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Cover: Connor W. Coley, Massachusetts Institute of Technology

Editorial Deadlines: October 2022 Issue: September 1, 2022
November 2022 Issue: October 1, 2022
Advances in laboratory automation promise to decrease the effort required to synthesize small molecule compounds, but determining how to synthesize a molecule is still a manual process that requires significant time investment from expert chemists. Computer-aided synthesis planning (CASP) focuses on accelerating this process by recommending synthetic pathways. This ability to formalize knowledge of reactivity in predictive models influences the overall process of molecular design by constraining the chemical space we are able to access, or access easily.

Machine learning and artificial intelligence have enabled new data-driven approaches to CASP where statistical models are trained directly on published experimental data. The two primary aspects of CASP—proposing retrosynthetic disconnections to connect the target to purchasable materials and validating proposed reactions in silico—are highly amenable to supervised learning approaches. We have developed several of these tools in a software suite, ASKCOS, that is capable of proposing retrosynthetic routes to new molecules, proposing reaction conditions for each step, and assessing the likelihood of experimental success. I will talk about the many learning tasks associated with the goal of synthesis planning, the progress that we and others in the field have made, and ongoing challenges in improving the fidelity of these models.

**Meeting Agenda**

6:30 - 7:00 pm  
Virtual Networking

7:00 pm  
• Opening by Carol Mulrooney, NESACS Chair  
• Featured Presentation by Connor W. Coley, MIT, Department of Chemical Engineering and the Department of Electrical Engineering and Computer Science

**Featured Presentation**

Data-Driven Synthesis Planning and Molecular Design  
Thursday, September 15th, 2022, 6:30 pm

**Zoom Link**

https://zoom.us/meeting/register/tJwudOGurzIqE9c-MxBGzmZfh0d0tRKIUgKY

**Featured Speaker**

Connor W. Coley  
Assistant Professor in the Department of Chemical Engineering and the Department of Electrical Engineering and Computer Science at the Massachusetts Institute of Technology

**Biography:**

Connor W. Coley is an Assistant Professor at MIT in the Department of Chemical Engineering and the Department of Electrical Engineering and Computer Science. He received his B.S. and Ph.D. in Chemical Engineering from Caltech and MIT, respectively, and did his postdoctoral training at the Broad Institute. His research group at MIT develops new methods at the intersection of data science, chemistry, and laboratory automation to streamline discovery in the chemical sciences with an emphasis on therapeutic discovery. Key research areas in the group include the design of new neural models for representation learning on molecules, data-driven synthesis planning, in silico strategies for predicting the outcomes of organic reactions, model-guided Bayesian optimization, and de novo molecular generation. Connor is a recipient of C&EN's “Talented Twelve” award, Forbes Magazine's “30 Under 30” for Healthcare, the NSF CAREER award, and the Bayer Early Excellence in Science Award.
The heterodimeric transmembrane receptor, integrin αvβ6 is a promising potential target for the treatment of idiopathic pulmonary fibrosis (IPF) and other fibrotic diseases. In this talk, we will describe the discovery of MORF-627, an orally bioavailable, selective avb6 integrin antagonist with activity in preclinical models of IPF. Optimization of early non-selective hits was accomplished via our MiNT platform, which integrates broad in vitro assay profiling, high-resolution X-ray co-crystal structure determination and in silico potency prediction using Free Energy Perturbation (FEP), to deliver a candidate with potency and pharmacokinetic (P.K.) properties that support a low projected human dose.

Featured Presentation

Discovery of MORF-627, an Orally Bioavailable, Selective avb6 Integrin Antagonist for the Treatment of Fibrotic Disease

By James Dowling

Organized by the Medicinal Chemistry Section of the Northeastern Section, American Chemical Society (NESACS)

Thursday, September 15th, 2022, 4:00 pm

Register for the September Webinar meeting at: https://american-chemical-society.zoom.us/webinar/register/WN_Oc5HA-EpTSSStEiop8l6Bqg

Visit: www.nesacs.org/medchem.html

Featured Speaker: James Dowling
Morphic Therapeutic

Biography:
Dr. James E. Dowling earned a B.S. in Chemistry from the University of Massachusetts at Boston under the mentorship of Prof. J.-P. Anselme and completed his Ph.D. work in heterocyclic chemistry with E.C. Taylor at Princeton. He began his medicinal chemistry career at Biogen as a member of the team that delivered Adentri, a selective Adenosine A1 receptor antagonist for the treatment of congestive heart failure. He moved to the oncology group at AstraZeneca in 2006 and worked extensively in the hit-to-lead space, applying fragment-based and encoded library approaches on a range of oncology targets, including the PIM kinase inhibitor AZD-1208 and antagonists of Wnt pathway signaling. In 2017 Jim joined Morphic to take up the challenge of developing oral integrin antagonists for the treatment of diseases with high unmet medical need.
The 10th Annual Advances in Chemical Sciences Symposium
Alkermes, Waltham, MA
October 7th, 2022

A day-long symposium focused on Medicinal Chemistry, Organic Synthesis, and Methodology, featuring eminent scientists from industry and academia.

Supporting Organizations: ACS, NESACS, RSC US and IUPAC

Symposium Speakers

Keynote Presentation: Bernard Feringa, Nobel Laureate, University of Groningen
Scott Miller, Yale University
Melissa Vasbinder, Ribon Therapeutics
M. Christina White, University of Illinois
Jared Lopes, Alkermes
Silvana Leit, Nimbus Therapeutics

Additional Symposium Details

Event Includes: A Day-long Vendor Exhibition Space & Closing Networking Reception
An onsite box lunch will be provided

Symposium registration fee: $75.00; Students: $25
On-line registration and payment: https://nemedchem.org/conference
Online registrations only. No onsite registrations will be allowed.

Symposium Location: Alkermes, 900 Winter St., Waltham, MA

If you need additional details, please contact any of the Organizing Committee:
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NESACS Area Students win ACS Graduate Student and Postdoctoral Scholar Recognition Program Awards

The ACS has announced (https://www.acs.org/content/acs/en/funding/awards/graduate-student-and-postdoctoral-scholars-recognition-program/past-recipients.html) that three graduate students from NESACS (and Northeastern University) were among the 2022 award winners in the ACS Graduate Student and Postdoctoral Scholar Recognition Program. These awards recognize graduate students and postdoctoral scholars who’ve demonstrated exemplary achievements in any of the three categories: Leadership in Mentoring, Leadership in the Promotion of Diversity, Equity, Inclusion, and Respect, and Leadership in the Promotion of Research Safety. The three Northeastern students won awards in all three categories:

