

Section II--Sponsor and Co-Sponsor Information:

1. Research Support Available

KOZLOWSKI, M. C.

ADC = annual direct costs

ATC = annual total costs

TDC = total direct costs (provided for instrumentation grants)

TC = total costs (provided for instrumentation grants)

ACTIVE

GOALI (Molander)	5/1/09 – 4/30/12	1.00 calendar
NSF	\$397,957(ADC) [MCK \$40,000 ADC]	
	\$500,000 (ATC) [MCK \$56,800 ATC]	

“High Throughput Experimentation for Reaction Optimization”

In collaboration with Merck, the use of high throughput experimentation and design of experiment principles will be examined in range of new reaction methods.

R56 CA109164 (Kozlowski)	7/1/09 – 6/30/10	1.50 calendar
NIH/NCI - ARRA	\$131,845 (ADC), \$196,173 (ATC)	

“Synthesis of Novel Anticancer Agents”

Perylenequinone natural products and analogs will be synthesized and examined as anticancer photodynamic therapeutics.

CHE-0911713 (PI Kozlowski)	9/1/09 - 8/31/12	1.00 calendar
National Science Foundation	\$102,724 (ADC), \$150,000 (ATC)	

“Oxidative Methods for C-C and C-N Bond Formation”

New oxidative processes targeted for development include: phenol couplings, bisnaphthoquinone and bisanthraquinone syntheses, and *N*-arylation reactions.

47616-AC1 (Kozlowski)	1/1/08 – 8/30/10	0.50 calendar
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CHE-0616885 (Kozlowski)	9/1/06 - 8/31/09	1.00 calendar
National Science Foundation	\$94,072 (ADC), \$139,000 (ATC)	

“Oxidative Methods for C-C and C-N Bond Formation”

This study focuses on the mechanism of Cu catalyzed oxidative naphthol couplings and related oxidative reactions..

CHE-0840438 (Lester) 2/1/09 – 1/31/12 0.10 calendar
NSF/CRIF \$226,854 (TDC), \$226,854 (TC)
“Purchase of an X-Ray Diffractometer”
Purchase of a departmental X-ray diffractometer to replace an aging instrument.

S10RR022442 (Smith) 9/30/06 – 9/29/08 0.10 calendar
NIH/NCRR \$500,000 (TDC), \$500,000 (TC)
“NMR systems: 2 Bruker Avance 500 Consoles”
Update of outdated user interfaces for NMR spectrometers critical for chemistry synthesis research.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

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[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

2. Sponsor's/Co-Sponsor's Previous Fellows/Trainees

Total previous predoctoral: 18

Total previous postdoctoral: 13

Representative trainees:

Erin DiMauro, predoctoral, B.A. Wesleyan Univ., Amgen, Research Scientist

Stephen Waters, predoctoral, B.S. Univ. Pittsburgh, postdoctoral with Sam Danishefsky at Sloan-Kettering, University of Vermont, Assistant Professor

V. Annamalai, predoctoral, B.S. Georgia Inst. Technology, postdoctoral with Laura Kiessling at Univ. Wisconsin

Michael Fennie, predoctoral, B.S. Canisus College, Sanofi-Aventis, Research Scientist

Barbara Jane Morgan, predoctoral, B.S. Kenyon College, postdoctoral at the Broad Institute

Bishwajit Ganguly, postdoctoral, Ph.D. Inst. of Science Bangalore, Central Salt and Marine Chemical Research Inst. India, Scientist E-1

3. Training Plan, Environment, Research Facilities

i) Ph.D. Candidacy Requirements: Ms. Podlesny has completed all the requirements for PhD candidacy at Penn including coursework, cumulative exams, and two semesters of teaching. Coursework consisted of organic chemistry mechanisms, organic synthesis, organometallic chemistry, heterocyclic chemistry, bioorganic chemistry, physical organic chemistry, organic materials chemistry, and chemistry literature/database searching.

ii) Meetings and Interactions: Joint group meetings between the Walsh (Organometallic Chemistry) and Kozlowski (Organic and Bioorganic Chemistry) groups are held weekly. After analyzing problems from the literature, one group member provides a formal presentation of their research from the last 6-9 months. Group discussion following the presentation provides a critique into the approaches taken and suggestions for further study. In conjunction, a written report is required, detailing the research from this time period. The reports are written in thesis format at a level of writing that would be appropriate for publication. Reports of this nature allow improvement of writing skills, self-evaluation of progress in the lab, and maintenance of satisfactory experimental records.

