Food and Drug Administration (FDA, USA) and the Ministry of Health, Labor and Welfare (Japan) and is pivotal to the efforts of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The CTD provides for a harmonized structure and format for new product applications. It is required in Europe, Japan, and Canada. It is "highly recommended" by the US FDA for marketing applications and is also accepted by this agency for investigational new drug applications (IND). The CTD format and content are also, of course, required for electronic CTD (eCTD) submissions. The eCTD will be required January, 2008 for all electronic submissions to the Center for Drugs Evaluation (CDER) at FDA.

The advent of the CTD not only allows for global harmonization of marketing applications, but also provides standards to prepare submission-ready documents in the IND phases. This standardization also benefits lifecycle, project, and information management and also facilitates drug development planning. Each section of the CTD can be treated as a technical report that can be written early in development and updated as needed until it is finalized for the submission.

Preparing the CTD from IND to NDA

Module 3 of the CTD, the "Quality" or CMC section, can be expanded from the IND to the NDA according to

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Preparing Documents

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requirements for each phase of development. The following table illustrates key differences between the IND and NDA regarding the Quality section.

IND	NDA
Detailed manufacturing flow chart is sufficient for phase 1	Complete manufacturing description, flow chart, manufacturing development history
Viral safety evaluation required; other process validation not required	Process validation summaries required for sterile products and non-standard processes
Assessment of critical method parameters	Complete method validation reports
Brief description of container closure	Complete container closure evaluation
Stability data support the duration of the clinical study	Stability data support the proposed marketing shelf life, per ICH
A.1 Facilities/Equipment not required	A.1 Facilities/Equipment, A.2 Adventitious Agents for biologics
The focus is on safety	*Complete details of CMC required*

Writing Submission-Ready Documents

SRDs should be planned for and written throughout the development process with four levels of reports in mind:

1) Full reports with raw data and appendices, e.g., method validation reports.
2) Summary reports without appendices, e.g., process development reports.
3) High level summaries suitable for the Quality Overall Summary
4) Reports to be kept on file and not submitted

All reports required for conformance with GMP must, of course, be kept on file (level 4) even if they do not need to be submitted. The entire level 1 report would be submitted. For a level 2 report, the full report would be written with a body of the report in a summary format, such as a section of Module 3. This should include a summary of the protocol, key data tables and figures, summaries of methods, and conclusions. Raw data and other appendices could be removed prior to the submission. It is recommended that all reports have an up-front executive summary (level 3) that introduces key findings, resolution of issues, and recommendations. The content of these summaries would be integrated into the Quality Overall Summary in Module 2.

Reports written early in development may be written in submission-ready format and amended or updated throughout the course of development. An example of this is the method validation report, where methods are often refined or changed completely from inception to the commercial process.

SRDs should be written in a modular format with subsections for different regions, such as differing specifications in Europe and the U.S.. Just prior to submission, the subsections not relevant to that region must be removed for the final report, with appropriate version control.

To facilitate the reviewers' job it is highly recommended to keep consistency between reports of the same type in the submission, e.g. stability reports or method validation reports. Training of authors should also include ensuring consistency of terminology in all submission documents.

Electronic submission tools afford some creative options in linking submissions to databases using XML. Ideally, the submission writer should not have write access to data (such as release and stability data under cGMP) protocols. Data tables within reports could be automatically populated from "Quality-controlled" databases using customized templates, with generation of graphs and statistical analysis.

Regulatory Project Management

Planning a submission is a major project that requires skill, experience, and teamwork (see Nucleus article dated January 2004 at www.ctdquqality.com). Using the CTD format to prepare submission-ready documents can greatly facilitate regulatory project management by mapping data, and reports to the CTD from the start. Project management software can be set up with sub-projects organized according to CTD subsections to track action items for each phase of development. This makes it easy to track and perform gap analysis.

In summary, planning and writing SRDs in development saves time and resources and enables building the marketing application (NDA, BLA, ANDA) from the clinical application (IND) throughout development. Chemists in the pharmaceutical industry need to be aware of this responsibility for writing documents destined for submission to supporting approval of clinical studies and marketing. Training in preparation of SRDs can contribute significantly to efficiency in preparing regulatory submissions.