**Leadership in Mentoring**
Suhasini Iyengar, Northeastern University

**Leadership in the Promotion of Diversity, Equity, Inclusion, and Respect**
Michael Bergman, Northeastern University

**Leadership in the Promotion of Research Safety**
Lynne LaRochelle Richard, Northeastern University

NESACS 2022 Election Results

<table>
<thead>
<tr>
<th>Position</th>
<th>Name</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Chair-Elect</td>
<td>183 Patrick Gordon</td>
<td>(W)</td>
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<tr>
<td>Treasurer</td>
<td>184 Stephen Canham</td>
<td>(W)</td>
</tr>
<tr>
<td>Trustee</td>
<td>138 Dorothy Phillips</td>
<td>(W)</td>
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<tr>
<td></td>
<td>49 Ashis Saha</td>
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<tr>
<td>Director-at-Large: (2)</td>
<td>133 Mark Tebbe</td>
<td>(W)</td>
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<tr>
<td></td>
<td>128 David Harris</td>
<td>(W)</td>
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<tr>
<td></td>
<td>84 Joseph Billo</td>
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<tr>
<td>Norris Award Committee: (2)</td>
<td>131 Lori Ferris</td>
<td>(W)</td>
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<td></td>
<td>83 Mark Tebbe</td>
<td>(W)</td>
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<td></td>
<td>75 Wayne Jones</td>
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<td></td>
<td>48 Chris Moreton</td>
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<td>Councilor/Alternate Councilor:</td>
<td>142 Mary Jane Shultz</td>
<td>(C)</td>
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<td></td>
<td>139 Malika Jeffries-EL</td>
<td>(C)</td>
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<td>136 Thomas R. Gilbert</td>
<td>(C)</td>
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<td></td>
<td>128 Mariam Ismail</td>
<td>(C)</td>
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<tr>
<td></td>
<td>127 Sofia Santos</td>
<td>(C)</td>
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<td></td>
<td>126 Sonja Strah-Pleynet</td>
<td>(C)</td>
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<td>114 Craig Sergeant</td>
<td>(A)</td>
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<td>109 Scott Edmondson</td>
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<td></td>
<td>108 Jens Brefkke</td>
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<td>108 Patrick Gordon</td>
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<td>105 Kap-Sun Yeung</td>
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<td>104 Daljit Matharu</td>
<td>(A)</td>
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<td></td>
<td>99 Zemen Berhe</td>
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<tr>
<td></td>
<td>99 Elizabeth Nye</td>
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<tr>
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<td>87 Lipin Ji</td>
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</table>

W - Elected
C - Councilor
A - Alternate Councilor
The annual Education Night, which celebrates the accomplishments of the students and teachers at schools, colleges, and universities within NESACS, took place on June 2, 2022, at one of the Section's monthly meetings. As was the case in 2021, this year’s event was held in virtual mode.

The technical skills of NESACS Chair, Carol Mulrooney, and Chair-Elect, Sonja Strah-Pleynet, resulted in a flawlessly produced 2.5-hour Zoom event, which included a 30-minute “meet-and-greet” session at the start and a 15-minute Q&A period with the guest speaker at the end. Anna Singer, the NESACS Administrative Secretary, skillfully crafted the online printed program for the meeting.

After welcoming the attendees as the presider of the event, Carol Mulrooney called on Morton Hoffman to introduce the speaker, Professor Malika Jeffries-EL of the Department of Chemistry and the Division of Materials Science at Boston University, and Associate Dean of the Graduate School of Arts and Sciences. She provided a very personal perspective about her upbringing in the New York City borough of Brooklyn, education at Wellesley College (B.A.) and George Washington University (Ph.D.), and professional career positions at Carnegie Mellon University (postdoc), Iowa State University (assistant to associate professor) and B.U. (associate professor to full professor). She shared her very deep feelings about science and social justice, as well as the importance of mentorship, championship, and sponsorship in her talk, “Moving the Needle: How Key Interventions Can Increase Diversity, Equity, and Inclusion in STEM.”

Student and Teacher Awards

Presiding over the presentations of awards and recognitions to students and teachers were Ruth Tanner and Steve Lantos; Michael Berger presented the Simmons University Award.

College and University Student Awards

Grants-in-Aid

The Grants-in-Aid are travel grants for undergraduates to attend ACS national meetings and to present their research at the Undergraduate Research Poster Sessions in the Division of Chemical Education; the funds are provided by NESACS and are matched by the students’ chemistry departments. Matthew Gage (University of Massachusetts Lowell) was the Chair of this year’s Grant Committee. The following four students were awarded grants, and presented posters about their research at the ACS meeting in San Diego in March 2022:

- Jennifer Pierre-Louis, Tufts University; Ira Caspari, Faculty Advisor Using Practical Epistemology Analysis to Address the Individuality Among Students In-The-Moment Learning in Introductory Chemistry and Physics.
DJ-1 is a Glycation Antagonist, Not an AGE Eraser.  

Jason Wu, Boston College; Shih-Yuan Liu, Faculty Advisor  
Stereoselective Carboboration and Hydroalkynylation of Internal 1,3 Enynes Enabled by Senphos-Palladium Complexes.

Naksha Roy, Massachusetts Institute of Technology; Zachary Smith, Faculty Advisor  
Sorption-Enhanced Mixed-Gas Transport in Amine Functionalized Polymers of Intrinsic Microporosity (PIMs).

For all these students, this was their first ACS national meeting. They were impressed by the variety of papers and programs, and enjoyed meeting students from other colleges and universities. It was an important introduction to the ACS for them.

Norris-Richards Scholarships  
The Norris-Richards Undergraduate Summer Research Scholarships are NESACS awards of $3,000 to each awardee for ten weeks of full-time research work during the summer plus $500 to the department for supplies related to the research work. Award winners are required to submit a written report for publication in The Nucleus. Jonathan Rochford (University of Massachusetts Boston) was the Chair of the Scholarship Committee. Five scholarships were awarded for 2022:

Anna Clark, Harvard University; Ted Betley, Faculty Advisor  
Exploration of Cu(O)₂ and Co(O)₂ Complex Reactivity on a Hindered Ligand Platform.

Hannah Duarte Ramos, University of Massachusetts Boston; Mariam Ismail, Faculty Advisor  
Synthesis of a Metal-Organic Framework (MOF), Mill-101(Cr), for Enhanced CO₂ Uptake.

Sunny Tang, Harvard University; Stuart Schreiber, Faculty Advisor  
Discovery of Molecular Glues via Chemical Inducers of Proximity DNA-Encoded Libraries.

Isabelle Nagle, Massachusetts General Hospital/Harvard University; Emmanouil Rousakis, Faculty Advisor  
Tissue Oxygen Sensing: “Smart” Bandages and Wearable Devices.

Noah Mason, University of Massachusetts Lowell; Michael Ross, Faculty Advisor  
Size-Dependent Phase Transitions in Plasmonic Post-Transition Metal Nanoparticles.