In addition, weekly Kozlowski group meetings will take place to review progress in the laboratory, troubleshoot problems, and identify new directions. As the total synthesis work draws to close, more time will be devoted to identifying the biological target(s) by meeting with collaborators in the Penn Medical School to develop further experiments. As the work on the chiral bisnaphthoquinones ramps up, opportunities for their use in materials chemistry will be explored via meetings with collaborators in Chemistry and the Laboratory for Research on the Structure of Matter (So-Jung Park, Andrew Feiring, Cheri Kagan).

iii) Seminars and Conferences: The University of Pennsylvania is at the hub of a vibrant region for science and research presenting an excellent environment for scientific discourse and numerous opportunities for continuing professional development. The Department of Chemistry alone maintains weekly seminar programs in four areas: Organic, Biological, Physical, and Inorganic Chemistry. In addition to academic speakers, speakers are drawn from local companies: Merck, Glaxo SmithKline, Wyeth, Bristol Myers Squibb, Aventis, Hoffmann LaRoche, etc., providing attendees with an appreciation of current biomedical topics of interest. Named and interdisciplinary lectureships from leaders in the field are held several times during the year. Students are also encouraged to attend seminars in their field outside of the Department Chemistry held at the Medical School, Wistar Institute, Laboratory for Research on the Structure of Matter, etc.

Ms. Podlesny is also a participant in the Chemical Biology Interface (CBI) program between the Department of Chemistry, the Department of Biology, and the Penn Medical School Biomedical Graduate Studies. The goal of the CBI training program is to provide students with the intellectual and technical skills required to solve important and complex biological problems that can be most effectively addressed by studies at the chemistry-biology interface and to create a group of graduating chemists and biologists who can effectively communicate and function successfully in multidisciplinary teams. The focus of the CBI training program will be mechanistic chemistry of proteins, which

is a theme that is of special interest to us with respect to the bisanthraquinone natural products. The CBI program includes coursework, monthly talks, and a twice annual mini-symposium centering on bioorganic chemistry. Even though Ms. Podlesney has completed the coursework required for the Ph.D. degree, she will take further courses in chemical biology, cell biology, and biochemistry to broaden her training and to be able to exploit the utility of her natural products.

Ms. Podlesney will attend national ACS meetings and NOS meetings on an annual basis to provide exposure to the broader scientific community. A further opportunity for professional development will be attendance of a Gordon Research Conference relative to her research interests in her fourth or fifth year to provide networking and prepare her for career after the Ph.D. degree. Finally, if her research moves into a specialized area (i.e. photodynamic therapy), then she will attend conferences or workshops in that area to gain further background and expertise.

iv) Research Environment and Facilities: The research community at Penn is vibrant. In Chemistry alone, there are ~190 doctoral students, ~70 postdoctoral fellows, and ~10 full-time scientific staff to support the ongoing research efforts. Approximately ~30 Ph.D. students graduate each year leading the School of Arts in Sciences at Penn. These students go on to high-profile postdoctoral, industrial, and academic positions. In addition, opportunities for interaction in the fields of biology and medicine abound with the School of Medicine, the Abramson Cancer Center, the Presbyterian Medical Center, and the Wistar Institute all located within a few blocks of the Chemistry department. For the chiral bisnaphthoquinones as organic materials, the strong ties to the Laboratory for Research on the Structure of Matter, Chemical Engineering, Materials Science, and the Penn Regional Nanotechnology Facility are in place.