Do a piece at a time to have peace in time.

M. Foster ◇

James Flack Norris

By Avery A. Ashdown[1] , M.I.T.

When James F. Norris began his assistantship in the Chemistry Department of the Massachusetts Institute of Technology in October 1895, he was twenty-four years old and fresh from the doctorate awarded by Johns Hopkins University in June of that year. Born in Baltimore, Maryland, January 20, 1871, he was one of nine children of the Reverend and Mrs. Richard Norris (Methodist). His elementary schooling was at Miss Jennie Gardner's School for Boys in Georgetown, D. C., where his father was serving as a pastor. Later he attended the Central High School in Washington. While in this school, he was a member of the Drum Corps, High School Cadets. Secondary education completed, he enrolled in Johns Hopkins University in 1889 and remained through years of graduate study, leading to the doctorate in chemistry in 1895. At what exact age chemistry began to hold his interest is not certain but it must have been before 1892 when he was teaching this subject in the University of Maryland. His final year at J.H.U., 1894-5, was brightened by an appointment as a Fellow (stipend $375, plus tuition). His life long pursuit of travel in summer, chiefly in Europe, began at this time. In 1892 he became the official delegate of the students of Johns Hopkins University to the 300th Celebration of the University of Dublin. In the summer of 1894 he worked with the U.S. Coast Survey, stationed at Lynn, Massachusetts. The summer of 1896 saw him, with Henry Fay (M.I.T.), touring England, France and Germany.

Not only teaching in the University of Maryland, but coaching classes in mathematics and science, in his final graduate year, at Johns Hopkins had, in a sense, prepared him for a life long devotion to teaching and research. In his first classes at M.I.T. he was associated with James Mason Crafts (of the Friedel and Crafts reaction) and gave a course in 0rganic preparations. The next year he added a series of lectures on the history of chemistry. In 1899 he gave the brief course in organic chemistry and became associated with Arthur Amos Noyes in the laboratory pursuit of organic preparations and reactions. The year 1900 saw him advanced to the rank of assistant professor of organic chemistry and engaged to Anne Bent Chamberlin, a student at the Museum of Fine Arts in Boston.

On February 4, 1902, Anne and he were married in St. John's Church, Washington, D. C. where her parents made their home while she was a student at the Museum. Henry Fay, also a young professor at M.I.T. and a close friend, was best man at the wedding. The new Norris family took up residence at 124 Anawan Avenue, West Roxbury (Boston), near the home of Professor Frank H. Thorp of M.I.T., already working on his *"Outlines of Industrial Chemistry,"* a text book for students, destined to be widely used. (First edition, October 1898, the third edition, in 1916, in collaboration with Warren K. Lewis, Professor of Chemical Engineering at M.I.T.)

The life-long friendship with Henry Fay began when both men came to M.I.T. as assistants in chemistry in 1895. Together they published their method for the *"Iodometric Determination of Selenous and Selenic Acids"* in volume 18, 1896, of the American Chemical Journal. This paper was the first bearing the name of Dr. Norris. It was followed at once by his thesis for the doctorate, *"The Action of Halogens on the Methylamines"* with Ira Remsen, appearing in the same journal, volume 19, 1896. These two papers head a list of seventy publications, mostly in the American Chemical Journal and the Journal of the American Chemical Society. Four books, all published by McGraw-Hill, also came from his pen.

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[1] From The NUCLEUS, 1996 LXXV (3), 4

James Flack Norris

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The first, *"The Principles of Organic Chemistry"* 1912, third edition, 1933, total issue over 70,000. The second book, "*Experimental Organic Chemistry,"* 1915, third edition, 1933, total issue also over 70,000. His textbook, *"Inorganic Chemistry for Colleges"* was published in 1921, third edition with Professor Ralph C. Young of M.I.T. in 1938. "*Laboratory Exercises in Inorganic Chemistry*," co-author Professor Kenneth L. Mark of Simmons College, appeared in 1922.