The students all expressed their eagerness to start on their research, and were looking forward to full time activities in the lab during the summer without the “distraction” and obligations of classes. They will present the results of their summer research at the Northeast Student Chemistry Research Conference (NSCRC) in April 2023.

Award Presentations  
Awards were given for excellent oral and poster presentations at the 2022 NSCRC, which was held virtually on April 23.
Strategies

- Remember that culture eats strategy for breakfast – Peter Drucker
  - Incremental advances will add up over time.
  - Mitigate biases and microaggressions.
  - Recruitment efforts are futile if retention is poor.
  - Representation matters, if you can diversify the faculty and you will diversify the students.

My early inspiration

Gregor Mendel, plant geneticist

Women Chemist of Color and the Ivory Tower

- 7,996 Total Faculty in 75 departments: 1,770 male (80.6%) and 346 female (19.4%)
- White: 1,736 (79.1%)
  - 1,417 male (81.6%) and 319 female (18.4%)
- Multi-race: 1 male
- Native American: 9 (0.4%)
  - 7 male (77.8%) and 2 female (22.2%)
- Hispanic: 69 (3.1%)
  - 47 male (68.1%) and 22 female (31.9%)
- Asian: 339 (15.0%)
  - 255 male (77.3%) and 75 female (22.7%)
- Black: 51 (2.3%)
  - 43 male (84.3%) and 8 female (15.7%)
The award for the Outstanding Presentation, sponsored by Strem Chemicals, was presented to Hannah Boyce, a senior at Northeastern University. Her research, *Carbon Monoxide Systems to Treat Inflammation*, was done in conjunction with Brigham and Women’s Hospital; her advisor, Giovanni Traverso, is at MIT. Hannah had recently returned from Germany as a member of the student delegation that participated in this year’s NESACS German Exchange.

Of special note was the presentation of the Phyllis A. Brauner Memorial Book Award to Naksha Roy (MIT) for her excellent talk based on her undergraduate research, *Sorption-Enhanced Mixed-Gas Transport in Amine Functionalized Polymers of Intrinsic Microporosity (PIMs)*. Her book-of-choice was “Energy and Civilization. A History” by Vaclav Smil. In addition, Naksha received very special virtual congratulations from Susan Brauner (daughter of Phyllis Brauner).

**High School Student and Teacher Awards**

**The Aula Laudis Society**

The Aula Laudis Society is the Hall of Fame for high school chemistry teachers within NESACS. Since 1985, induction into the Society has recognized distinguished contributions to chemical education, and has acknowledged outstanding teaching as noted by letters of support from inductees’ students, colleagues, and supervisors. This year’s inductee was Abigail Gay of Weston High School, who “reaches all students through her getting to know them both in and out of the classroom. She uses anecdotes and metaphors to improve student comprehension and connect chemistry to the real world.” Among her colleagues, she is a collaborator and morale booster, is always willing to share with others and she continues her own learning as it benefits her teaching. Abigail Gay received a plaque acknowledging her induction into the Society.

**The Richards Award**

The Theodore Williams Richards Award for Excellence in Teaching Secondary School Chemistry, which is the highest NESACS “Teacher of the Year” recognition, honors the long-term achievements of a high school teacher within the Section who, through innovation and dedication, has inspired potential chemists, has communicated chemistry to non-chemists, and has influenced other chemistry teachers.

The 2022 awardee was Brian Faulk of Phillips Andover Academy, who was presented with a plaque and a $1,500 cash prize. The following are quotations from his nomination letter and letters of support from past students, current colleagues, and headmaster:

- “Brian has shown great range in being able to connect with students at all levels, meeting them where they are and challenging them to grow to their fullest potential. He instills in his students a love of chemistry, and helps them build confidence to take on the most challenging problems.”

- “Brian’s empathetic, yet challenging approach, gives opportunities for students to develop skills and deepen their understanding. He is constantly seeking ways to improve how students can discover the scientific process and how science works through active learning.”
• “He teaches up and down the curriculum with the same passion and excitement for sharing chemistry with his students in each and every class, with the belief that all students deserve the strongest grounding in science and finding ways to succeed.”

• “When I entered Mr. Faulk’s Organic Chemistry class, I felt extremely nervous as I heard it was impossibly hard. Mr. Faulk taught it with such passion that I felt inspired every day to work my hardest, and I finished the course with plans to major in chemistry and wrote several college essays about my new love of organic chemistry. Mr. Faulk makes learning fun, and he helped us when we struggled, continually emphasizing that ‘learning chemistry is thermodynamic, not kinetic’. Because of his kindness, humor, and exciting teaching style, chemistry is my favorite class.”

• “At Andover, Mr. Faulk is widely loved by his students. He’s the teacher who has influenced me the most. If I could sum up Mr. Faulk’s Organic Chemistry course in a word, it would be mind-boggling. He was clear, always using analogies to explain complicated concepts, the problems always creative and applicable; his ‘out of the box’ presentations truly allowed me to become a stronger chemist and thinker. He encouraged us to apply to various research camps and wrote incredible recommendations, which helped me to enter MIT this Fall with great help from his teaching, guidance, and encouragement.”

For all of these superb qualities, NESACS proudly presented Brian Faulk with the 2022 Richards Award.

The Ashdown Exam and the Simmons University Awards

The High School Student Awards are based on the results of the annual Avery Ashdown Exam, which was held virtually again this year with technical support provided by the ACS K-12 Office for Education and experienced administration of the exam by Alan Crosby (Newton South High School). This year, 32 schools participated from across NESACS with more than 100 students sitting for the exam.

The first-place winner was Neil Chowdhury (Phillips Exeter Academy; Teacher: Jeffrey Ward). Remarkably, Neil’s score on the exam placed him in the top five in the three previous years, and the second year in a row to win first place! Neil went on to take the U.S. National Chemistry Olympiad (USNCO) Exam, and qualified among the top 20 competitors in the country to attend the USNCO Study Camp in preparation for the International Chemistry Olympiad (IChO), both held virtually this year as was the case in 2021. Unfortunately, Neil didn’t move on to the top four to represent Team USA at the IChO in July. Nevertheless, we honor his accomplishments over the past four years of participation in the Ashdown Exam, and wish him well at his next level of education at MIT. Neil was unable to attend the Education Night celebration, but was represented by his mother, Rina Chowdhury, who connected from Seattle.