The research facilities at Penn for this work include the standard facilities in Chemistry as well significant additional resources as conditions warrant from the institutes and centers listed above. The Chemistry facilities undergo constant renewal with recent instrumentation grants having updated the NMR, X-ray, and MS facilities. The Chemistry complex is comprised of four buildings with older facilities being renovated on a rotating basis. Our laboratory space is located in the 11-year old Vagelos Laboratories.

v) Additional Required Training or Technical Skills: Training in departmental instrumentation will continue to be provided by Dr. George Furst (Director, NMR Services), Dr. Rakesh Kohli (Director, MS Services), and Dr. Patrick Carroll (Director, Crystallographic Facility). Under the tutelage of Dr. Steven Johnson (University of Pennsylvania Medical School, Department of Hematology/Oncology), all of the necessary equipment and training for cancer cell assays is available. Should these assays prove encouraging, then Theresa Busch (University of Pennsylvania Medical School, Department of Radiation Oncology) will provide further training and guidance in testing of the photodynamic therapeutic properties of the bisanthraquinone natural products including clonogenic cell assays, animal toxicity studies, and animal tumor model studies. Both these collaborations are firmly established with our ongoing work using the perylenequinone natural products (*J. Am. Chem. Soc.* **2009**, *131*, 9413–9425).

vi) Applicant's Career Goals: With strong interests in organic synthesis and a desire to pursue a career in basic research, an individual development plan will be devised and examined periodically with Ms. Podlesney. The current version combines strong training in the core area of organic synthesis combined with interdisciplinary training in biological chemistry and/or materials science. Regardless of the precise direction the research develops, Ms. Podlesney will emerge with the skills to solve complex chemical problems in a team environment.

4. Number of Fellows/Trainees to be Supervised During the Fellowship

Total predoctoral: 8

Total postdoctoral: 2

5. Applicant's Qualifications and Potential for a Research Career

Ms. Podlesny received her BS in Chemistry from Gettysburg College. [REDACTED] She was an undergraduate researcher in two laboratories, one at Gettysburg and one at the University of Virginia. [REDACTED]

This assessment is in line with her performance here at Penn [REDACTED] [REDACTED] has gotten off to an impressive start in her first year in the laboratory. For example, in Amos Smith's total synthesis class she was assigned one of the axially chiral bisanthraquinone synthetic targets that my group was considering (she is now moving forward with this synthesis following one of the plans she designed). For the class, two synthesis proposals were required, one utilizing enantioselective induction and one starting from commercially available chiral materials. While the first synthesis could be devised using our catalytic asymmetric oxidative naphthol coupling, the second was very challenging since axially chiral compounds are not abundant precursors (i.e. available from commercial sources at less than \$1 per gram). She came up with a synthesis commencing from BINOL that was both clever and insightful. Prof. Amos Smith, Prof. Patrick Walsh, and I all commented on how innovative her proposal was as we had never seen any synthesis starting from BINOL, which is now relatively inexpensive (~35 cents per gram).

In her one year in my laboratory, Ms. Podlesny has made excellent progress in her project on the bisnaphthoquinones and the corresponding bisanthraquinone natural products. [REDACTED] she has been the most productive among the four students from her class in my group.

My philosophy toward student training is to provide a preliminary plan with missing details and important concepts. Ms. Podlesny has shown that she can manage such input and she has significantly developed the very preliminary project outline that I gave her. She has identified further natural products, developed completely new synthetic routes, and tackled significant difficulties in implementation of the research plan. Already, she is growing into the role of an interesting and innovative coworker vs a novice student. As she continues to mature, I will challenge her to develop new projects and new ideas based both on her current work and her developing interests via one-on-one meetings as well as group discussions. I find that this method may result in slower research progress initially since I do not lay out every experiment. However, the ultimate result is a well-developed, confident student who can identify important problems and develop plans for experimental implementation fully independently. Activities to foster this development will include writing manuscripts, identifying and researching new projects for younger coworkers and grant applications, supervising undergraduate students and junior graduate students, reviewing important literature topics for the group, and ultimately writing research proposal sections.

At this stage in her development, Ms. Podlesny compares to the best students that have come out of my lab. I am excited to work with her further to complete her development as an independent scientist.