In 1900, advancement to Assistant Professor of Organic Chemistry at M.I.T. gave him a larger share in the chemistry department. In spite of this favorable development, his official connection with M.I.T. was interrupted in 1904 by appointment to Professor of Chemistry at Simmons College, organized in Boston in 1899 and destined to be known, for a time, as the M.I.T. for women students. Through eleven years he devoted himself to building up the chemistry department at Simmons. While at Simmons, he took a sabbatical leave in 1910 to study physical chemistry with Professor Fritz Haber in the Technische Hochschule at Karlsruhe in Baden, Germany. With Mrs. Norris be took up living quarters; in a pension in Karlsruhe. Dr. Norris always took great satisfaction from this phase of his post-doctoral experience. He found, increasingly, that the physical chemical points of view he gained, gave him new insight into organic chemistry. The year was not all laboratory work. Dr. and Mrs. Norris passed a winter vacation in Berlin and Dresden. In the spring recess they traveled in Italy. During the summer of 1911, three of Dr. Norris' sisters joined them for a grand tour, including Paris, Holland, England, and Scotland.

Came the year 1915, Dr. Norris resigned his position at Simmons to accept the professorship of chemistry in Vanderbilt University in Nashville, Tennessee. Association with this outstanding University in the Southland, although very rewarding, was to be for only one year.

In June, 1916, he was asked to return to M.I.T. where, in October, he became Professor of General Chemistry. When he left Vanderbilt, students and staff combined to present him with a silver cigarette case, bearing the inscription "Sunny Jim." This appellation he accepted with great pleasure. In fact, all of his associates, both at that time and thereafter, recognized his new name as most descriptive of his general disposition and character.

By the autumn of 1916, World War I, increasing in fury in Western Europe for two years, had been building up a condition of deep concern for the United States. In October 1917, Dr. Norris was granted leave of absence from M.I.T. for one year, to "render special service to the government in the present emergency." He worked first at the Bureau of Mines in Washington, D. C., on gas problems. Later he was in charge of "Offence Chemical Research" at the Bureau. Early in 1918 he was appointed Lieutenant Colonel, Chemical Warfare Service, U.S. Army. His headquarters were in London. In 1919 he was appointed to the Interallied Gas Conference. Finally, (1919) Dr. Norris was in charge of investigating the manufacture of war gases in the German chemical plants. His final war service was with the American University at Beaunne, France. Honorably discharged from the service in July 1919, he returned to Boston to resume duties at M.I.T.

This renewed association with M.I.T. was to be enjoyed for twenty-one years, until his death on August 3, 1940. He remarked of his position, as Professor of Organic Chemistry, that it was the kind of job he had wanted all his life. Graduate students came from far and wide to work with him on researches leading to advanced degrees.

Dr. Norris' service to chemistry broadened with his association with M.I.T. He was an early chairman of the Northeastern Section (1904). All of his life he remained very loyal to his home section. In 1924 he became chairman of the Section on Chemistry and Chemical Technology of the National Research Council in Washington, D.C. He was granted a leave of absence from M.I.T. for this work. However, he was in Boston two days each week and

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James Flack Norris

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thus able to keep in contact with his graduate students. In 1925 he was made an Honorary Member of the Royal Institution of Great Britain. In the same year he was elected President of the American Chemical Society, a position he held for a second term. For three years, 1925-1928, he was Vice President of the International Union of Pure and Applied Chemistry. Eventually, association with the Union took him on several trips abroad, to Rumania in 1925, to Warsaw in 1927, to Lucerne, Switzerland, in 1936, and to Rome, Italy, in 1938. His long term as a Director of the national American Chemical Society ended in 1934 with a testimonial luncheon in New York

Two other activities were also in this period. First came the address on *"Chemistry in National Defense"* before the Institute of Politics at Williamstown, Massachusetts, in August 1926. Second, in June, 1928, he was chosen a member of the educational Delegation to the USSR, of which John Dewey of Columbia was chairman.