Inasmuch as both Neil and the second place award winner, Daniel Jeon, who is also from Phillips Exeter Academy (Teacher: Alison Hobbie), were previous cash award winners, and thus were ineligible to receive cash awards this year, the Simmons University Award of $500 went to the third place winner, Brian Li, from Acton-Boxborough Regional High School

For Education Night 2022, attendees enjoyed networking and learning from faculty members and students from the highest-achieving schools in the region. Attendees included Hannah Boyce (Northeastern University), Brian Faulk (Phillips Andover Academy), Rina Chowdhury, Brian Li (Acton-Boxborough RHS), and Ira Caspari (Faculty Advisor).
Dear Readers,

For those of you interested in learning more about plastics recycling in the US, here are a couple links to websites by the American Chemistry Council:

- [www.americanchemistry.com/better-policy-regulation/plastics/recycling-recovery-goals](http://www.americanchemistry.com/better-policy-regulation/plastics/recycling-recovery-goals)
- [www.plasticfilmrecycling.org](http://www.plasticfilmrecycling.org)

(Teacher: Leah Marsh) Brian was also selected for this year’s USNCO Study Camp. The award was presented to Brian by Michael Berger of Simmons University. It should be noted that all of the top five awardees for this year’s exam were also the top five awardees of the 2021 exam. As we acknowledge the accomplishments of these outstanding students, we urge other students from across NESACS to compete and make it to the next top five!

**Study Camp and the International Chemistry Olympiad (IChO)**

Three NESACS students (Neil Chowdhury, Brian Li, and Gideon Tzafriri [Lexington High School; Teacher: Parul Kumar]) advanced to the Study Camp, which was held this year over 12 days in early June; the Camp is attended by the top twenty USNCO scorers, who learn and train for the IChO. The fact that we had three of the top 20 at the Camp (comprising 15% of the students) speaks well about their hard work and the outstanding chemistry teaching across the Section. Once again, Esther Hines (Billerica High School) served as the Camp Head Mentor. At the end of the Camp, a series of exams were taken by the campers leading to the selection of the top four students, who went on to represent the United States at the IChO in July. This year, Gideon Tzafriri made Team USA, which is a phenomenal feat. Gideon is a three-time top-five scorer on the Ashdown Exam with second place in both 2020 and 2021, and fourth place this year.

**Looking Ahead**
With good fortune, the annual Education Night meeting will return next year to a live setting that will feature shared conversation around a good meal, another outstanding speaker, and more honors to the students and teachers from across the Northeastern Section.

_Congratulations to all the award winners and inductees!! We look forward to celebrating Education Night in-person next year_
It’s not often that undergraduate students get the chance not only to do science, but also to impact how that science is done through ACS-led advocacy work.

On June 17, a group of students from Harvard University, their professor, Dr. Heidi Vollmer-Snarr, and a high school student joined Dr. Doris Lewis, chair of the NESACS Government Relations Committee, in a meeting with 4th District Rep. Jake Auchincloss and his staff to discuss bills to be included in the USICA/COMPETES Act. While Drs. Lewis and Vollmer-Snarr had experience meeting with government representatives, for the students this was their first chance to glean an inside look at how science policy traveled from idea to document to impact.

Rep. Auchincloss began the meeting, to the students’ surprise, with introductions. The students were able to introduce themselves not just as scientists-to-be but as constituents as well, with roles both in furthering scientific research and in seeing research interests served by government priorities. Dr. Lewis, Dr. Vollmer-Snarr, and the students all appreciated the chance to tell Rep. Auchincloss a bit about themselves and their journeys to studying chemistry, adding faces and individual stories to the interests of scientific research.

The student-led group focused on presenting bills H.R. 476, Innovation Centers Acceleration Act; H.R. 204, STEM Opportunities Act; H.R. 74, Protecting Local Communities from Harmful Algal Blooms Act; H.R. 2307, Energy Innovation and Carbon Dividend Act; and H.R. 1512, Climate Leadership & Environmental Action for our Nation’s (CLEAN) Future Act. These bills addressed a range of issues: inclusion in the sciences for women, minorities, and immigrants (H.R. 204); STEM funding for young scientists from under-resourced regions; prevention of natural disasters caused by toxic algae blooms; and awareness about
supply chains for helium. Each student was able to connect the bill they presented with stories from their own personal background or causes important to them, weaving advocacy for chemistry research with a genuine conversation.

After the students had presented the bills, the meeting drifted towards an open discussion, with Rep. Auchincloss interested in learning more about the state of scientific research in Massachusetts and nationwide. The conversation covered the growth of medicinal chemistry, academia, and international collaboration, in conjunction with policymaking and ACS’s interests. As a representative for Massachusetts, one of the biggest scientific communities in the nation, Rep. Auchincloss shared his experiences working with Congress on these and similar bills. The group learned from Rep. Auchincloss about the different ways to overcome logistical hurdles in implementing pieces of science-related policy, like how language from smaller bills could be appended to larger legislative packages as “report language”. Specifically, the group dived into the complexity around immigration waivers for PhD candidates and the importance of international partnerships across boundaries to advance the sciences, with Rep. Auchincloss ultimately offering to take closer looks at some of the bills presented. Coming out of the meeting, the young scientists were grateful to have been able to share their experiences, build stronger connections with representatives, and participate in some small way in growing the relationship between the researchers who drive science and the government officials who shape how science is completed.

Participating in the meeting were Tessa Haining, Harvard senior and undergraduate researcher at the Dana-Farber Cancer Institute; Brammy Rajakumar, Harvard senior and research assistant at the Department of Chemistry and Chemical Biology’s advanced undergraduate laboratories; and Dr. Heidi Vollmer-Snarr, Director of Advanced Undergraduate Laboratories and Senior Preceptor on Chemistry and Chemical Biology at Harvard University. Zach Snarr is a student at Concord-Carlisle High School and the Harvard Extension School. Dr. Vollmer-Snarr is a member of the ACS Committee on Chemistry and Public Affairs and has a leadership role in involving research students in public policy.

“Education is the key to unlock the golden door of freedom”
– George Washington Carver
A New Generation of Targeted Therapies for Cancer, Autoimmune, and Infectious Diseases