From early years, Dr. Norris was asked to be a special lecturer on organic chemistry at several different colleges. The first of these lectureships was at Simmons College in 1903. Next came Harvard for two years, 1912 to 1913. Among his students at Harvard was Louis P. Hammett, who, inspired by Dr. Norris, became the founder of physical organic chemistry in America. In 1913 he lectured on organic chemistry at Clark University in Worcester, Massachusetts. He had three periods of extended association with Bowdoin College, at Brunswick, Maine. This was the college of Hawthorne, Longfellow and President Franklin Pierce. In January 1925 Dr. Norris was named visiting professor at Bowdoin. In 1929 and in 1931 he was again a visiting Professor at Bowdoin. The college conferred on him an honorary Sc.D. in 1925.

A very important part of the life of Professor and Mrs. Norris was the several summers they passed at North Bridgton on Long Lake in western Maine. There they built a house in 1906 after plans drawn by Professor Harry W. Gardner of the Department of Architecture at M.I.T. They named their summer home "Good Cheer." The center of social life of their home was the "porch" where, often, there were record dances in the evening. Dr. Norris had a den for study and writing detached from the main house where he worked every morning, writing his books. After lunch he swam in the lake with companions and in the evening mingled with guests on the porch.

Dr. and Mrs. Norris were patrons of art galleries both in the United States and in Europe. Dr. Norris was an ardent movie fan and a devoted follower of Sir Harry W. Lauder, Scottish comedian and entertainer for half a century. Many people, still living *[that was in 1965!, ed.]*, will recall such Harry Lauder songs as, "I Love a Lassie," "Roamin' in the Gloamin'" and "It's Nice to Get Up in the Mornin' but its Nicer to Lie in My Baid."

Many honors came to Dr. Norris. He was elected to the Society of the Sigma XI, Phi Beta Kappa and Alpha Chi Sigma, the professional chemical fraternity. He was a member of the American Academy of Arts and Sciences, the National Academy of Sciences and a fellow of the American Association for the Advancement of Science. He held honorary membership in the Chemical Society of Rumania and in the Royal Institution of Great Britain. He was elected vice-president of the American Academy of Arts and Sciences in 1936. He was Chairman of the Faculty of M.I.T., 1937-1939. Dr. Norris was very proud of the award of the Medal of the Institute of Chemists, conferred on him in May, 1937. In accepting the award he wrote to Dr. M. L. Crossley of the Institute of Chemists.

"I appreciate very much the high honor and will be much pleased to accept the Medal. I was gratified to learn that the award was made for both teaching and research. So far as I know, the Medal, awarded by your Institute, is the only one in which emphasis is placed on a man's influence, as a teacher, on young men electing to enter the profession of the chemist. I feel that a man can do a great deal in this world in influencing those who are undertaking a professional life."

The troubled situation in Europe in 1939, fomented by Hitler, argued against a walking tour in Germany, or Austria or Switzerland. Instead, Professor and Mrs. Norris toured Hawaii, California and Northwestern United States in June of that year.

The next summer, June 1940, the development of a cataract in his right eye, necessitated surgery which was successful. However, his troubles were not over. On July 1, 1940, phlebitis set in. On July 18th he was back in the Phillips House of the Massachusetts General Hospital for blood transfusions. In spite of all the resources of the hospital, his condition worsened steadily. He died on August 3, 1940, half way through his seventieth year. Funeral services were held at Mt. Auburn Cemetery, on August fifth, in Cambridge, Massachusetts, where his grave is in the Norris lot. The day was bright and full of sunshine as if to capture some of the "Good Cheer" of the North Bridgton home and of the encouragement Dr. Norris had given his students and colleagues and friends over many years.

The original article was accompanied by eight pages of photographs and a listing of 41 students who received doctoral or master's degrees for work under his guidance.◇

Images from the Boston ACS Meeting

all photos by Robert Lichter

Sisters in Science Symposium, August 22, 2007

Organized by Pam Mabrouk, Immediate Past NESACS Chair

Professor Sharon Neal, University of Delaware

Professor Gilda Barabino, Georgia Institute of Technology

NESACS Reception

NESACS Chair Mukund Chorghade

German Exchange participants with NESACS YCC Chair, Laila Dafik

Committee on Minority Affairs lunch, August 20, 2007

ACS President Katie Hunt with luncheon speaker Shanandeen Begay, former ACS Scholar and current graduate student at Boston University

German Exchange Dinner, August 24, 2007

New Red Sox Fans!!