By Philip S. Low, Purdue University

Dr. Low is the 2021 recipient of the Gustavus John Esselen Award

My circuitous path into drug discovery

My interest in designing ligand-targeted drugs to treat human diseases was motivated by an unexpected result from an experiment on cultured soybean cells. I had been asked by Monsanto to determine the mechanism by which inoculation of one leaf of a soybean plant with a pathogenic bacterium would rapidly confer resistance to the pathogen throughout the entire plant. After isolating an active component from an homogenate of the pathogenic bacterium, Pseudomonas aeruginosa, and demonstrating that it induced cultured soybean cells to release an intense burst of hydrogen peroxide (i.e. an observation that lead to our discovery of the oxidative burst defense response in the plant kingdom [1], we undertook to determine the number of receptors on soybean cells that existed for the above bacterial component and whether these receptors endocytosed into soybean cells (i.e. a process that was widely considered impossible in the plant kingdom because of the very high turgor pressure pushing the plasma membrane out against the cell wall). To address these issues, I asked a graduate student to radiolabel the pathogenic component and quantitate its binding and internalization by the cultured soybean cells. The student surprisingly responded that he would be unable to perform the study because he was opposed to working with radioactivity. To accommodate this unexpected preference, I then suggested that the student might consider labeling the bacterial component with biotin and monitoring its internalization with a fluorescent streptavidin conjugate. Although the resulting experiment clearly demonstrated that the bacterial component both bound and entered soybean cells by receptor-mediated endocytosis [2, 3], the graduate student considered the experiment to be a failure because his biotinylated “control” protein (bovine serum albumin) also bound and entered soybean cells by endocytosis. To comfort my discouraged student, I suggested that his unexpected result might indicate that a biotin receptor was also present on soybean cells and that the receptor was capable of mediating endocytosis of biotin. After confirming this hypothesis by establishing the internalization of many biotinylated proteins, we then wondered whether animal cells might similarly have receptors for biotin and perhaps other vitamins. Investigation into this latter question revealed that biotin receptors did indeed exist on some animal cells, but that folate receptors were almost exclusively expressed on cancer cells [4]. This latter serendipitous finding changed my career, prompting me to discontinue experiments on plants and focus future efforts on the use of folate to target attached drugs to cancer cells [5]. Our natural expansion of this effort has subsequently led to our discovery of multiple other targeting ligands for many other diseases [6-14].

Development of folate-targeted drugs for imaging and treatment of cancers

In order to confirm that folic acid could indeed deliver attached drugs specifically to cancer cells, we co-cultured a cancer cell line (KB cells) with a nonmalignant cell line (WI38 cells) in the same flask and evaluated which cells in the co-culture might take up the fluorescent folate-linked fluorescein conjugate later named EC17. As anticipated, the cancer cells rapidly became brightly fluorescent, while the nonmalignant cells remained dark [15]. Encouraged by these data, we then conjugated folate to a cytotoxic drug and conducted related experiments in which malignant and nonmalignant cells were concurrently exposed to the cytotoxic conjugate in the same flask. Again, as predicted, the folate-cytotoxin conjugate killed the cancer cells while leaving the nontransformed cells unharmed [15]. Recognized by these data, we then conjugated folate to a cytotoxic drug and conducted related experiments in which malignant and nonmalignant cells were concurrently exposed to the cytotoxic conjugate in the same flask. Again, as predicted, the folate-cytotoxin conjugate killed the cancer cells while leaving the nontransformed cells unharmed [15]. Recognizing that this specificity might have clinical applications if folate conjugates were to similarly avoid uptake...
by healthy cells in vivo, we then synthesized a folate-targeted radioimaging agent ($^{111}$In-DTPA-folate) and examined its biodistribution in tumor-bearing mice. The resulting radioimages revealed significant uptake in both the tumors and kidneys, with little if any retention in any other tissues. Moreover, when the folate-targeted imaging agents were replaced with folate-conjugated cytotoxic drugs, no elevated blood urea nitrogen (BUN), proteinuria or serum creatinine levels were observed, suggesting that the cytotoxic folate conjugates were passing through the kidneys without causing measurable toxicity. Buoyed by these results, we then imaged the biodistribution of $^{111}$In-DTPA-folate in humans to determine whether it might display any retention in healthy tissues, and as shown in Fig. 1 (left panel), we obtained results that closely replicated those seen in mice; namely, prominent accumulation of the drug in tumors and kidneys with minimal uptake in other tissues [16]. Then, anticipating that human kidneys remain as unharmed by folate-targeted cytotoxic drugs as murine kidneys, we proceeded in subsequent years to develop a number of folate-targeted therapeutic and imaging agents (EC17[17-21], EC20[22, 23], EC145[24], EC225[25, 26], EC489[27], EC776, EC1456[28, 29], EC1496[30], OTL38[32, 33]) for clinical trials in patients expressing folate receptor positive tumors (i.e. cancers of the ovary, lung, kidney, endometrium, breast, bladder and colon). While only one of these drugs has obtained FDA approval to date (i.e. OTL38; a.k.a. pafolacianine and Cytalux), several others have displayed promise in clinical trials and much has been learned that has guided our development of other ligand-targeted drugs. Some of the lessons learned from these investigations are as follows:

1. Folate receptors are not only upregulated on epithelial cancer cells (i.e., folate receptor alpha, FRα) [34], but also on activated myeloid cells (folate receptor beta, FRβ) that infiltrate solid tumors (e.g. tumor associated macrophages (TAMs) and myeloid derived suppressor cells (MDSCs)). [35]

2. Folic acid will deliver almost any small molecule payload to a folate receptor (FRα or FRβ) expressing cell in vivo. [4, 5, 20-35]

3. Low molecular weight folate conjugates will reach and enter the vast majority of FR-positive cells in a solid tumor. [24]

4. FR-targeted cytotoxic drugs do not measurably harm the kidneys.

5. Cancers that express low numbers of folate receptors can only be successfully treated with very potent cytotoxic drugs, but cancers that significantly upregulate folate receptors can be eliminated with less potent payloads. [36]
A New Generation of Targeted Therapies for Cancer, Autoimmune, and Infectious (continued)

6. Approximately 40% of human cancers have sufficient FR to be imaged with folate-targeted optical and radioimaging agents. [36]

7. Folate-targeted therapeutic drugs will fail if their attached drug is released either before the conjugate is internalized by its target cell or too slowly after the drug is internalized to reach a concentration required for therapeutic efficacy.

8. Folate-targeted drugs that do not require release of their payloads for efficacy (e.g. radiotherapeutic agents, imaging agents, TLR 3, 7, 8, or 9 agonists, or immunogenic haptons, etc.) are generally both safer and more effective than those that do. [38, 39]

9. Tumor uptake of FR-targeted drugs can be enhanced by inserting a pharmacokinetic extender into the conjugate that can prolong the conjugate's circulation time (and therefore increase its AUC).

10. Tumor-specific targeting ligands can be developed for many other receptors that are over-expressed on cancer cells and other pathologic cell types. [7-15]

11. Because well-designed ligand-targeted drugs will concentrate in receptor-bearing cells and be excluded from receptor negative cells, their potencies will be increased and their toxicities decreased relative to their nontargeted counterparts. [36]

As noted above, one of our folate-targeted drugs (OTL38) was recently approved by the FDA for use in assisting surgeons to find and resect malignant lesions during cancer surgeries[37]. This folate receptor-targeted near infrared cyanine dye was shown in phase III clinical trials to enable surgeons to locate and remove otherwise undetected cancer in ~27% of all ovarian cancer patients [38]. Because unresected cancers can continue to grow and eventually kill a patient, use of this and other tumor-targeted fluorescent dyes currently under development can potentially save lives[39]. Indeed, the only sure cure for cancer is to resect all malignant tissue, and rendering malignant tissue brightly fluorescent should enhance a surgeon's ability to quantitatively find and remove it (Fig. 1, center panel).

Development of folate-targeted drugs for reprogramming the tumor microenvironment

During the course of characterizing FR-positive cells in cancer tissues, we observed that cells with myeloid markers can also express a folate receptor, only in this case the FR expressed is the beta isoform (FRβ) of the folate receptor [35, 40]. More detailed analysis of these cells then revealed that the myeloid cells can be either pro- or anti-inflammatory (i.e. M1- or M2-like) and that the vast majority of FRβ+ cells in tumor tissues are anti-inflammatory [35]. Thus, FRβ+ cells in malignant lesions were observed to secrete immunosuppressive cytokines (e.g. TGFβ and IL-10), release growth factors (e.g. PDGF, FGF3, and EGF, etc.) and express checkpoint receptors (e.g. PD-1), i.e. all of which can promote tumor growth and survival. Fortunately, subsequent experiments were able to demonstrate that reprogramming the tumor-infiltrating macrophages (TAMs) and myeloid-derived suppressor cells (MDSCs) by systemic injection of a folate-targeted TLR7 agonist could strongly suppress tumor growth, even in solid tumors in which the malignant cells expressed no FR [35]. The additional observation that nontargeted TLR7 was not only highly toxic but also ineffective in reducing tumor growth provided a convincing example of lesson 11 above, i.e. that ligand targeting can improve both the safety and efficacy of a nontargeted drug [35]. Interestingly, more detailed exploration of the mechanisms underpinning the tumoricidal activities of folate-TLR7 agonists has revealed that the conjugate not only repolarizes both TAMs and MDSCs to a tumoricidal phenotype, but also indirectly reprograms other immune cells in the same malignant mass (e.g. CD8+ T cells, regulatory T cells, antigen presenting cells, and myofibroblasts) from a tumor-supporting to tumor-inhibiting phenotype [35]. Because myeloid cells in healthy tissues (e.g. tissue resident macrophages, splenic macrophages, and circulating monocytes, etc.) do not express FR, folate-TLR7 agonist mediated activation of myeloid cells appears to be restricted to TAMs and MDSCs in a tumor mass [35]. This remarkable specificity is very fortunate, since it allows tumoricidal activation of immune cells in cancer tissue without inducing the same cytotoxic immune cell phenotype in healthy tissues.

Development of folate-targeted drugs for imaging and treatment of autoimmune diseases

While conducting the above cancer-focused studies, concurrent experiments on other diseases were revealing that FRβ+ myeloid...
cells were also abundant in virtually all autoimmune lesions [41-43]. Thus, FRβ+ M1-like macrophages were found to accumulate in inflammatory lesions from patients with rheumatoid arthritis, Crohn’s disease, multiple sclerosis, psoriasis, atherosclerosis, osteoarthritis and systemic lupus erythematosus, etc. [43], while FRβ+ M2-like macrophages were similarly observed to concentrate in anti-inflammatory lesions such as idiopathic pulmonary fibrosis [44-46], nonalcoholic steatohepatitis [47], cardiac fibrosis, and chronic kidney disease. Moreover, as with solid tumor masses, FRβ+ macrophages were documented to be largely absent from healthy tissues in the same diseased patients [48]. Because the etiologies of most autoimmune diseases are believed to involve an imbalance between pro- and anti-inflammatory arms of the immune system, we have posited that use of an appropriate FRβ+ targeted immune modulator could potentially restore an immune imbalance to its healthy state and thereby treat such diseases. Indeed, multiple studies on many animal models now support this hypothesis. Thus, we have shown that folate-linked immunosuppressive drugs such as methotrexate, aminopterin, everolimus, and dexamethasone can suppress the symptoms of pro-inflammatory diseases [49-52] while folate-linked immunostimulatory drugs (e.g. TLR7 agonists) can reverse to over-activated healing responses in fibrotic diseases [46]. In all cases, selective reprogramming of aberrant FRβ+ macrophages leads indirectly to a similar repolarization of other immune cells in the same autoimmune lesion, resulting in a more global shift in the immune system towards a better balance between pro- and anti-inflammatory responses [35, 43].

**Design of novel ligands to target folate receptor negative pathologies**

Encouraged by the successes of the above folate-targeted drugs, we undertook to explore the use of unrelated targeting ligands to deliver both imaging and therapeutic cargos to other diseased cell types. Our first foray into this space was enabled by publication of the crystal structure of prostate specific membrane antigen (PSMA), which we immediately employed to design a low molecular weight ligand that bound to the active site of PSMA and served as a targeting ligand for delivery of attached drugs to prostate cancer lesions [6]. After demonstrating that a PSMA-targeted ⁹⁹mTc radioimaging agent could image malignant lesions in both animal models and human prostate cancer (PCa) patients (Fig. 1, right panel), we employed the same ligand (DUPA) to design a PSMA-targeted near infrared fluorescent dye for fluorescence guided surgery of prostate cancer (now in phase 2 clinical trials) [53, 54] and synthesized a PSMA-targeted DOTA chelating agent for use in radiotherapy of the same patient populations [55]. While both agents yielded highly specific images of PCa tissue, a slightly modified version of the radiotherapeutic agent was shown to successfully treat otherwise refractory metastatic castration resistant prostate cancer (mCRPC). The drug, ¹⁷⁷Lu-PSMA-617, was purchased by Novartis from Endocyte Inc. (a company I founded) and then evaluated in phase III clinical trials for treatment of mCRPC. The results of this clinical trial reveal that ¹⁷⁷Lu-PSMA-617 reduces the risk of death in mCRPC patients by 38%, lowers their risk of disease progression or death by 60%, increases progression free survival from 3.4 to 8.7 months, and achieves a complete response in 9.2% of patients [56]. Since mCRPC patients in general do not respond to current therapies, ¹⁷⁷Lu-PSMA-617 was awarded “breakthrough status” by the FDA and is expected to be granted regulatory approval in 2022.