Abstracts and Bios

Continued from page 5

chemico-physical and pharmacokinetic properties, and high efficacy in *in-vivo* tumor models, the compound MP-529 was ultimately selected for further development.

Dr. Hariprasad Vankayalapati received his Ph.D. degree in Pharmaceutical sciences UDCT, at the University of Bombay, India. He moved to the US as a postdoctoral fellow in the laboratories of Professor Hurley, at the College of Pharmacy, Arizona Cancer Center, Tucson, AZ. Presently, he serves as Director of Medicinal Chemistry at SuperGen Inc. Salt Lake City, UT. His research interests are in the areas of synthesis of small molecule heterocyclic kinase inhibitors and Topoisomerase-II and G-quadruplex interactive agents. Dr. Hariprasad has published over 50 peer reviewed articles in national and international journals and holds several patents.

Adrian Hobson

Applications of Parallel Synthesis in Hit-to-Lead

Adrian Hobson received his Ph.D. in organic chemistry from University of Sheffield (UK) under the supervision of Dr. C.M. Marson. He then joined Knoll Ltd. as a principal scientist where he was responsible for all medicinal chemistry activities. In early 2000 Dr. Hobson accepted a team leader position at Abbott Bioresearch Center, Worcester, MA. Over the next 5 years, he has mainly been involved in the Hit-to-Lead generation program. Presently, he serves as group leader and manages the Hit-to-Lead team.

Vinod F. Patel

The Discovery of Motesanib (AMG 706), a Multi-Kinase Angiogensis Inhibitor for Treatment of Human Cancers: From Crystal to Clinic

A structure-guided approach to the discovery of a potent and highly selective VEGF-R2 inhibitor, AMG 706 will be presented. The preclinical properties that led to its selection as a development candidate and the subsequent initial Phase I experience with AMG 706 will also be discussed.

Vinod Patel received a B.Sc. degree (First Class Honors) in Applied Chemistry from Leicester Polytechnic (UK) and a Ph.D. in Organic Chemistry from Nottingham University (UK) under the supervision of Professor Gerry Pattenden. He moved to the US as a postdoctoral fellow in the labs of the late Professor Dick Schlessinger at the University of Rochester, where he was engaged in the total synthesis of natural products. In 1990, Dr. Patel accepted a position at Eli Lilly & Co. (Indianapolis) where, over the next 9 years, he was principally involved in discovering and developing oncolytics. In early 1999, he returned to the east coast to join Kinetix Pharmaceuticals (Medford, MA), a start-up firm specializing in kinase research. In late 1999, Amgen acquired Kinetix and Vinod accepted the role of Head of Medicinal Chemistry at the newly-opened Amgen Cambridge Research Center (CRC). Over the past 7 years at AMA, he has contributed to the growth of the site, especially the medicinal chemistry group, and has had the privilege of leading the KDR program that discovered AMG 706. Presently, he serves as Director of Medicinal Chemistry and manages a group of medicinal chemists with interests in Neuroscience and Oncology drug discovery programs.

Tomi Sawyer

Exploring Chemical Space in Protein-Protein Interaction Drug Discovery: Bridging Nature to Breakthrough Medicines

Protein-protein interactions have incredible scope in the modulaton of biological activities and disease mechanisms. Inhibition or mimicry of such protein-protein interactions with small-molecules or natural products has been incredibly challenging, whereas peptide/protein strategies have been limited by cell penetration and in vivo pharmacological properties. Nevertheless, there exists a significant potential to develop a new class of drugs that are capable of modulating protein-protein interactions to switch "off" or "on", for example, signal transduction pathways in many disease states. Examples of therapeutic targets as well as pioneering research to advance drug discovery