Encouraged by the success of these PSMA-targeted drugs, we next looked for receptors that were upregulated in still other human diseases with the expectation that ligand-targeted therapies for these maladies could similarly improve both the safety and efficacy of existing drugs. These investigations lead to the discovery of targeting ligands for carbonic anhydrase IX [11, 57, 58], hydroxypatite [59], fibroblast activation protein [13, 14], EGF receptor [12], cholecystokinin 2 receptor [7], luteinizing hormone releasing hormone receptor [8], neurokinin 1 receptor [9], PD-L1 [60], asialoglycoprotein receptor [61], and urokinase-type plasminogen activator receptor (uPAR) among others [62]. Importantly, targeted drugs constructed using the first four ligands above are already undergoing preclinical development in preparation for human clinical trials, and targeted drugs designed with the latter six ligands are currently being optimized in animal models.
Design of nontargeted drugs to treat malaria and sickle cell disease

In the studies above, we exploited over-expression of internalizing receptors to deliver attached drugs to diseased cells. Unfortunately, there are several cell types that do no internalize receptors and therefore cannot be targeted with receptor-binding drugs. Because the human erythrocyte constitutes one of these cell types, erythrocyte-specific diseases such as malaria and sickle cell disease must be addressed with different targeting strategies. For this purpose, we have looked for aberrant processes in malaria-infected and sickle erythrocytes that contribute prominently to their pathologies but are largely absent from healthy cells. The result of this search led to a phosphorylation pathway in erythrocytes that transiently weakens the erythrocyte membrane in response to appropriate stimuli, but is pathologically over-activated in both malaria-infected and sickle cells. This pathway, which involves Syk-catalyzed phosphorylation of the anion transporter, band 3, triggers localized dissociation of the spectrin-actin cytoskeleton from the erythrocyte membrane and thereby induces membrane destabilization [63, 64]. Global activation of this pathway in malaria-infected cells destabilizes the erythrocyte membrane sufficiently to promote its vesiculation and allow escape of the enclosed parasites from infected erythrocytes at the end of their 48 hour life cycle, i.e. thereby releasing the merozoites into circulation to continue their propagation in uninfected erythrocytes [65, 66]. Not surprisingly, inhibition of this pathway was found to block parasite escape from infected red cells and thereby terminate their parasitemia [67]. More importantly, phase II clinical data [68] obtained on malaria patients in the jungles of Vietnam confirmed that addition of a Syk kinase inhibitor to the current malaria therapy blocks parasite egress and thereby eliminates the parasitemia much more rapidly and with fewer side effects than seen with the standard therapy. Moreover, our Syk inhibitor supplemented therapy appears to be impervious to drug-resistant strains of *P. falciparum* malaria, because no delay in parasite clearance is observed in any patients treated with the new therapy, even though ~1/3 of patients on the standard therapy still contain measurable parasites at the end of their 3-day treatment. Given that drug-resistant strains of malaria are spreading throughout Southeast Asia, the availability of a new therapy with a novel mechanism of action that cannot be easily circumvented by parasite mutagenesis could constitute a useful tool for enabling global control of malaria.

Curiously, a similar over-activation of erythrocyte Syk kinase may well be responsible for the pathology of sickle cell disease [63, 69]. That is, the major symptoms of sickle cell disease derive from vaso-occlusive events that occur when microscopic embolisms reduce perfusion of blood through essential organs. Chronically elevated phosphorylation of the same anion transporter, band 3, in sickle cells leads to a similar destabilization of the membrane that induces release of hemoglobin, free heme, and membrane-derived microparticles into the bloodstream [69]. Unfortunately, discharge of heme can activate toll-like receptors on endothelial cells, inducing upregulation of adhesion receptors on the vascular endothelium [70]. Release of hemoglobin can scavenge NO required for capillary vasodilation, leading to harmful constriction of the microvasculature [71], and blebbing off of membrane vesicles from sickle cells can stimulate thrombin activation, initiating a clotting cascade that can lead to thrombus formation [71]. When activated concurrently, the above processes are envisioned to create conditions that can limit blood flow to essential organs. Recognizing that inhibition of Syk might block these processes, we examined the effect of a relatively safe FDA-approved tyrosine kinase inhibitor (imatinib) with off-target activity against Syk on the above pathways in model systems and found it to prevent all three [69]. Based on these results and two anecdotal publications reporting that imatinib suppressed the symptoms of sickle cell disease in two sickle cell patients [72, 73], we have initiated a clinical trial to test the efficacy of imatinib in treating sickle cell disease. While imatinib's retardation of a child's growth may prevent its eventual chronic use in children [74, 75], its good safety record in adults may allow its application in more mature patients with sickle cell disease.

Conclusions

Although the contribution that ligand-targeted drugs will eventually make to human health remains to be determined, the toxicities that nontargeted drugs can cause when
they distribute indiscriminately into all tissues of the body are well-established. We have attempted to reduce such toxicities by linking desired drugs to targeting ligands that can concentrate their therapeutic cargoes in pathologic cells and prevent their uptake by healthy cells. We have also designed our ligand-drug conjugates to be small in size so that their penetration into diseased tissues is unimpeded. Although area under the curve (AUC) deficit. Based on the data summarized above, we believe that low molecular weight "smart drugs" that “home” to pathologic cells and avoid collateral damage to healthy cells will assume an increasingly prominent role in human medicine and find applications in the treatments of almost all human diseases.

A New Generation of Targeted Therapies for Cancer, Autoimmune, and Infectious (continued)


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Northeastern Section
American Chemical Society
For more than a decade now, NESACS has been hosting a Red Sox game each year at Fenway Park. This never fails to provide great enjoyment to our members and also often attracts members that are not otherwise seen at other NESACS events.
The Northeastern Section of the American Chemical Society (NESACS) will provide Grants-in-Aid of $500 to each of four undergraduates to attend the 265th ACS National Meeting in Indianapolis, IN, and to present a paper at the Undergraduate Research Poster Session in the Division of Chemical Education. In the event the meeting is held in virtual mode, the Grant will pay the registration fee.

Eligibility: Applications will be accepted from students at colleges and universities within the Northeastern Section of the ACS. 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 undergraduate research. The institutions of the successful applicants are expected to match the awards to their students.

Application: Application forms may be obtained from the NESACS web site at https://www.nesacs.org/award/grants-in-aid/#nominations. The deadline for receipt of completed applications by Professor Matthew Gage, Chair of the Grants-in-Aid Committee, is October 4, 2022. Send all application materials by electronic transmission to email: Matthew_Gage@uml.edu.

Notification: Applicants will be notified of the results by e-mail on October 11, 2022. The deadline for the electronic submission of abstracts to the American Chemical Society in Washington, D.C., is October 17, 2022, 11:59 PM.
Call for Nominations
The Gustavus John Esselen Award for Chemistry in the Public Interest

The Northeastern Section of the American Chemical Society (NESACS) is inviting nominations for the 36th Gustavus John Esselen Award for Chemistry in the Public Interest. This prestigious annual award is given to a chemical scientist whose scientific and technical work has contributed significantly to the public well-being thereby communicating the positive values of the chemical profession. The awardee shall be a living resident of the United States or Canada at the time of nomination and the public impact of the work should have become apparent within the five years preceding 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 2023 meeting of the Section. The Awardee is expected to deliver an address on the subject of the work for which the honor is conferred, or for work in progress which is also directed toward chemistry in the public interest.

Nominations should be submitted as a single pdf file including: 1) a letter signed by the primary sponsor with a description of the nominee’s work recognized as making a major contribution to the public welfare and as communicating positive values of the chemical profession, plus the names of two co-sponsors; 2) short supporting co-sponsor statements; 3) the nominee’s professional biography including a list of no more than ten of the nominee’s publications selected for their pertinence to the work nominated for recognition; and 4) copies of popular and technical press news or feature articles indicative of public benefit and interest. Further information is available at www.nesacs.org.

Nominations Are Due October 14, 2022 to Katherine Mirica at katherine.a.mirica@dartmouth.edu with cc to Jeananne Piper Grady at jpiipergrady@gmail.com. Award recipients will be notified by January 31, 2023.

Inquiries may be directed to the above emails or to Dr. Katherine Mirica, Tel. (603) 646-8188 or Jeananne Piper Grady, Tel. (617) 620-8315. Address: 11 Thaxter St., Hingham, MA 02043.
Esselen Award Dinner

The 2022 Gustavus John Esselen Award for Chemistry in the Public Interest awardee, Dr. Philip S. Low and his wife Joan at the Esselen Award social hour.

Dr. R. Graham Cooks, Prof Low’s Nominator and his guest, NESACS Dr. Cathy Costello.

Dr. Mike Filosa and Dr. Frederick Greene catch up.

Dr. Low chatting with Catherine Esselen and Jane Esselen Blocker at the social hour.
Dr. Daljit Matharu and Dr. David Smith at the social hour.

Dr. Katherine Lee with Dr. Bill Eykamp and NESACS Chair Carol Mulrooney. Mr. Bernie Hafrey in the background.

Dr. Muthiah Manoharan, Dr. Arthur Krieg and Dr. Anna French, guests of Dr. Low heading into dinner.
The Head Table *(standing L to R)*: Dr. Carol Mulrooney (2022 NESACS Chair), Mrs. Joan Low, Dr. Philip Low (2022 awardee), Dr. R. Graham Cooks (Dr. Low’s nominator); *(seated L to R)*: Mr. Tom Allen, Dr. Karen Allen (2022 Esselen Committee Chair), Dr. Cathy Costello.

The Esselen Family *(standing L to R)*: Mr. Alan Kurd, Dr. Katherine Esselen, Mrs. Catherine Esselen, Mr. Michael B. Hanson; *(seated L to R)*: Mrs. Jane Esselen Blocker, Mr. Malcolm Bell, Mrs. Nancy Bell, Mrs. Joanna Hanson Stengle.
Dr. Low’s Guests standing (L to R): Dr. Laura Green, Dr. David E. Golan, Dr. Muthiah Manoharan; seated (L to R) Mr. Isaac Barchas, Mr. Malcolm Kottler, Mr. Bernie Hafrey

Dr. Low’s Guests (L to R): Dr. Arthur Krieg, Ms. Jennifer Marie Swensen, Mr. Martin Low, Ms. Amanda Campbell
The Esselen Award Ceremony took place at the Harvard Faculty Club and was live-streamed on zoom. Top left: Dr. Karen Allen (Esselen Committee Chair) opened the award ceremonies with a welcome and brief history of the award. Bottom left: She was followed to the podium by Mrs. Jane Esselen Blocker, daughter of the Award’s founder and granddaughter of the Award’s namesake who presented the Award Medal and check to Dr. Philip S. Low. Right: Mrs. Jane Esselen Blocker and Dr. Philip S. Low with the Award Medal.
Following the presentation, Dr. R. Graham Cooks, Dr. Low’s nominator, introduced Dr. Low and his work to the audience.
One of these chemists who could have produced the orbital symmetry rules before Woodward and Hoffmann was Harvard’s William Lipscomb. He was an expert in valence isomerizations of highly complex, multi-ring structures. And it was in his group — one of whose members was the graduate student Roald Hoffmann — that the extended Hückel program was developed and first used. Indeed, it could even have been the Woodward-Lipscomb rules, had R. B. Woodward sought out Lipscomb instead of Hoffmann. And Lipscomb wasn’t the only possible candidate. His story and those of others, including Richard Bader, R. Stephen Berry (another Harvard alumnus), David Craig, William Moffitt (Harvard also), Leslie Orgel, Massimo Simonetta, will be told in Paper 5 of Jeffrey I. Seeman’s series on the history of the Woodward-Hoffmann rules.
Many local employers post positions on Facebook and on the NESACS job board. Find yours at

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For details, see [https://www.acs.org/content/acs/en/membership/membership-packages.html](https://www.acs.org/content/acs/en/membership/membership-packages.html).

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**Calendar**

Check the NESACS home page for late Calendar additions: [http://www.NESACS.org](http://www.NESACS.org)

Note also the Chemistry Department web pages for travel directions and updates.

These include:

- **Boston College**
  - [https://www.bc.edu/content/bc-web/schools/mcas/departments/chemistry/news-and-notes.html#events](https://www.bc.edu/content/bc-web/schools/mcas/departments/chemistry/news-and-notes.html#events)

- **Boston University**
  - [https://www.bu.edu/chemistry/seminars/colloquium](https://www.bu.edu/chemistry/seminars/colloquium)

- **Brandeis University**
  - [https://www.brandeis.edu/chemistry/events.html](https://www.brandeis.edu/chemistry/events.html)

- **Harvard University**
  - [https://chemistry.harvard.edu/calendar/upcoming](https://chemistry.harvard.edu/calendar/upcoming)

- **MIT**
  - [https://chemistry.mit.edu/events](https://chemistry.mit.edu/events)

- **Tufts University**
  - [https://chem.tufts.edu/news-events/events](https://chem.tufts.edu/news-events/events)

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**September 2022**

**September 12**
- **Prof. Puja Goyal** (Birmingham Univ.)
  - BU, 11:15 am

**September 13**
- **Prof. Mary Watson** (Univ. Delaware)
  - BC, Merkert 130, 4:00 pm

**September 14**
- **Prof. Monika Raj** (Emory Univ.)
  - BC, Merkert 130, 4:00 pm

**September 15**
- **Prof. David MacMillan** (Princeton)
  - PhotoRedox catalysis and reaction development
  - MIT, Rm 10-250, 4:00 pm

**September 16**
- **Prof. David MacMillan** (Princeton)
  - Micromapping: An approach to discovering new biology
  - MIT, Rm 10-250, 4:00 pm

**September 20**
- **Prof. Martin Oestreich** (Technische Universität Berlin, Germany)
  - From minus to plus: Our journey in silicon chemistry
  - BC, Merkert 127, 4:00 pm

**September 27**
- **Prof. Gaël Ung** (UConn)
  - UNH, Parsons N104 11:10 am

**September 28**
- **Prof. Ralph Kleiner** (Princeton)
  - Illuminating RNA biology metabolically incorporated ribonucleoside probes
  - BC, Merkert 130, 4:00 pm

**September 29**
- **Prof. Bo Li** (Univ. N. Carolina, Chapel Hill)
  - MIT, Rm 6-120, 4:00 pm

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**Notices for The Nucleus Calendar should be sent to:**
Samurdhi Wijesundera,
Email: samu.amameth@gmail.com