Abstracts and Bios

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will be described. Exploring known protein-protein interactions has revealed that alpha-helical protein ligand/receptor type binding mechanisms are key to such molecular recognition processes. Noteworthy has been recent investigations providing proof-of-concept that synthetic alpha-helical peptides are capable of binding and modulating specific therapeutic targets utilizing protein-protein interactions. Furthermore, hydrocarbon bridging of key alpha-helical peptides has advanced a promising class of biologics possessing unique cell-penetrating and *in vivo* pharmacological efficacies. Examples of such "stapled" alpha-helical peptides that mimic the BH3 domain alpha-helix of BID, a pro-apoptotic BCL-2 family member, will be highlighted with respect to their effective *in vitro* and *in vivo* anti-cancer activities for leukemias. The significance of this concept and technology platform to exploit the chemical space in protein-protein interaction drug discovery suggests an extraordinary opportunity for bridging nature to breakthrough medicines.

Tomi Sawyer recently joined AILERON Therapeutics (Cambridge) as Chief Scientific Officer and Senior Vice-President of Drug Discovery and Innovative Technologies. He will lead AILERON's development of a first-generation of breakthrough medicines directed at intracellular protein-protein interaction targets by leveraging a proprietary "stapled peptide" technology platform with application for the treatment of cancer and other diseases. Tomi was previously Senior Director, Pfizer Research Technology Center (Cambridge) and concurrently served on Pfizer's Global Chemistry Leadership Team. Prior to Pfizer, Dr. Sawyer held several leadership positions in drug discovery at ARIAD Pharmaceuticals including Senior Vice-President, Drug Discovery, where he led chemistry campaigns which successfully advanced the mTOR inhibitor AP23573 (recently partnered with

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Abstracts and Bios

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Merck) and the second-generation Src/Abl kinase inhibitor AP24534 (a clinical candidate). He began his career at The Upjohn Company as a peptide chemist and drug design scientist before moving on to a position at Parke-Davis/Warner-Lambert Company where he last served as Head, Structure-Based Design Chemistry. Dr. Sawyer is the recipient of several international academic and corporate awards for outstanding drug discovery and innovative technologies. He is an inventor of more than 60 issued or filed scientific patents and is an author of more than 200 scientific publications including books, reviews, commentaries and research articles. Dr. Sawyer currently holds academic and research advisory appointments at the University of Massachusetts Medical School and the University of Massachusetts-Amherst. He is the Founding Editor-in-Chief of Chemical Biology & Drug Design. Dr. Sawyer received a B.Sci. with Honors in chemistry from Moorhead State University and a Ph.D. with Distinction in organic chemistry from the University of Arizona. ◇

What exactly goes on at NESACS' monthly Board meetings?

www.nesacs.org/reports

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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http://www.unh.edu/chemistry/seminars.html

Dec 3

Mohammad Movassaghi (MIT)
"Cascade Reactions in Complex Alkaloid Synthesis"
Boston Univ., Life Science and Engineering Building Auditorium (B01)
4:00 pm

Dec 4

Prof. Ray Fort Jr. (Univ. of Maine, Orono)
"Exploring the Chemistry of Hemicelluloses"
Univ. New Hampshire, Iddles Room L103
11:10 am

Dec 6

Prof. Nick Melosh (Stanford Univ.)
"Bio-Electronic Interfaces and Plasmonic Integration with Molecular Electronics"
Boston College, Merkert Chemistry Center, Rm. 130
4:00 pm

Dec 10

Dr. Klavs Jensen (M.I.T.)
Jeanne and Martin Sussman Endowed Lectureship
TBA
Tufts Univ. Science and Technology Center
11:30 am

Dr. Jeffrey Bode(Univ. of California, Santa Barbara)
TBA
Brandeis Univ, Gerstenzang 122
3:45 pm

Dec 11

Prof. Matthias Brewer (Univ. Vermont)
TBA
Univ. New Hampshire, Rm. L103
11:10 am

Dr. Erving Bigio (Boston Univ.)
"Elastic Light Scattering Spectroscopy for the Detection of Early Cancer and pre-cancer"
New England Section Society for Applied Spectroscopy
Hampton Inn - Natick (just off the Mass Pike)
7:30 pm

Notices for The Nucleus Calendar of Seminars should be sent to:

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